Eur J Vasc Endovasc Surg (2019) 58, 446–454

REVIEW

Closed Incision Negative Pressure Wound Therapy in Vascular Surgery: A Systematic Review and Meta-Analysis

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WHAT THIS PAPER ADDS

Post-operative surgical site infection rates remain persistently high despite various interventions including surgical technique and systemic antibiotic therapy. Closed incision negative pressure wound therapy (CiNPT) has been shown to reduce surgical site infections in other surgical disciplines, and may be a valuable adjunct. Randomised controlled trials of CiNPT in vascular surgery have been published recently demonstrating encouraging results; however to date, no meta-analysis has been published. While this meta-analysis has shown evidence supporting the efficacy of CiNPT in reducing Szilagyi Grades I and III infections, as well as the risk of surgical re-intervention, there were no differences in other important clinical outcomes potentially limiting its clinical relevance. Furthermore, the current sample size remains small hence reducing the statistical power of these findings. A larger, well designed randomised controlled trial is needed to establish these findings.

Background: Closed incision negative pressure wound therapy (CiNPT) may be a valuable treatment option for surgical site infections. This systematic review and meta-analysis sought to compare CiNPT against conventional wound care after vascular procedures.

Methods: This study conformed to the PRISMA guidelines. An electronic search was performed on Medline/Pubmed, EMBASE, and the Cochrane Library. The date of last search was July 11 2018. Relative risks and mean differences for primary and secondary outcomes were calculated. A random effects model was used for substantial heterogeneity ($I^2 > 30\%$). The Cochrane Risk of Bias tool was employed to rate the methodological quality of the included studies, whilst the GRADE approach was use to grade the level of evidence for the observed effects.

Results: Of 47 studies, five randomised controlled trials (RCTs) were included, comprising 662 patients, of which 47.9% underwent CiNPT and 52.1% received conventional care. The overall risk of infection (RR = 0.31, 95% CI 0.21–0.47) (high quality), Szilagyi Grades I (RR = 0.35, 95% CI 0.20–0.60) (high quality), and III (RR = 0.17, 95% CI 0.04–0.68) (high quality) infections, need for antibiotics (RR = 0.36, 95% CI 0.20–.64) (high quality), and surgical re-intervention (RR = 0.27, 95% CI 0.27–0.98) (high quality) were lower in the CiNPT group. However, there were no significant differences in the risk of Grade II (RR = 0.59, 95% CI 0.10–3.66) (moderate quality), as well as length of hospital stay (mean difference, MD = −0.59, 95% CI −2.48 to 1.31) (moderate quality), and 30 day mortality (RR = 3.95, 95% CI 0.17–94.76) (high quality).

Conclusion: While there is evidence demonstrating that CiNPT reduces the risk of Grades I and III infections and re-interventions, there was a noticeable lack of difference in other important post-operative outcomes. Further well designed RCTs are needed to corroborate these findings.

Keywords: Closed incision negative pressure wound therapy, Vascular surgery, Surgical site infections
Article history: Received 15 August 2018, Accepted 22 December 2018, Available online 1 August 2019
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https://doi.org/10.1016/j.ejvs.2018.12.021

INTRODUCTION

Surgical site infection (SSI) after vascular procedures remain a significant issue with prevalence rates ranging from 6% to 30%,[1,2] and is the most common cause of re-admissions.[3]

Fortunately, use of preventive measures can reduce the risk by up to 40%.[4] Among various strategies including systemic antibiotic therapy and surgical techniques, only antibiotic therapy has shown to be effective.[5,6] The persistently high rates of SSIs warrant the need for alternatives. Since its introduction in the late 1990s, negative pressure wound therapy (NPWT) has been widely regarded as an effective treatment option for various wound conditions, including complex open wounds, infected wounds, traumatic wounds, degloving injuries, and high energy trauma wounds.[7,8] This has subsequently led to the concept of closed incision NPWT (CiNPT), which was first proposed by Stannard *et al.*, in 2006.[8] This primarily involves the use of negative pressure therapy (NPT) on closed surgical incisions to aid healing by primary intention and prevent wound dehiscence.[8]

Since then, two meta-analyses[9,10] have collectively shown that CiNPT reduces surgical site infection rates compared with conventional care. In the vascular area, various randomised controlled trials (RCTs) evaluating the efficacy of CiNPT have emerged recently.[11–15] To date however, there has been no meta-analysis of CiNPT in vascular surgery. It is the aim of this systematic review and meta-analysis was to compare the efficacy and safety of CiNPT with conventional care in adult patients who had undergone vascular procedures.

METHODS

Literature search

This study was conducted in accordance with the Cochrane Handbook of Systematic Reviews and Meta-analysis, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines.[16]

An electronic search was performed in the following databases: Medline, EMBASE, and the Cochrane library from inception to November 30 2018. In Medline, the following search terms were combined using Boolean operators (closed incision negative pressure therapy.mp. OR negative pressure wound therapy.mp. OR ciNPT.mp.) AND surgical site infection.mp. AND (vascular surgery.mp. OR vascular surgery/ OR peripheral arterial disease.mp. OR peripheral occlusive artery disease/). In EMBASE, the following terms were used (negative-pressure wound therapy/or closed incision negative pressure therapy.mp. OR CiNPT.mp.) AND (surgical site infection.mp. or surgical wound infections/) AND (peripheral arterial disease/or vascular surgical procedures/or vascular surgery.mp.). In Cochrane database, the following terms were used (negative-pressure wound therapy [MeSH] OR closed incision negative pressure therapy OR ciNPT) AND (surgical wound infection [MeSH]) AND (peripheral arterial disease [MeSH] OR vascular surgery). The exact search strategy can be found in Appendix 1. The reference lists of included articles were also searched to identify additional relevant studies.

Eligibility criteria

Any randomised study that compared CiNPT with conventional post-operative wound dressing in adults (greater than 18 years) who had undergone a vascular procedure were included. The use of any devices was permitted, including PREVENA™, PICO™ or VAC®. Only English language studies were included. Conference abstracts were considered only if sufficient data were reported for meaningful synthesis and analysis. Studies investigating NPT for open wounds were excluded. Case reports and case series were excluded due to the high risk of known selection and publication bias. Animal and laboratory studies were also excluded.

Outcome measures

Primary outcome measures were overall wound infections, as well as wound infections classified using the Szilagyi classification (Grades I to III).[17] Grade I was limited to the dermis but included lymphatics from the closed incision. Grade II was defined as extension to the subcutaneous skin layers, and Grade III was defined as arterial involvement. Secondary outcome measures included length of hospital stay (days), frequency of antibiotic treatment, surgical re-intervention, and 30 day mortality.

Selection of studies and data extraction

Two reviewers (I.W., N.S.) independently screened and assessed the studies for inclusion, first by their titles and abstracts. Subsequently, the full text of articles included in the first stage was retrieved for review if the relevance of the studies for inclusion could not be confirmed. Conflicts were resolved by consensus, or by appeal to a third author (A.C.). A data sheet was used to extract the following data from text, tables, and figures in each study: first author, year and type of publication; age, gender, patient comorbidities, type of surgery, and primary and secondary outcomes. Data extraction was performed independently by two reviewers (I.W., N.S.), and conflicts were resolved by consensus or by appeal to a third author (A.C.).

Risk of bias assessment and quality assessment

The Cochrane Risk of Bias tool was used to assess the risk of bias of included RCTs, which included seven key items measuring selection bias, performance bias, detection bias, attrition bias, and reporting bias. Two reviewers (I.W., N.S.) independently assessed the quality of studies, and consensus was reached after resolution of conflicts or by appeal to a third reviewer (A.C.).

To underpin the evidence base for the findings of this study and recommendations for clinical practice, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was employed. The following grading system was used: low heterogeneity when $p > .05$; moderate heterogeneity when $p > .01$ but $< .05$, which requires a downgrading of evidence by one level; high heterogeneity when $p \leq .01$, which requires a downgrading of evidence by two levels. However, if there was a consistent direction based on visual inspection of the forest plots in a specific outcome, the quality of evidence was not downgraded. Based on the aforementioned, the overall reliability of the pooled data was evaluated as “very low”, “low”, “moderate”, or “high”.[18]

Data analysis

All statistical analyses were performed using Review Manager 5 (RevMan 5.3, The Cochrane Collaboration, Copenhagen) and Stata software. A random effects meta-analysis was conducted to pool the dichotomous data on adjusted rate ratios (RR) in case of substantial statistical heterogeneity (I^2 above 30%). Data were pooled with a fixed effects model if statistical heterogeneity could not be demonstrated (I^2 below 30%). The mean and standard deviation for continuous outcomes were estimated using methods described by Hozo *et al*.[19]

RESULTS

Search results

The systematic search yielded 47 articles, of which 32 were excluded after title and abstract screening. The remaining 15 articles were reviewed in their entirety, and 11 were excluded, leaving five randomised controlled trials for final inclusion in the meta-analysis.[11–14,20] The screening process is shown in the PRISMA flow diagram (Fig. 1). There was a total of 662 patients, of which 317 (47.9%) underwent CiNPT and 345 (52.1%) received conventional care. Considering that some patients had more than one incision, this translated to a total of 691 incisions, of which 332 (48.0%) underwent CiNPT and 359 (52.0%) received conventional care.

Baseline characteristics

The mean age ranged from 68 years to 71 years in the CiNPT group, and from 65 years to 68 years in the control group. The prevalence of male was 65.3% and 74.8% in the CiNPT and control groups respectively. In terms of risk factors and comorbidities between the CiNPT and control groups, the prevalence of DM was 41.9% and 36.7% respectively, prevalence of renal insufficiency was 25.6% and 23.9%, proportion of smokers was 63.6% and 69.3% respectively, and the prevalence of hypertension was 86.6% and 92.3% respectively. A variety of vascular procedures were performed. Of those who underwent CiNPT, 7.0% underwent either endovascular aortic repair (EVAR) or thoracic endovascular aortic repair (TEVAR), and 93.0% underwent lower limb revascularisation. In the control arm, 6.4% underwent either EVAR or TEVAR, and 93.6% underwent lower limb revascularisation. A variety of control treatments were employed, including standard sterile gauze dressing, absorbent adhesive dressing (ABE®, Meditrade GmbH, Kiefersfelden, Germany), Cosmopore E wound

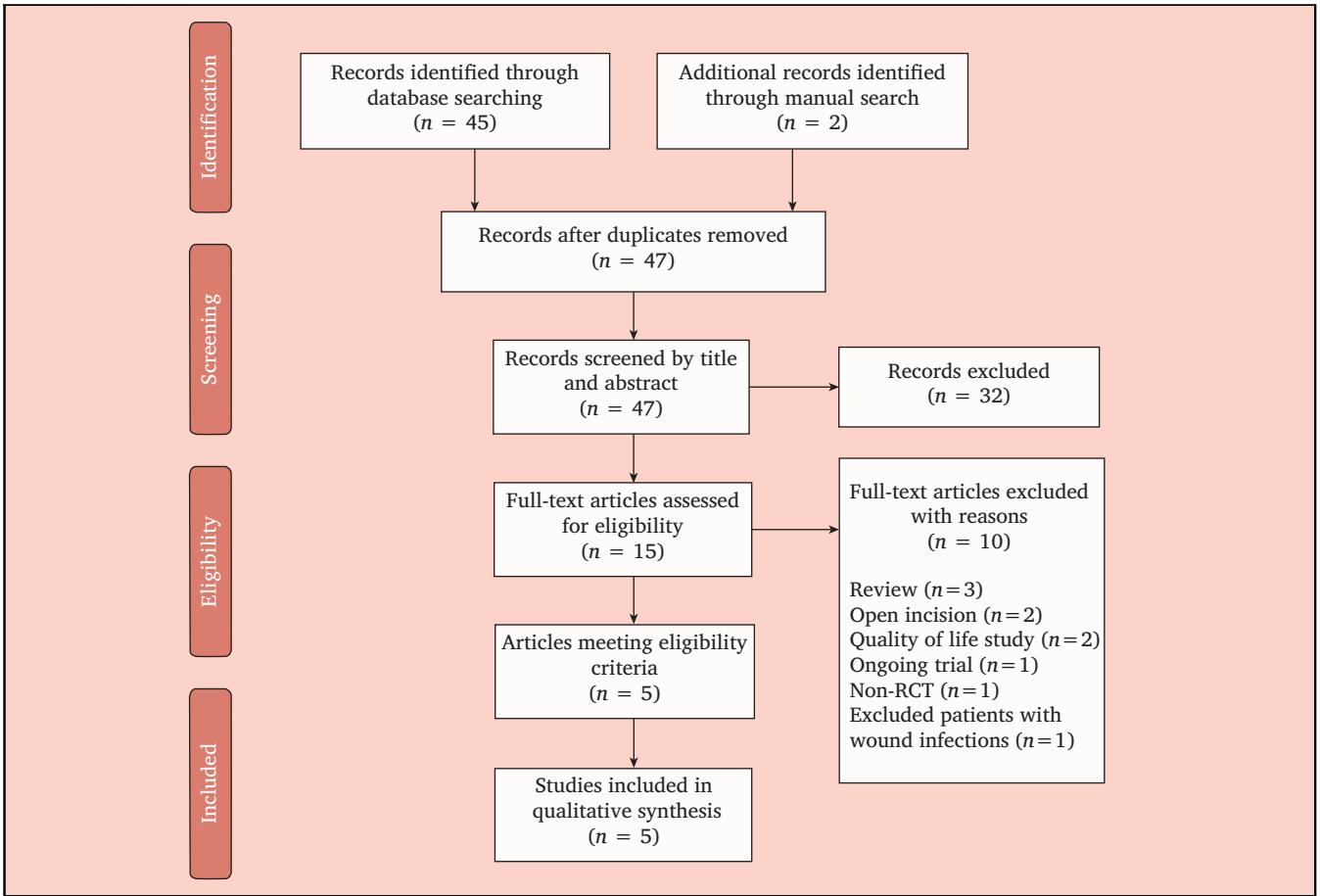

Figure 1. PRISMA flow diagram for literature search to identify randomised controlled trials of closed incision negative pressure wound therapy in vascular surgery. RCT = randomised controlled trial; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

dressing (Hartmann, Heidenheim, Germany), and conventional adhesive plaster. A summary of baseline characteristics can be found in Table 1.

Primary outcomes

Using a fixed effects model, the overall risk of infection was lower in the CiNPT group than in the control arm (RR = 0.31, 95% CI 0.21—0.47) (high quality) (Fig. 2).

Using a fixed effects model, the risk of Grade I (RR = 0.35, 95% CI 0.20—0.60) (high quality) (Fig. 3), and III infections (RR = 0.17, 95% CI 0.04—0.68) (high quality) (Fig. 4) were lower in the CiNPT group. However, there was no significant difference in the risk of Grade II infections (RR = 0.60, 95% CI 0.16—2.23) (moderate quality) (Fig. 5).

Secondary outcomes

Using a random effects model, there was no significant difference in the length of hospital stay (mean difference, MD = −0.59, 95% CI −2.48 to 1.31) (moderate quality) (Fig. 6). However, using fixed and random effects model respectively, there was a significantly decreased need for the use of antibiotics (RR = 0.36, 95% CI 0.20—0.64) (high quality) (Fig. 7), and a significantly lower risk of surgical re-intervention in the CiNPT group (RR = 0.27, 95% CI 0.27—0.98) (high quality) (Fig. 8). However, there was no significant difference in 30 day mortality between both groups (RR = 3.95, 95% CI 0.17—94.76) (high quality) (Fig. 9). A summary of primary and secondary outcomes, as well as the overall quality of evidence can be found in Table 2.

Risk of bias and overall quality of evidence

Amongst the five RCTs, there was overall a low risk of bias (Fig. 10). There was overall a low risk of selection bias, with two studies that failed to report random sequence generation and allocation concealment.[14,20] Overall, there was high risk of performance and detection bias. However, the nature of the therapy prevented double blinding of the participants, assessors, and surgeons. There could be high risk of sponsor bias in one trial as it was funded by Acelity (San Antonio, TX, USA), the manufacturer of the CiNPT devices.[13]

Based on the GRADE approach, all outcomes except the risk of Grade II infections (moderate quality) and length of hospital stay (moderate quality), had a high quality of evidence. The quality of evidence was downgraded by one level given the moderate statistical heterogeneity in both outcomes.

DISCUSSION

The benefits of CiNPT are numerous. It reduces oedema, and incision line tension, while providing an airtight seal.[21] Overall, the findings suggest that CiNPT reduces the risk of wound infection, particularly Grade I and III infections. In addition, there was also a reduced risk of re-intervention in

Table 1. Patient demographics, types of graft, and type of surgery in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery.

First author, year	Study design	Arm	Surgery				Patients		Graft material			
			No. of incisions	Redo surgery	EVAR/ TEVAR	RVC	Age	Male	PTFE	Dacron	Bovine pericardium	Autologous
Lee, 2017[11]	RCT	CiNPT	53	0/53	0/53	53/53	69 ± 10	34/53	9/53	13/53	11/53	8/53
		Standard sterile gauze dressing	49	0/49	0/49	49/49	68 ± 10	45/49	14/49	10/49	3/49	15/49
Engelhart, 2018[12]	RCT	CiNPT	64	NR	0/64	64/64	Median 72 (64—75)	48/64	15/64 alloplastic[a]		46/64	3/64
		Absorbent adhesive dressing[b]	68	NR	1/68	67/68	Median 70 (60—78)	57/68	22/68 alloplastic[a]		42/68	4/68
Gombert, 2018[13]	RCT	CiNPT	98	46/98	0/98	98/98	68 ± 10	70/98	34/98	12/98	29/98	13/98
		Cosmopore E wound dressing[c]	90	39/90	0/90	90/90	65 ± 8	62/90	32/90	10/90	30/90	9/90
Pleger, 2018[14]	RCT	CiNPT	58	NR	19/43	24/43	71 ± NR (54—89)	29/43	4/43	12/43	0/43	5/43
		Conventional adhesive plaster	71	NR	16/57	41/57	65 ± 8 (41—86)	43/57	6/57	22/57	0/57	7/57
Kwon, 2018[20]	RCT	CiNPT	59	26/59	9/59	NR	65 (44—83)	26/59	NR	NR	NR	NR
		Gauze covered by Tegaderm[d]	81	25/81	5/81	NR	68 (41—89)	51/81	NR	NR	NR	NR

RC = retrospective cohort; RCT = randomised controlled trial; CiNPT = closed incision negative pressure wound therapy; NR = not reported; PTFE = polytetrafluoroethylene; EVAR = endovascular aortic repair; TEVAR = thoracic endovascular aortic repair; RVC = revascularisation.
[a] Alloplastic stands for an artifical material substituted for a tissue graft.
[b] ABE®, Meditrade GmbH, Kiefersfelden, Germany.
[c] Hartmann, Heidenheim, Germany.
[d] 3M, St. Paul, MN.

Study	CiNPT Events	CiNPT Total	Control Events	Control Total	Weight	Risk Ratio M–H Fixed, 95% CI
Engelhart 2018[12]	4	64	10	68	11.5%	0.42 [0.14, 1.29]
Gombert 2018[13]	13	98	30	90	37.1%	0.40 [0.22, 0.71]
Kwon 2018[20]	2	59	17	81	17.0%	0.16 [0.04, 0.67]
Lee 2017[11]	2	53	2	49	2.5%	0.92 [0.14, 6.31]
Pleger 2018[14]	5	58	30	71	32.0%	0.20 [0.08, 0.49]
Total (95% CI)		**332**		**359**	**100.0%**	**0.31 [0.21, 0.47]**
Total events	26		89			

Heterogeneity: $Chi^2 = 3.91$, df = 4 ($p = .42$); $I^2 = 0\%$
Test for overall effect: Z = 5.52 ($p < .0001$)

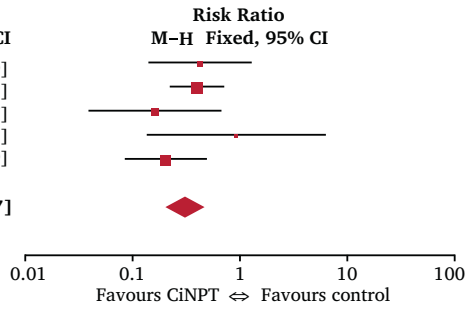

Figure 2. Risk ratio of overall infection rates in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

Study	CiNPT Events	CiNPT Total	Control Events	Control Total	Weight	Risk Ratio M–H Fixed, 95% CI
Engelhart 2018[12]	3	64	10	68	21.6%	0.32 [0.09, 1.11]
Gombert 2018[13]	8	98	24	90	55.8%	0.31 [0.15, 0.65]
Kwon 2018[20]	0	59	3	81	6.6%	0.20 [0.01, 3.71]
Lee 2017[11]	0	53	0	49		Not estimable
Pleger 2018[14]	4	58	8	71	16.0%	0.61 [0.19, 1.93]
Total (95% CI)		**332**		**359**	**100.0%**	**0.35 [0.20, 0.60]**
Total events	15		45			

Heterogeneity: $Chi^2 = 1.20$, df = 3 ($p = .75$); $I^2 = 0\%$
Test for overall effect: Z = 3.77($p = .0002$)

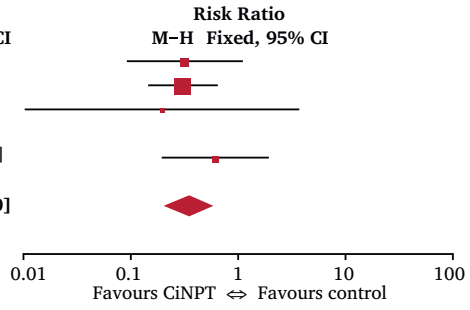

Figure 3. Risk ratio of Grade I infection rates in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

Study	CiNPT Events	CiNPT Total	Control Events	Control Total	Weight	Risk Ratio M–H, Fixed, 95% CI
Engelhart 2018[12]	0	64	0	68		**Not estimable**
Gombert 2018[13]	0	98	2	90	17.6%	0.18 [0.01, 3.78]
Kwon 2018[20]	0	59	10	81	60.1%	0.07 [0.00, 1.09]
Lee 2017[11]	1	53	1	49	7.0%	0.92 [0.06, 14.38]
Pleger 2018[14]	0	59	2	71	15.2%	0.24 [0.01, 4.99]
Total (95% CI)		**332**		**359**	**100.0%**	**0.17 [0.04, 0.68]**
Total events	1		15			

Heterogeneity: $Chi^2 = 1.94$, df = 3 ($p = .58$); $I^2 = 0\%$
Test for overall effect: Z = 2.51 ($p = .01$)

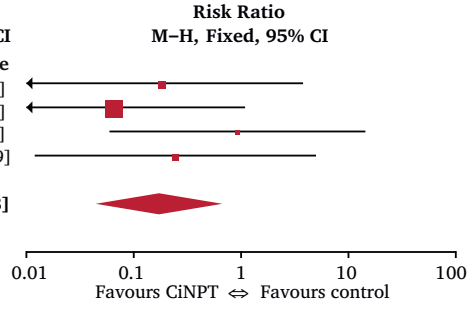

Figure 4. Risk ratio of Grade III infection rates in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

Study	CiNPT Events	CiNPT Total	Control Events	Control Total	Weight	Risk Ratio M–H, Random, 95% CI
Engelhart 2018[12]	1	64	0	68	11.8%	3.18 [0.13, 76.78]
Gombert 2018[13]	5	98	4	90	28.7%	1.15 [0.32, 4.14]
Kwon 2018[20]	2	59	4	81	24.2%	0.69 [0.13, 3.62]
Lee 2017[11]	1	53	1	49	14.4%	0.92 [0.06, 14.38]
Pleger 2018[14]	1	58	20	71	20.8%	0.06 [0.01, 0.44]
Total (95% CI)		**332**		**359**	**100.0%**	**0.60 [0.16, 2.23]**
Total events	10		29			

Heterogeneity: $Tau^2 = 1.12$; $Chi^2 = 8.50$, df = 4 ($p = .07$); $I^2 = 53\%$
Test for overall effect: Z = 0.76 ($p = .45$)

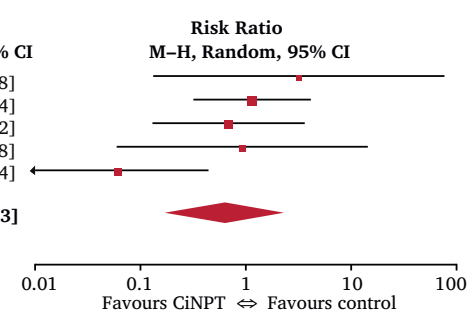

Figure 5. Risk ratio of Grade II infection rates in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

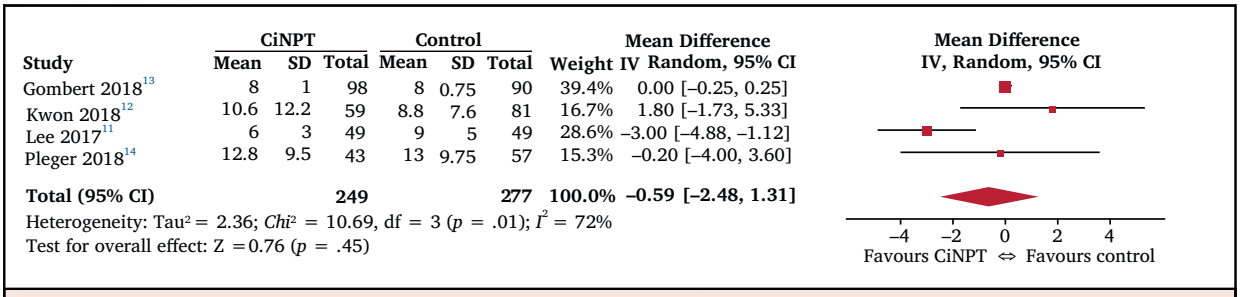

Figure 6. Mean difference of length of hospital stay in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

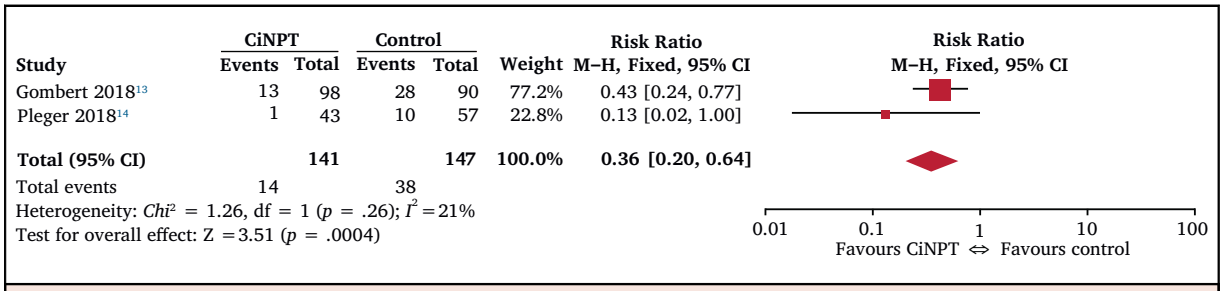

Figure 7. Risk ratio of antibiotic treatment in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

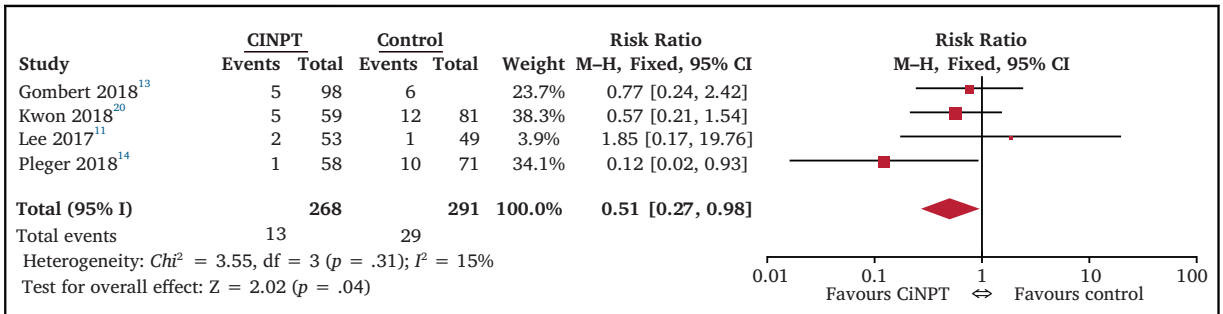

Figure 8. Risk ratio of surgical re-intervention in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

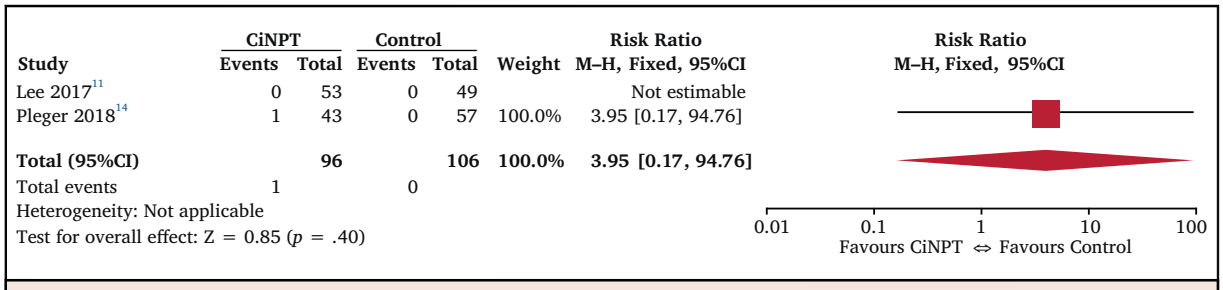

Figure 9. Risk ratio of 30 day mortality in randomised controlled trials reporting use of closed incision negative pressure wound therapy in vascular surgery. CiNPT = closed incision negative pressure wound therapy; M-H = Mantel–Haenszel test; CI = confidence interval.

the CiNPT group. However, it is evident in this analysis that the study by Gombert *et al.*[13] carried a disproportionate statistical weight of almost 45%, which could be attributed to the larger number of events (Grade I infections) in this study. Despite that, the heterogeneity remains low, hence improving the validity of these findings. In terms of safety outcomes, CiNPT did not increase the risk of mortality or length of hospital stay.

These results are in agreement with previously published meta-analyses on non-vascular procedures.[9,10] While it is important to note that there is a decrease in risk of Grade I infections, it is the fewer Grade III infections and surgical re-

Table 2. Summary of outcomes and quality of evidence assessment based on the GRADE approach in the five randomised controlled trials of closed incision negative pressure wound therapy in vascular surgery.

Outcomes	Pooled effect estimates		Pooled relative effect Risk ratio (95% CI)	Number of studies	Number of incisions or patients	Statistical heterogeneity (%)ik	*p*	Quality of evidence (GRADE)
	CiNPT%	Control%						
Overall risk of infection	7.8	24.8	0.31 (0.21 − 0.47)	5	691	0	.42	++++
Grade I infection	4.5	12.5	0.35 (0.20 − 0.60)	5	691	0	.75	++++
Grade II infection	3.0	8.1	0.60 (0.16 − 2.23)	5	691	43	.07	+++[a]
Grade III infection	0.3	4.2	0.17 (0.04 − 0.68)	5	691	0	.58	++++
Length of hospital stay − d	9.1	9.4	MD −0.59, −2.48 to 1.31	4	526	792	.01	+++[a]
Use of antibiotics	9.9	25.9	0.36 (0.20 − 0.64)	2	288	21	.26	++++
Surgical re-intervention	4.9	10.0	0.51 (0.27 − 0.98)	4	559	15	.31	++++
Mortality	1.0	0.0	3.95 (0.17 − 94.76)	2	202	NA		++++

CiNPT = closed incision negative pressure therapy; CI = confidence intervals; MD = mean difference; NA = not available.
++++ = high quality of evidence; +++ = moderate quality of evidence; ++ = low quality of evidence; + = very low quality of evidence.
[a] Downgraded by one level for moderate statistical heterogeneity.

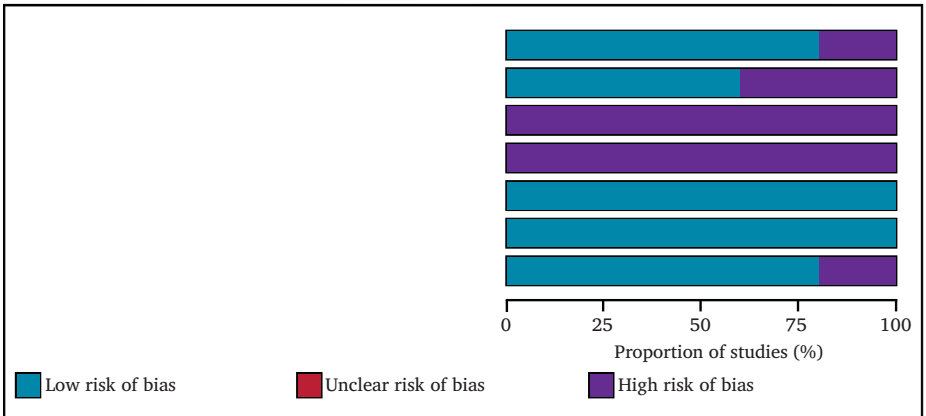

Figure 10. Risk of bias amongst the five randomised controlled trials of closed incision negative pressure wound therapy for surgical site infection.

interventions that are particularly relevant clinically. However, interestingly, this did not translate to improvements in other major clinical outcomes including mortality, length of hospital stay, and Grade II infections. Hence, caution must be exercised when interpreting these outcomes. Although CiNPT seems to have reduced the risk of Grade III infections significantly, this effect is largely driven by one study.[20] In that study, however, patients included in the randomisation were those deemed to be already at high risk of wound complications, as determined by the presence of certain criteria including a body mass index above 30 kg/m^2, poorly controlled diabetes, poor nutrition, and significant overlying abdominal pannus. Hence it is perhaps unsurprising that a standard dressing may not suffice and CiNPT plays a larger role in reducing the risk of wound infections in these high risk patients. Furthermore, results from such a risk stratified population may be less generalisable.[20] A similar trend was noted for re-intervention, which was driven by one study by Pleger *et al.*[14] In the subgroup analysis of this study however patients in the CiNPT group with a hospital stay longer than eight days had significantly fewer re-interventions as compared with the control group. This would suggest that the combination of prolonged CiNPT use and hospital stay may prevent wound complications that occur much later after the initial surgery. Furthermore, the early removal of CiNPT could lead to wound contamination during wound dressing changes, subsequently leading to complications that may require revision surgery.[14] Hence, it may be reasonable to extend the application time of CiNPT in order to maximise its potential benefits.

While diabetes, renal failure, age, and obesity are known risk factors for wound infections,[22,23] these confounding factors could not be accounted for by performing a meta-regression analysis, given the small number of studies. Recently, an international multidisciplinary consensus recommendation by Willy *et al.*[21] recommended CiNPT for patients with one or more risk factors, or in those who has a significant history for developing surgical site complications. Albeit contrary to the consensus recommendations,[21] Pleger *et al.*[14] in their RCT, constructed a scoring system in which risk factors with the highest significance were assigned two points while risk factors with a lower significance were assigned one point. A minimum threshold of 8 points was used to justify the indication for CiNPT.[14] The need for a scoring system could stem from the considerably higher costs of CiNPT compared with conventional wound dressings,[12] and should be a consideration that future

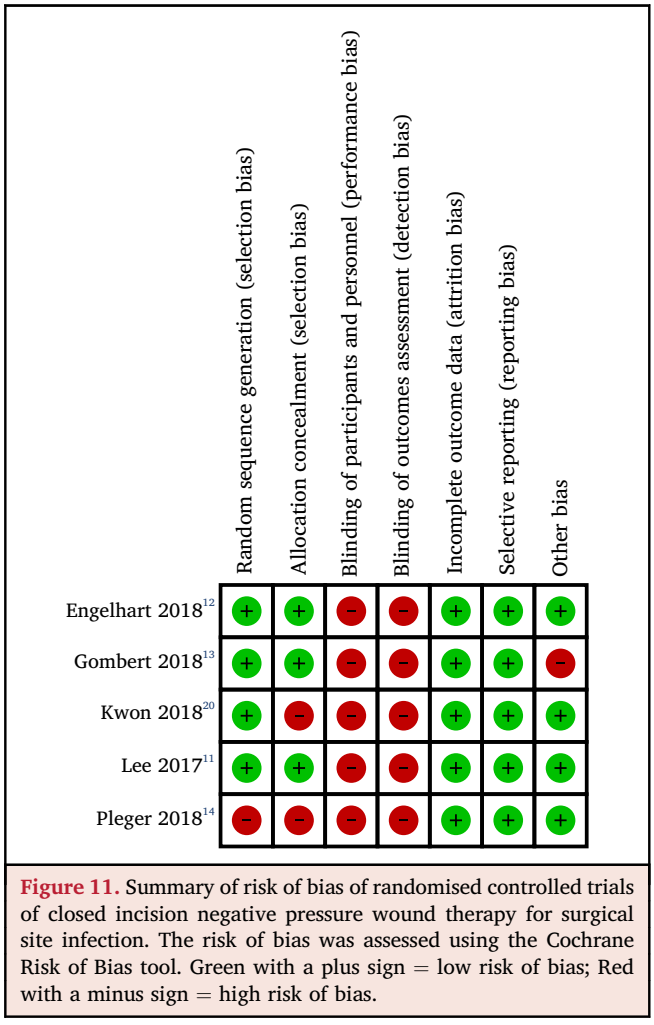

Figure 11. Summary of risk of bias of randomised controlled trials of closed incision negative pressure wound therapy for surgical site infection. The risk of bias was assessed using the Cochrane Risk of Bias tool. Green with a plus sign = low risk of bias; Red with a minus sign = high risk of bias.

studies might consider incorporating. A single PREVENA™ unit for instance, costs $495, as reported by Matatov *et al*.[1] However, the study was not able to perform a cost analysis due to the lack of data. Although such upfront costs may be justified by the prevention of subsequent, additional health care costs arising from complications,[10] it remains a controversial issue with relatively weak evidence,[24] warranting the need for large cohort studies investigating cost savings in all surgical disciplines.

Based on the GRADE system, a weak recommendation can be made regarding the use of CiNPT in vascular surgery. This is given the low confidence in the effect estimates and lack of clinical relevance since were no improvements in major clinical outcomes. The aspect of cost has not been adequately studied and is also a potential trade off for the use of CiNPT.

Unfortunately, this study was not able to compare various NPT systems. The RCTs included in this meta-analysis employed the PREVENA™ Incision Management Therapy System, which raises the issue of whether other systems are as effective and safe for vascular surgery. The PICO™ Single Use Negative Pressure Wound Therapy System (Smith & Nephew, London, UK), for instance, is similar to the PREVENA™ in removing wound secretions by evaporation and using less negative pressure.[14] However, only one RCT by Svensson *et al*.[15] used the PICO™ system. Hence, further research on other devices is urgently needed.

Despite being only RCTs, these findings must be interpreted in the context of known limitations. Clinical heterogeneity was also inevitable as the studies assessed different surgical procedures. Lastly, publication bias was not accounted for because of the lack of studies.

CONCLUSION

There is evidence demonstrating that closed incision negative pressure therapy (CiNPT) reduces the risk of Grade I, Grade III surgical site infections and re-interventions following vascular surgery. Interestingly, while the decrease in Grade III surgical site infections and re-interventions are clinically relevant, this has not translated into differences in Grade II infection and other post-operative outcomes including length of hospital stay, and 30 day mortality. Using the GRADE approach, a weak recommendation can be made regarding the use of CiNPT. However, further well designed randomised controlled trials with larger sample sizes, should be performed, particularly on other devices.

DISCLOSURES

All authors have no conflicts of interest to disclose.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.12.021.

REFERENCES

1 Matatov T, Reddy KN, Doucet LD, Zhao CX, Zhang WW. Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients. *J Vasc Surg* 2013;**57**:791–5.
2 Turtiainen J, Saimanen E, Partio T, Karkkainen J, Kiviniemi V, Makinen K, et al. Surgical wound infections after vascular surgery: prospective multicenter observational study. *Scand J Surg* 2010;**99**:167–72.
3 Syed MH, Hussain MA, Khoshhal Z, Salata K, Altuwaijri B, Hughes B, et al. Thirty-day hospital readmission and emergency department visits after vascular surgery: a Canadian prospective cohort study. *Can J Surg* 2018;**61**:257–63.
4 Humphreys H. Preventing surgical site infection. Where now? *J Hosp Infect* 2009;**73**:316–22.
5 Giovannacci L, Eugster T, Stierli P, Hess P, Gurke L. Does fibrin glue reduce complications after femoral artery surgery? A randomised trial. *Eur J Vasc Endovasc Surg* 2002;**24**:196–201.
6 Stewart AH, Eyers PS, Earnshaw JJ. Prevention of infection in peripheral arterial reconstruction: a systematic review and meta-analysis. *J Vasc Surg* 2007;**46**:148–55.
7 Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg* 1997;**38**:553–62.
8 Stannard JP, Robinson JT, Anderson ER, McGwin Jr G, Volgas DA, Alonso JE. Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma. *J Trauma* 2006;**60**:1301–6.

9 Hyldig N, Birke-Sorensen H, Kruse M, Vinter C, Joergensen JS, Sorensen JA, et al. Meta-analysis of negative-pressure wound therapy for closed surgical incisions. *Br J Surg* 2016;**103**:477–86.

10 Semsarzadeh NN, Tadisina KK, Maddox J, Chopra K, Singh DP. Closed incision negative-pressure therapy is associated with decreased surgical-site infections: a meta-analysis. *Plast Reconstruct Surg* 2015;**136**:592–602.

11 Lee K, Murphy PB, Ingves MV, Duncan A, DeRose G, Dubois L, et al. Randomized clinical trial of negative pressure wound therapy for high-risk groin wounds in lower extremity revascularization. *J Vasc Surg* 2017;**66**:1814–9.

12 Engelhardt M, Rashad NA, Willy C, Muller C, Bauer C, Debus S, et al. Closed-incision negative pressure therapy to reduce groin wound infections in vascular surgery: a randomised controlled trial. *Int Wound J* 2018;**15**:327–32.

13 Gombert A, Babilon M, Barbati ME, Keszei A, von Trotha KT, Jalaie H, et al. Closed incision negative pressure therapy reduces surgical site infections in vascular surgery: a prospective randomised trial (aims trial). *Eur J Vasc Endovasc Surg* 2018;**56**:442–8.

14 Pleger SP, Nink N, Elzien M, Kunold A, Koshty A, Boning A. Reduction of groin wound complications in vascular surgery patients using closed incision negative pressure therapy (ciNPT): a prospective, randomised, single-institution study. *Int Wound J* 2018;**15**:75–83.

15 Svensson-Bjork R, Hasselmann J, Acosta S. Evaluation of inguinal vascular surgical scars treated with closed incisional negative pressure wound therapy using three-dimensional digital imaging-A randomized controlled trial on bilateral incisions. *Wound Repair Regen* 2018;**26**:77–86.

16 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Plos Med* 2009;**6**:e1000097.

17 Szilagyi DE, Smith RF, Elliott JP, Vrandecic MP. Infection in arterial reconstruction with synthetic grafts. *Ann Surg* 1972;**176**:321–33.

18 Schünemann HBeJ, Guyatt G, Oxman A. *Handbook for Grading the Quality of Evidence and the Strength of Recommendations Using the GRADE Approach*. 2013 [cited 2017 25 Sep]. Available from: https://gdt.gradepro.org/app/handbook/handbook.html.

19 Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;**5**:13.

20 Kwon J, Staley C, McCullough M, Goss S, Arosemena M, Abai B, et al. A randomized clinical trial evaluating negative pressure therapy to decrease vascular groin incision complications. *J Vasc Surg* 2018;**68**:1744–52.

21 Willy C, Agarwal A, Andersen CA, Santis G, Gabriel A, Grauhan O, et al. Closed incision negative pressure therapy: international multidisciplinary consensus recommendations. *Int Wound J* 2017;**14**:385–98.

22 Neumayer L, Hosokawa P, Itani K, El-Tamer M, Henderson WG, Khuri SF. Multivariable predictors of postoperative surgical site infection after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg* 2007;**204**:1178–87.

23 Imai E, Ueda M, Kanao K, Kubota T, Hasegawa H, Omae K, et al. Surgical site infection risk factors identified by multivariate analysis for patient undergoing laparoscopic, open colon, and gastric surgery. *Am J Infect Control* 2008;**36**:727–31.

24 Tuffaha HW, Gillespie BM, Chaboyer W, Gordon LG, Scuffham PA. Cost-utility analysis of negative pressure wound therapy in high-risk cesarean section wounds. *J Surg Res* 2015;**195**:612–22.