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Randomized controlled trial comparing post operative pain outcome between suture and tissue glue wound apposition post-circumcision in the pediatric age group

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AGA KHAN UNIVERSITY

Postgraduate Medical Education Programme
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RANDOMIZED CONTROLLED TRIAL COMPARING POST-OPERATIVE PAIN OUTCOME BETWEEN SUTURE AND TISSUE GLUE WOUND APPOSITION POST-CIRCUMCISION IN THE PEDIATRIC AGE GROUP

By

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A dissertation submitted in part fulfillment of the requirements for the degree of Master of Medicine in General Surgery

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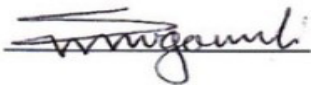

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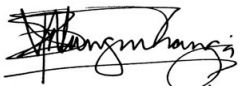

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DEDICATION

This book is dedicated to my father and mother for always being available for professional and emotional support

ABSTRACT

Introduction

Circumcision is one of the oldest and most common surgical procedures in the male population. Of the various circumcision techniques, sutures and tissue glue are utilized for wound closure in the free-hand techniques. Locally, sutures are routinely used for wound closure in the free-hand techniques. Whilst there are studies comparing the two wound apposition techniques using various outcomes, pain as a primary outcome comparing the two has been poorly researched. One hypothesis is that local ischemia at the suture site contributes to post-circumcision pain. It is against this background that we sought to explore differences in pain between these two methods of wound apposition.

Method

This was a prospective randomized controlled trial comparing post-operative pain following tissue glue and suture wound apposition post-circumcision. Secondary objectives were to establish the difference in post-operative bleeding, wound dehiscence and duration of surgery between the two interventions. Eligible participants were male children between 2 and 12 years coming for circumcision at the Aga Khan University Hospital, Nairobi from September 2021 to April 2022. They were allocated into the two intervention arms of sutures versus tissue glue following simple randomization. Duration of surgery was noted in the operation notes and populated in the data sheet. At 24 and 48 hours post-operatively, the Parents Post-Operative Pain Measure questionnaire was administered telephonically to assess pain. A pain score of more than or equal to 6 out of 15 was considered clinically significant. Outcomes of bleeding and wound dehiscence were obtained at the post-operative clinic review and populated on the data sheet. A small sample analysis was done. Continuous data was expressed as means ± standard deviation and differences between groups were assessed using the student's t-test.

Results

Eighteen patients were analyzed in the present study with twelve in the suture arm and six in the tissue glue arm. The mean age of the participants was 6 ½ years (Range 2- 11years, SD 2.55). The mean level of pain at 24 hours was 1.3 (SD 1.55) and 0 at 48 hours. There was a statistically significant difference in pain in patients with suture apposition compared to glue apposition ($t(16) = 2.066$, $p = 0.045$). This was, however, not clinically significant given as the mean level of pain was less than the clinically significant level of 6 as indicated on the Parents Post-Operative Pain Measure questionnaire. There was no bleeding noted in either groups at one week. Wound dehiscence was noted in one patient in the glue apposition group. However, this was not statistically significant when the two groups were compared ($t(16) = 1.46$, $p = 0.16$). The mean duration of surgery in the glue group was found to be slightly longer compared to the suture group (26.5 versus 21.3 minutes). However, this did not reflect a significant statistical difference ($t(16) = -1.418$, $p = 0.175$)

Conclusion

In view of the limited sample size, the present study's results may not be generalizable. The trends from the small sample analysis suggests that despite there being a statistically significant difference in pain, there was no clinically significant difference in post-operative pain during the first 24 – 48 hours, with more patients complaining of pain in the suture apposition group. The trends in the present study similarly demonstrated no statistically significant difference in post-operative bleeding rates, duration of surgery as well as wound dehiscence rates between the two groups.

LIST OF ABBREVIATIONS USED

AKU	-	Aga Khan University
AKUHN	-	Aga Khan University Hospital, Nairobi
KGS	-	Kilograms
PPPM	-	Parents Post-Operative Pain Measure score
SPSS	-	Statistical Program for Social Sciences

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My gratitude to the library staff as well for their support.

Thank you all

DECLARATION

I declare this dissertation does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university and that to the best of my knowledge it does not contain any material previously published or written by another person except where due reference have been made in the text.

Signature of Candidate

30th May, 2022

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CHAPTER 1: INTRODUCTION

Circumcision is one of the oldest and most common surgical procedures in the male population (1). It is defined as the removal of the prepuce or foreskin and has been described in history from as far back as ancient Egypt where the procedure was identified in mummies and documented in wall paintings (2). It is practiced extensively in African populations, with the prevalence of circumcision in Kenya at 84% (3).

There are several reasons why circumcision is undertaken including cultural, religious and medical reasons. Several studies have detailed the medical value of circumcision. These include hygiene, decreased risk of urinary tract infections, sexually transmitted infections and penile cancer (4,5)

Circumcision can be done at any age. However, early male circumcision has been on the rise. The American Academy of Pediatrics (AAP) recommends newborn male circumcision for its preventive and public health benefits that have been shown to outweigh the risks of newborn male circumcision. It has been associated with prevention of urinary tract infections, balanitis and phimosis in the infantile period. This recommendation is strengthened by a systematic review by Morris et al in which they analyzed 140 articles. They found early medical male circumcision was associated with immediate and lifelong benefits including protecting against infections, improved male hygiene and prevention against STIs (4).

Despite the value of circumcision, there are contraindications to performing this procedure. These include congenital abnormalities of the phallus such as hypospadias, epispadias, megalourethra, webbed penis, prior circumcision and any other condition that renders treatment more difficult. Others are prematurity and bleeding disorders.

As much as there have been several high-quality studies endorsing the practice of circumcision in the pediatric age-group, there have been opposing views to this, especially with regards to neonatal circumcision. Opponents of this, such as Van Howe et al, O'Hare et al, Darby et al and others highlighting post-circumcision complications such as bleeding, long-term negative psychological impact and interference with subsequent sexual function. Much of the literature with opposing views remained largely unpublished (6). An analysis by Morris et al as a systematic review concluded that arguments opposing male circumcision were based mostly on low quality evidence and opinions not backed by any strong scientific evidence (6).

1.1 Relevant anatomy of the penis

The penis is divided into 3 parts:

- The root- it is the most proximal part of the penis. It is located in the superficial perineal pouch and provides attachment to the pelvic floor
- Body- the free part of the penis between the glans and the root. Composed of three erectile muscles, 2 corpora cavernosum and the corpora spongiosum. It is covered by the Buck's fascia, dartos fascia and the skin.
- Glans- this is the most distal part of the penis. It is formed as a distal expansion to the corpus spongiosum. It contains the opening of the urethra and is normally covered by foreskin (prepuce) in the uncircumcised penis.

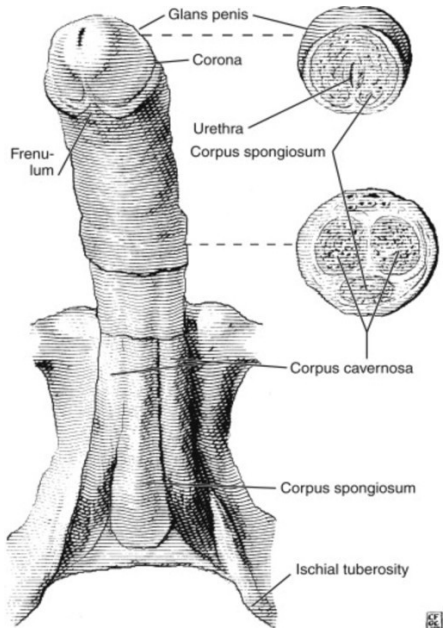

Figure 1: Anatomy of the penis, Manual of Surgical Pathology, 3rd Edition (7)

1.2 Methods of circumcision

Various techniques of circumcision have been described in literature:

- Freehand techniques- these include dorsal slit technique, guillotine technique and sleeve technique
- Circumcision using circumcision devices- these include the Plastibell technique, the Gomco clamp, and Mogen clamp

Dorsal slit technique

The prepuce is freed from the glans via adhesiolysis with the aid of an artery forceps placed at 10 o'clock and 1 o'clock, followed by a 12 o'clock cutting of both layers of the prepuce to some few millimeters of the corona. The prepuce is then excised circumferentially, and the wound edges apposed.

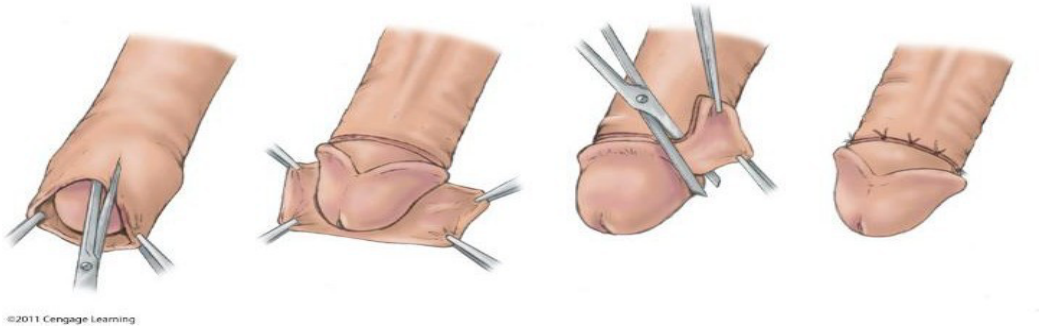

Figure 2: Dorsal slit technique, cengage learning (7)

This technique carries a risk of injury to the urethral meatus. It has found increased usage in treatment of medical conditions requiring circumcision due to excellent visualization of the glans.

Sleeve technique

In this procedure, the prepuce is retracted over the glans penis and a circumferential incision made around the shaft as far back as the scar line is to be made, distal to the corona. The prepuce is then returned to cover the glans and another circumferential incision is made around the shaft at the same position as the first one. A longitudinal incision is made between the two circumferential ones and strip of skin removed. The free raw edges are then apposed.

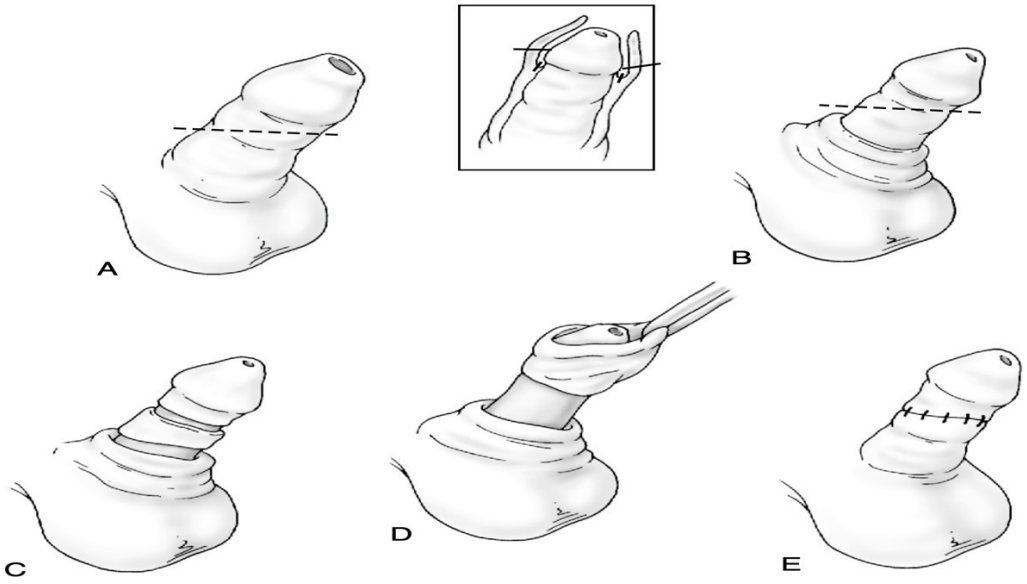

Figure 3: Sleeve technique, Ashcraft pediatric surgery (8)

This technique has better cosmetic outcomes. The glans is well visualized during the procedure and reduces the risk of injuries to the glans but is slower compared to other techniques and takes longer to teach.

Guillotine technique

In this procedure, the foreskin is grasped with 2 artery forceps at the 6 o'clock and 12 o'clock position and tension applied equally to stretch the prepuce uniformly. A long artery forceps is then placed just distal to the tip of the glans, making sure not to catch the glans and locked. Both layers of the prepuce are then cut, hemostasis achieved and free edges of the skin apposed.

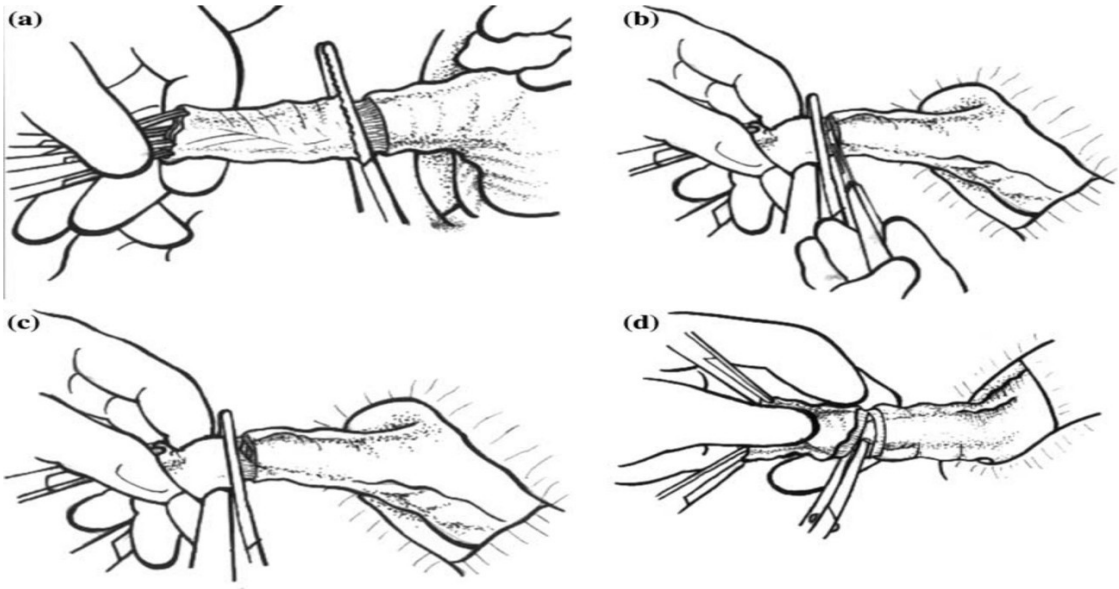

Figure 4: Guillotine technique, Basar et al (9)

This technique is easier to learn and faster to perform but can lead to injuries of the glans since it is not visualized during the surgery.

Circumcision devices

Several circumcision devices have been described. These include the Plastibell, Gomco clamp and the Mogen clamp among others.

The most used circumcision device in our set-up is the Plastibell circumcision device. The Plastibell device is slipped between the glans and the prepuce after an initial dorsal slit. The prepuce is then pulled slightly forward, and suture material looped around in the groove and tied tightly. The suture cuts off blood supply to the prepuce distal to the groove, which withers and drops off in 7-10 days.

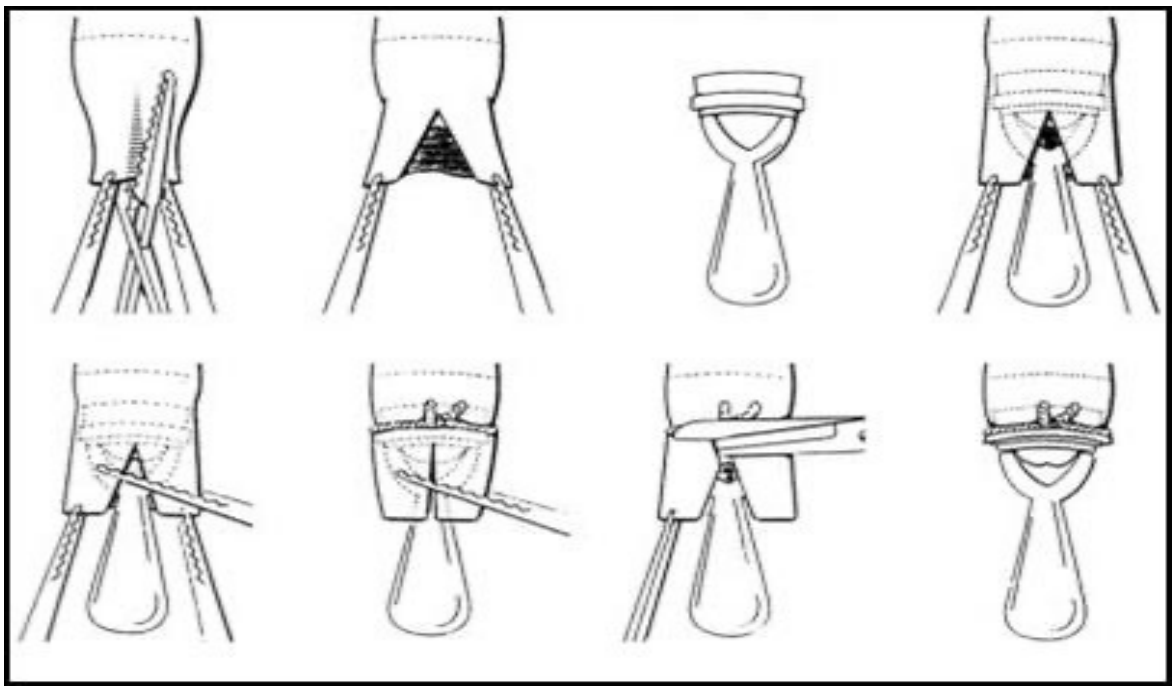

Figure 5: Plastibell technique, drmomma.org (10)

This technique has lower risks of bleeding, is quicker to perform and doesn't require a theatre setting. However, the device needs to be worn for approximately a week and is not commonly used in older children.

The following complications have been described in literature following circumcision procedures. These include:

- Excessive bleeding
- Infection
- Phimosis resulting when insufficient outer and inner preputial layers have been removed, leading to healing with fibrosis necessitating repeat circumcision
- Urethro-cutaneous fistulas
- Necrosis of the glans
- Meatal stenosis
- Buried penis
- Glans to inner skin synechiae/adhesions

- Iatrogenic epispadias and hypospadias due to injury to the glans and urethra

While no current gold standard method of circumcision exists in the literature, each method has its merits and demerits. The goal of all the methods is to remove an adequate amount of prepuce to uncover the glans while protecting function and achieving a good cosmetic outcome. With advancement in age, the open techniques tend to be done more frequently than the use of the circumcision devices. This is more so evident in our local practice whereby the Plastibell device is mostly in the neonatal and infant age groups. Whichever method is chosen, the surgeon must be familiar and adept with the procedure to avoid complications.

1.3 Apposition with Tissue Glue

The method of apposition of wound edges is also in evolution. Traditionally, the standard of wound closure following circumcision has been by use of interrupted absorbable sutures (11). However, novel techniques of wound apposition have been used, one of which is using tissue glue.

CHAPTER 2: LITERATURE REVIEW

Tissue glue has been used from as early as the 1970's for wound apposition with noted promise with regards to surgical wound closure. Use of tissue glue for apposition of circumcision wounds has also been extensively investigated.

Cheng et al comparing tissue glue versus sutures for circumcision wound apposition concluded that there was no difference in complication rates when utilizing tissue glue over sutures for circumcision wound apposition (12) but found the duration of surgery to be significantly longer in the tissue glue group (19.8 min vs 16.5 min, P= 0.002). Elemen et al, however, documented a shorter duration when using tissue glue (13) (12.04 ± 2.86 versus 24.10 ± 3.51 ($p<0.05$) minutes in the tissue glue and suture groups respectively). Several other studies support a similar outcome (14, 15,16).

Usage of tissue glue has also been associated with reduced post-operative bleeding. Van Haute C et al (19) and by Elemen et al (13) showed significantly less occurrence of bleeding post circumcision while utilizing tissue glue for wound apposition. This is an important outcome measure since bleeding is one of the most common and earliest complications of circumcision, necessitating presentation to the emergency department (14,17,18). The mechanism by which tissue glue leads to less bleeding post circumcision is not well understood. Pain is a frequent and expected post circumcision complication. Literature comparing pain post circumcision with suture closure and tissue glue is limited. There are only a few studies which have analyzed this as a primary post-circumcision outcome. Most of these studies were also not powered to detect a difference in pain and employed inconsistent tools to assess pain outcomes. They also varied significantly in their methodology. The key differences noted in these studies are:

1. The lack of standardized circumcision technique.

   Subramaniam et al (22) used CO2 laser as the instrument for circumcision, though it is not a standard in many institutions. Others used scalpel only, as seen in the study by Arunachalam et al (15) as well as Elemen et al (13), while others used both scalpel circumcision and the Gomco clamp for circumcision (14).

2. Mixed interventions in the different arms:

   Most had separate arms for suture versus tissue glue, however, in other studies, as those by Arunachalam et al (15) and Elmore et al (14), sutures and glue were used simultaneously in one arm while sutures only used in the other. These could likely have had a bearing in assessing the pain outcomes.

3. The failure to use a standardized validated tool in assessing pain as an outcome.

4. The use of retrospective study designs or collecting data on pain retrospectively.

   Recall bias would interfere with effective reporting of outcomes, as seen in the study done by Van C Haute et al (16).

Consequently, there is currently no consensus on outcomes of post-surgical pain between the two groups. A systematic review by Maurizio et al (17), on the use of tissue glue for circumcision in children, failed to conclude on the superiority of either method in post-operative pain outcomes, recommending more prospective trials to assess this relationship.

2.1 Pain Outcome measure tool

The Parents Post-Operative Pain Measure score is a behavioral checklist based on non-verbal pain cues children show after surgery. It was developed by Chambers et al for use by parents as a measure of pain post-surgery (23).

It contains 15 items identifying behavioral cues likely to suggest pain post-operatively (See appendix 2). A score of 6 or more is considered to represent clinically significant levels of pain.

It has been validated as an accurate measure of pain for children between 2-12 years of age post-surgery (25) and has been used in several publications assessing pain post-operatively.

CHAPTER 3: STUDY JUSTIFICATION

Circumcision is one of the most common surgical procedures carried out in the male population. The uptake of early male circumcision in on the rise due to its reported benefits (4,5).

The complication rate between glue and suture wound apposition is comparable as demonstrated in literature (17). However, pain as an outcome measure has been poorly researched with available studies being of poor evidence (13-22).

To our knowledge, there is no randomized control trial comparing pain scores between the suture and tissue glue closure methods for circumcision as the primary outcome. This study was conducted to determine if tissue glue wound closure is comparable to suture wound closure in post circumcision pain and complication rate.

CHAPTER 4: METHODOLOGY

4.1 Study question

Is there a difference in the level of pain in tissue glue compared to suture wound apposition post circumcision?

4.2 Null Hypothesis

We hypothesized that there would be no difference in the severity of pain in the glue and suture groups.

4.3 Primary Objective

The primary objective was to compare post-operative pain using a validated pain assessment tool between tissue glue and suture wound apposition in pediatric patients undergoing circumcision.

4.4 Secondary Objectives

The secondary objectives were to look for any differences in rates of post-operative bleeding and wound dehiscence, and duration of surgery between the tissue glue group and the suture group.

4.5 Study design

This was a single center randomized controlled trial comparing pain scores among patients undergoing tissue glue wound apposition with those undergoing suture wound apposition during circumcision.

4.6 Study Population

The study included all the male children between 2 years and 12 years of age coming for circumcision at the Aga Khan University Hospital, Nairobi between September 2021 to April 2022.

4.7 Sample size

Using the formulae stated below:

$$n = f(\alpha, \beta/2) \times 2 \times \sigma^2 / d^2$$

where:

f = is the normal deviate

Significance level (α) = 2.5% one-sided

Power (β) = 90

Standard deviation of outcome (σ^2): using the formulae shown below, and utilizing standard deviations obtained from Elemen et al (11) in their clinical study, the pooled standard deviation was calculated at 0.671

$$SD_{pooled} = \sqrt{\frac{(SD_1^2 + SD_2^2)}{2}}$$

Equivalence limit (d): the equivalence limit was set at 0.6 to exclude a difference in means of more than 0.6

Sample size was calculated at a total of 66 participants with 33 participants in either arm

4.8 Inclusion Criteria

- Male children aged between 2 – 12 years coming in for circumcision
- Consent to randomization to either procedure

4.9 Exclusion Criteria

Male children known to have:

- Bleeding disorders,
- Congenital malformations:
    - Hypospadias,
    - Chordee,
    - Epispadias,
    - Disorders of sexual differentiation,
    - Micro-penis
    - Buried penis.
- Patients undergoing other procedure plus circumcision
- Known adverse reactions to bupivacaine, paracetamol, ibuprofen, mupirocin, and tissue glue
- Contraindications to above medications
- Language barrier leading to inability to apply the pain assessment tool

4.10 Materials and Methods

Participant selection:

Patients attending the pediatric surgical outpatient clinics requesting circumcision or referred due to medical reasons requiring circumcision who satisfied the inclusion criteria were

recruited to participate in the study. An informed consent explaining the procedures, interventions, risks and benefits was obtained**.**

The standard pre-operative consent form was signed by the parent/guardian detailing the procedure to be done, circumcision, in this case. The expected benefits and complications were fully elucidated in this form, which was signed once the parent/guardian had fully understood what the procedure entailed.

The parent/guardian was provided with a consent form for the study (in addition to the standard surgery consent) once they had accepted to participate in the study and their children fit in the inclusion criteria. An assent form tailored for this study was provided to children between the age of 7 – 12 years, explaining the procedure and the role of the study. Children between age 7-12 years were recruited into the study once they had fully understood and signed the assent form and once their parents/guardians had consented to the study as well.

Group assignment

The participants were randomized into the two arms using computer generated random numbers through simple randomization.

Interventions:

The interventions were carried out by two pediatric surgeons with experience in both suture and glue wound apposition post circumcision.

General anesthesia was administered to the participants in both arms. Dorsal penile block and ring block using bupivacaine at 0.5mg/kg was also administered prior to start of the procedure.

Sleeve technique of circumcision was utilized in both arms. The sleeve technique ensured there was a circumferential sub-coronal cuff and avoided the inverted V at the frenulum which would have been problematic in glue application and was a risk of bleeding due to the presence of the frenular artery (the most common cause of post-circumcision bleeding) and a cause of pain. The study base is the hypothesis that the sutures cause local ischemia and drive the pain. The sleeve technique spares the frenulum thus avoiding the hemostatic frenulum stitch. The frenulum as well as the corona, as per the study done by Halata and Munger (24), have been reported to have sensory receptors called genital corpuscles which have higher sensitivity compared to other penile regions due to the higher density of these receptors in the named regions. This receptor distribution has been reported to contribute to post-circumcision pain. We therefore avoided frenulum division and the hemostatic frenulum stitch in both arms. Hemostasis intra-operatively was achieved by use of bipolar electrocautery.

Wound closure procedures:

- In participants in the suture wound closure arm, suturing was done using interrupted Vicryl Rapid 4/0 on a cutting needle. An 8- point suture technique was utilized with interrupted sutures placed at 12, 3, 6 and 9 o'clock with single sutures interspersed between these points, after which the wound was dressed with a single layer of bactigrass gauze and secured with a sterile gauze and Coban™ bandage wrapped in three turns. The dressing was removed after 24 hours and application of the antibacterial cream started.
- Wound apposition in the tissue glue closure arm was performed using 2-Octyl cyanoacrylate (Dermabond™), a tissue adhesive. This was applied circumferentially and the tissues held for 1 minute until the glue dried. To avoid and protect the urethral opening from the adhesive, a sterile gauze was used to cover the glans during the tissue

glue application. No dressing was applied following application of the tissue glue to prevent adhesion of dressing material to wound site. However, an antibacterial cream was applied once the glue had dried.

Duration of surgery, defined as the time from incision to the completion of intervention, was noted and recorded.

Participants in both arms were discharged on weight-based dosages of paracetamol at 15mg/kg up to four times daily and ibuprofen at 10mg/kg thrice daily for 3 days. They were advised to wear free flowing clothing for 1 week after circumcision and take sponge baths for 3 days after circumcision. Both arms were discharged with a topical antibiotic cream to be applied twice daily for 1 week. They limited out-door play activities during this period.

Follow-up was done at 24 hours and 48 hours post-operatively. This was done telephonically by a research assistant who was unaware of the initial intervention done. The Parents post-operative pain measure (PPPM) tool was administered by the research assistant telephonically to the parents, scored and recorded.

Follow-up was done at 1 week at the pediatric surgery clinic. Parameters assessed included:

- Post-operative bleeding - this was assessed by presence or absence of a hematoma.
- Wound dehiscence - this was assessed and graded as: dehiscence requiring no intervention or dehiscence requiring intervention.

In the event of any adverse events prior to the 1-week follow-up, the participants were advised to report to the pediatric accident and emergency department for assessment. The primary consultant was informed and a management plan as per the attending physician instituted.

4.11 Data analysis

Data was entered and analyzed using Statistical Program for Social Science (SPSS) version 26.0. Continuous data was expressed as mean ± standard deviation (SD) while categorical data was presented as proportions. Differences between groups was assessed using students t-test. Data was presented in tables and figures.

A p value of <0.05 was considered significant.

4.12 Ethical considerations

Ethical clearance was sought from the AKU ethics and research committee.

An informed consent detailing the rights of the participants including the right to refuse or withdraw from the study at any given point and the risks and benefits was sought prior to enrollment in the study.

A research permit was obtained from the National Commission for Science, Technology and Innovation (NACOSTI). The primary investigator reported any serious adverse events to the Institutional Review Board.

Serious adverse events included but were not limited to any adverse event that:

- Results in death
- Is life-threatening (places the patient at risk of death)
- Requires hospitalization or prolongs an existing hospitalization
- Causes persistent or significant disability or incapacity
- Requires medical intervention to prevent one of the above outcomes

4.13 Data handling

All data obtained were treated with utmost confidentiality and only used for the intended purpose.

All questionnaires and data collection forms were anonymized by coding using serial numbers and would not bear patient identifiers. They were stored in a locked cabinet accessible only to the primary investigator.

All data sheets were password protected and accessible only to the primary investigator.

The study was registered on the RCT tracking.

All data collection tools utilized in this study will be handed over to the Aga Khan University research office as per the institution's policies on completion of the study.

CHAPTER 5: RESULTS

The present study aimed to recruited sixty-six participants. However, due to limitations brought about by the restrictions placed due to the COVID-19 pandemic, eighteen participants were recruited for the study. The data were captured using an interview administered questionnaire, coded and a small sample analysis done using SPSS Version 26.0, as participant recruitment to achieve the target sample size continues.

The data obtained was grouped into frequencies and percentages, and presented in tables and figures.

5.1 Participant's Characteristics

A total of eighteen participants were recruited for the study with twelve in the suture apposition arm and six in the glue apposition arm. The participants had a mean age of 6 $^{1}/_{2}$ years (SD 2.55). The youngest participant was two years, while the oldest was eleven years. The participants had a mean weight of 31.64 kilograms with a minimum of 14 kilograms, while the maximum was 75 kilograms.

(See Table 1)

Table 1: Participant's characteristics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	18	2	11	6.56	2.55
Weight	18	14	75	31.64	15.77

The mean age of participants that had their circumcision wound closed by suture was 7.33, while the mean age of those that had their circumcision wound closed by the glue method was 5.00. Further, the mean weight of participants who had their circumcision wound closed by suture was 35.29 kilograms, while the glue method was 24.33 kilograms. (See Table 2)

Table 2: Age and Weight Comparison with Intervention

	Intervention	N	Mean	Std. Deviation	Std. Error Mean
Age	Suture	12	7.33	2.35	0.68
	Glue	6	5.00	2.37	0.97
Weight	Suture	12	35.29	17.52	5.06
	Glue	6	24.33	8.64	3.53

5.2 Comparison of Means of Age and Weight Against Intervention

Table 3 shows no statistically significant difference in age for participants who had their circumcision wound closed by suture and those who had it closed by glue method *(t (16) =1.982, p = 0.065).* Similarly, there was no statistically significant difference in weight for participants who had their circumcision wound closed by suture and those closed by glue method *(t (16) =1.432, p = 0.171).* (See Table 3)

Table 3: Comparison of means of age and weight against intervention

		t-test for Equality of Means		
		T	**Df**	**Sig. (2-tailed)**
AGE	Equal variances assumed	1.982	16	0.065
	Equal variances not assumed	1.977	10.031	0.076
WEIGHT	Equal variances assumed	1.432	16	0.171
	Equal variances not assumed	1.777	15.984	0.095

5.3 Indication for Surgery

Majority of the participants sought circumcision for ritual purposes (66.7%). Twenty-two percent (22.2%) had the procedure due to phimosis, while 11.1% of participants listed balanitis as the indication for surgery. (See Figure 6)

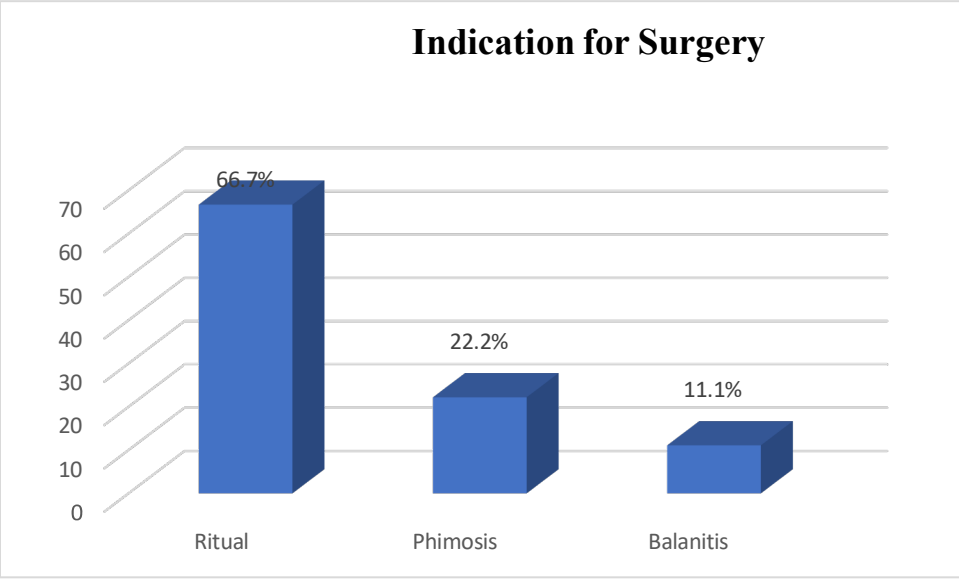

Figure 6: Indication for Surgery

5.4 Comparison of the Level of Pain Between Tissue Glue and Suture Wound Apposition Post Circumcision

The mean level of pain at 24 hours was at 1.3 (SD 1.55) for children that had circumcision wound closed by suture. Since the score was less than six, it meant that there were no clinically significant levels of pain. The most common behavior change that was exhibited by the children was whining or complaining more than usual. The children that had their circumcision wound closed by the glue method exhibited no pain at 24 hours. There was no pain reported at 48 hours in both suture and tissue glue groups. (See Table 4 below)

Table 4: Comparison of the level of pain between tissue glue and suture wound apposition post circumcision

	Intervention	N	Mean	Std. Deviation	Std. Error Mean
PAINAT24HOURS	Suture	12	1.3333	1.557	0.44947
	Glue	6	0.000	0.000	0.000
PAINAT48HOURS	Suture	12	0.000	0.000	0.000
	Glue	6	0.000	0.000	0.000

5.5 Comparison of Means of Level of Pain Between Those Who Used Suture and Glue Wound Apposition Post Circumcision

As shown in Table 5, there was a statistically significant difference in the level of pain for participants who had their circumcision wound closed by suture and those who had it closed by glue method. There was less pain noted in the glue apposition group *(t(16) =2.066, p = 0.045).*

Table 5: Comparison of means of level of pain between those who used suture and glue wound apposition post circumcision

	t-test for Equality of Means			
	t	**df**	**Sig. (2-tailed)**	**Mean Difference**
Equal variances assumed	2.066	16.000	0.045	1.333
Equal variances not assumed	2.966	11.000	0.013	1.333

5.6 Difference in bleeding rates post -operatively between glue and suture

The estimated blood loss for suture was 4 milliliters while glue method was 3 milliliters. However, there was no statistically significant difference in estimated blood loss between glue method and suture *t (8.525) =1.37, p = 0.206).* There was no bleeding at one week for either glue method or suture. (See Table 6)

Table 6: Difference in Bleeding Rates Post -Operatively Between Glue and Suture

		Group Statistics			t-test for Equality of Means		
	Intervention	N	Mean	Std. Deviation	Std. Error Mean	t	df	Sig. (2-tailed)
BLEEDAT ONE WEEK	Suture	12	1.00	0.00	0.00	1.467	16	0.162
	Glue	6	1.00	0.00	0.00			
ESTIMATED BLOOD LOSS	Suture	12	4.08	1.38	0.40	1.37	8.525	0.206
	Glue	6	3.00	1.67	0.68			

5.7 The difference in rates of wound dehiscence between tissue glue and suture wound apposition

Seventeen participants (94.4%) had no wound dehiscence with either glue or suture wound apposition. However, one of the participants whose wound was apposed with glue (5.6%) had dehiscence. This required intervention, where suturing was done.

This difference was, however, not found to be statistically significant (*t (16) =1.46, p = 0.16).* (See Table 7 below*)*

Table 7: Difference in rates of wound dehiscence between tissue glue and suture

	Intervention	N	Mean	Std. Deviation	Std. Error Mean	t	df	Sig. (2-tailed)
Dehiscence	Suture	12	1.00	0.00	0.00	-1.46	16	0.16
Intervention	Glue	6	1.17	0.41	0.17			

5.8 The difference in duration of surgery between tissue glue and suture wound apposition

The average duration of surgery with tissue glue wound apposition was 26.5 minutes while for suture was 21.3 minutes. (See Table 8 below)

Table 8: The difference in duration of surgery between tissue glue and suture wound apposition

	Intervention	N	Mean	Std. Deviation	Std. Error Mean
DURATION	Suture	12	21.333	8.060	2.327
	Glue	6	26.500	5.206	2.125

5.9 Comparison of means of duration of surgery between tissue glue and suture wound apposition

There was no statistically significant difference in the duration of surgery between tissue glue and suture wound apposition *(t (16) = -1.418, p = 0.175).* (See Table 9).

Table 9: Comparison of means of duration of surgery between tissue glue and suture wound apposition

		t-test for Equality of Means				
		t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Duration	Equal variances assumed	-1.418	16	0.175	-5.167	3.645
	Equal variances not assumed	-1.640	14.622	0.122	-5.167	3.151

CHAPTER 6: DISCUSSION

Tissue glue has been used from as early as the 1970's for wound apposition with noted promise with regards to surgical wound closure. Use of tissue glue for apposition of circumcision wounds has also been extensively investigated, with most studies finding it comparable in terms of complication rates (12,13,19). However, there are very few poor quality studies assessing pain as an outcome measure between tissue glue and sutures (17).

The present study was conducted in a private tertiary facility in Kenya, East Africa, with the aim of comparing post-operative pain following tissue glue and suture wound apposition post-circumcision. The secondary objectives were to assess possible differences in bleeding rates post- operatively between glue and suture, differences in rates of wound dehiscence between tissue glue and suture wound apposition and differences in duration of surgery between tissue glue and suture wound apposition.

6.1 Participant's characteristics

The mean age of the participants in the present study was six and a half years (SD 2.5). The oldest participant was eleven years, while the youngest was two years. The mean age of participants that had their circumcision wound closed by suture was seven years (SD 2.35), while for the glue method was five years (SD 2.37). However, there was no statistically significant difference in age between participants who had their circumcision wound closed by suture and those closed by glue method *(t (16) =1.982, p = 0.065).*

The average weight for the participants was 31.6 kilograms. The mean weight of participants who had their circumcision wound closed by suture was 35.29 kilograms, while the glue

method was 24.33 kilograms. Nevertheless, there was no statistically significant difference in weight for participants who had their circumcision wound closed by suture and those closed by glue method *(t (16) =1.432, p = 0.171).*

6.2 Comparison of pain level between tissue glue and suture wound apposition

The present study's findings on the comparison of pain level between tissue glue and suture wound apposition post-circumcision indicated that the mean level of pain at 24 hours was at 1.3 for children with circumcision wounds closed by suture. However, there was no pain elicited with tissue glue wound apposition. Consequently, there was a statistically significant difference in the pain level for participants who had their circumcision wound closed by suture and those who had it closed by glue method in the first 24 hours *(t (16) =2.066, p = 0.045).* However, at 48 hours, there was no pain reported in both groups. This finding may be attributed to sutures causing local ischemia and driving the pain in the first 24 hours.

The present study did not find any clinical difference in pain between the tissue glue and suture wound closure. It however showed that the participants with tissue glue wound closure had less pain when compared with those with suture wound closure in the first 24 hours.

The present study, therefore, demonstrates no clinical superiority of tissue glue wound apposition over suture wound apposition. However, suture wound apposition is associated with more pain in the early post-operative period. These findings are comparable to findings by Maurizio et al (17), who failed to conclude on the superiority of either method in post-operative pain outcomes.

6.3 Comparison of bleeding rates post operatively

The comparison in bleeding rates post-operatively between glue and suture wound apposition revealed that there was no statistically significant difference in bleeding rates between the glue method and suture, since no bleeding was exhibited with both methods *t (16) =1.467, p = 0.162).* The estimated blood loss for suture was 4 milliliters while the glue method was 3 milliliters. This difference, however, was not found to be statistically significant (*t (8.525) =1.37, p = 0.206).* These finding differ from other studies, with both Van Haute C et al (19) and Elemen et al (13) which found that there was significantly less occurrence of bleeding post circumcision while utilizing tissue glue for wound apposition.

6.4 Comparison of duration of surgery

The average duration of surgery with suture wound apposition was 21.3 mins while for tissue glue was 26.5 mins. This difference was, however, not found to be statistically significant (*(t (16) = -1.418, p = 0.175)*). The findings are comparable to those of Cheng et al (12), who found that the duration of surgery was significantly longer in tissue glue group compared to suture (19.8 min vs 16.5 min, P= 0.002). In contrast, Elemen et al (13), documented a shorter duration when using tissue glue vs suturing. The study findings also contrast those of prior studies that have found that the operation time was shorter when using tissue glue (14, 15,16). This may be explained by the operator's learning curve, given that suture wound apposition was practiced more than tissue glue wound apposition prior to the study duration.

6.5 Comparison of wound dehiscence

The present study revealed that there was one case of wound dehiscence early on with glue wound apposition. This could be due to technical application during the early phase. Suture wound apposition had no cases of wound dehiscence. This difference was, however, not found

to be statistically significant ((*t (16) =1.46, p = 0.16).*) Consistent with the results, Cheng et al (12) concluded that there was no difference in complication rates when utilizing tissue glue over sutures for circumcision wound apposition.

Despite lack of demonstration of statistically significant wound dehiscence, this does not rule out a clinically significant difference between the two arms of intervention. This may be attributed to the present study's small sample size.

6.6 Study limitation

Due to unforeseen circumstances and restriction measures placed due to the COVID 19 pandemic, the present study was unable to recruit its targeted sample size in the given time duration. This may affect the generalizability of its findings.

CHAPTER 7: CONCLUSIONS

Owing to the limitation cited above, the results of the present study may not be generalizable. The sample analysis of the present study demonstrates the following trends:

1. The present study does not demonstrate a trend towards a clinically significant difference in post-operative pain between tissue glue apposition and suture wound closure. There were, however, more patients complaining of pain in the suture wound closure group than in the tissue glue wound apposition group during the first 24 hours.
2. The present study shows no significant difference in bleeding rates post-operatively between glue and suture wound apposition.
3. The present study does not show a trend towards a significant difference in the duration of surgery between tissue glue and suture wound apposition.
4. The present study has no statistically significant difference in wound dehiscence between the tissue glue apposition and suture wound closure.

CHAPTER 8: RECOMMENDATIONS

We recommend the translation and validation of the Parents Post-Operative Pain Measure tool to a local dialect, as this will aid in local studies examining pain as an outcome measure in children

We recommend analysis of the final score of the target sample size to facilitate generalizability of the results.

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APPENDICES

APPENDIX 1: PATIENT GUARDIAN AND INFORMATION SHEET AND CONSENT FORM

CONSENT FORM: RANDOMIZED CONTROLLED TRIAL COMPARING POST-OPERATIVE PAIN OUTCOME BETWEEN SUTURE AND TISSUE GLUE WOUND APPOSITION POST-CIRCUMCISION IN THE PEDIATRIC AGE GROUP

My name is Dr Happiness Obare. I am a postgraduate doctor in the department of surgery at Aga Khan University Hospital, Nairobi. I am conducting a study to find out the post-surgical outcomes of children between 2-12 years who undergo circumcision at our facility.

The purpose of this study is to find out differences in the pain levels and the final outcomes between children who get their circumcision wounds closed with sutures and those closed with tissue glue.

The surgery was performed by the primary consultant doctor in the standard technique and all pain eradication measures taken as is standard for circumcision procedures. There was randomization into two arms of interventions for the circumcision wound closure. Randomization entails allocation of the participants a given method of wound closure randomly, meaning that the probability of landing one wound closure technique over another will be by chance and not pre-determined. The circumcision wound was closed by either suturing or by using tissue glue depending on the group your child is randomly allocated. The study would not interfere in any way with the standard fashion of how the procedure is carried out.

This kind of surgery with similar interventions (suture versus tissue glue in circumcision) has been used before safely in both pediatric and adult age groups while evaluating other outcomes. What we do not know is if there is a difference with regards to pain and discomfort after surgery when comparing the two closure techniques. Pain as an outcome while comparing these two closure techniques has not been studied adequately and hence is the basis of this study.

The benefits of the study are to evaluate if the pain outcomes after using glue for wound closure are comparable to those with suture closure. Common complications of circumcision include bleeding and surgical site infection. All these have been taken into account and necessary measures have been put into place to minimize these complications: Adequate control of bleeding intra-operatively using electro-cautery and local antibiotic ointment to be utilized post-operatively.

Standard post-surgical pain medication (paracetamol and ibuprofen) in addition to the local antibiotic ointment (Mupirocin) shall be administered as part of the local standard discharge medication.

We shall then contact you via telephone at the 24-hour mark and the 48-hour mark and ask questions regarding the behavior exhibited by your child post-surgery. The interview should last approximately 15 minutes. Your child shall be followed up by your primary doctor in our surgical outpatient clinics after one week and assessed.

I am inviting you and your child to be part of this study as you lie within my target study population which includes children between 2-12 years undergoing circumcision in our facility.

Should you choose to participate in the study, any information you give us shall be anonymized so that it cannot be traced back to you. It shall be stored in a secure locker and a password protected computer within the institution. No one will have access to it other than the research team. The final study results can be availed to you on request and may be published in medical journals. No patient personal information will be published.

Involvement in the study is voluntary will not result in payment or promise of better care and the decision not to be involved in this study will not result in your child being denied treatment.

I (Name & Surname)..... (Parent or Legal guardian) do give consent for the investigators to include my child in this study and be randomized in either suture closure or tissue glue closure wound closure following circumcision.

Signature……. Date…….

Investigator (Name & Surname) ……..……. Signature……

Witness (Name & Surname) ……Signature…….

You can contact us at any time with questions about this study on our contacts:

Dr. Mugambi Machoki: 0725103850 or email stanley.mugambi@aku.edu

Dr. Happiness Obare: 0727408944 or email happiness.obare@aku.edu

If you have any questions or concerns regarding your rights as a research subject, you may also contact the Aga Khan research office at 020-366 2138/1136 or email research.supportea@aku.edu.

APPENDIX 2: ASSENT FORM

ASSENT FORM FOR AGES 7 TO 12 YEARS OLD: RANDOMIZED CONTROLLED TRIAL COMPARING POST-OPERATIVE PAIN OUTCOME BETWEEN SUTURE AND TISSUE GLUE WOUND APPOSITION POST-CIRCUMCISION IN THE PEDIATRIC AGE GROUP

I am Dr. Happiness Obare from Aga Khan University Hospital.

I am doing a study about pain after a circumcision has been done.

A study is a way to learn more about things or people.

For this study:

- The boys are going to undergo circumcision as planned with their doctor and parents/guardians.
- The circumcision method is the same for all the boys.
- The only differences will be:
    - One group will have the skin closed with sutures
    - The other group will have the skin closed with glue

At the moment both methods (glue and suture) have been used for many boys without any difference in problems normally associated with this surgery.

What we do not know is if there is a difference between the two methods in terms of level of pain and discomfort after surgery.

That is what we will be looking to find out.

If you agree to be in the study the method used to close your skin will depend on chance (like flipping a coin) so that the study can truly tell us which is better.

The doctor will only use the method according to the side which the ‘coin-flip’ lands.

You will get to know the method after surgery.

The two methods work well though after surgery pain and discomfort may be experienced but the pain will be controlled with medicine as usual for this surgery.

I would like you to know that:

- You will not get into trouble if you do not want to be part of the study
- You can stop being part of the study at any point.
- You are free to ask any questions about the operation and the study at any point
- Your parents/guardians are aware of the study and were asked if it is OK for you to be part of the study.

You may sign this form only if:

- You completely understand what the study is about and what is needed for it
- You and your parents have talked about it and are ok with being part of the study
- You are ok with the study and agree to be part of the study

You will not be paid to be in the study OR given any gifts for being in the study.

The study itself is going to help others in the future when deciding to use either glue or sutures.

If you decide you want to be in this study, please sign your name.

I, ..., agree to be in this research study.

Sign your name here…….

Date……

APPENDIX 3: PARENTS' POST-OPERATIVE PAIN MEASURE (PPPM)

Children sometimes have changes in behavior when recovering from surgery. The following is a list of behaviors that your child may or may not have exhibited while recovering from surgery between _____ and _____ today. For each of the behaviors below, circle the appropriate response, yes or no.

When your child was recovering from surgery between _____ and _____ today, did s/he . . .

1) Whine or complain more than usual? ..... Yes No

2) Cry more easily than usual? .... Yes No

3) Play less than usual? .... Yes No

4) Not do the things s/he normally does? ..... Yes No

5) Act more worried than usual? .... Yes No

6) Act more quiet than usual? .... Yes No

7) Have less energy than usual? .... Yes No

8) Refuse to eat? ..... Yes No

9) Eat less than usual?.....Yes No

10) Hold the sore part of his/her body? ..... Yes No

11) Try not to bump the sore part of his/her body? ..... Yes No

12) Groan or moan more than usual? .... Yes No

13) Look more flushed than usual? ....Yes No

14) Want to be close to you more than usual? ..... Yes No

15) Take medication when s/he normally refuses? .....Yes No

Note on Administration and Scoring: Parents are asked to complete the measure between a specific time period (i.e., between breakfast and lunch, between lunch and supper, or supper and bedtime). The number of items parents have circled "Yes" are summed for a total score out of 15. A score of at least 6 out of 15 signifies clinically significant pain.

APPENDIX 4: DATA COLLECTION SHEET

STUDY IDENTIFIER .....

AGE (IN YEARS) .....

INTERVENTION ARM .....

DURATION OF SURGERY (IN MINUTES) .....

PPPM SCORE

AT 24 HOURS .....

AT 48 HOURS .....

POST OPERATIVE BLEEDING AT 1 WEEK

- YES
- NO

WOUND DEHISCENCE AT 1 WEEK

- YES
  - REQUIRING NO INTERVENTION
  - REQUIRING INTERVENTION
- NO