

Outcomes of 2-octyl cyanoacrylate skin adhesives following musculoskeletal oncology surgery

A STROBE-compliant observational study

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Abstract

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

We enrolled 99 patients who underwent musculoskeletal surgery. 2OCA was chosen for wound closure and was performed by a specific surgeon for all patients. The drying times for the adhesive were recorded, and photographs were obtained intra-operatively. Posttreatment follow-up consisted of queries regarding pain level and recording incisional dehiscence, wound infection, hematoma, and incisional bleeding. Data collection was performed postoperatively at 48 hours, 5 to 10 days, 14 days, and 30 days. Other adverse events were documented.

2OCA was applied to 110 incisions in 99 patients, comprising 62 female 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 was 2.37 on a postoperative 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 percentages of dehiscence, hematoma and keloid formation were considerably low.

In this study, 2OCA was safe for musculoskeletal oncology surgical incisions. The incidence of postoperative adverse events was low. However, some patients develop hematomas. Postoperative pain was low, and patient satisfaction was high. 2OCA can be a practical alternative to traditional suture closure for skin incisions after musculoskeletal surgery.

Abbreviations: 2OCA = 2-octyl cyanoacrylate, Dx = diagnostic, TSA = topical skin adhesive, VAS = visual analogue scale.

Keywords: 2-octyl cyanoacrylate, musculoskeletal oncology surgery, topical skin adhesive

1. Introduction

Surgery in oncology patients demands additional measures and precautions owing to the patient's health condition and possible repeat surgical interventions. Intra- and postoperative wound healing remains a significant concern, occasionally due to patients' vulnerability to infection. The wound healing process serves as a significant 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 involved in routine 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, significantly affecting wound healing. Macrophages, which are part of the innate wound

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

This retrospective chart review study involving human participants was conducted following the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Human Research Ethics Committee of the Chulabhorn Research Institute (Approval Number: RAA 054/2563).

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

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healing response, are used by cancer cells in disease metastasis^[5]; hence, focusing on rapid intra-operative or postoperative wound healing is essential.

In modern surgery, topical skin adhesives (TSAs) are chosen over traditional sutures for better and rapid wound healing. Octyl-2-cyanoacrylate or 2-octyl cyanoacrylate (2OCA) skin adhesives are preferred over sutures because of the painless process and 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 other surgical processes.^[9] These studies reported better outcomes with TSA than with sutures.

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

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

In addition, no recent studies have reported the use of TSA in musculoskeletal surgery. Thus, the present study aimed to report that the application of 2OCA is safe and effective for surgical wound healing in musculoskeletal oncology. The primary objective of this retrospective study was to understand 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 patient satisfaction with the wound scar.

2. Materials and methods

2.1. Study design

TSA 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 complied with the STROCSS guidelines^[14] and was designed to understand the effectiveness of 2OCA skin adhesive application for wound closure after musculoskeletal surgery in cancer patients. The

study was conducted at the Chulabhorn Cancer Center, Bangkok, Thailand, from August 28, 2017 to August 17, 2020.

2.2. 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 this study. The inclusion and exclusion criteria for participants were as follows:

Inclusion criteria were as follows: diagnosis of soft tissue or bone tumor (including metastasis), tumor-like lesion in the extremities and back area; any age and sex; and use of 2OCA for skin closure.

Exclusion criteria were as follows: no precise diagnosis; previous surgical wound before surgery; allergy to 2OCA; pre-operative radiotherapy; and skin disorder.

2.3. 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 made using linear vertical incisions.

2.4. Postoperative treatment and follow-up

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

2.5. 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 was performed according to the ethical standards of the 1975 Declaration Helsinki.

2.6. Data collection and statistical analysis

A total of 15 parameters were considered in the present study: diagnosis, demographic, surgery-related, wound healing, side effects, infection, and patient outcome-related parameters. All statistical analyses were conducted using the R software (version 3.6.1, Auckland, New Zealand). Descriptive analysis of each parameter was performed. Numerical data are presented as mean



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.

\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 appropriate. Correlation analysis was conducted using Pearson r , Spearman ρ , and Kendall tau-b method to understand the possible relationship between the wound and other parameters. The significance of sex-based differences was evaluated using Pearson chi-square test.

3. Results

Each parameter was scrutinized following the study objective, and statistical assessments were performed for descriptive and inferential observations. The specific objective of these observations was to understand the possible relationships between essential parameters, such as sex, age, wound length, and drying

time. However, every variable was keenly inspected for any plausible impact they may have had on patient outcomes.

3.1. Clinical observations

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

3.2. Observations and outcomes

Most of the subjects who participated in this study were between 40 and 70 years (Fig. 3A). The mean patients' age was 50.41 (± 16.83) years (Fig. 3B). The mean age of the female patients was 50.46 (± 16.36) years, and the mean age of the male patients was 50.32 (± 17.80) years. The total number of female participants in

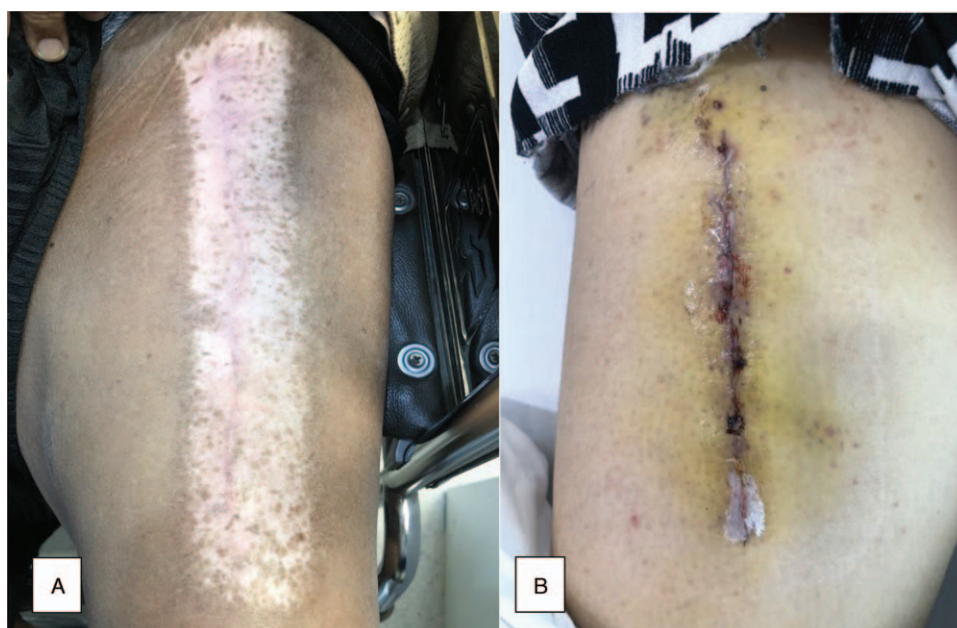


Figure 2. (A) Postoperative findings 180 days after wide resection and postoperative radiotherapy (RT) 60 days after liposarcoma resection in the left thigh. (B) Example of a postoperative hematoma in a patient's right thigh on day 14.

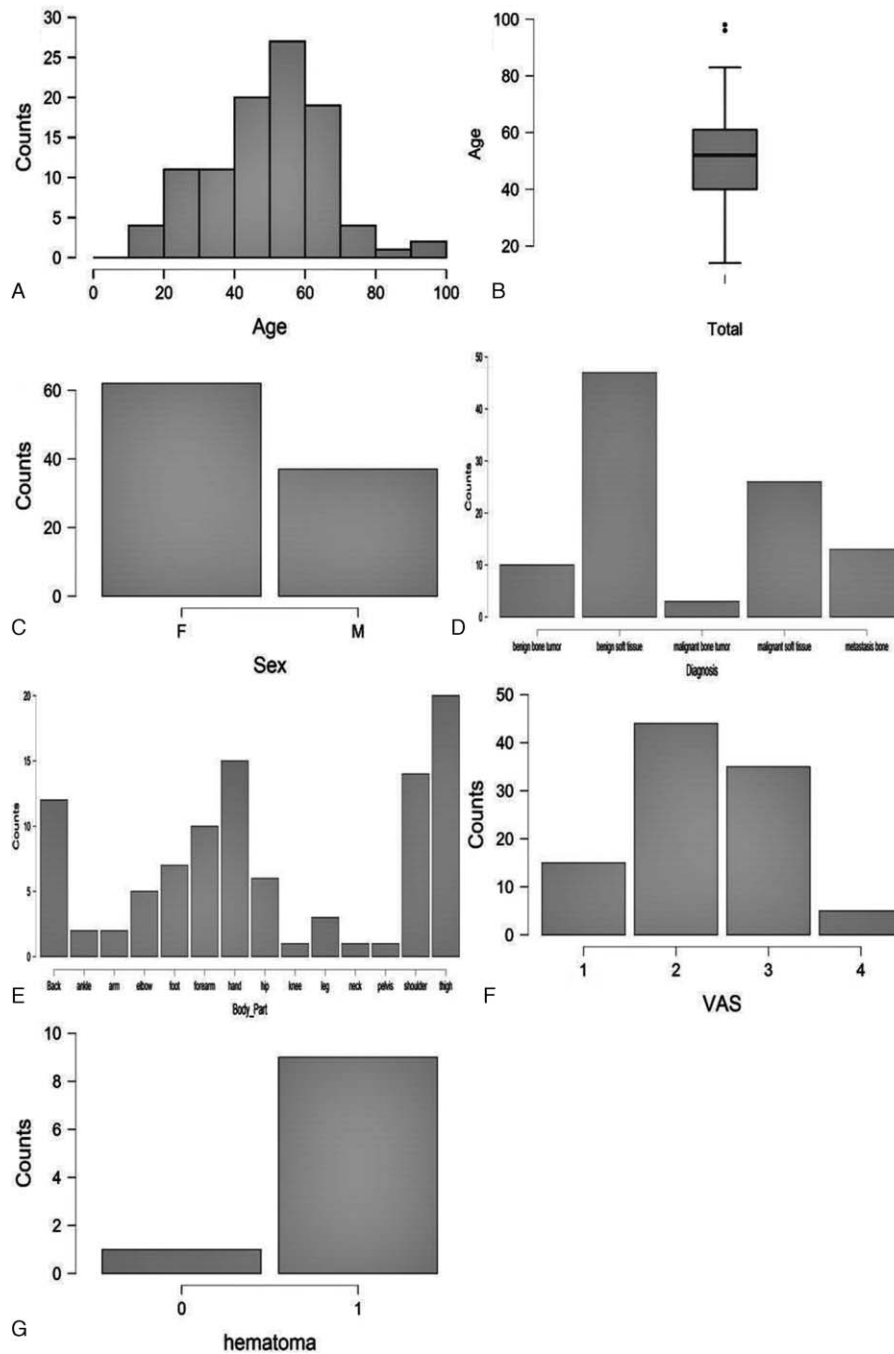


Figure 3. Distribution of the descriptive parameters. (A) Patients’ age distribution; (B) box plot presenting the 25th, 50th, and 75th percentile of the age distribution; (C) distribution of the patients based on sex; (D) diagnosis-related outcome distribution; (E) body part/region undergoing operation and wound treatment; (F) wound healing outcomes according to the visual analogue scale (VAS) scores; and (G) frequency of postoperative hematoma.

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 based on the diagnostic (Dx) categories (Table 1) and the type of cancer (Fig. 3D). The Dx categories included 26 cases of lipoma (26.26%) and 14 cases of liposarcoma (14.14%), followed by ganglion cysts (n=8, 8.08%) (Table 1). Metastasis was observed in 13/99 cases (13.13%).

Patients’ diagnoses were categorized based on the type of tumor, benign, malignant, or metastatic. Additionally, in the

benign group, benign bone tumors (n=10, 10%) and benign soft tissue tumors (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 patients (Fig. 3D).

Inspection and demographics of the tumor or diagnosed cancer were also performed based on 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 40 (40.40%)

Table 1
The observed distribution of the Dx code among the participants.

| Dx code | Frequency | Percent |
|--------------------------|-----------|---------|
| Desmoid fibromatosis | 2 | 2.020 |
| Epidermal inclusion cyst | 1 | 1.010 |
| Ewing 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 |

Dx = diagnostic, GCT = giant cell tumor, MPNST = malignant peripheral nerve sheath tumor, PNST = peripheral nerve sheath tumor, UPS = undifferentiated pleomorphic sarcoma.

patients 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. 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 scars was performed using a VAS (Fig. 3F), with a scale range of 1 to 4, with most patients reporting scores of 2 or 3 (Fig. 3F). The hematoma was observed in 10 patients during postoperative follow-up (Fig. 3G). Table 1 presents the distribution of the diagnosed cases based on 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 included the following: curettage and cementation, intramedullary nailing, marginal resection, curettage, cementation, and cephalomedullary nailing; curettage, cementation, and intramedullary nailing; curettage, cementation, and plating; endoprosthesis; hemiarthroplasty; marginal resection; open biopsy; and wide resection. Most surgeries were performed either with marginal resection ($n=44$, 44%) or wide resection ($n=40$, 40%) (Table 2).

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

The mean drying time was 1.81 (± 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%) 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

Table 2
Categorization of the subjects based on 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 |

CMN = cephalomedullary nailing, IMN = intramedullary nailing.

patients regarding using the adhesive as a surgical wound treatment and closure method.

3.3. Adverse event assessment

Careful monitoring was performed for possible intra- and postoperative adverse events. Two patients developed minor infections, keloid formation was observed in 5 patients, and poor wound healing, as dehiscence was observed in 7% of patients. In 3% of the patients, postoperative incisional bleeding was recorded, and a hematoma was observed in 10 patients (Fig. 3G).

3.4. 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 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 ($P=.019$) and female patients ($P=.010$).

These findings motivated us to conduct Pearson chi-square test to detect statistically significant differences between male and female patients. However, for the considered parameters, no statistically significant difference was observed in the observed outcomes between the sexes (Table 3).

4. Discussion

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

Different procedures and techniques have been adopted for wound closure after musculoskeletal surgery in cancer patients, microsurgery,^[20] and vacuum-assisted wound closure for complicated wounds affected by radiation and subsequent resection of musculoskeletal tumors.^[21,22] However, complications associated with postoperative wound healing, especially in musculoskeletal oncology patients, remain a challenge. Reports have been available for such complications in soft tissue-associated sarcomas for decades.^[23–25] Several associated factors,

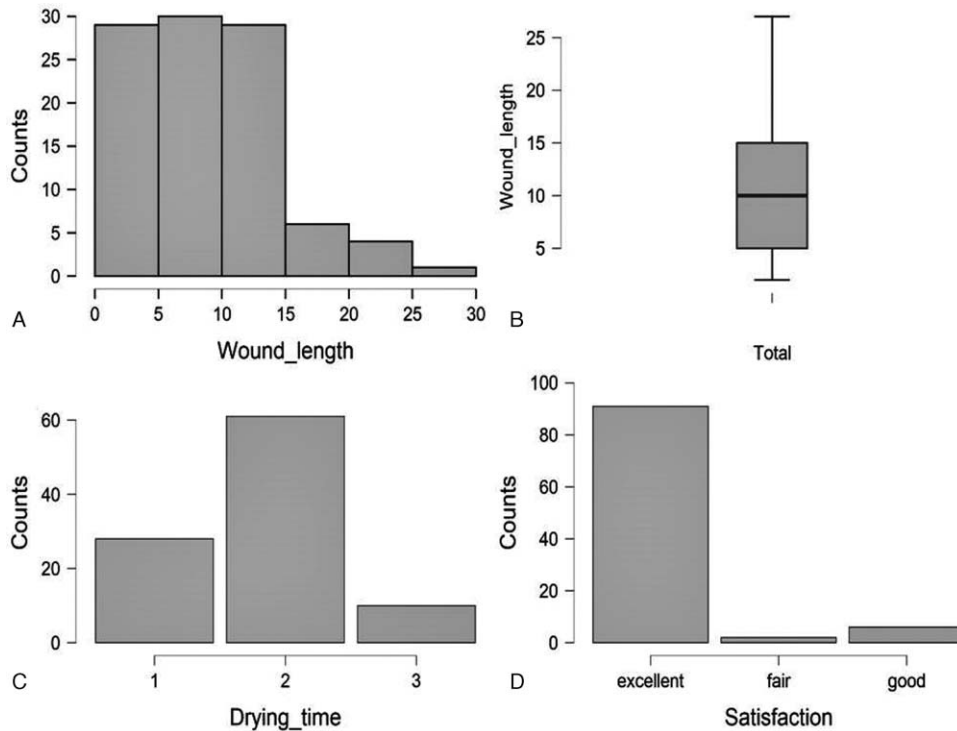


Figure 4. Observations related to (A) wound length; (B) box plot of wound length; (C) wound drying time; and (D) patient satisfaction survey results.

such as dehiscence, infection, and fistula, have been examined to understand their effects on complicated surgical wounds.^[26]

Developing applications and growing interest in using TSAs have led to better patient outcomes, as reported in a previous

study on the prevalence of TSA application in oncology patients.^[27] 2OCA skin adhesives are chosen more often because of their better postoperative healing outcomes in oncology patients. Specific applications have also been reported in single-

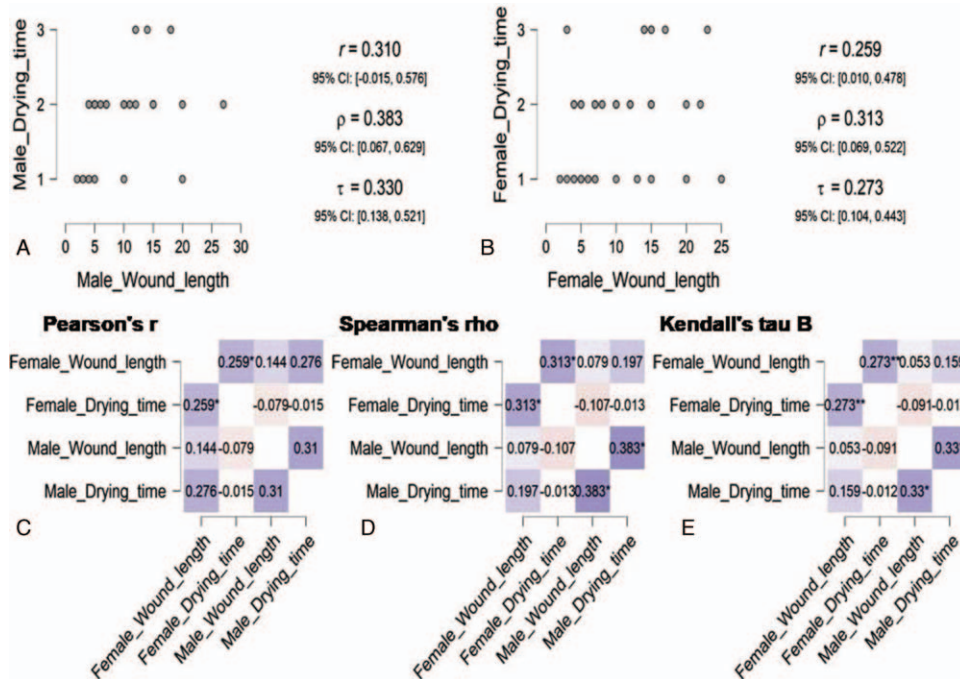


Figure 5. Comparative sex-based statistical correlation analysis results of wound length and drying time. (A) Wound length and drying time in male subjects and (B) wound length and drying time in female subjects. Statistical correlation and heatmap representation using (C) Pearson r correlation, (D) Spearman rho correlation, and (E) Kendall tau-b correlation for wound length and drying time for both sexes.

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

| Parameter | Chi-squared | Degree of freedom | P value |
|----------------------|-------------|-------------------|---------|
| Age | 747.71 | 756 | .578 |
| Dx | 128.58 | 156 | .9469 |
| Diagnosis | 9.8284 | 12 | .631 |
| Operation | 28.386 | 28 | .4441 |
| Body part | 54.48 | 63 | .7692 |
| Wound length | 122.68 | 156 | .9773 |
| VAS | 5.5561 | 9 | .7834 |
| Drying time | 1.031 | 4 | .9051 |
| Patient satisfaction | 0.25628 | 2 | .8797 |

Dx = diagnostic, VAS = visual analogue scale.

incision laparoscopic surgery in patients with colorectal cancer.^[28] In addition, the comparative economic and clinical outcomes associated with 2OCA as an effective skin adhesive have been studied very recently.^[29,30]

Reports evaluating 2OCA in patients with musculoskeletal cancer are 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 postoperative wound healing in musculoskeletal oncology patients. The observations and outcomes were satisfactory, with most patients highly satisfied with the adhesive results in wound healing. However, a small number of patients developed hematomas and incisional bleeding.

Keloid formation was observed in 5 patients. Three of these 5 patients also had wound dehiscence. Therefore, wound dehiscence may be a factor in the development of keloid formation in our study. The true incidence and prevalence of keloids are unknown, 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 the heredity of keloids.^[32] Clinical observations show that the disorder is more common among sub-Saharan Africans, African Americans, and Asians, with unreliable and extensive estimated prevalence rates ranging from 4.5–16%.^[33,34] The hematoma was observed in 10 cases. All patients had a wound length of more than 10 cm. The drainage of postoperative bleeding may not be enough by surgical drainage tube and the bleeding cannot through the wound that used 2OCA. The wound dehiscence (7% of the patient) occurs in the incision near the joint. Those patients had not restricted the postoperative mobilization.

A significant statistical relationship between wound length and drying time was observed in both men and women. Hence, using TSA in minimal surgical incisions accelerates recovery and reduces scarring. 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 indicated by 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 patients required surgery in the upper extremities compared with the lower extremities. The average wound lengths in the upper and lower extremities and the back region were 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) minutes, 1.92 (\pm 0.65) minutes, and 2.16 (\pm 0.38) minutes, 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.

4.1. Study limitation

The present study was a single-center study with small sample size. Multicenter studies with more extensive and more diverse samples may provide conclusive and generalized insights to support the observations recorded in the present study. In addition, a large randomized controlled trial may provide exciting insights into the application of skin adhesives and their better impact on wound recovery.

5. Conclusion

Our study outcomes suggest 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. The rapid drying time also supported a shorter operation time and quick postoperative recovery. Hence, skin adhesives can be considered adequate, painless wound healing treatments for musculoskeletal oncology patients, as well as for recurrent sarcomas.

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