Are Topical Skin Adhesives An Option For Wound Closure Following Musculoskeletal Oncology Surgery? A STROCCS-Compliant Observational Study

Thanapon Chobpenthai (✉ dseero@gmail.com)

HRH Princess Chulabhorn College of Medical Science <https://orcid.org/0000-0002-2482-8203>

Thanate Poosiripinyo

Khon Kaen University Faculty of Medicine

Pakjai Tuntarattanapong

Prince of Songkla University Faculty of Medicine

Pichaya Thanindratarn

Chulabhorn Hospital

Warayos Trathitephun

Chulabhorn Hospital

Research

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Abstract

Background:

2-octyl cyanoacrylate (2OCA) is a high-viscosity medical-grade tissue adhesive used routinely. However, no studies have evaluated its use in musculoskeletal oncology surgery.

Methods:

We enrolled 99 patients undergoing musculoskeletal oncology surgery. 2OCA was chosen for wound closure, and it was applied by a specific surgeon for all patients. Drying times for the adhesive were recorded, and photographs were obtained intra-operatively. Post-treatment follow-up constituted queries regarding pain level, and recording incisional dehiscence, wound infection, hematoma, and incisional bleeding. Data collection was performed post-operatively at 48 hours, 5–10 days, 14 days, and 30 days. Other adverse events were documented.

Results:

2OCA was applied to 110 incisions in 99 patients constituting 62 female patients and 37 male patients. The mean age of patients was 50.41 (± 16.83) years; mean incision length was 10.24 (± 5.7) cm; and the mean pain score using a visual analogue scale (VAS) was 2.37 on post-operative day 7. The mean drying time was 1.81 (± 0.59) minutes; 91 (91%) patients reported excellent and superior satisfaction, and the remaining patients reported “good” (6%) and “fair” (2%) satisfaction. The percentage of dehiscence, hematoma, and keloid formation was considerably low.

Conclusion:

2OCA was safe in musculoskeletal oncology surgical incisions in this study. The incidence of post-operative adverse events was low. However, some patients developed a hematoma. Post-operative pain was low, and patient satisfaction was high. 2OCA can be a practical alternative to traditional suture closure for skin incisions after musculoskeletal surgery.

Introduction

Surgery in oncology patients demands additional measures and precautions owing to the patient's health condition and possible repeat surgical interventions. Intra- and post-operatively, wound healing remains a major concern, occasionally owing to patients' vulnerability to infection. The body's wound healing process serves as a major line of defense against infection, and cancer may impact the natural healing efficiency by impairing the cellular plasticity of the epidermal cell populations [1]. Cascading and orchestrated signaling pathways that are involved in normal wound healing are distorted with cancer development [2]. The roles of stem cell plasticity [3] and stroma [4] are altered during cancer development and metastasis, which significantly affects wound healing. Macrophages, which are part of the innate

wound healing response, are used by cancer cells in disease metastasis [5]; hence, focusing on rapid wound healing intra- or post-operatively is important.

In modern surgery, topical skin adhesives (TSA) are being chosen over traditional sutures for better and rapid wound healing. Octyl-2-cyanoacrylate or 2-octyl-cyanoacrylate (2OCA) skin adhesives are preferred compared with sutures because of the painless process and their rapid action. Comparisons of sutures and adhesives have been performed for facial wound healing [6], wound closure in cholecystectomy incisions [7], congenital cleft lip [8], and in other surgical processes [9]. These studies reported better outcomes with TSA compared with sutures.

2OCA skin adhesive has been found to be effective and superior in many applications. A comparative analysis suggested that adhesives are effective and better than staples in managing wounds related to incisional surgical site complications (SSCs) [10]. Similarly, 2OCA was found to be effective compared with sutures in another study [11]. Clinically relevant characteristics have also been evaluated for different skin adhesives that are presently being used routinely, and these adhesives were found suitable [12]. Moreover, *in vivo* evaluation helped establish the superiority of octyl-cyanoacrylate-based adhesives compared with adhesives that are butyl-cyanoacrylate-based [13]. Hence, in oncology-related surgery, where wound healing could be an issue, TSAs may provide an alternative support to achieve better and rapid wound healing. However, certain aspects, such as allergic reactions, and other possible adverse events should be addressed before careful application of any topical skin adhesive.

Musculoskeletal oncology requires a complex surgical process, often demanding repeat operations, depending on the disease condition. Hence, using TSA, especially 2OCA, could be a better choice. Skin adhesive-based treatment can be considered because it involves less skin wedging compared with traditional sutures, especially with recurrent tumors requiring re-operation. The benefits of using this approach includes 1) fast skin closure, which is particularly helpful in oncology patients as it is well-known that the more the operative time, the more is the risk of infection; 2) no skin mark along the wound as observed in traditional sutures. In case of tumor recurrence, it is not required to wedge the skin over the sutures; hence, there is less skin loss; 3) easy wound care as no dressing is required and it is water resistant; 4) good cosmetic outcomes; and 5) painless wound healing.

In addition, no recent studies have reported about TSA use in musculoskeletal surgery. Thus, this present study aimed to report that the application of 2OCA is safe and effective for musculoskeletal oncology surgical wound healing. The primary objective of this retrospective study was understanding the clinical outcomes and possible adverse events following the application of 2OCA in topical incision closure for musculoskeletal surgery. As secondary outcomes, we evaluated the drying time and patients' satisfaction with the wound scar.

Materials And Methods

Study design

Topical skin adhesive is a modern complementary addition to traditional sutures, and the application of 2OCA has been encouraging in many aspects in this context. The present retrospective study was complying with STROCCS guideline [14] and designed to understand the effectiveness of 2OCA skin adhesive application for wound closure after musculoskeletal surgery in cancer patients. The study was conducted at Chulabhorn Cancer Center, Bangkok, Thailand, from 08/28/2017 to 08/17/2020.

Study participants and eligibility criteria

A total of 99 participants were selected for the present study following strict eligibility criteria. Both sexes were included in the study. The inclusion and exclusion criteria for the participants were as follows:

Inclusion criteria: (1) Diagnosis with soft tissue or bone tumor (including metastasis), tumor-like lesion in extremities and back area; (2) Any age and sex; (3) Use 2OCA for skin closure

Exclusion criteria: (1) Not clear diagnosis; (2) Previous surgical wound before surgery; (3) Allergy to 2OCA; (4) Pre-operative radiotherapy; (5) Skin disorder

Surgical specifications and patient characteristics

We carefully recorded the incision characteristics, such as the specific upper and lower extremities and back region, and the diagnosis requiring surgery, such as malignant soft tissue tumors, benign soft tissue tumors, malignant bone tumors, benign bone tumors, and bone metastasis. All incisions were linear vertical incisions.

Post-operative treatment and follow-up

The focus of the study was surgical closure of the skin wound in adult patients using 2OCA, which was applied by a specifically designated surgeon. We recorded adhesive drying times and performed photography intra-operatively. Post-treatment follow-up was conducted with queries of patients' pain levels assessed using a visual analogue scale (VAS), as well as evaluation of incision dehiscence, wound infection, hematoma, and incisional bleeding. Follow-up was performed post-operatively at 48 hours, 5–10 days, 14 days, and 30 days. Specific intra-operative regimens were followed where wound edges were manually approximated by fingers or forceps. The physicians painted the 2OCA over the manually apposed wound edges with the applicator tip and were careful not to apply adhesive between the wound edges. The wound was held for drying. For each incision, the drying times were tested by a light touch of the forceps to ensure that the wound was closed, and the drying time was recorded. We closed deep layer and subcutaneous layer with Vicryl 1/0 and 2/0 or 3/0, respectively, before applying the topical skin adhesive in all cases.

Ethical considerations

This study was approved by the Human Research Ethics Committee of our institution (Chulabhorn Cancer Center, Bangkok, Thailand; project code: 054/2563), and the study was performed in accordance with the ethical standards of the 1975 Declaration of Helsinki.

Data collection and statistical analysis

A total of 15 parameters, diagnosis, demographic, surgery-related, wound healing, side effects, infection, and patient outcome-related parameters, were considered in the present study. All statistical analyses were conducted using R (version 3.6.1). A descriptive analysis of each parameter was performed. Numerical data are presented as mean $\pm$ standard deviation, and ordinal and categorical data are presented as percentages. The numerical variables were further analyzed for quartile distributions and are represented as box plots. Histograms and bar plots were considered, as appropriate. Correlation analysis was conducted using Pearson's r , Spearman's ρ , and Kendall's Tau-b method to understand the possible relationship between the wound and other parameters. The significance of sex-based differences was evaluated using Pearson's Chi-square test.

Results

In accordance with the study objective, each parameter was inspected carefully, and statistical assessment was performed for descriptive and inferential observations. The specific objective of these observations was to understand the possible relationships between the important parameters, such as sex difference, age, wound length, and drying time. However, every variable was keenly inspected for any plausible impacts they may have had on patient outcomes.

Clinical Observations

All resections involved linear vertical incisions. Some patients developed hematoma after almost 2 weeks of surgery, and examples are presented in Fig. 1 and Fig. 2 as observed post-operatively.

Observations And Outcomes

Most of the subjects who participated in this study were aged between 40 and 70 years (Fig. 3A). The mean patients' age was 50.41 ($\pm$ 16.83) years (Fig. 3B). The mean age of the female patients was 50.46 ($\pm$ 16.36) years, and the mean age of the male patients was 50.32 ($\pm$ 17.80) years. The total number of female participants in this study was 62 (62.62%), and the number of male participants was 37 (37.37%) of the 99 subjects selected for the study (Fig. 3C).

All selected participants underwent proper diagnosis and were categorized on the basis of the diagnostic (Dx) categories (Table 1) and the type of cancer (Fig. 3D). The Dx categories constituted 26 cases of lipoma (26.26%) and 14 cases of liposarcoma (14.14%), followed by ganglion cyst (n = 8, 8.08%) (Table 1). Metastasis was observed in 13/99 cases (13.13%).

Table 1
Observed distribution of the diagnosis codes among the participants.

Dx Code	Frequency	Percent
Desmoid fibromatosis	2	2.020
Epidermal inclusion cyst	1	1.010
Ewing's sarcoma	2	2.020
Fibrosis	2	2.020
GCT of the distal radius	6	6.061
GCT of bone	2	2.020
GCT of the tendon sheath	5	5.051
Ganglion cyst	8	8.081
Hemangioma	3	3.030
Leiomyosarcoma	1	1.010
Lipoma	26	26.263
Liposarcoma	14	14.141
MPNST	1	1.010
Metastasis	13	13.13
Osteosarcoma	1	1.010
PNST	3	3.030
Sarcomatoid sarcoma	1	1.010
UPS	3	3.030
Fibrosarcoma	1	1.010
Hemangioma	1	1.010
Leiomyosarcoma	3	3.030
Total	99	100.000
GCT, giant cell tumor; MPNST, malignant peripheral nerve sheath tumor, PNST, peripheral nerve sheath tumor; UPS, undifferentiated pleomorphic sarcoma		

Patients' diagnoses were categorized on the basis of the type of the tumor, benign, malignant, or metastatic. Additionally, in the benign group, benign bone tumors (n = 10, 10%) and benign soft tissue tumor (n = 47, 47.47%) were diagnosed and recorded. Similarly, in the case of malignancy, malignant

bone tumor (n = 3, 3.03%) and malignant soft tissue tumors (n = 26, 26.26%) were identified. Bone metastasis was observed in 13 cases (Fig. 3D).

Inspection and demographics of the tumor or diagnosed cancer were also performed on the basis of the body part of origin (Fig. 3E) to understand the most predominant body part affected by musculoskeletal cancer; 59 cases (59.59%) had musculoskeletal cancer in the upper extremities and back, and, in contrast, 40 (40.40%) cases had cancer in the lower extremities. Most cancers in the upper extremities were observed in the shoulder, forearm, and hand (Fig. 3E); several cases were recorded in the back region as well. The thigh and hip were the most affected areas in the lower body (Fig. 3E).

Analysis of the pain intensity due to the surgical wounds and the scars was performed using a VAS (Fig. 3F), with a scale range of 1–4, and with most patients reporting scores of 2 or 3 (Fig. 3F). Hematoma was observed in 10 patients during the post-operative follow-up (Fig. 3G). Table 1 presents the distribution of the diagnosed cases on the basis of the Dx category and shows a predominance of lipoma (n = 26, 26%), liposarcoma (n = 14, 14%), and metastasis (n = 13, 13%) (Table 1).

We further analyzed the surgical operations that were performed, which constituted the following: curettage and cementation and intramedullary nailing (IMN); marginal resection; curettage, cementation and cephalomedullary nailing (CMN); curettage, cementation and IMN; curettage, cementation, and plating; endoprosthesis; hemiarthroplasty; marginal resection; open biopsy; and wide resection. The majority of the surgeries were performed either with marginal resection (n = 44, 44%) or by wide resection (n = 40, 40%) (Table 2).

Table 2
Patient categorization according to the surgery.

Surgery type	Frequency	Percent
Curettage and cementation and IMN	1	1.010
Marginal resection	5	5.051
Curettage and cementation and CMN	3	3.030
Curettage and cementation and IMN	1	1.010
Curettage and cementation and plating	1	1.010
Endoprosthesis	2	2.020
Hemiarthroplasty	1	1.010
Marginal resection	44	44.444
Open biopsy	1	1.010
Wide resection	40	40.404
Total	99	100.000
IMN, intramedullary nailing; CMN, cephalomedullary nailing		

The distribution of the wound length, drying time, and patients' responses are shown in Fig. 4. Most surgical wounds were within 15 cm (Fig. 4A), and the mean incision length was 10.24 ($\pm$ 5.7) cm (Fig. 4B).

The mean drying time was 1.81 ($\pm$ 0.59) minutes. In most cases, the adhesive dried within 2 minutes after application (Fig. 4C). All patients were requested to provide feedback on the treatment outcomes (Fig. 4D). Of the 99 patients, 91 (91%) patients reported excellent satisfaction with the treatment approach (Fig. 4D). The remainder of the patients reported scores of "good" (6%) and "fair" (2%). No negative feedback was received from any of the patients regarding the use of the adhesive as a method of surgical wound treatment and closure.

Adverse Event Assessment

Careful monitoring was performed for possible adverse events intra- and post-operatively. Two patients developed minor infections, keloid formation was observed in five patients, and poor wound healing as dehiscence was observed in 7% of patients. Post-operative incisional bleeding was recorded in 3% of the patients, and hematoma was observed in 10 patients (Fig. 3G).

Statistical Evaluation Of Wound Length And Drying Time

We performed a correlation analysis for the wound length and drying time (Fig. 5), with separate analyses for the male (Fig. 5A) and female (Fig. 5B) patients. Although the correlation values were similar between the sexes (Fig. 5C–E), the relationship between the wound length and drying time was significant for both male patients ($P = 0.019$) and female patients ($P = 0.010$).

These findings motivated us to conduct Pearson's Chi-square test to detect statistically significant observations that differed between the male and female patients. However, for the considered parameters, no statistically significant difference was observed for the observed outcomes between the sexes (Table 3).

Table 3 Evaluation of statistically significant differences between the sexes using Pearson's Chi-square test.

Parameter	Chi-squared	Degree of freedom	p-value
Age	747.71	756	0.578
Dx	128.58	156	0.9469
Diagnosis	9.8284	12	0.631
Operation	28.386	28	0.4441
Body Part	54.48	63	0.7692
Wound Length	122.68	156	0.9773
VAS	5.5561	9	0.7834
Drying time	1.031	4	0.9051
Patient satisfaction	0.25628	2	0.8797

Dx, diagnostic classification; VAS, visual analogue scale

Discussion

Sutures have been used traditionally for wound closure and recovery; however, they have mechanical and physical effects and psychological impact on the patient that alter the healing process. Modern wound closure techniques include staples and adhesives as well as sutures [15]. However, there are discrepancies regarding selection of the closure technique intra-operatively [16–17]. Several studies attempted to compare these techniques to understand the advantages and disadvantages related to specific contexts, such as arthroplasty [18–19].

Different procedures and techniques have been adopted as wound closures after musculoskeletal surgery in cancer patients, micro-surgery [20] and vacuum-assisted wound closure for complicated wounds affected by radiation and following resection of musculoskeletal tumors [21–22]. However, complications associated with post-operative wound healing, especially for musculoskeletal oncology patients, remain a challenge. Reports have been available for such complications in soft tissue-associated sarcoma for decades [23–25]. Several associated factors, such as dehiscence, infection, and fistula, have been examined to understand their effects in complicated surgical wounds [26].

Developing applications and growing interest in using TSAs have led to better patient outcomes as reported in a previous study of the prevalence of TSA application in oncology patients [27]. 2OCA skin adhesives are being chosen more often for their better post-operative healing outcomes in oncology patients. Specific applications have also been reported in single-incision laparoscopic surgery in colorectal cancer patients [28]. In addition, the comparative economic and clinical outcomes associated with 2OCA as an effective skin adhesive have been studied very recently [29–30].

The availability of reports evaluating 2OCA in musculoskeletal cancer patient treatment is limited. The present study was conducted to understand the clinical outcomes, patient satisfaction regarding pain relief, and adverse events following the application of 2OCA skin adhesive for post-operative wound healing in musculoskeletal oncology patients. The observations and outcomes were satisfactory, with most patients highly satisfied with the results of the adhesive in wound healing. However, a small number of patients developed hematoma and incisional bleeding.

Keloid formation was observed in 5 patients. Three of these 5 patients also had wound dehiscence. So, wound dehiscence may be one factor for developing keloid formation in our series. True incidence and prevalence of keloid is not known as no population study has assessed the epidemiology of this disorder. In his 2001 publication, Marneros [31] stated that “reported incidence of keloids in the general population ranges from a high of 16% among the adults in Zaire to a low of 0.09% in England,” quoting from Bloom’s 1956 publication on heredity of keloids [32]. Clinical observations show that the disorder is more common among sub-Saharan Africans, African Americans and Asians, with unreliable and very wide estimated prevalence rates ranging from 4.5–16% [33, 34].

A significant statistical relationship between wound length and drying time was observed for both men and women. Hence, using TSA in minimal surgical incisions accelerates recovery and reduces the scar. These observations suggest that TSA can be a better alternative to sutures for surgical wound healing even in musculoskeletal oncology patients with long incisions. TSA is a painless remedy, as shown in the VAS scores in the present study. However, other important factors, such as allergic reactions [35], wound length, hematoma, and keloid should be carefully evaluated before TSA application.

The present study indicated that most cases required surgery in their upper extremities compared with the lower extremities. The average wound length in the upper and lower extremities and the back region was 8.53 ($\pm$ 4.75) cm, 12.25 ($\pm$ 6.69) cm, and 10.25 ($\pm$ 3.27) cm, respectively. Similarly, the average respective drying times for the upper and lower extremities, and the back were 1.63 ($\pm$ 0.52) mins, 1.92 ($\pm$ 0.65) mins,

and 2.16 ($\pm$ 0.38) mins, respectively. An abundance of female patients was observed in this study compared with male patients, and marginal and wide resection was chosen, depending on the assessment of the disease conditions. Statistically, a significant relationship was observed between drying time and wound length for both sexes.

Study Limitation

The present study was a single-center study with a small sample size. Multi-center studies with larger and more diverse samples may provide conclusive and generalized insight to support the observations recorded in the present study. In addition, a large randomized controlled trial may provide interesting insight for applying skin adhesives and their better impact on wound recovery.

Conclusion

Our study outcomes suggested that the application of 2OCA is safe and effective for surgical wound healing. The number of adverse events, such as incisional bleeding, hematoma, keloid, and dehiscence was low. Rapid drying time also supported shorter operation time and quick post-operative recovery. Hence, skin adhesives can be considered effective, painless wound healing treatments for musculoskeletal oncology patients as well as for recurrent sarcoma.

Abbreviations

2OCA, 2-octyl cyanoacrylate

VAS, visual analogue scale

TSA, topical skin adhesives

Dx, diagnostic

IMN, intramedullary nailing

CMN, cephalomedullary nailing

Declarations

Competing interests

The authors declare that they have no competing interests.

Funding

All authors certify that no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest.

Consent for publication

All Patients acknowledged and signed informed consent regarding publishing their data and photographs.

Ethics approval and consent to participate

The Human Research Ethics Committee of the Chulabhorn Research Institute acknowledged and approved this study. (Approval Number: RAA 054/2563). Informed consent was deemed not applicable since the study is purely retrospective in nature, and therefore written informed consent for participation was not obtained for adults or children under 16 years of age.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors's contributions

TC Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Visualization, Supervision, Project administration. TP Validation, Formal analysis, Investigation, Writing - Original Draft. PAT Methodology, Validation, Formal analysis, Writing - Review & Editing. PIT Investigation, Data Curation, Visualization, Writing - Review & Editing. WT Methodology, Investigation, Data Curation, Writing - Review & Editing.

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Figures

Figure 1

Representative case of wide resection of the distal femur and reconstruction with an endoprosthesis. The outcome indicated appropriate wound healing with no complications, and excellent patient satisfaction was recorded.

Figure 2

(A) Post-operative findings 180 days after wide resection and post-operative radiotherapy (RT) 60 days after liposarcoma resection in the left thigh. (B) Example of a post-operative hematoma in a patient's right thigh on day 14.

Figure 3

Distribution of the descriptive parameters. (A) Patients' age distribution; (B) Box plot presenting the 25th, 50th, and 75th percentile of the age distribution; (C) Distribution of the patients on the basis of sex; (D) Diagnosis-related outcome distribution; (E) Body part/region undergoing operation and wound treatment; (F) Wound healing outcomes according to the visual analogue scale (VAS) scores, and; (G) Frequency of post-operative hematoma.

Figure 4

Observations related to (A) wound length; (B) box plot of wound length; (C) wound drying time, and; (D) patient satisfaction survey results.

Figure 5

Comparative sex-based statistical correlation analysis results of wound length and drying time. (A) Wound length and drying time in male subjects and (B) wound length and drying time in female subjects. Statistical correlation and heatmap representation using (C) Pearson's r correlation, (D) Spearman's rho correlation, and (E) Kendall's Tau-b correlation for wound length and drying time for both sexes.

Supplementary Files

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