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Negative Pressure Wound Therapy vs Conventional Wound Treatment in Subcutaneous Abdominal Wound Healing Impairment
The SAWHI Randomized Clinical Trial

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IMPORTANCE Negative pressure wound therapy (NPWT) is an established treatment option, but there is no evidence of benefit for subcutaneous abdominal wound healing impairment (SAWHI).

OBJECTIVE To evaluate the effectiveness and safety of NPWT for SAWHI after surgery in clinical practice.

DESIGN, SETTING, AND PARTICIPANTS The multicenter, multinational, observer-blinded, randomized clinical SAWHI study enrolled patients between August 2, 2011, and January 31, 2018. The last follow-up date was June 11, 2018. The trial included 34 abdominal surgical departments of hospitals in Germany, Belgium, and the Netherlands, and 539 consecutive, compliant adult patients with SAWHI after surgery without fascia dehiscence were randomly assigned to the treatment arms in a 1:1 ratio stratified by study site and wound size using a centralized web-based tool. A total of 507 study participants (NPWT, 256; CWT, 251) were assessed for the primary end point in the modified intention-to-treat (ITT) population.

INTERVENTIONS Negative pressure wound therapy and conventional wound treatment (CWT).

MAIN OUTCOMES AND MEASURES The primary outcome was time until wound closure (delayed primary closure or by secondary intention) within 42 days. Safety analysis comprised the adverse events (AEs). Secondary outcomes included wound closure rate, quality of life (SF-36), pain, and patient satisfaction.

RESULTS Of the 507 study participants included in the modified ITT population, 287 were men (56.6%) (NPWT, 155 [60.5%] and CWT, 132 [52.6%]) and 220 were women (43.4%) (NPWT, 101 [39.5%] and CWT 119 [47.4%]). The median (IQR) age of the participants was 66 (18) years in the NPWT arm and 66 (20) years in the CWT arm. Mean time to wound closure was significantly shorter in the NPWT arm (36.1 days) than in the CWT arm (39.1 days) (difference, 3.0 days; 95% CI 1.6-4.4; $P < .001$). Wound closure rate within 42 days was significantly higher with NPWT (35.9%) than with CWT (21.5%) (difference, 14.4%; 95% CI, 6.6%-22.2%; $P < .001$). In the therapy-compliant population, excluding study participants with unauthorized treatment changes (NPWT, 22; CWT, 50), the risk for wound-related AEs was higher in the NPWT arm (risk ratio, 1.51; 95% CI, 0.99-2.35).

CONCLUSIONS AND RELEVANCE Negative pressure wound therapy is an effective treatment option for SAWHI after surgery; however, it causes more wound-related AEs.

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Invited Commentary

Supplemental content

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Complication rates after major surgery are a substantial global public health concern.[1] Subcutaneous abdominal wound healing impairment (SAWHI) manifests itself either in spontaneous dehiscence, the need for reopening of the suture, or in wounds left open after surgery owing to high risk of infection or significant tissue loss while the abdominal fascia is still closed. Subcutaneous abdominal wound healing impairment is often triggered by surgical site infection.[2] Other reasons include hematoma and seroma formation, mechanical obstacles to wound closure, and various technical reasons (eg, sutures breaking). The most serious complication with a high mortality rate is fascia dehiscence, where the wound separates completely, exposing the underlying organs.[3] Several patient-related factors, such as morbid obesity or malnutrition, smoking and alcohol abuse, advanced age, or concomitant diseases, promote the development of SAWHI.[4,5] Subcutaneous abdominal wound healing impairment is commonly treated with conventional wound dressings, applied based on scientific evidence, patient's preference, physician's experience, and the wound situation.[6] Treatment options for open surgical wounds include the use of negative pressure wound therapy (NPWT). Negative pressure wound therapy generally entails putting a dressing into the wound cavity and sealing the area with an adhesive film.[7] A tube is connected to a vacuum device that delivers a controlled negative pressure within the range of −50 mm Hg to −125 mm Hg. Negative pressure of 125 mm Hg was shown to reach a maximum increase in blood flow.[8] Positive effects of NPWT on wound healing were demonstrated in various basic studies.[8,9] In practical use, NPWT shows its advantages in promoting granulation tissue formation, reducing the frequency of dressing changes by keeping anatomically challenging wounds clean, removing high volumes of wound exudate, and reducing odor.[7] Nevertheless, NPWT can also lead to adverse events (AEs), which are usually avoidable by correct application and adequate precautions.[10] The clinical evidence before this study largely consisted of clinician perception, case reports and series, small cohort studies, and weakly powered or low-quality randomized clinical trials (RCTs) in various clinical settings.[11-14] To our knowledge, only 1 retrospective single-arm study of DeFranzo et al[15,16] reviewed the medical records of 63 patients with partial-thickness postsurgical abdominal wound healing impairment treated with NPWT.[15,16] Between 2013 and 2019, NPWT was increasingly being used on surgical wounds healing by secondary intention,[2] in the open abdomen,[17] and prophylactically on closed incisional wounds to prevent surgical site complications,[18] but many RCTs have methodologic weaknesses and a high risk of bias.[2,18-20] Comparative studies assessing effectiveness and safety of NPWT in SAWHI are still missing. The aim of the SAWHI study was to compare effectiveness and safety of NPWT and conventional wound treatment (CWT) in SAWHI after surgery in clinical practice to provide sound evidence as a basis for clinical therapy decisions.

Key Points

Question Is negative pressure wound therapy (NPWT) an effective and safe treatment option for subcutaneous abdominal wound healing impairment (SAWHI) after surgery?

Findings In the randomized clinical SAWHI study that included 507 adults, wounds were closed significantly faster and more often in the NPWT arm (36.1 days for 92 of 256 study participants) than with conventional wound treatment (39.1 days for 54 of 251 participants). The number of participants with wound-related adverse events was higher in the NPWT arm (48 of 234) than in the conventional wound treatment arm (27 of 201).

Meaning For SAWHI after surgery, NPWT is an effective treatment alternative to conventional wound treatment but causes more wound-related adverse events.

Methods

Study Design

This multinational, multicenter, randomized clinical superiority trial with blinded assessment of wound photographs was conducted in 34 abdominal surgical departments in Germany, Belgium, and the Netherlands. Study sites were selected by means of a qualification checklist, which included criteria such as treatment standards, experiences with NPWT, and wound treatment strategies. The study protocol (Supplement 1) and the informed consent documents were approved by the lead ethical committee of the University of Witten/Herdecke. The study protocol was published open access.[21]

Participants

Adult patients (age ≥18 years) with spontaneous wound dehiscence after abdominal surgery or active reopening of the suture and patients with open postsurgical abdominal wounds that could not be closed by primary intention were screened for study participation by the local clinical investigators. Correct application of the NPWT device requires a minimal wound opening area to insert the sponge into the wound cavity and ensure optimal drainage of wound exudate; thus, owing to the random treatment allocation, a minimum wound size was required. The initially defined wound size limitation was deleted because this was not in line with clinical practice and led to difficulties with patient inclusion. Inclusion, randomization, adequate wound pretreatment (debridement or thorough wound cleansing), and start of therapy was to be performed within 48 hours after diagnosis of the SAWHI. This included the closure of a possible defect of the abdominal fascia, which was an exclusion criterion. The initially planned period of 24 hours was extended to provide a sufficient timeframe for completing the inclusion procedure, which included wound pretreatment, possibly surgical revision, baseline documentation, and obtaining written informed consent. Patients unable or unwilling to comply with the protocol and study-related requirements, or participating in another trial, which was thought to interfere with the study procedures, patient's compliance, wound healing, or targeted end points, were excluded from study participation. Patients were also excluded when receiving concomitant therapies or procedures deviating from the clinical standard wound treatment or with investigational character within 30 days prior to screening or with the need for concomitant therapies or procedures directly affecting wound healing.

Randomization and Masking

After providing written informed consent, patients were randomly allocated to NPWT or CWT in a 1:1 ratio using a computer-generated list created by the trial statistician located on a centralized web-based tool hosted by a professional information technology service. The randomization list consisted of permuted blocks of variable length, which were randomly arranged. Patients were stratified by study site and wound size (≤60 cm^3 and >60 cm^3). Each registered investigator received individual access to the randomization tool without knowing the randomization sequence, which ensured allocation concealment. The investigators were responsible for adequately implementing the assigned therapy. Neither study participants nor medical staff were blinded to the treatment assignment. Independent treatment-blind health care and clinical research professionals who received standardized training in wound assessment performed verification of wound closure based on wound photographs and determined wound size using the Wound Healing Analyzing Tool (WHAT).

Procedures

At baseline, patients received an extensive examination of the study wound, actual surgical history, and overall health status. After wound debridement or thorough wound cleansing, study therapy started either in-hospital or outpatient and should to be continued in outpatient care whenever possible. In the intervention arm, commercially available CE-marked Vacuum Assisted Closure (VAC) Therapy systems of the manufacturer Kinetic Concepts Incorporated, an Acelity company, were used in the discretion of the clinical investigator and according to manufacturer's instructions.[22] Mainly GranuFoam dressings were used as indicated for dehisced wounds. WhiteFoam dressings (Acelity) and GranuFoamSilver dressings (Acelity) were used for superficial and sensitive wounds and for wounds with need for barrier to bacterial penetration, respectively. Negative pressure wound therapy as interim therapy was discontinued once the condition of a wound was suitable for closing, either by epithelialization or surgically. Control therapy was any local wound treatment regularly used in the respective study site that did not have an experimental status or was NPWT according to the hospitals' local clinical standards and guidelines. The applied wound therapy included wound cleansing; surgical debridement; measures for wound margin protection; wound drainage; and the application of dressings of the following categories: gauze, hydrocolloid, alginate, hydrofiber, foam, collagen, antimicrobial materials, active coal compresses, hydrogel, elastomeric matrices, transparent films, and composite dressings. Application was based on the individual needs of the wound in the process of healing with special attention to the amount of exudate and the local infections status. Study visits needed to be performed weekly until the end of maximum study treatment time at day 42 and included a complete wound examination. All study participants were followed up until 132 days after randomization. An additional follow-up was performed on day 87 for study participants with open wounds on day 42.

Outcomes

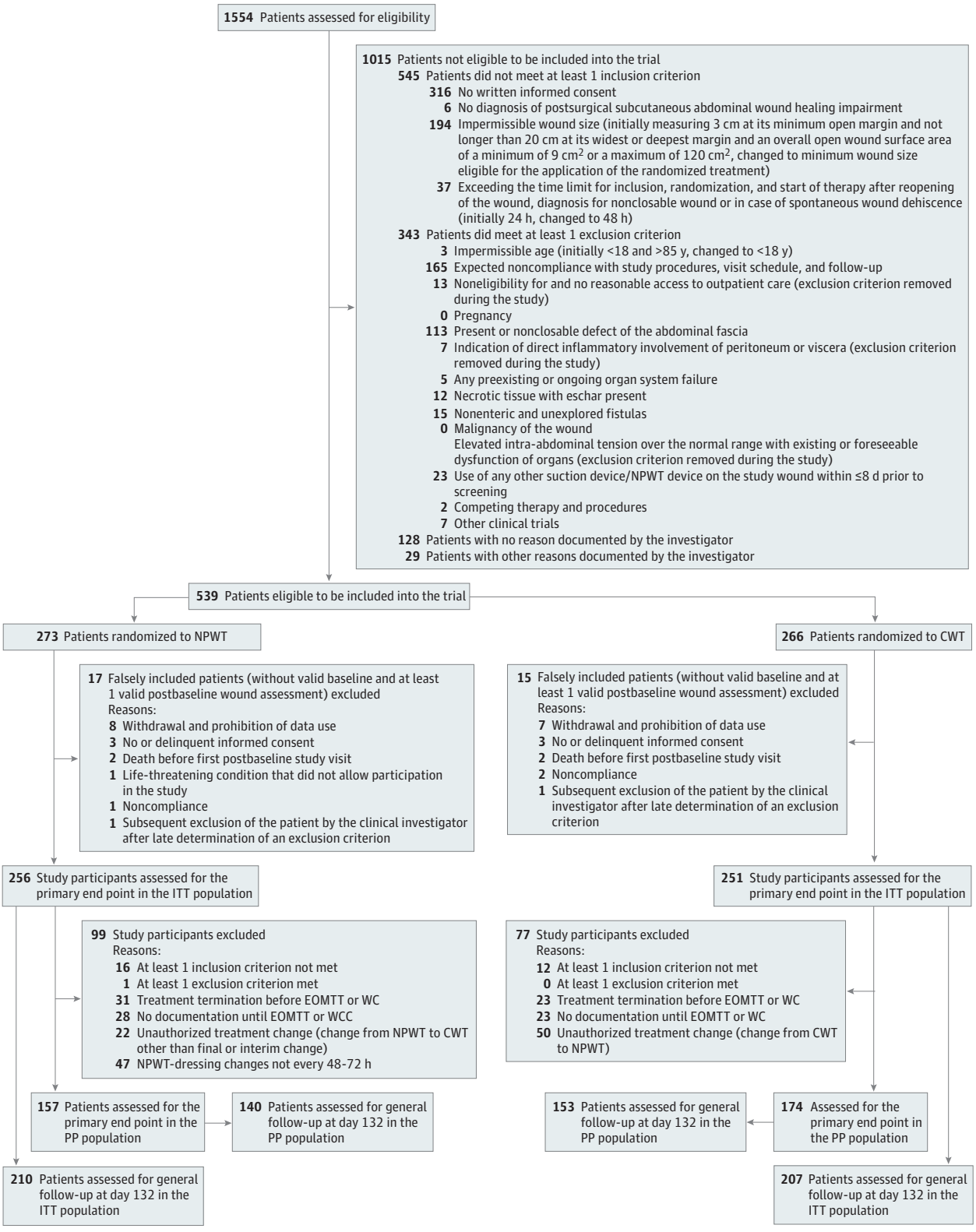
Taking into account the clinical and patient-relevant focus on eliminating the wound healing impairment and all its consequences as quickly as possible, time until wound closure (100% epithelialization of the wound, no drainage, no suture material, and no need for wound dressing or adjuvants) was chosen to be the primary end point of this study. Wound closure could be achieved either by secondary intention (epithelization) or by surgical intervention, both after generating a sufficient granulation tissue matrix, needed to sustain for a minimum of 14 days, and was to be confirmed by independent blinded observers using photographs.

Secondary outcomes were wound closure rate within 42 days, recurrence of the wound healing impairment after wound closure within 132 days, and reduction of wound size within 42 days. Quality of life (QoL) was measured using the physical and the mental component summary score of the Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) questionnaire at wound closure, at day 42 in case of a residual open wound, hospital discharge, and at general follow-up after 132 days. Because an initially used pain diary proved to be unmanageable for the study participants, the assessment of wound-associated pain on a numerical rating scale (0 to 10) was limited to the study visits. Patient satisfaction was evaluated using an adapted questionnaire based on specific scales of the validated Cologne Patient Questionnaire.[23,24] Incidence of AEs, unsustained wound closures within 42 days, and serious adverse events (SAEs), including mortality within 132 days, were safety end points of this trial. As an add-on, health economically relevant parameters were collected and will be reported separately.

Statistical Analysis

To the best of our knowledge, only 1 study[15,16] evaluating partial thickness abdominal wounds was available for study planning. The average NPWT time was 13 days (range, 11-14 days). Wounds were mainly closed surgically without any indication of a time to wound closure. To be on the safe side, the treatment period was tripled, and, considering the clinical experience that showed that on average 10% to 15% more wounds can be closed with NPWT within 1 month, we assumed a complete wound closure rate of 50% in the CWT arm and a minimum difference of 12.5% between the treatment arms after 42 days. A number of 492 study participants was calculated[25] to be necessary to achieve 80% power ($\beta = 0.2$) with $\alpha = .05$. One planned interim analysis was performed after 250 participants completed 42 days. We adjusted α using the O'Brien-Fleming method ($\alpha = .005$ for the interim analysis and $\alpha = .048$ for the final analysis),[26] which led to a marginal increase of the sample size of 498 participants. Interim results did not show the predefined positive effect at P less than .005 or a negative effect at a P less than .05 level for NPWT, and the study was continued. The initially planned sample size adjustment after the interim analysis was not performed because this approach turned out not to be appropriate. All final analyzes were based on a modified intention-to-treat (ITT) population that included all randomized participants with a valid baseline and at least 1 postbaseline wound assessment (**Figure 1**). Addition-

Figure 1. Study Participant Flow in the Subcutaneous Abdominal Wound Healing Impairment (SAWHI) Randomized Clinical Trial



Patient flow according to Consolidated Standards of Reporting Trials (CONSORT), including all reasons for exclusions from the intention-to-treat (ITT) and the per protocol (PP) population. CWT indicates conventional wound treatment; EOMTT, end of maximum treatment time; NPWT indicates negative pressure wound therapy; WC, wound closure.

ally, a per protocol analysis was performed excluding patients violating inclusion and exclusion criteria, with unauthorized treatment changes, deviations from the recommended frequency of NPWT dressing changes, early treatment termination, or without valid documentation until wound closure confirmation or end of maximum treatment time. Owing to the high number of treatment changes and the fact that adverse events were a frequent reason for treatment change, the adverse event analysis could not be performed based on the as-treated population. Safety results are presented first for the modified ITT population without regard to the causality of the event and second for the population without unauthorized treatment changes considering the relationship to device, CWT, and wound.

Time to complete wound closure is presented using Kaplan-Meier curves and was compared between the treatment arms using a log-rank test. Missing values and unsustained wound closures were included as censored values. Incidence of complete wound closure was analyzed using Fisher exact test. In case of missing data, the outcome was considered not achieved. Total percentage reduction of wound surface and volume are presented by calculating the area under the curve of the repeated wound size measurements within 42 days as a summary measure for each participant as an aggregated value. The statistical tests used to compare the secondary and safety outcomes are listed in the corresponding tables. Missing values of the progression parameters wound size and pain were imputed by carrying the last observation forward. SPSS statistical software, version 23 (IBM Inc), was used for all analyses.

Results

A total of 539 patients were randomized in 34 study sites between August 2, 2011, and January 31, 2018. A total of 507 study participants (NPWT, 256; CWT, 251) were included in the modified ITT analysis (Figure 1). In 18 study sites, there were at least 1 and a maximum of 4 exclusions from the ITT population (N = 32). Baseline characteristics of the patients included in the ITT population were similar in the treatment arms (**Table 1**). The clinical investigators documented up to 10 reasons for SAWHI per patient (eTable 1 in Supplement 2).

Wound Closure

The mean time to complete, sustained, and verified wound closure within 42 days was significantly shorter in the NPWT arm (difference, 3.0 days; 95% CI, 1.6-4.4; $P < .001$; **Figure 2**). Because 71.2% of the wounds (NPWT, 64.1%; CWT, 78.5%) were not closed within 42 days, it was not possible to calculate the median time to wound closure. Significantly more wounds were closed within 42 days when treated with NPWT and thus had a lower risk of remaining open than those treated with CWT (risk ratio [RR], 0.489; 95% CI, 0.329-0.725; $P < .001$; **Table 2**).

In the NPWT arm, more wounds were sutured, whereas in the CWT arm, slightly more wounds healed by secondary intention (Table 2). The significant positive effect of NPWT on wound closure did not change when adjusted for study site and wound size (Figure 2). The risk of a verified complete wound closure not

Table 1. Baseline Characteristics of the ITT Study Population

Baseline parameter	No. NPWT (n = 256)	No. CWT (n = 251)
Age, median (IQR), y	66 (18)	66 (20)
Sex, No. (%)		
Male	155 (60.5)	132 (52.6)
Female	101 (39.5)	119 (47.4)
Weight, median (IQR), kg	85 (24)	81 (25)
Height, median (IQR), cm	172 (16)	170 (13)
BMI, median (IQR)	28.7 (8.6)	27.9 (7.8)
Smoking, No./total No. (%)	65/256 (25.4)	55/251 (21.9)
Packs/d	62	54
Mean (SD)	0.9 (0.5)	0.8 (0.5)
Years	56	52
Mean (SD)	32.1 (12.4)	29. 6 (13.5)
Alcohol use, No./total No. (%)	111/255 (43.5)	114/250 (45.6)
Recreational	97	102
Chronic	15	13
Drug use, No./total No. (%)	3/256 (1.2)	3/251 (1.2)
Recreational	3	1
Chronic	0	2
Nutritional status		
Well-nourished	235	222
Moderately or suspected of being malnourished	18	26
Severely malnourished	3	3
Wound volume, cm^3		
≤60	149	142
>60	107	107
Coagulation (laboratory values) during screening[a]		
Prothrombin time %	149	148
Mean (SD)	88.3 (16.2)	88.3 (17.8)
INR	145	145
Mean (SD)	1.1 (0.2)	1.1 (0.2)
pTT	146	146
Mean (SD), s	33.9 (10.8)	32.5 (10.4)
Diagnosis of abdominal wound healing disorder		
Spontaneous dehiscence	57	52
Active reopening	198	193
Wound left open after surgery	2	9
Clinical signs of local infection during screening? No./total No. (%)		
No	122/256 (47.7)	116/250 (46.4)
Not assessable	29/256 (11.3)	24/250 (9.6)
Yes	105/256 (41.0)	110/250 (44.0)
Level of surgical site infection according to CDC classification, No./total No. (%)		
Superficial incisional	65/104 (62.5)	67/110 (60.9)

(continued)

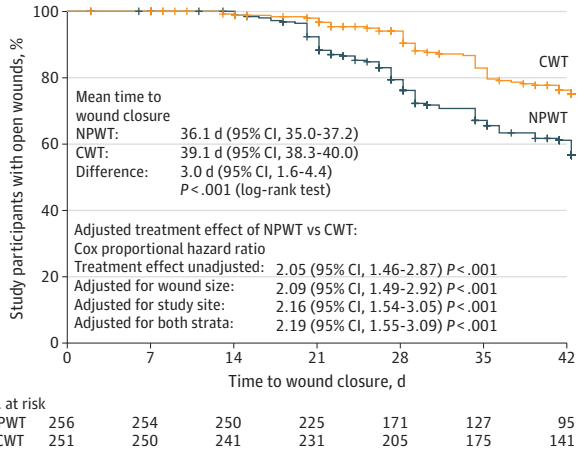
Table 1. Baseline Characteristics of the ITT Study Population (continued)

Baseline parameter	No. NPWT (n = 256)	CWT (n = 251)
Deep incisional	37/104 (35.6)	39/110 (35.5)
Organ or space infection	2/104 (1.9)	4/110 (3.6)
Clinical signs of local infection at randomization, No. (%)		
No	133 (53.8)	130 (53.1)
Not assessable	39 (15.8)	36 (14.7)
Yes, No./total No. (%)	75/247 (30.4)	79/245 (32.2)
Level of surgical site infection according to CDC classification, No./total No. (%)		
Superficial incisional	43/73 (58.9)	43/79 (54.4)
Deep incisional	28/73 (38.4)	34/79 (43.0)
Organ or space infection	2/73 (2.7)	2/79 (2.5)
Main procedure that caused the abdominal wound healing impairment, available No./total No.	255/256	248/251
Intestinal surgery, No./total No. (%)	165/255 (64.5)	156/248 (62.9)
Incision, excision, resection and anastomose of the small and large intestine	94	93
Other operations on the small and large intestine	35	30
Appendix surgery	14	13
Rectal surgery	22	20
Anal surgery	0	0
Nonintestinal surgery, No./total No. (%)	90/255 (35.3)	92/248 (37.1)
Esophagus surgery	0	2
Gastric incision, excision, and resection	6	4
Extended gastric resection and other gastric surgery	3	0
Liver surgery	8	8
Gall bladder and bile ducts surgery	23	17
Pancreatic surgery	13	11
Closure of abdominal hernias	18	13
Operations on other abdominal regions	15	27
Other	4	10

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CDC, US Centers for Disease Control and Prevention; CWT, conventional wound treatment; INR, international normalized ratio; IQR, interquartile range; NPWT, negative pressure wound therapy; pTT, partial thromboplastin time.

[a] Laboratory values are provided with the respective SI unit.

Figure 2. Time to Wound Closure in the Intention-to-Treat (ITT) Population



No. at risk

NPWT	256	254	250	225	171	127	95
SCWT	251	250	241	231	205	175	141

Starting point of the presentation are 100% open wounds on the day of randomization/initiation of the study therapy (negative pressure wound therapy [NPWT] or conventional wound treatmen [CWT]). Kaplan-Meier curves are used to show the decrease in the number of open wounds within the study treatment/observation period of 42 days. The number of study participants at risk (with open wounds) is shown below the diagram for each survey time (randomization/initiation of therapy and weekly study visits) and the end of the maximum treatment time after 42 days. The course was censored for each study participant if this participant achieved the study goal complete, verified, and sustained wound closure. Mean time to wound closure is shown in days for each treatment arms and as difference between the treatment arms together with 95% CI. Mean time to wound closure was compared between the treatment arms using the log-rank test.

to sustain for a minimum of 14 days was only slightly higher in NPWT arm than in the CWT arm (RR, 1.14; 95% CI, 0.54-2.37; P = .71; Table 2).

Secondary Clinical Outcomes

No recurrences occured after complete, sustained, and verified wound closure in any of the treatment arms. Total reduction of wound surface area within 42 days calculated from width and length was significantly greater in the NPWT arm than in the CWT arm (difference, 253 mm^2; 95% CI, −711 to 1217; P = .007) (eTable 2 in Supplement 2). Owing to extreme and largely scattered values, the total wound surface reduction calculated with WHAT was not significantly different between the treatment arms (eTable 3 in Supplement 2). Total reduction of wound volume within 42 days was also significantly greater in the NPWT arm (difference, 395 mm^3; 95% CI, −1065 to 1855; P = .002) (eTable 4 in Supplement 2).

Patient-Reported Outcomes

Mean SF-36 physical and mental component summary scores were lower than the mean scores for healthy participants both in study participants achieving wound closure and in those with persisting wounds after 42 days. The scores did not significantly differ between the treatment arms at any evaluation time (eTable 5 in Supplement 2). Overall, pain levels were very low and decreased further during the study treatment time (eTable 6 in Supplement 2). Subjective satisfaction with the treatment was marginally better with NPWT (eTables 7-9 in Supplement 2).

Treatment Compliance

Within 42 days, 201 study participants were treated exclusively with CWT. Fifty participants underwent a treatment change from CWT to NPWT, resulting in 306 study participants treated with NPWT. The most common reasons for treatment changes were fascia dehiscence, heavy exudation, and wound infection (eTable 10 in Supplement 2).

Table 2. Wound Closure Within 42 Days in the ITT Population

Wound closure, unsustained wound closure in the ITT population	No./total No. (%)		
	NPWT (n = 256 [100])	CWT (n = 251 [100])	Difference between the treatment arms
Dropouts and/or withdrawals during study treatment time (until day 42), No.	15	9	4
Missing documentation of treatment outcome (no wound closure and wound closure confirmation or no wound status documentation at end of maximum treatment time), No.	16	14	2
Study participants with complete, verified and sustained wound closure within 42 d			
No./total No. (%) [95% CI]	92/256 (35.9) [30.1-41.8]	54/251 (21.5) [16.4-26.6]	38 (14.4) [6.6-22.2]
P value	NA	NA	.003[a]
Study participants with delayed primary wound closure after wound bed preparation (suturing)[b]	65/92 (70.7)	27/54 (50)	38 (20.7)
Study participants with wound closure by secondary intention (continuous wound bed preparation and subsequent epithelization)[b]	27/92 (29.3)	31/54 (57.4)	4 (28.1)
Study participants with unsustained wound closure within 42 d[c]			
No./total No. (%) [95% CI]	18/110 (16.4) [9.7-25.8]	9/63 (14.3) [6.5-27.1]	9 (2.1) [−7.9 to 12.1]
P value	NA	NA	.72[a]

Abbreviations: CWT, conventional wound treatment; ITT, intention-to-treat; NPWT, negative pressure wound therapy.

[a] χ^2 Test (α = .05).

[b] For 2 study participants in the NPWT arm and 6 participants in the CWT arm, the clinical investigators documented both suturing of the wound and closure by secondary intention. For 2 patients in each treatment arm, no information was given on the type of wound closure.

[c] Unsustained wound closure is defined as a wound closure not confirmed to be sustained for a minimum of 14 days after achieved complete and verified closure.

Safety

In the modified ITT population, both treatment arms had approximately the same risk for AEs (RR, 1.04; 95% CI, 0.88-1.24), but after excluding study participants with unauthorized treatment changes, the relative risk for AEs was higher in the NPWT arm (RR, 1.20; 95% CI, 0.97-1.47) (**Table 3**). In the TC population, adverse device events exclusively occurred in participants treated with NPWT. Additionally, more study participants in the NPWT arm had wound-related AEs (RR, 1.51; 95% CI, 0.99-2.35). The most frequently documented wound-related AEs were periwound macerations and local infections with signs of inflammation. Most AEs were recovered during the study observation period. None of the deaths was related to the NPWT device, CWT, or the wound.

Per Protocol Analysis

In the per protocol population, the mean time to wound closure within 42 days was significantly shorter in the NPWT arm (34.7 days) than in the CWT arm (38.6 days) (difference, 3.9 days; 95% CI, 2.2-5.6; $P < .001$) (eFigure in Supplement 2). Significantly more study participants achieved wound closure within 42 days when treated with NPWT (75 of 157 [47.8%]) than with CWT (48 of 174 [27.6%]) (difference, 20.2%; 95% CI, 9.9-30.5; $P < .001$) (eTable 11 in Supplement 2). The results for recurrences within 132 days and wound size reduction, QoL, pain, and patient satisfaction within 42 days show no relevant deviations from those of the ITT population (eTables 11-19 in Supplement 2).

Discussion

In the SAWHI study, complete, sustained, and verified wound closure was achieved significantly faster and more often in study participants treated with NPWT than in those treated with CWT. The benefits of NPWT, demonstrated in various clinical trials with other wound types, were confirmed by the results of our study.[2,7,11] Most wounds in the NPWT arm were sutured. In the CWT arm, a slightly higher rate of wounds healed by secondary intention. The rates of unsustained wound closures and recurrences were very low, with no relevant difference between the treatment arms. Therefore, there is no indication of an influence of the type of wound closure on the sustainability of treatment success. However, the choice of wound closure technique was in the discretion of the unblinded clinical investigator, which has a potential bias on wound closure time and rate taking into account that wound healing by secondary intention is slower and may not be achieved within 42 days. Nevertheless, NPWT has advantages in exudate removal and granulation tissue formation,[2,8,9] which possibly led to an improved basis for surgical closure.

Quality of life scores were lower than the mean scores for healthy participants but did not differ significantly between the treatment arms. The type of treatment did not influence study participants' QoL more than the underlying disease or the wound healing disorder.

While the risk for an AE was approximately the same in the ITT population in both treatment arms, the exclusion of the study participants with therapy changes showed that a higher number of AEs occurred in the NPWT arm. This increased number resulted mainly from technical malfunctions of the device, as well as from a higher number of wound-related AEs, which represent actual unfavorable effects of wound treatment. The reported accumulation of the known AE periwound macerations, which was higher in the NPWT arm, is usually caused by a lack of drainage of wound exudate from the wound margin and avoidable with adequate protection.[6] Local infections with signs of inflammation can be quickly eliminated by adequate therapy mea-

Table 3. Adverse Events Within 42 Days and Serious Adverse Events Including Mortality Within 132 Days in the Modified ITT Population and in Study Participants Compliant With the Treatment Allocation

Safety	No./Total No. (%)	
	NPWT	CWT
Study participants with AEs in the modified ITT population	133/256 (52.0)	125/251 (49.8)
No. of AEs in the modified ITT population	276	231
Outcome of AEs in the modified ITT population		
Recovered	211/276 (76.5)	181/231 (78.4)
Recovered with sequelae	15/276 (5.4)	12/231 (5.2)
Not recovered	7/276 (2.5)	7/231 (3.0)
Fatal (death)	24/276 (8.7)	15/231 (6.5)
Unknown	7/276 (2.5)	8/231 (3.5)
Missing	12/276 (4.4)	8/231 (3.5)
Study participants with SAEs in the modified ITT population	92/256 (36.0)	89/251 (35.5)
No. of SAEs in the modified ITT population	153	134
Study participants with AEs in the TC population	117/234 (50)	84/201 (41.8)
No. of AEs in the TC population	240	136
Outcome of AEs in the modified TC population		
Recovered	180/240 (75)	105/136 (77.2)
Recovered with sequelae	14/240 (5.8)	6/136 (4.4)
Not recovered	6/240 (2.5)	4/136 (2.9)
Fatal (death)	24/240 (10)	14/136 (10.3)
Unknown	4/240 (1.7)	2/136 (1.5)
Missing	12/240 (5)	5/136 (3.7)
Study participants with SAEs in the TC population	80/234 (34.2)	57/201 (28.4)
No. of SAEs in the TC population	133/240 (55.4)	81/201 (40.3)
Study participants with ADEs (AEs definitely related to the NPWT-device) in the TC population	13/234 (5.6)	NA
No. of ADEs (AEs related to the NPWT-device) in the TC population	23/240 (9.6)	NA
Device		
Low/critical battery	1	NA
Burning smell/smoke	1	NA
Off/on, lock/unlock, language	1	NA
False alarms; inactive therapy	1	NA
Battery defect (not rechargeable; not maintaining charge)	2	NA
Continuous nonidentifiable alarm	3	NA
Not keeping the pressure settings	1	NA
Noisy device (suction noises)	1	NA
Canister		
Empty, but alarm indicates full canister	1	NA
Blockage	3	NA
Drape		
No adherence	5	NA
Allergic reaction to drape (periwound level)	1	NA
Other	2	NA
Study participants with CWT-related AEs in the TC population	1/234 (0.4)	1/201 (0.5)
No. of CWT-related AEs in the TC population	1/240 (0.4)	1/136 (0.7)
Study participants with wound-related AEs in the TC population	48/234 (20.5)	27/201 (13.4)
No. of wound-related AEs in the TC population	80/240 (33.3)	41/136 (30.1)
Periwound maceration	21	9
Local infection with signs of inflammation	28	12
Minor, serious, or fatal bleeding	3	4
Irritation or sensitivity to the drape	2	0
Burst abdomen	3	1
Fascia defect	3	4
Fistula	2	0
Other	18	11

Abbreviations: ADE, adverse device event; AE, adverse event; CWT, conventional wound treatment; ITT, intention-to-treat; NA, not applicable; NPWT, negative pressure wound therapy; SAE, serious adverse event; TC, treatment compliant.

sures, which in case of contaminated abdominal wounds should also be frequently performed when applying NPWT.[22]

Limitations

The SAWHI study has several limitations. Blinding of study participants and medical staff was not possible owing to the nature of NPWT. The ITT population was adapted, but the number of patients excluded after randomization was low (NPWT, 6.2%; CWT, 5.6%), and no clustering in a study site was observed. Because more than 50% of the wounds were not closed within 42 days, the chosen treatment and observation time was unfortunately too short. During study planning, only 1 retrospective trial reported the use of NPWT in SAWHI after surgery, which provided only limited information on treatment time and no information on the time necessary for complete closure.[15,16]

Owing to intensive marketing and despite the lack of proof of benefit, NPWT represents an established treatment in clinical practice. This affected the investigators compliance with the randomized treatment arm and resulted in a high number of treatment changes from CWT to NPWT. Furthermore, missing standardization of CWT and very different and partly low inclusion numbers in the study sites within a long recruitment period may be limitations of the SAWHI-study but represent the clinical practice realistically.

The typical clinical practice of wound reopening and secondary suture after achieving wound bed granulation caused a nonlinear wound size progression and large scatter of the values. Using the relative reduction of the wound size over time is therefore questionable. Because very few patients with wounds left open after surgery were enrolled, future research should focus on this type of wound and determine an appropriate treatment time and a longer observation time for wound closure.

Conclusions

To our knowledge, the SAWHI study is the first RCT to demonstrate that NPWT is superior to conventional dressings in achieving complete closure of subcutaneous abdominal wounds after surgery while not affecting patients' QoL more than the underlying disease; however, NPWT more frequently causes AEs mainly related to the device itself and the wound.

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