นิพนธ์ต้นฉบับ

Original Article

การศึกษาเปรียบเทียบผลลัพธ์ทางคลินิกระหว่างการทำแผลแบบความดันลบด้วยอุปกรณ์ CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) และอุปกรณ์แบบดั้งเดิมในบาดแผลเปิด

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บทคัดย่อ

ที่มาของงานวิจัย : บาดแผลแบบเปิดมักต้องการการรักษาด้วยการทำแผลแบบความดันลบ (Negative Pressure Wound Therapy, NPWT) ซึ่งอุปกรณ์ทำแผลแบบความดันลบ CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) ถูกพัฒนาขึ้นมาเพื่อแก้ไขข้อจำกัดของอุปกรณ์แบบดั้งเดิมในด้านความคุ้มค่า ราคา และความสะดวกสบายของผู้ป่วย

วัตถุประสงค์ : การศึกษานี้ซึ่งมีผู้ป่วย 48 คน มีเป้าหมายเพื่อเปรียบเทียบ CKANPD กับอุปกรณ์ NPWT แบบดั้งเดิมในด้านอัตราการสร้างเนื้อเยื่อแกรนูเลชันและอัตราการติดเชื้อ

วิธีการศึกษา : การศึกษาแบบ double-blind randomized controlled trial ถูกนำมาใช้ โดยอัตราการสร้างเนื้อเยื่อแกรนูเลชันเป็นผลลัพธ์หลัก และอัตราการติดเชื้อและความพึงพอใจของผู้ป่วยเป็นผลลัพธ์รองผลการศึกษา

ผลการศึกษา : กลุ่มที่ใช้ CKANPD มีอัตราการสร้างเนื้อเยื่อแกรนูเลชันภายในหนึ่งสัปดาห์สูงกว่าอุปกรณ์แบบดั้งเดิมอย่างมีนัยสำคัญทางสถิติ (93.09 ±4.76% เทียบกับ 88.41 ±5.71%, p=0.004) โดยไม่พบความแตกต่างในอัตราการลดขนาดแผล และทั้งสองกลุ่มไม่มีการติดเชื้อเพิ่มเติม

สรุปผลการศึกษา : อุปกรณ์ทำแผลแบบความดันลบ CKANPD เป็นทางเลือกที่ไม่ด้อยกว่าอุปกรณ์แบบดั้งเดิมในการส่งเสริมการสร้างเนื้อเยื่อแกรนูเลชัน โดยไม่เพิ่มความเสี่ยงต่อการติดเชื้อ ผลการศึกษานี้ชี้ให้เห็นถึงความเป็นไปได้ในการศึกษาเพิ่มเติมในผู้ป่วยนอก ซึ่งสอดคล้องกับวัตถุประสงค์ของการพัฒนา CKANPD และควรมีการศึกษาต่อเนื่องเพื่อตรวจสอบผลในระยะยาวต่อไป

คำสำคัญ : การทำแผลแบบความดันลบ, การทำแผลแบบสุญญากาศ, การสร้างแกรนูเลชั่น, บาดแผลแบบเปิด, อุปกรณ์ทำแผลความดันลบแบบพกพา, อุปกรณ์ CBH-KMITL Ambulatory Negative Pressuring Device(CKANPD)

Randomized controlled trial compares Clinical Outcome between Negative Pressure Wound Therapy(NPWT) with CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) and Conventional Device in Open Traumatic Wound

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Abstract

Background: Open traumatic wounds often require Negative Pressure Wound Therapy (NPWT) for treatment. The CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD), a cost-effective, portable NPWT device, has been developed to address the limitations of conventional devices.

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Objective: This study of 48 patients aimed to compare the CKANPD and conventional NPWT devices in terms of granulation tissue formation rate and infection rates.

Methods: A double-blind randomized controlled trial was conducted. The primary outcome was the rate of granulation tissue formation, with secondary outcomes including infection rates and patient satisfaction.

Results: The CKANPD group demonstrated a significantly higher rate of granulation tissue formation after one week of NPWT (93.09 ±4.76% vs 88.41 ±5.71%, p=0.004). No significant difference was observed in wound size reduction between the two methods. Both methods had an infection rate of 0, indicating excellent safety profiles.

Conclusion: The CKANPD is a non-inferior alternative to conventional NPWT devices, promoting faster granulation tissue formation without increasing infection risk. These promising results pave the way for the next phase of study in outpatient settings, aligning with the primary goal of CKANPD development. Further research is needed to confirm these findings and assess long-term outcomes.

Keywords : Negative Pressure Wound Therapy (NPWT), Vacuum-Assisted Wound Closure (VAC), granulation tissue formation, open traumatic wounds, portable NPWT device, CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD)

Background

Open Traumatic wounds, varying in characteristics and severity, are a frequent encounter in medical practice. These wounds can range from superficial abrasions to significant tissue loss, often impacting underlying structures such as soft tissue, tendons, and even internal organs[1,2]. One widely accepted treatment for open wounds that cannot be immediately covered with soft tissue is Negative Pressure Wound Therapy (NPWT), also known as Vacuum-Assisted Wound Closure (VAC)[3].

NPWT promotes granulation tissue formation by applying controlled negative pressure to the wound, which reduces edema, increases perfusion, and removes exudate, thereby lowering the bacterial load. Granulation tissue, characterized by new connective tissue and microscopic blood vessels, forms on the surfaces of a wound during the healing process, providing a foundation for epithelialization. NPWT creates mechanical deformation at the cellular level, stimulating cell proliferation, migration, and angiogenesis through microstrain. It upregulates growth factors like VEGF, FGF, and PDGF, essential for wound healing, and enhances the formation of the extracellular matrix by fibroblasts. Studies by Morykwas et al. and Argenta and Morykwas demonstrate its effectiveness in both animal models and clinical settings, confirming the significant role of NPWT in enhancing wound healing and granulation tissue formation[4-6]. This method has demonstrated efficacy in accelerating the healing of open fractures[7], promoting the formation of granulation tissue, and maintaining a clean wound bed[8]. A systematic review and meta-analysis conducted in 2018 further corroborated these findings, indicating that NPWT significantly reduces infection rates and enhances wound healing[9-15].

Some studies have questioned the cost-effectiveness of NPWT[9]. These studies found no significant difference in wound healing rates, infection rates, patient quality of life, and cost-effectiveness between NPWT and traditional wet dressing. However, some study has suggested that home-based NPWT could potentially reduce costs by more than $20,000[16].

In the United States, outpatient NPWT has been implemented, with patients receiving guidance on using portable NPWT devices at home. However, there is a lack of research comparing the outcomes of this approach, and even the manufacturer's website does not provide any information on this. In Thailand, particularly in tertiary hospitals, the use of portable NPWT devices remains a challenge due to the high cost of the equipment, which is over 50,000 baht per device, and the consumable materials that need to be replaced each time cost about 3,500 baht. The current NPWT equipment used in Chonburi Center Hospital is bed-attached, necessitating prolonged hospital stays and bed rest for patients.

The researchers aim to address this issue by developing a portable NPWT device that can be carried by the patient. This project is a collaboration with the Department of Biomedical Engineering, Faculty of Engineering, King Mongkut's Institute of Technology Ladkrabang. The device, named CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD),Figure 1, can be produced at a unit cost of no more than 5,000 baht. This device will be used for NPWT in the context of tertiary hospitals and is expected to benefit patients in the future.

Fig 1 CBH-KMITL Amburatory Negative Pressuring Device (CKANPD)

Objective

Primary outcome : To compare the rate of granulation tissue formation between negative pressure wound therapy using the CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) and the conventional device in open traumatic wounds.

Secondary outcome :

1. To compare the infection rates between negative pressure wound therapy using the CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) and the conventional device in open wounds.

2. To study patient satisfaction with the CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD).

Material and Methods

An approval of this study (48/65/R/h1) was obtained by the institutional review board of Chonburi Hospital (IRBCBH 087/256).

The participants of this study were 60 patients diagnosed with open traumatic wounds where immediate soft tissue coverage could not be achieved. The inclusion criteria encompassed patients with open surgical wounds that could not be immediately covered with soft tissue, patients requiring wound dead space management, patients with exposed bone or degloved skin or exposed tendons, and patients with open joint injuries. The age range for participation was limited to 18 to 60 years.

Exclusion criteria were determined to ensure patient safety and the validity of the study results. Patients were excluded if they had contraindications for vacuum-assisted closure therapy, including the presence of necrotic tissue and black eschar, chronic bone infection, exposed blood vessels, nerves, or vascular anastomosis sites. Furthermore, patients who were eligible for immediate flap coverage were also excluded from the study.

The sample size for this study was determined based on a literature review. No previous research has compared the granulation rate between different types of Negative Pressure Wound Therapy (NPWT) devices. However, a study by Bayoumi et al[17], examining the use of a conventional wall suction device, reported an average granulation rate of 78.68% ± 18.12% (P=0.0001) after a week of NPWT. As such, under this non-inferiority study design with a non-inferiority margin set at 15%, a minimum of 21 patients per group was deemed necessary. To account for a projected 5-10% dropout or withdrawal rate, the total sample size was adjusted to 48 patients. Nonetheless, adhering to the principles of the Central Limit Theorem as per BartZ's (1999) suggestion, an extended sample size of 30 patients per group was considered.

Randomization in this study was performed using a block of 4 method. The statistical analysis was scheduled to occur at three points: a preliminary analysis mid-study (7 blocks, N=28), at the calculated end point (12 blocks, N=48), and, if no statistical significance was observed, the study, with the approval of the Institutional

Review Board of Chonburi Hospital / Ethic Committee, was allowed to continue up to 15 blocks (N=60). These scheduled analyses, particularly the preliminary analysis mid-study and the extended study group, are based on the theoretical equivalence of CKAPD and convention, both using the same 125mmHg NPWT.

This study was conducted as a double-blind Randomized Controlled Trial (RCT) using a per-protocol design in the Department of Orthopedics at Chonburi Hospital, Thailand, from 1st December 2022 to 30th November 2023. Blinded physicians performed surgical debridement and evaluated granulation. The Blinded surgical team collects wound data according to the research protocol after performing excisional debridement. The surgeon decides the size and amount of granulation tissue. If the primary surgeon is a third-year resident or higher, they make the assessment. If the primary surgeon is a lower-level resident, the chief resident on duty (third year or higher) will assess and determine the size and amount of granulation tissue. The boundaries of the granulation tissue are outlined and photographed with a digital camera with a resolution of more than 20 megapixels and a color depth of at least 8 bits. The information is then fully recorded in the data collection form. The wound is then closed aseptically using sterile foam/sponge covered with 3M™ Ioban™ and an 18-gauge NG tube is placed. The pressuring devices were employed within the inpatient ward and managed by registered nurses according to the study protocol, the administration of which was randomized and fully informed. The medical and multidisciplinary team monitors the treatment and nursing care of patients with negative pressure wound therapy as usual (continuous NPWT with 125mmHg without opening wound or change Vac dressing instrument for 7 days), opening wounds in the ward for infection assessment only if the medical team suspects an infection specifically due to the wound, not from other causes. Blood tests, including procalcitonin levels, are taken to aid in the evaluation. An infection is defined as the presence of pus from the wound and/or the patient exhibiting at least one of the following symptoms: pain, swelling, redness, or heat, combined with a procalcitonin level greater than 0.05 micrograms per liter. If an infection is confirmed, the study is terminated, and the patient undergoes surgical debridement as soon as possible,

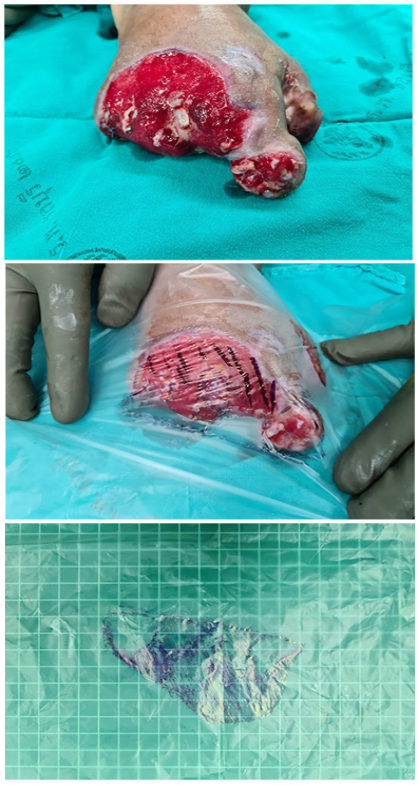

Fig 2 : Demonstrated granulation formation measurement. A : granulation tissue after NPWT. B: wound area was drawed, and granulation tissue was shadowed on sterile plastic sheet
C : Plastic sheet was taken photo on flat reference measurement mat.

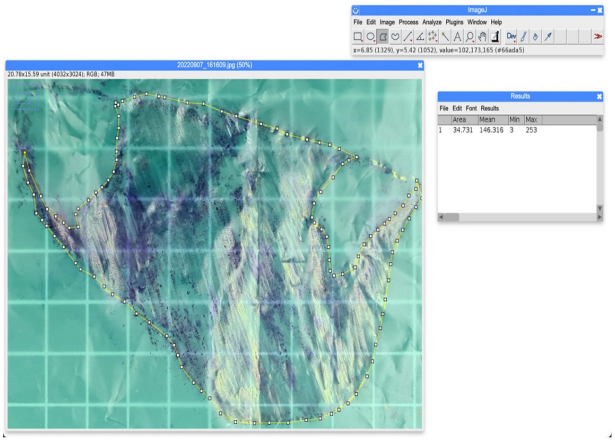

Fig 3 : Demonstrated granulation area measurement using ImageJ image processing program

with tissue samples sent for pathology and culture. If the wound is not infected, it is closed using the same negative pressure wound therapy device, and the process continues NPWT for 7 days. The rate of granulation formation was obtained by measuring the percentage of granulation formation at day 7th of NPWT utilizing ImageJ® imaging processing software as shown in Figure 2,3.

The CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) models CKAND V.1, identified by device codes ANPD-01 through ANPD-06, utilized in the intervention arm, were rigorously evaluated by a research and development team of engineers from the Department of Biomedical Engineering, Faculty of Engineering, King Mongkut's Institute of Technology Ladkrabang. The devices were also inspected closely for quality, accuracy, and electrical safety in compliance with the IEC 60601-1 international standard, utilizing a DALE601E safety analyzer device. This electrical safety assessment was conducted at the TPA Medical Equipment Calibration Lab, which adheres to the Thai Industrial Standards Institute (TISI) standards. The evaluative details are as follows:

1. The negative pressure level was directly measured at 125 mmHg, providing a confidence interval of approximately 95%. The pressure fluctuation did not exceed 2.8 mmHg, in accordance with the measurement standards set by the National Institute of Metrology of Thailand.

2. The electrical safety was verified according to the IEC 60601-1 international standard using the DALE601E safety analyzer device. The testing confirmed the absence of electrical leakage. Detailed test results are provided in the supplementary documentation.

In the Concern of infection prevention, the CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) was designed as an active negative pressure system with an air buffer mechanism to inhibit the backflow of contaminants into the wound. The system incorporates a buffering air chamber and an air suction tube to maintain a contamination-free environment. The wound closure device (Ioban™) is affixed to the wound area, and a nasogastric tube is connected to collect waste in a Redivac drain bottle. All components passed standard infection control equipment employed in hospitals. As shown in Figure 2 compare with conventional NPWT.

Statistical analysis for this study was planned to be performed using the STATA/MP statistical analysis program version 17. Descriptive data pertaining to demographics were to be represented using means±SD for continuous data, and percentages for categorical data. To analyze the primary outcome, which is the rate of granulation (percentage per week), independent T-tests or Mann-Whitney U tests were designated.

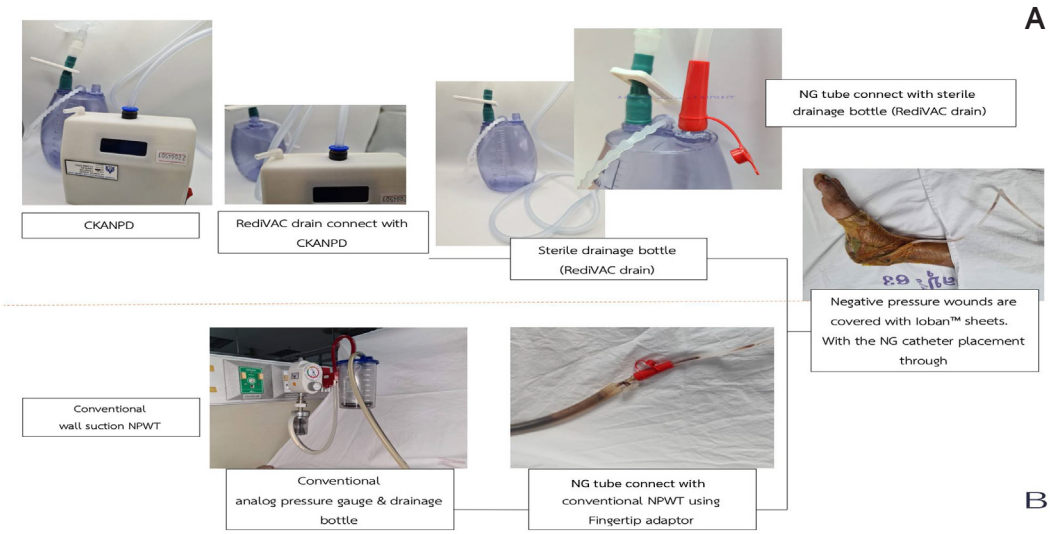

Fig 4 : Demonstrated NPWT device assembly. A : Conventional NPWT, B : CKANPD

Result

For the analysis calculated end point of the study, 48 patients (comprising 12 groups) were enrolled in accordance with the inclusion criteria. The mean age of the patients was 29.5 ± 9.56 years, ranging from 18 to 55 years. In the conventional group, the average age was 28.9 ±10.1, compared to 30.1 ± 9.19 in the CKANPD group.

As depicted in Table 1, the demographic data reveals the homogeneity between the control and intervention groups. The lower limb was the most commonly affected body part in both groups, and the prevalent mechanism of injury was motorcycle accidents. The majority of soft tissue defects were managed with skin grafts.

Table 1 : Demographic data

	Total N=48	**Conventional** N=24	***CKANPD*** N=24
Sex			
Male	30 (62.5)	14 (58.3)	16 (66.7)
Female	18 (37.5)	10 (41.7)	8 (33.3)
Age	29.5±9.56	28.9±10.1	30.1±9.19
Affected part			
Lower (leg)	39 (81.3)	21 (87.5)	18 (75.0)
Lower (foot)	3 (6.3)	0 (0)	3 (12.5)
Upper (forearm)	5 (10.4)	2 (8.4)	3 (12.5)
Upper (hand)	1 (2.1)	1 (4.2)	0 (0)
Mechanism of injury			
Motorcycle accident	31 (64.6)	16 (66.6)	15 (62.6)
Car accident	6 (12.5)	2 (8.4)	4 (16.6)
Secondary to procedure	6 (12.5)	4 (16.6)	2 (8.4)
Fasciotomy	5 (10.5)	2 (8.4)	3 (12.5)
Occupational	26.7±16.2	28.7±18.6	24.8±13.5
Initial wound size (cm^2)			
Soft tissue defect closure	45 (93.8)	22 (91.6)	23 (95.8)
Skin graft	3 (6.3)	2 (8.4)	1 (4.2)
Flap±Skin graft	3 (10.7)	2 (14.3)	1 (7.14)

After a week of applying NPWT, the granulation formation and wound size reduction was satisfied in both CKANPD (Figure 5) and conventional group as shown in table 2. All patients undergo excisional debridement after 7 days of NPWT, during this procedure, wound size and granulation tissue measurements are recorded. Subsequently, wound coverage is achieved using secondary procedures such as split-thickness skin grafting or flap reconstruction as shown in table 1.

Fig 5 : Demonstrated result of CKANPD. A : Soft tissue defect at initial before NPWT. B: Granulation formation and wound size reduction after 1 week of NPWT with CKANPD

Table 2 presents a comparative analysis of granulation formation and wound size reduction between the Conventional and CKANPD groups. Initially, there was no significant difference in the percentage of granulation between the two groups (2.71 ±3.49% for Conventional vs. 3.18 ±3.89% for CKANPD, p=0.353). However, after one week of NPWT, the CKANPD group exhibited a significantly higher percentage of granulation (96.3 ±4.21%) compared to the Conventional group (91.24 ±4.11%, p=0.004). The rate of granulation per week was also statistically significantly higher in the CKANPD group (93.09 ±4.76%) compared to the Conventional group (88.41 ±5.71%, p=0.004), as shown in Figure 6.

Successful soft tissue coverage is achieved using split-thickness skin grafts (STSG) and flap procedures. Notably, both the NPWT and conventional treatment groups achieve successful soft tissue coverage by the 7th day, despite the conventional group exhibiting a lower percentage of granulation tissue formation

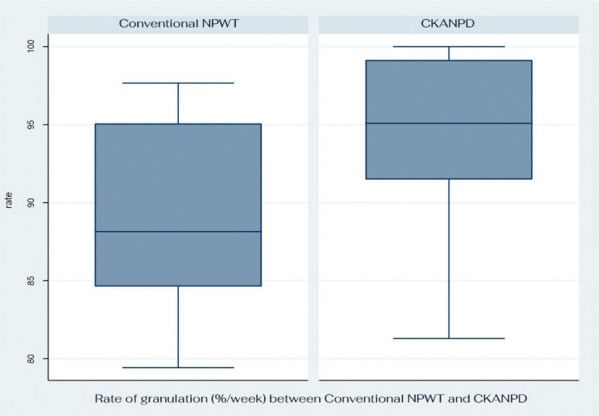

Fig 6 : Rate of granulation(%/week) between Conventional and CKANPD

In terms of wound size reduction, there was no significant difference between the Conventional and CKANPD methods (13.41 ±8.56%vs. 15.50 ±12.16% p=0.494). Furthermore, both methods demonstrated excellent safety profiles, with an infection rate of 0 in both groups.

Table 2 : Result compare between Conventional and CKANPD

	Total N=48	**Conventional** N=24	***CKANPD*** N=24	**p-value**
Granulation formation				
Percent of Granulation				
intital (%)	2.71 ±3.49	3.18 ±3.89	2.23 ±3.07	0.353
1 week (%)	93.54 ±4.51	91.24 ±4.11	96.3 ±4.21	0.004
Rate of granulation (%/week)	90.83 ±5.70	88.41 ±5.71	93.09 ±4.76	0.004
Wound size reduction	14.46±10.46	13.41 ±8.56	15.50 ±12.16	0.494
infection rate	0	0	0	

Patient satisfaction, encompassing aspects of convenience, device endurance, and safety, was evaluated in this study. Out of the 14 patients who were administered the CKANPD, 10 returned the completed questionnaire. The feedback received was predominantly positive, with responses ranging from good to excellent across all assessed parameters. However, due to the absence of a standardized questionnaire, a formal statistical analysis could not be performed.

Discussion

The results of this study suggest that the CBH-KMITL Ambulatory Negative Pressuring Device (CKANPD) is a non-inferior alternative to conventional Negative Pressure Wound Therapy (NPWT) devices for the treatment of open traumatic wounds. The CKA-

NPD group demonstrated a significantly higher rate of granulation tissue formation after one week of NPWT, indicating that the device may promote faster wound healing. However, the clinical significance of this finding should be considered carefully, as it may vary based on the physician's application and hospital setting.

The superior statistical significance of the CKANPD could be attributed to its automatic pressure regulation, digital gauge, and smaller pressure gap due to a smaller pump diaphragm. In contrast, conventional devices require manual pressure regulation by a nurse every 4-8 hours, use an analog gauge, and have a larger pressure gap.

Interestingly, there was no significant difference in wound size reduction between the CKANPD and conventional methods. This suggests that while the CKANPD may promote faster granulation tissue formation, it does not necessarily lead to a faster reduction in wound size. This could be due to various factors, such as the severity and location of the wound, the patient's overall health status, and the quality of wound care.

The infection rate was zero in both groups, indicating that the CKANPD instrument safety profile is as safe as conventional NPWT devices in terms of infection rate. This is an important finding, as infection is a major complication of open traumatic wounds and can significantly delay wound healing and increase healthcare costs.

While these results are promising, further research is needed to confirm the efficacy and safety of the CKANPD. Future studies should include a larger sample size and longer follow-up periods to assess the long-term outcomes of the CKANPD. The significant result of non-inferiority of CKANPD will lead to the next phase of study in outpatient settings, which is the primary goal of CKANPD development.

Conclusion

In conclusion, our study introduces the CKANPD as a promising, cost-effective, and safe alternative to traditional NPWT devices for the treatment of open traumatic wounds. Its potential for use in outpatient care could significantly impact the management of such injuries, offering benefits that extend beyond the clinical to include economic advantages. Further research is essential to fully ascertain the long-term benefits and potential wider application of this innovative device in wound care management.

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