Negative Pressure Wound Therapy Versus Conventional Wound Care In Cancer Surgical Wounds: A Meta-analysis of Observational Studies and Randomized Controlled Trials

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Abstract

The application of negative pressure wound therapy (NPWT) in cancer surgical wounds is still controversial, despite its promising usage, due to the risks of increased tumorigenesis and metastasis. This study aimed to review the risks and benefits of NPWT in surgical wounds with the underlying malignant disease compared to conventional wound care (CWC). The first outcome was wound complications, divided into surgical site infection (SSI), seroma, hematoma, and wound dehiscence. The secondary outcome was hospital readmission. We performed a separate meta-analysis of observational studies and randomized controlled trials (RCT) with CI 95%. Thirteen observational studies with 1923 patients and seven RCTs with 1091 patients were included. NPWT group showed significant decrease in the risk of SSI (RR = 0.48) and seroma (RR = 0.61) in observational studies with P value <0.05, as well as RCTs but were not significant (RR = 0.88 and RR = 0.68). Wound dehiscence (RR = 0.74 and RR = 1.15) and hospital readmission (RR = 0.90 and RR = 0.62) showed lower risks in NPWT group but were not significant. Hematoma (RR = 1.08 and RR = 0.87) showed no significant difference. NPWT is not contraindicated in cancer surgical wounds and can be considered a beneficial palliative treatment to promote wound healing.

Keywords

cancer wound, malignant wound, meta-analysis, negative pressure wound therapy, vacuum-assisted closure

Key Messages

- Negative pressure wound therapy (NPWT) reduces postoperative complications of various surgeries, but its application in cancer surgical wounds is still controversial.
- A meta-analysis of observational studies and RCTs was conducted to review postoperative wound complications and hospital readmission.
- NPWT is not contraindicated in cancer surgical wounds and can be considered a beneficial palliative treatment to promote wound healing.

1. INTRODUCTION

One of the leading causes of death globally is malignancy, which is a wound associated with cancer.[1] According to a 2019 research by the World Health Organization (WHO) cancer ranks first and second as the foremost cause of death in 112 of 183 countries and fourth in 23 others.[2] Most patients with cancer have a combination of treatment, such as surgery with chemotherapy and/or radiation therapy.[3] However, despite the disease itself, chemotherapy and radiation therapy can delay postoperative wound healing.[4] Wounds that are slow to heal can turn into chronic wounds, which can easily increase complications including seroma, wound dehiscence, infection, hematoma, or other problems that can reduce the quality of life.[5]

Negative Pressure Wound Therapy (NPWT), also recognized as Vacuum-Assisted Closure (VAC), is a system used to close large and complicated wounds by applying sub-atmospheric pressure.[6] The mechanism of NPWT involves wound contraction, extracellular fluid removal, and wound environment stabilization which results in a decrease of tissue edema and bacterial colonization, increase in blood flow, angiogenesis, granulation formation, and faster wound healing.[7] NPWT decreases the biological destruction caused by local harmful substances to the body. Meanwhile, the continuous negative pressure significantly increases the flow rate of local microcirculation and the diameter of microvessels.[8] This technique is applied to promote the formation of granulation tissue in open wounds, clean surgical incisions and cover skin grafts.[9] NPWT gave advantages by reducing the wound healing time and the risk of surgical complications, including surgical site infection (SSI)[10], seroma, hematoma, and wound dehiscence[11].

Despite its promising clinical usage, previously, NPWT was an absolute contraindication for wounds with underlying malignant diseases due to risks of increased tumorigenesis and metastasis.[12] This belief is derived from the study of normal tissues, and to the authors' knowledge, there has been no literature that directly supports the hypothesis that NPWT regulates tumor progression. However, with the development of new research, regarding its benefits for the palliative treatment of malignant wounds, the NPWT use in cancer wounds has changed from absolute contraindications to relative contraindications.[13] In patients with malignancy, the normal wound healing process is often interrupted, influenced by both the malignancy itself and the treatment's course[14], which resulted in consideration of NPWT use.

Presently, there is no substantial evidence that prevents the use of NPWT on wounds with underlying malignant diseases. Therefore, we aim to conduct a meta-analysis assessing the risks and benefits of NPWT in surgical wounds with the underlying malignant disease compared to conventional wound care (CWC), thus NPWT can be considered as a beneficial palliative treatment to promote wound healing.

2. MATERIALS AND METHODS

2.1 Study selection

Three reviewers (LB. Adzalika, R. Pramanasari, IL. Putri) searched for observational studies and randomized controlled trials (RCT) that compared NPWT with CWC for wounds with the underlying malignant diseases and compared postoperative wound complications after interventions between the two groups. Only human studies reported in English with full-text availability were included. Any disagreement was solved by negotiation or a consensus meeting with the fourth investigator (CDK. Wungu).

The main outcome was wound complications divided into SSI, seroma, hematoma, and wound dehiscence. The secondary outcome was hospital readmission. We eliminated studies with unspecific wound complications and studies without comparators.

2.2 Literature search

This systematic study was carried out with the meta-analysis appropriate with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA), as shown in Figure 1.

Some of the keywords used to carry out this study are negative pressure wound therapy (NPWT), NPWT, VAC, vacuum-assisted closure, cancer, malignant/malignancy, wound, included their synonyms and controlled vocabulary (MeSH or Emtree terms) when ready. The search term was such as ("negative pressure wound therapy" OR "vacuum-assisted closure" OR "NPWT" OR "VAC") AND (malignan* OR cancer) wound.

Figure 1 illustrates the search strategy in detail. Three researchers identified relevant studies from PubMed, ScienceDirect, Web of Science, ProQuest, and the registry trial (www.clinicaltrials.gov) from July 15, 2021, to July 28, 2021. All studies were then exported to Mendeley to be sorted out.

2.3 Data extraction

We independently selected data on authors, publication year, country, study design, population, mean age, follow-up periods, type of cancer, type of surgery, NPWT pressure, mode, length of use, the occurrence of SSI, seroma, hematoma, dehiscence, and readmission (Table 1, 2). Data were extracted from preliminary studies and cross-checked to eliminate discrepancies.

2.4 Risk of bias and quality assessment

The observational studies' quality, such as case-control and cohort studies, was evaluated applying the Newcastle-Ottawa Scale (NOS) (Table 3, 4) and the Jadad scale for RCT studies (Table 5). The score is considered high quality if the score is 7 or higher for the NOS score[15] and 3 or higher for the Jadad scale[16].

2.5 Statistical analysis

RevMan 5.4 statistical software (Cochrane Collaboration) was used to determine Statistical analysis with a relative risk ratio (RR) of 95% confidence intervals (CIs) applied to analyze the random or fixed-effect models. Furthermore, the significant outcome of the two-sided statistical tests was determined with a P-value <0.05. This study uses the inconsistency index statistic (I^2) to assess heterogeneity, and the value of the I^2 statistic also reflects the level of heterogeneity. If I^2 was >50% and P-value <0.05, the trials were used to determine the heterogeneous, and random-effects models. Otherwise, the fixed-effects model was chosen. A funnel plot was performed to estimate publication bias.

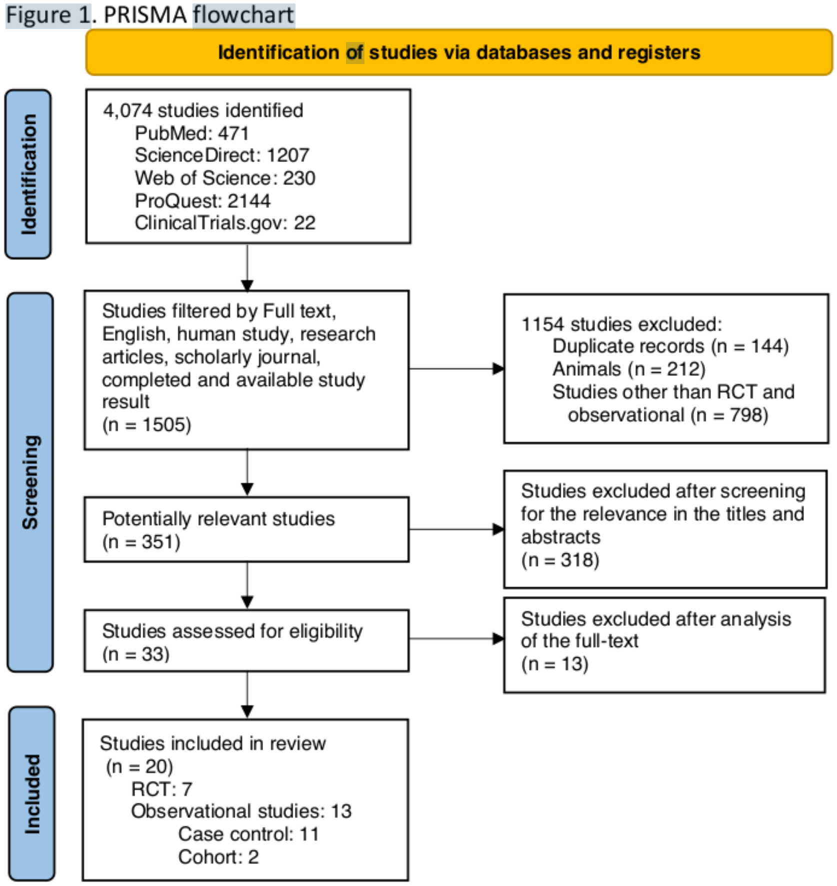
3. RESULTS

3.1 Study selection and characteristics

A total of 4,074 studies were retrieved from various databases: 471 studies from PubMed; 1207 studies from ScienceDirect; 230 studies from Web of Science; 2144 studies from ProQuest; 22 studies from ClinicalTrials.gov, of which 1,505 were included after filtering by full-text availability, English language, human study, research articles, scholarly journal, completed and available study results. These studies were then exported to Mendeley. A total of 1154 studies were excluded for not being relevant: duplication (n = 144); animal studies (n = 212); studies other than observational studies or RCT (n = 798).

Based on the screening criteria for the relevance in titles and abstracts, 318 studies were removed. After full-text reviews, we eliminated 13 studies. Finally, 20 eligible studies were selected for a qualitative review, including 13 observational studies and 7 RCTs. The flowchart of the study selection process can be seen in figure 1.

Figure 1. PRISMA flowchart



Observational Studies. The thirteen observational studies, including eleven case-control studies and two cohort studies, encompassed 1,923 patients between the years 2013 to 2021, 662 patients were using NPWT and 1261 patients were in the CWC group. All of the included studies were from developed countries according to International Statistical Institute[17] in 2020. The mean age ranged from 53.2 to 72.1 years, and the follow-up ranged from 30 to 90 days. The malignancy type varies from skin cancer, breast cancer, pancreatic cancer, colorectal cancer, peritoneal cancer, gynecological cancer, urothelial carcinoma to spinal cancer, as well as the surgery types. More details can be seen in table 1. The most widely used amount of pressure for NPWT use was -125 mmHg, all used continuously, ranging from 2 to 9 days, with the most number of days used was 4 days.

RCTs. The seven RCTs included 1,091 patients between the years 2017 to 2021, with 543 patients underwent surgery with NPWT and 548 patients underwent surgery without NPWT. Only one study was from a developing country, China, a study by Yang et al in 2020.

The mean age ranged from 56.25 to 73.18 years, and the follow-ups were all in 30 days. The malignancy type also varies from gastrointestinal cancer, pancreatic cancer, colorectal cancer, peritoneal cancer, to gynecological cancer, as well as the surgery types. The most widely used amount of pressure for NPWT use was -125 mmHg, most of them were used continuously, ranging from 3 to 7 days, with the most number of days used was 7 days. More details can be seen in table 2.

Table 1. Included observational studies' characteristics

Author, y, country, design	Population	Mean Age (y)	Follow Up (d)	Malignancy	Surgery	NPWT pressure (mmHg), mode, duration (d)
Blackham[35], 2013, USA, CC	N: 104 C: 87	N: 57.1 C: 57.1	30	Colorectal cancer Peritoneal cancer Pancreatic cancer	Right colectomy Left colectomy Subtotal colectomy Low anterior resection Abdominoperitoneal resection Cytoreduction/HIPEC with colon resection Cytoreduction/HIPEC without colon resection Pancreaticoduodenectomy Distal pancreatectomy	-125, continuous, 4
Burkhart[36], 2017, USA, CC	N: 120 C: 274	n/a	30	Pancreatic cancer	Pancreaticoduodenectomy	-125, continuous, 4
Chadi[37], 2014, Canada, CC	N: 27 C: 32	N: 62 C: 61	30	Rectal cancer SCC of anus	Abdominoperineal resection Abdominoperineal resection + proctocolectomy Pelvic exenteration	-125, continuous, 5
Chambers[38], 2020, USA, CC	N: 64 C: 192	N: 59 C: 60.9	n/a	Cervical cancer Ovarian cancer Fallopian tube cancer Peritoneal cancer Uterine cancer	Hysterectomy Radical hysterectomy &/ en-bloc resection Small bowel surgery Large bowel surgery Ileostomy Colostomy Splenectomy Pelvic lymphadenectomy Paraaortic lymphadenectomy	-125, continuous, 7
De Rooij[39], 2021, Netherland, CC	N: 50 C: 111	N: 65.4 C: 65.1	90	Breast cancer	Mastectomy + sentinel node Mastectomy + axillary lymph node dissection	-80, continuous, 4
Gupta[40], 2017, USA, CC	N: 25 C: 36	N: 61.1 C: 64.1	n/a	Pancreatic cancer	Pancreaticoduodenectomy	-80, continuous, 7-10
Joice[41], 2020, Italy, CC	N: 104 C: 54	N: 69.7 C: 70.5	90	Urothelial carcinoma	Radical cystectomy	-125, continuous, 3
Jorgensen[42], 2019, Denmark, CC	N: 14 C: 41	N: 59.93 C: 57.88	90	Melanoma	Inguinal lymph node dissection Abdominoperineal resection	-125, continuous, 5-7
Kaneko[43], 2021, Japan, CC	N: 51 C: 95	N: 67 C: 64.25	n/a	Rectal cancer Anal cancer Melanoma Gynecological cancer	Pancreaticoduodenectomy Subtotal pancreatectomy Distal pancreatectomy Total pancreatectomy	-125, continuous, 5

				Peritoneal cancer Paget's disease		
Lynam[44], 2016, USA, CC	N: 22 C: 208	N: 54.9 C: 53.2	90	Cervical cancer Uterine cancer Ovarian cancer	Laparotomy	-125, continuous, 2-5
Marti[45], 2021, Spain, CC	N: 58 C: 85	N: 63.28 C: 61.51	30	Ovarian cancer Cervical cancer Endometrial cancer Vulvar cancer	Cytoreductive surgery Laparotomy	-125, continuous, 2-9
Mueller[46], 2021, USA, Cohort	N: 16 C: 35	N: 61.5 C: 63.6	60	Spinal cancer	Spinal surgery	-125, continuous, 7
Quercia[47], 2020, Italy, Cohort	N: 7 C: 11	N: 71.3 C: 72.1	n/a	Vulvar cancer	Radical vulvectomy	-100-(-125), continuous, 4-5

Abbreviations: C, conventional wound care; CC, case-control; HIPEC, hyperthermic intraperitoneal chemotherapy; N, negative pressure wound therapy.

Table 2. Included RCT studies' characteristics

Author, y, country, design	Population	Mean Age (y)	Follow Up (d)	Malignancy	Surgery	NPWT pressure (mmHg), mode, duration (d)
Andrianello[48], 2021, Italy, RCT	N: 32 C: 40	N: 69 C: 64	30	Ampullary cancer Cystic Distal bile duct cancer Duodenal cancer Neuroendocrine tumor Pancreatic ductal adenocarcinoma	Pancreaticoduodenectomy Total pancreatectomy	n/a, intermittent, 3-7
Kuncewitch[49], 2019, USA, RCT	N: 36 C: 37	N: 64.75 C: 61.5	30	Pancreatic cancer	Laparotomy	-125, continuous, 4
Leitao[50], 2021, USA, RCT	N: 254 C: 251	N: 56.25 C: 58	30	Ovarian cancer Fallopian tube cancer Peritoneal cancer Uterine cancer Cervical cancer	Laparotomy	-125, continuous, 7
Shen[51], 2017, USA, RCT	N: 132 C: 133	N: 57.25 C: 58.75	30	Gastrointestinal cancer Pancreatic cancer Peritoneal cancer	Bowel resection Colorectal resection Pancreaticoduodenectomy Distal pancreatectomy Total pancreatectomy Cytoreduction/HIPEC	-125, continuous, 4
Teoh[52], 2020, USA, RCT	N: 43 C: 38	N: 59.6 C: 58.4	30	Gynecologic cancer	Laparotomy	n/a
Wierdak[53], 2021, Poland, RCT	N: 35 C: 36	N: 61.6 C: 62.4	30	Colorectal cancer	Ileostomy reversal Hemicolectomy Colectomy Anterior resection of rectum Intersphincter resection Transanal total mesorectum excision	n/a
Yang[54], 2020, China,	N: 11 C: 13	N: 73.18 C: 69.85	30	Rectal carcinoma	Abdominoperineal resection	n/a

RCT							

Abbreviations: C, conventional wound care; HIPEC, hyperthermic intraperitoneal chemotherapy; N, negative pressure wound therapy; RCT, randomized controlled trial.

3.2 Studies' quality assessment and bias risk

The mean NOS score was 7.3/9, indicating high quality of the included observational studies and the mean Jadad scale was 2.3/5 for RCT studies, indicating low quality. Table 3 and 4 presents the quality of eleven included case-control and two cohort studies evaluated by NOS. Meanwhile, table 5 presents the quality of RCT studies evaluated by the Jadad scale.

Funnel plot analysis of included observational studies showed no significant publication bias (Figure 2). We identified an outlier by De Rooij 2021. After temporarily excluding the study, there was no significant effect. Funnel plot analysis of included RCT studies was not performed because of the limited studies.

Most of the studies were considered representative and were in line with the studies we included, as most malignant tumors are treated in medical centers. All included studies reported surgical site infection, and some studies reported other complications, i.e. seroma, hematoma, dehiscence. Most of the studies reported hospital readmission, therefore we added it as the secondary outcome.

Table 5. Quality of included RCT studies evaluated using Jadad scale

Study	Randomization	Double-blinding	Follow Up	Total Score
Andrianello 2021	2	1	0	3
Kuncewitch 2019	1	0	1	2
Leitao 2021	2	1	0	3
Shen 2017	2	0	0	2
Teoh 2020	1	0	0	1
Wierdak 2021	2	1	0	3
Yang 2020	1	0	1	2

Figure 2. Funnel plot of included observational studies

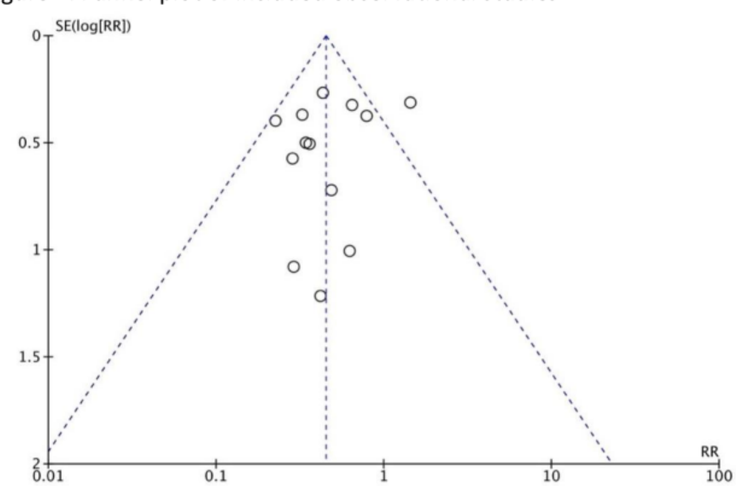


Table 3. Quality of included observational studies (case-control) evaluated using Newcastle-Ottawa Scale (NOS)

Study	Selection				Comparability	Exposure			Total Score
	Case definition adequate (1)	Representativeness of the cases (1)	Selection of controls (1)	Definition of controls (1)	Comparability based on design or analysis (2)	Ascertainment of exposure (1)	Same method of ascertainment for cases and controls (1)	Non-response rate (1)	
Blackham 2013	1	1	1	0	2	1	1	1	8
Burkhart 2017	1	1	1	0	2	1	1	1	8
Chadi 2014	1	1	1	1	2	0	1	1	8
Chambers 2020	1	1	1	0	2	0	1	1	7
De Rooij 2021	1	1	1	1	2	0	1	0	7
Gupta 2017	1	1	1	0	2	0	1	1	7
Joice 2020	1	1	1	0	2	0	1	1	7
Jorgensen 2019	1	1	1	0	2	0	1	1	7
Kaneko 2021	1	1	1	0	2	0	1	1	7
Lynam 2016	1	1	1	0	2	1	1	1	8
Marti 2021	1	1	1	0	2	1	1	1	8

Table 4. Quality of included observational studies (cohort) evaluated using Newcastle-Ottawa Scale (NOS)

Study	Selection				Comparability	Outcome			Total Score
	Representativeness (1)	Selection of the non-exposed cohort (1)	Ascertainment of exposure (1)	Demonstration outcome of interest (1)	Comparability based on design or analysis (2)	Assessment of outcome (1)	Followed up long enough (1)	Adequacy of follow up (1)	
Mueller 2021	1	1	1	0	2	0	1	1	7
Quercia 2020	1	1	1	0	2	0	0	1	7

3.3 The primary outcomes

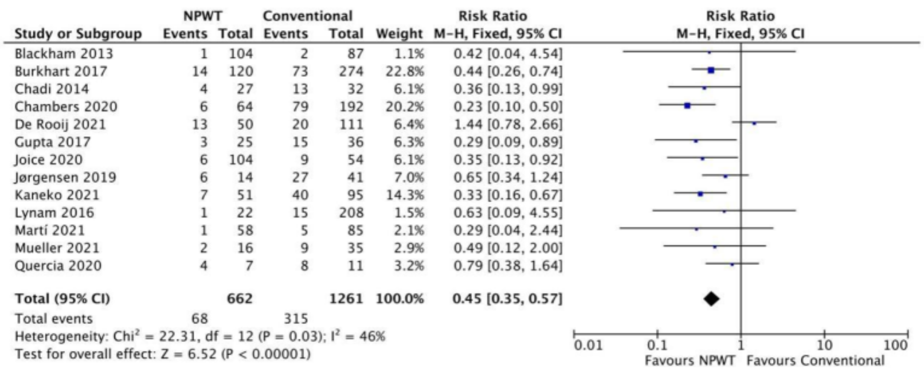
Surgical Site Infection

Observational Studies. Thirteen observational studies reported the data on the SSI risk after NPWT use or CWC. The SSI rate in the NPWT group was 10.27% and in the CWC was 25%. The use of NPWT was associated with a significant decrease in the risk of SSI in patients with cancer compared with CWC (RR = 0.45; 95% CI 0.35-0.57; P<0.00001). There was no statistical heterogeneity among the evaluated studies (I^2=46%; P=0.03) (Figure 3A).

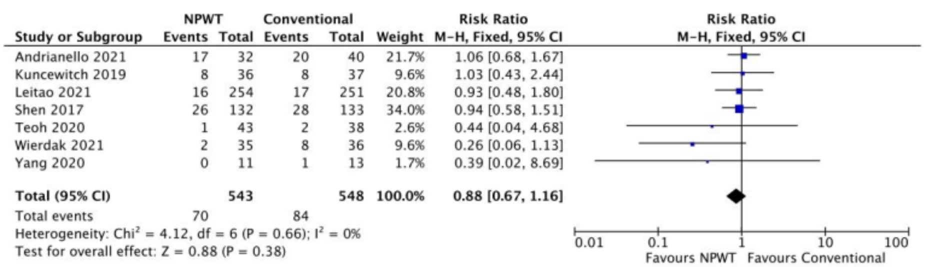
RCTs. Seven RCTs reported the data on the risk of SSI after NPWT use or CWC. The SSI rate in the NPWT group was 12.89% and in the CWC was 15.32%. The NPWT occurred due to the decrease in risk of SSI in cancer patients, which is insignificant (RR = 0.88; 95% CI 0.67-1.16; P=0.38). There was no statistical heterogeneity among the evaluated studies (I^2=0%; P=0.66) (Figure 3B).

Figure 3. Surgical site infection

A. Observational studies



B. RCT



Seroma

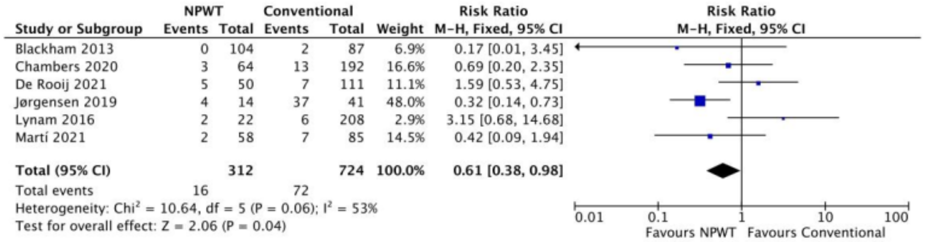
Observational Studies. Six observational studies reported the data on the seroma risk after NPWT use or CWC. The seroma rate in the NPWT group was 5.12% and in the CWC group was 10%. The significant decrease in the occurrence of seroma in patients suffering from cancer was associated with CWC (RR = 0.61; 95% CI 0.38-0.98; P=0.04). Furthermore, the evaluated studies have no statistical heterogeneity (I^2=53%; P=0.06) (Figure 4A).

RCTs. Five RCTs reported the data on the risk of seroma after NPWT use or CWC. The seroma rate in the NPWT group was 4.7% and in the CWC group was 7.04%. The use of NPWT was correlated with a decrease in the SSI risk in patients with cancer compared with

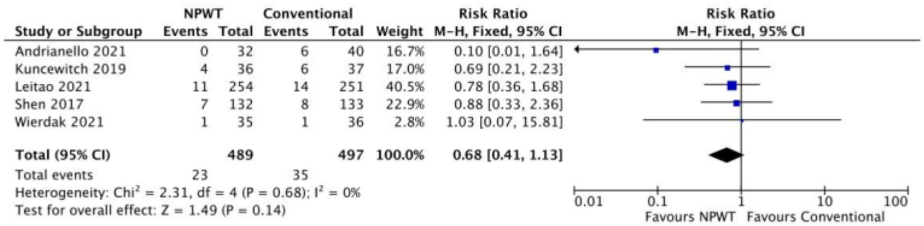
CWC, but was not significant (RR = 0.68; 95% CI 0.41-1.13; P=0.14). There was no statistical heterogeneity among the evaluated studies (I^2=0%; P=0.68) (Figure 4B).

Figure 4. Seroma

A. Observational studies



B. RCT



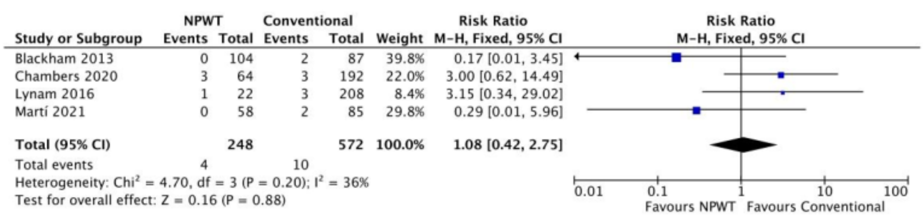
Hematoma

Observational Studies. Approximately 4 observational studies were used to analyze the data associated with the hematoma risk after NPWT or CWC. The hematoma rate in the NPWT group was 1.6% and in the CWC was 1.74%. The use of NPWT showed no significant difference in decreasing the hematoma risk (RR = 1.08; 95% CI 0.42-2.75; P=0.88). There was no statistical heterogeneity among the evaluated studies (I^2=36%; P=0.20) (Figure 5A).

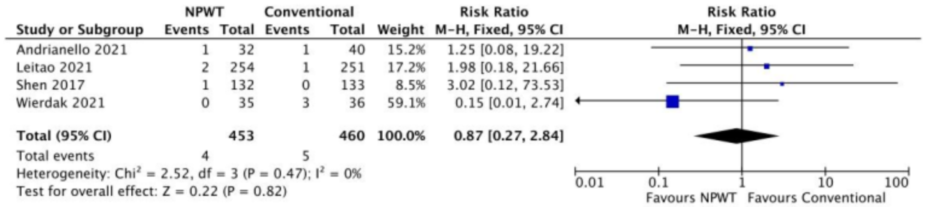
RCTs. Four RCTs reported the data on the risk of hematoma after NPWT use or CWC. The NPWT and CWC groups hematoma rates of 0.88% and 1.08%. The use of NPWT also showed no significant difference in decreasing the risk of hematoma (RR = 0.87; 95% CI 0.27-2.84; P<0.82). Furthermore, there was no statistical heterogeneity associated the evaluated studies (I^2=0%; P=0.47) (Figure 5B).

Figure 5. Hematoma

A. Observational studies



B. RCT



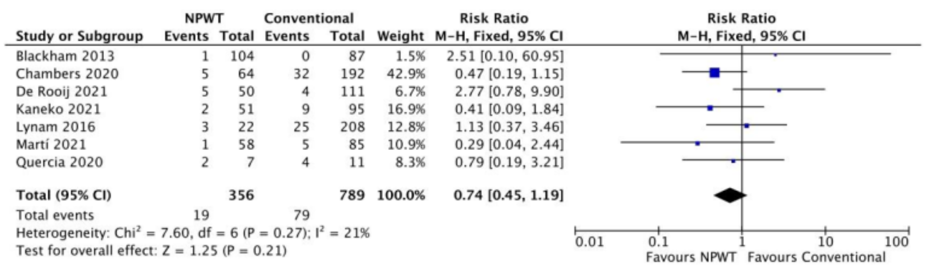
Wound Dehiscence

Observational Studies. A total of 7 observational studies were used to determine the data associated with the risk of wound dehiscence after the occurrence of NPWT and CWC. The dehiscence rate in the NPWT group was 5.33% and in the CWC was 10%. The use of NPWT was correlated with a decrease in the wound dehiscence risk in patients with cancer compared with CWC, but was not significant (RR = 0.74; 95% CI 0.45-1.19; P=0.21). There was no statistical heterogeneity among the evaluated studies (I^2=21%; P=0.27) (Figure 6A).

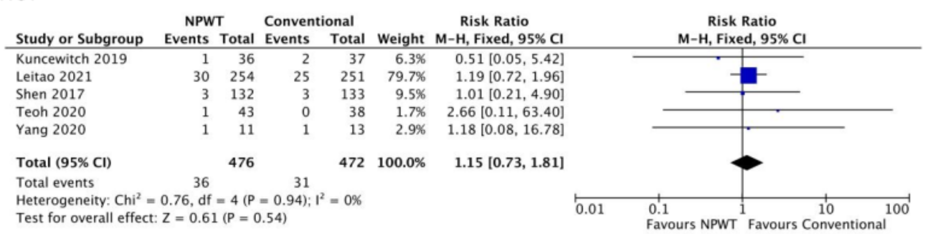
RCTs. Five RCTs reported the data on the risk of wound dehiscence after NPWT use or CWC. The wound dehiscence rate in the NPWT group was 7.56% and in the CWC was 6.56%. CWC is correlated with a reduction in the risk of wound dehiscence in patients suffering from cancer compared with NPWT, but was not significant (RR = 1.15; 95% CI 0.73-1.81; P=0.54). Furthermore, there was no statistical heterogeneity inherent the evaluated studies, as shown in Figure B (I^2=0%; P=0.94).

Figure 6. Wound dehiscence

A. Observational studies



B. RCT



3.4 Secondary outcome

Hospital Readmission

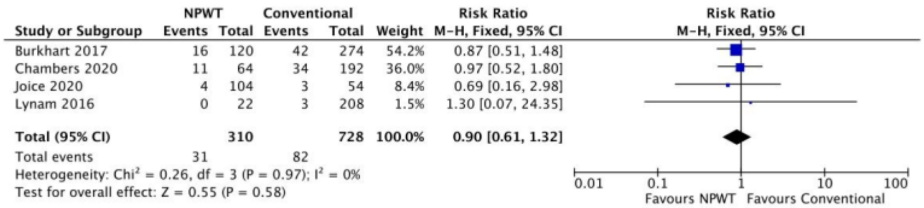
Observational Studies. Four observational studies reported the data on the hospital readmission risk after NPWT use or CWC. The hospital readmission rate in the NPWT group was 10% and in the CWC group was 11.2%. The possibility of readmitting patients with cancer decreases with NPWT use compared with CWC (RR = 0.90; 95% CI 0.61-1.32; P=0.58).

Figure 7A shows there was no statistical heterogeneity associated with the evaluated studies (I^2=0%; P=0.97) (Figure 7A).

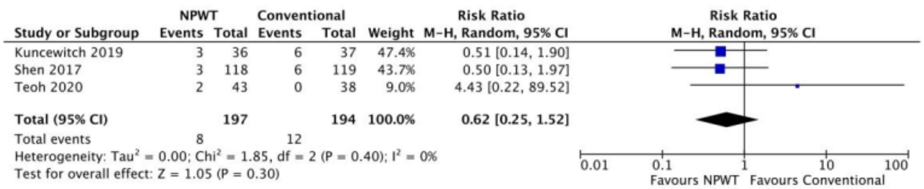
RCTs. Three RCTs reported the data on the risk of hospital readmission after NPWT use or CWC. The hospital readmission rate in the NPWT group was 4.06% and in the CWC group was 6.18%. NPWT is associated with a decrease in the rate at which patients with cancer are readmitted into the hospital (RR = 0.62; 95% CI 0.25-1.52; P=0.30). There was no statistical heterogeneity among the evaluated studies (I^2=0%; P=0.40) (Figure 7B).

Figure 7. Hospital readmission

A. Observational studies



B. RCT



4. DISCUSSION

According to Mendez-Eastman[18] the use of NPWT is inappropriate with malignancy because when the mechanical stretch is performed to normal cells, it leads to increased proliferation. Furthermore, in malignancy, cancerous cells often are not anchored due to their inability to respond to the stimuli, thereby making NPWT ineffective. However, several studies have been done using NPWT in cancer surgical wounds and gave interesting results.

This research summarized the available evidence associated with the effects of NPWT for cancer surgical wounds. Almost all of the studies included were from developed countries[19]. Only one study, an RCT, was from a developing country, China. Nevertheless, that did not correlate with the completeness of the data. The ratio of subjects treated with NPWT and CWC in observational studies was 1:2, demonstrating that the use of NPWT in malignancies was lower may be due to its high cost, less availability, fear of harming patients, and risk of accelerated metastasis, although none have provided solid evidence to support this hypothesis. A recent meta-analysis[20] consisted of three case series and three observational studies that evaluated local oncological recurrence of NPWT use in cancer surgical wounds without residual malignancy and its complications revealed that there was no significant difference between NPWT and CWC. The differences with our study were that we performed a meta-analysis of observational studies consisted of thirteen studies and RCTs consisted of seven studies, and evaluated more detailed postoperative wound complications divided into SSI, seroma, hematoma, wound dehiscence, and hospital readmission. Overall, our analysis revealed a better result in SSI and seroma rates in observational studies and no significant difference in other parameters.

As a risk factor for cancer in 2021, the National Cancer Institute stated that the median age of patients diagnosed with cancer was 66 years, which means half of all cancers occur in people older than this age and half in people younger than this age for several common cancers, such as breast cancer, colorectal cancer, prostate cancer, and lung cancer.[21] Meanwhile, a study that analyzed the incidence and mean age at diagnosis for global cancer stated that the average age of cancer incidence in the world was 65.73 years.[22] In this study, the patients' mean age was 60.96 years ranged from 53.2 to 73.18 years.

The follow-up period of all included studies lasted for a minimum of 30 days, as the postoperative wound complication can take place up to 30 days after the surgery, particularly for SSI, and influencing the incision or deep tissue at the operation site.[23] Another study[24] showed a similar postoperative follow-up ranged from 28 to 42 days but was most commonly limited to a 30-day-follow-up as advised by the CDC guidelines[25].

Most of the included studies were using NPWT with the pressure of -125 mmHg with a continuous mode that lasted for 2 to 10 days. Two observational studies were using -80 mmHg and one study was using -100 mmHg pressure. This corresponds to the meta-analysis done by Borgquist in 2010, which stated the clinical standard pressure for treating wounds with NPWT is -125 mmHg[26]. Kairinos (2008) carried out a research to determine the standard pressure on wounds and the clinical inconsistencies associated with the use of NPWT[27]. According to Kairinos, higher magnitudes inflict pain on the patient as opposed to negative pressure, which lowers it from -125 to -50 mmHg. Secondly, care need to be taken when determining the vascularity of compromised tissue because the high levels of negative pressure causes ischemia. According to preliminary studies, negative-pressure wound therapy contradicts due to inconsistency in vascularity. Miller and Lowery stated that the specific suction pressures universally accepted is -125 mmHg[8]. Contrary to complete data of NPWT in observational studies, four out of seven RCTs did not state the pressure, mode, and duration of NPWT. This could lead to immeasurable results of the study.

Observational studies indicated a significant SSI risk reduction in the NPWT group, which is consistent with the results of several previous reviews in other surgical wounds[29,30]. NPWT is suggested to reduce the infection rate for the following reasons: For wound care, NPWT systems reduce the frequency of dressings, the wound site would be less exposed[29]. NPWT tends to create a positive wound healing environment by removing inhibitors such as metalloproteinases, microorganisms[31], promoting better microvascular circulation to reduce bacterial colonization[32].

The seroma rate was also significantly lower in the NPWT group in observational studies, which is in accordance with several past study[33,34]. It is not fully understood how NPWT leads to a reduced seroma formation in the wound. Horch et al.[35] suggested that NPWT leads to a significant increase in tissue perfusion and oxygenation.

Both hematoma rates in observational studies and RCTs did not show significant differences, while a study done by Ge in 2018[36] showed a significant result in reducing hematoma risk on various surgical wounds. Nevertheless, the incidence rate was low in both analyses (1.6% and 0.88%) because NPWT application was done in the operating room so that excellent wound hemostasis could be ensured.

We found that the wound dehiscence rate in observational studies favored the NPWT group. Contrary to that, RCTs showed a trend toward a lower wound dehiscence rate in patients treated with CWC. Nonetheless, there was not much difference in the incidence of wound dehiscence in the two groups (7.56% and 6.56%). This could be due to the low quality of the included RCT studies, which also did not show significant results in all analyses. Some of the studies did not include the pressure, mode, and duration of the installed NPWT, so a thorough look could not be done.

The hospital readmission rate in both analyses favored towards NPWT group, which indicated fewer complications in the NPWT group compared to conventional wound care only, therefore no need for re-hospitalization. A study[37] also stated that patients who smoked or patients with alcohol/drug abuse had a higher hospital readmission rate.

Overall, the NPWT groups showed a better improvement in decreasing the complications rate in both observational studies and RCTs. However, all of these RCT analysis results may require more exploration with a higher number and better quality of RCTs.

5. LIMITATION

Our study has some limitations. Because the number of RCTs performed was limited compared to observational studies, and the included RCT studies were low in quality due to the nature of inability to double-blind the intervention, coupled with the large number of patients who dropped out, led to the ratio of poor quality to good quality RCTs into 4:3. Another limitation was this study did not analyse the tumor recurrence, but only the postoperative wound complications and hospital readmission.

6. CONCLUSION

Our meta-analysis revealed the best results in the risk of SSI and Seroma between NPWT and conventional wound care in cancer surgical wounds. The NPWT use was correlated with fewer complications such as SSI, seroma, hematoma, wound dehiscence, and hospital readmission. Therefore, NPWT is not contraindicated in cancer surgical wounds and can be considered a beneficial palliative treatment to promote wound healing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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