Application of Topical Negative Pressure (Vacuum-Assisted Closure) to Split-Thickness Skin Grafts

A Structured Evidence-Based Review

Ernest Anthony Azzopardi, MRCSEd, MSc Surg, MD,† Dean E. Boyce, MD, FRCS, FRCSEd, FRCS(Plast),† William A. Dickson, MBE, FRCS(Glas) FRCS,† Elayne Azzopardi, BSc, Hons, MSc,‡ James Hamish Ellsworth Laing, BSc, MBBS, FRCS(Plast),† Iain S. Whitaker, MA(Cantab), PhD, FRCS(Plast),† and Kayvan Shokrollahi, BSc, MB ChB, MSc, MSc LLM MRCS(Eng), FRCS(Plast)†§*

Introduction: Significant controversy surrounds the effectiveness of negative pressure wound therapy although it has been in use for decades. Although many clinicians favor this modality in relation to its practicality, ease of use especially in complex wounds, it has faced the same challenges as other dressings in relation to evidence base of efficacy in relation to a number of outcome measures. In view of the current financial pressures on health care systems worldwide, this structured review systematically challenges the evidence for perioperative application of topical negative pressure (TNP) to split-thickness skin grafts (STSGs) through evidence-based critical appraisal, and extrapolate the mechanisms of action on the mechanisms through which TNP may aid wound healing. Weighted evidence-based recommendations regarding the impact of TNP on split skin graft quality and quantity of take as outcomes.

Methods: Phase 1: Structured literature search. Phase 2: Retrieved articles were critically appraised for rigor and methodological validity by 3 independent authors, then stratified according to a validated "levels of evidence" framework. Graded "current best evidence" recommendations could therefore be proposed.

Results: Of the 220 studies retrieved in the initial search, 38 studies satisfied our quality of evidence criteria. Current best evidence supports 2 complementary trends explaining the mechanisms whereby STSG benefits from TNP. *Active stimulation of epithelial mitosis*: TNP creates mechanical stretch which stimulates multiple signaling pathways up-regulating growth- and mitosis-associated epithelial transcription factors. Topical negative pressure also promotes microcirculatory flow (graft and wound edge), stimulates angiogenesis and basement membrane integrity (grade C). *Prevention of complications:* significant reduction of graft lift-off by edema, exudates, subgraft hematoma, and reduction of shear when compared to traditional dressings (grade B). Topical negative pressure promotes significant qualitative improvement in the final STSG result studies (level 1B). The role of TNP in prevention of infection is, however, equivocal and further research is required. No evidence of harm from TNP application was reported.

Conclusions: Topical negative pressure increases quantity and quality of split skin graft take compared to traditional bolster dressings. The advantages are increased in irregularly contoured, technically difficult wounds and suboptimal recipient wound beds where it seems to be the best modality currently available. Large-scale randomized clinical controlled trials remain scanty in all areas of wound dressing research including negative pressure therapy.

Key Words: topical negative pressure, VAC, negative pressure wound therapy, split-thickness skin graft

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Split-thickness skin grafting (STSG) is a simple and versatile technique that has been applied with varying success across many specialties for a variety of indications. Simultaneously, topical negative pressure (TNP) has made significant inroads into wound care across the breath of specialties,[1–4] since it was originally described by Morykwas et al[5] and first published in the *Annals of Plastic Surgery*. Marriage of both techniques may result in increased wound healing rates and has become a well-recognized option for skin graft application and immobilization. However, the benefit of perioperative TNP application to STSG and, indeed, the mechanisms whereby TNP exerts its purported effects remain contentiously debated.

Several mechanisms for this technology have been proposed[6,7] but the literature still lacks an exhaustive critical appraisal of current best evidence on which adoption of this expensive technique may be justified. The lack of randomized control trials (RCTs) specific to this subject invalidates the adoption of a standard Cochrane approach. Our multicenter study group, therefore, adopted a structured current best evidence-based approach to review perioperative application of TNP to STSG, the proposed mechanisms of action and outcomes through a critical appraisal analysis and synthesis of the literature. Thereafter, the mechanisms supported by best evidence are presented as possible means through which TNP may affect wound healing. A beneficial effect from pretreating recipient beds with TNP therapy before eventual final reconstruction with STSG was very recently described.[8]

Bolster dressings are traditionally applied to secure the graft to the wound bed and probably remain the most common method for small to moderate wounds. Burns surgeons commonly cover extensive areas of body surface using staples or sutures without bolsters, but no meaningful objective comparison has been undertaken looking at graft take with different modalities. There is some evidence to show that irregularly contoured recipient sites, exuding wounds, poorly healing areas, and the presence of shear stress significantly reduce the success rate of STSG with traditional bolster dressings, increasing morbidity, pain, hospital stay, and cost.[6,9,10] Topical negative pressure wound therapy has been advocated as a potential solution to some of these issues. This review presents a structured, critical appraisal of the evidence investigating the role of TNP to STSGs, leading to graded, evidence-based recommendations.

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From the *Tissue Engineering and Reparative Dentistry, School of Dentistry, Cardiff University, Heath Park, Cardiff; †Welsh Centre for Burns and Plastic Surgery, Morriston Hospital, (Canolfan Llosgiadau a Llawfeddygaeth Blastig Cymru, Ysbyty Treforys), Swansea; ‡Research Institute for Health and Social Change, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Elizabeth Gaskell Campus, Manchester; and Mersey Regional Burns and Plastic Surgery Unit, Whiston Hospital, Liverpool, United Kingdom.

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Reprints: Kayvan Shokrollahi, BSc, MB ChB, MSc, LLM, FRCS(Plast), MRCS(Eng), Welsh Centre for Burns and Plastic Surgery, Morriston Hospital, Swansea, United Kingdom. E-mail: kshokrollahi@hotmail.com.

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METHODS

A multiplatform electronic and manual search was constructed across multidisciplinary databases including PubMed, Ovid EBSCO, CINAHL, AMED, and the Cochrane databases and unpublished doctoral theses databases for articles published in the last 10 years, in any language. Gray literature, manufacturer information, and doctoral theses repositories were also searched. A standardized approach was required to sieve through peer-reviewed literature published in the last decade. Although a limited amount of studies were encountered, these varied vastly from laboratory studies, mechanistic models, computerized simulation prediction, to clinical studies and included qualitative, quantitative, and mixed methodological approaches.

An evidence-based approach integrates the best available research to clinical practice,[11] such that clinical bedside decisions can be based on robust and valid rationale. It entails a reproducible literature strategy reducing literature retrieval. An evidence-based approach allows an in-depth appraisal of the literature for methodological rigor, reproducibility, impact, internal validity, and applicability and brings out recommendations for clinical practice and future research.[12,13]

To assign the contribution of each piece of research, a weighting of the quality of evidence presented therein, a critical analysis of each included article was performed independently by 2 authors, arbitrated by a third. These appraisals were based on validated appraisal frameworks for both qualitative[14] and quantitative[15] research. A "hierarchy of evidence framework" was applied to provide weighting to the published evidence according to its robustness and validity.[16,17]

The retrieval methodology is reported in Table 1. The retrieved primary literature was assessed for relevance by 3 authors in plenum. Each paper was graded based on the hierarchy proposed by the Oxford Centre for Evidence-Based Medicine.[16]

LITERATURE REVIEW

Two main themes arise in the literature which try and explain the effects of TNP application to STSG. The first proposes that TNP exerts its effects through enhancement of wound healing. This may occur quantitatively, through increased local blood flow, microdeformation stimulating mitosis, and local milieu equilibrium-shifts toward healing,[6,7,18] and qualitatively.[19] The second trend attributes the success of TNP application to STSG through preventing complications of bacterial infection, graft shear, and graft lift-off, especially in technically difficult areas.[6,20] The evidence underscoring both trends is analyzed below.

Promotion of Split-Thickness Graft Healing by TNP

The original study of Morykwas et al[5] on porcine models explored 5 possible mechanisms for TNP-mediated healing in secondary intention wounds. Their prospective cohort design (Table 2) reported a 4-fold increase in blood flow, an increased rate of granulation tissue formation and bacterial clearance. Their reproducible outcome measures and objective data collection methods increased internal validity and robustness of design. Two-sided paired *t* tests were used with Bonferroni correction. Bonferroni correction is useful when testing a number of independent hypotheses but it is very conservative and unlikely to reject the null hypothesis.[21] These results suggest that TNP increased local blood flow, which may be beneficial to skin grafts in watershed areas. A possible flaw is the lack of randomization which may have introduced sample bias. In fact, cohort studies are particularly poor in the assessment of treatment efficacy.[22] Also, the healing process was only observed for 30 minutes, in contrast to Chen et al[18] who continued follow-up until day 9. Follow-up was therefore insufficient and the study could only be classified at level 4 in our hierarchy of evidence model.[16]

Wackenfors et al[7] expanded on the study of Morykwas et al[5] through a cohort design to investigate the effects of TNP on microcirculation with increased distance from the wound edge and variable negative pressure. They reported a sustained increased perfusion of the wound edge with cyclic TNP. They also noted that the exerted effect was dependent on the type of tissue (increase in blood flow occurred closer to the wound edge in muscular as compared to subcutaneous tissue (3 cm, at −75 mm Hg). In practice, this may imply the need to vary TNP settings depending on the graft bed. Their rigorous approach is illustrated by the extensive reference to previous literature, use of clearly defined controls, and previously validated objective data-collection methods. The authors did not report how randomization of suction pressures was achieved or the study samples' baseline characteristics, including freedom from intercurrent disease. Data collection was not blind, increasing the possibility of observer bias. After these considerations, this study was classified as a poor quality cohort study (level 4 in Phillips et al[16]). Wackenfors et al[7] demonstrated an increased benefit from cyclical versus continuous TNP at the wound edge. Interestingly, Philbeck et al[23] suggested that intermittent therapy may provide rhythmic perfusion, hence, also stimulate mitosis. However, this may be limited by the pain experienced by some patients on cyclical TNP.

A cohort study by Chen et al[18] to investigate TNP-mediated wound healing found that TNP "promoted capillary blood flow velocity, increased capillary caliber and blood volume, stimulated endothelial proliferation and angiogenesis, narrowed endothelial spaces, and restored the integrity of the capillary basement membrane" (Table 3). Previous literature was extensively reviewed and used to justify the data collection methods. Data were triangulated and a longer follow-up was used than Morykwas et al.[5] These considerations increased the rigor and validity of the results. However, sample and reporting biases may have been introduced by the absence of sample randomization and double-blinding. Study units were not matched for baseline characteristics, possibly introducing confounding factors. Two-tailed independent *t* tests were used to compare studies and controls, however, a Bonferroni correction factor was not applied (the Bonferroni correction is a safeguard against multiple tests of statistical significance on the same data falsely giving the appearance of significance, as one out of every 20 hypothesis-tests will seem to be significant at the $\alpha = 0.05$ level purely due to chance). Their results suggest that TNP may be responsible for increasing capillary caliber, stimulation of angiogenesis, and blood volume. At the same time, TNP may improve circulation, restore membrane integrity, and reduce vessel permeability, hence wound edema. This cohort study was therefore classified as level 2b.[16]

Micromechanical forces exerted by TNP may significantly improve epithelial mitoses, and robust evidence derived from histological sections harvested after TNP application agrees with basic science research proving that mechanical stretch up-regulates epithelial growth and mitosis.[24–28] Saxena et al[19] investigated the observation that TNP achieved superior healing rates compared to traditional dressings, even when little exudate was extracted. A computer-generated model of TNP-wound interaction was generated using data derived from histological sections after TNP. Their simulation reported an undulating pattern of strain between 5% and 20%.

TABLE 1. The Literature Retrieval Process

Search terms	(((Vacuum AND Assisted AND Closure) OR (Negative AND Pressure AND Closure) OR Topical AND Negative AND Pressure)) AND (Split AND Thickness AND Skin AND Graft$))
Databases	AMED, PubMed; Cochrane Database of Systematic Reviews British Nursing Index; BMC, NLM, CINAHL; EMBASE; Ovid-MEDLINE In-Process and other non-indexed citations

TABLE 2. Study Summary (Morykwas et al[5])

Aim	A series of animal experiments are presented to form the foundation for a new subatmospheric pressure method for treating wounds	
Study design	Five arms	
Ethical considerations	Institutional approval reported	
Sample	Twenty-five 20-kg Cheshire pigs	
Arm	Data collection method	Result
1. Blood flow studies (cohort; control)	Laser needle probe—measured change in blood flow	Fourfold increase for intermittent TNP at 5 min VAC+ 2 min rest. Greatest increase at 125 mm Hg
2. Granulation tissue with continuous TNP (cohort; control)	Volume of granulation tissue	63.3% ± 26.1%
3. Granulation tissue with continuous TNP (cohort; control)	Volume of granulation tissue	103.4% ± 35.3%
4. Bacterial clearance (cohort; control)	Log organisms per gram of homogenized cultured tissue	$<10^5$ CFU/g in all sample units
5. TNP to flap (TNP presurgery and postsurgery; TNP presurgery TNP postsurgery; no TNP control)	Flap survival was expressed as a percentage of total	Pretreated and posttreated flaps had greatest survival at 72.2% ± 10%

They suggested that TNP may produce its effects through production of micromechanical forces that trigger cells to mitose in the presence of soluble growth factors. Their computer simulation suggests that a foam-based pressure delivery system may contribute to this stretch-induced mitotic induction. Mechanical stretching of cells has is in fact been well documented to stimulate epithelial growth and mitosis.[24–26] Mechanically induced changes in gene expression are thought to work via a variety of signaling pathways, leading to altered expression of transcription factors.[27,28] To study this, extensive research has been carried out by Peake and coworkers[29–31] regarding the mechanical induction of c-fos gene which has a role in the regulation of cellular proliferation. Analysis of the pathways responsible for mediating c-fos mechanoinduction was carried out using multiple inhibitors (of calcium signaling, stretch responsive membrane channels, and integrin-mediated cell attachment) and promoter (deletion) analysis. The results indicate that both integrin-mediated cell-matrix interactions and calcium signaling via mechanosensitive ion channels are required for c-fos induction, and these are integrated via multiple response elements in the c-fos promoter.

Table 5 summarizes 101 cases of technically difficult grafts including neovaginal, penile, and chronic ulcer resurfacing reported in the literature. Over a spread of 101 cases, 75 to 125 mm Hg of negative pressure (μ = 106 mm Hg; mode continuous) applied to split skin graft (range, 13–19/1000 thickness 3–5 mm mode average: meshed) was concordant to a mean successful graft take of 95%. The dangers of case-series bias on validity are well known.[32] However, this summary statistic compares favorably to an expected STSG failure rate of 15% to 30% when using bolster dressings.[33–35] This finding is in concordance with Blume et al[36] whose 10-year retrospective review found significantly improved graft survival.

TABLE 3. Study Summary (Chen et al[18])

Focus	"To study the mechanism through which vacuum-assisted closure (VAC) induces an increase in blood flow and reduces edema on skin wounds."
Background	TNP is widely accepted, however, the mechanism through which it influences wound healing and reduce tissue edema is unknown
Terms of reference	To assess (secondary aims) • Change in blood flow velocity and capillary caliber • Change in capillary density • Change in ultra structure of capillaries and endotheliocytes • To evaluate the process of wound healing
Study design	Nonrandomized nonblinded 4 armed cohort study with experimental controls on animal models. Thirty-two study units divided into 4 study groups as previously mentioned. On each, 1 ear was used as study and 1 as control. On each wound pressures of −5, −10, −15, and −20 kPa were used, for 20 min each separated by a 10-min interval. A control group (petrolatum gauze only). Microcirculation microscopy and image pattern analysis were used to observe the variation in wound microcirculation
Results	"VAC promoted capillary blood flow velocity, increased capillary caliber and blood volume, stimulated endothelial proliferation and angiogenesis, narrowed endothelial spaces, and restored the integrity of the capillary basement membrane."
Ethical consideration	Animals anesthetized. Institutional board review not mentioned.
Data analysis	Two-tailed independent *t* tests
Data presentation	Graphical representation, *t* tests with *P* values. Salient results: TNP increasing capillary caliber, stimulate angiogenesis and blood volume. At the same time TNP may improve circulation, restore membrane integrity, and reduce vessel permeability, hence wound edema.
External validity	This study illustrates the mechanisms through which TNP may benefit STSG in stages of healing: Through reduced wound edema, close graft-bed apposition may be achieved thus aiding adhesion and serum imbibition. Stimulation of angiogenesis and blood flow may aid revascularization.

TABLE 4. Study Summary (Moues et al[20])

Aim	"The aim of this study was to examine whether the increased rate of wound healing found in VAC-treated wounds could be explained by an effect on the bacterial balance"
Randomization	Achieved using sealed envelope method
Exclusion criteria	"Malignant disease, deep fistulas, sepsis, active bleeding, uncontrolled diabetes, psychiatric patients, and unstable skin around the wound"
Sample size	N = 54
Power calculation	Reported
Were the groups treated equally?	The same procedures were used for allocated treatment. No information is provided as to further wound handling or dressing; procedures to avoid cross-contamination.
Statistical analysis	Student 1-sample *t* test was applied to the regression gradient of logarithmically transformed data, to test whether the average reduction within a group was statistically significant. The 2-sample *t* test analysis was used to compare the average reduction between groups.
Objectivity of results	Validated bacterial culture methods were used. The authors described a double-blind RCT
Results	No significant difference in the number of organisms grown between the sample and control

Prevention of Complications

TNP and Bacterial Count

A common reason for STSG failure is infection.[37,38] The only RCT retrieved[20] did not find a significant reduction in total bacterial load through TNP. Patients were randomized to TNP or non-TNP treatment, and regular incision biopsies were cultured on several media. Clearly defined exclusion criteria (Table 4) reduced the risk of type 1 error. Reporting the method used for sample randomization reduced the risk of sample bias, whereas power calculations decreased the risk of type 2 error. Biopsies were cultured using standard techniques, and all patients were accounted for reducing risk of attrition bias. However, this study did have limitations, that is, the study was performed on a mixed hospital population, and no measures were described to avoid cross-contamination. Furthermore, patients with known immunosuppression were not excluded. The complex statistical analysis was poorly described and difficult to appraise. Despite using incision biopsies, culture results were not expressed per gram of homogenized tissue, as in the original RCT by Morykwas et al.[5] The complete absence of β-hemolytic streptococcal infection was surprising considering the destruction this can cause when present even in small numbers, and the conclusions should be viewed with caution when applied to the typical patient population requiring skin grafts. Because of the previously mentioned considerations, this study was placed at level 2b in Phillips et al[16] ("individual cohort study or low-quality randomized controlled trials").

Prevention of Graft Shear and Lift-off

Graft shear is a lateral force applied to a graft in relation to its bed, reducing the likelihood of successful graft take. Several studies[9,10,39–44] (Table 5) have explored the role of TNP in preventing this complication. Both shear and lift-off separate the graft from its recipient bed, resulting in graft failure. Commonly observed causes of lift-off in local practice include wound exudates and hematoma formation, usually secondary to oozing from the wound bed. Traditional bolster dressings rely on their absorbent nature to "mop up" this exudate. This may be successful in small wounds; however, the amount of edema or blood that can be absorbed is finite, and is an excellent culture medium for pathological organisms.

The ability of TNP to prevent graft lift-off by exudates was reported in 2 early studies by the original Wake Forest University Team.[5,45] These 2 cases series reported excellent success rates (>90% and approximately 100% take, respectively) and described the technique's versatility over a spectrum of acute/chronic conditions, age extremes, and technically difficult areas. A qualitative methodology served to illustrate initial results, forming a credible basis for future studies. However, the authors did not outline their data collection methods, and there was no evidence of baseline patient comparability, reducing the study's rigor. The results were difficult to follow through, raising concerns with internal validity. The study was therefore classified at level 4.[16]

The 101 individual cases reported in the literature[9,10,39–44] have been retrieved from the literature indicate a mean graft take of 95.5%. Publication bias and the nature of case reporting can lend little weight to this body of evidence perhaps with the exception of perhaps providing a credible starting point to demonstrate safety, applicability, and practicality. Also, the authors did not state the length of follow-up or the methods used to assess the take-rate. Nevertheless, these patients had remarkable comorbidities, contrasting sharply to Moisidis et al[46] who reported no significant quantitative differences in graft take. Interestingly, the results of Dainty et al[9] using intermittent pressure contrast with the earlier assertions of Schneider et al[45] that "high pressure is not required for a graft to take, but continuous contact certainly is."

Scherer et al[42] retrospectively compared a series of patients whose skin grafts were secured with either TNP dressings or traditional bolster dressings, and determined outcome as number of successes or failures. The authors[42] concluded that TNP dressings are a "safe and effective method for securing STSG, and are associated with improved graft survival." This study's clearly defined primary and secondary aims, and stepwise methodological description and clear reporting of basic data and results increase its reproducibility. However, the methodology elicits some concerns. Cases were defined as originating from the same level 1 trauma center; however, no specific inclusion/exclusion criteria were reported and data collection was neither randomized nor blinded exerted a confounding influence on the results, including introduction of retrieval and selection bias through lack of blinding. The authors do not discuss why 1-way analysis of variance was used when their 2-group case is more appropriately analyzed with Gosset *t* test. Furthermore, the authors used regrafting rate as the primary outcome measure, which is an unsatisfactory indicator of success/failure. In 2 control cases (traditional bolster), where the patient refused regrafting they were excluded from data analysis. This may have distorted data which would otherwise have been statistically robust. This study was thus classified as a poor-quality case-control design (level 3b).[16] Notwithstanding the apparent skew of results against TNP, the authors still reported a positive outcome.

In an individual case-control study on a porcine model, Simman et al[47] compared TNP-secured to traditionally bolstered STSG. They reported decreased edema, earlier resolution of the acute inflammatory phase, and faster narrowing of the separation plane. Taking

TABLE 5. Synthesis of Data From Case Studies and Case-Series

Author	Site	Case and Intercurrent Conditions	n	TNP (mm Hg)	Type of Pressure Applied	Mesh	Take
Blackburn et al[39]	Leg	Chronic leg ulcer vascular insufficiency	1	125	Continuous	1.5:1	95%
	Leg	Traumatic amputation	1	125	Continuous	1.5:1	98%
	Groin	Cystic hydradenitis suppurativa	1	125	Continuous	1.5:1	100%
Dainty et al[9]	Vagina	Neovagina postrecurrent ca cervix HIV HTN	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
	Vagina	Stage II Adenocarcinoma; IDDM HTN	1	100	Intermittent	1.5:1; 13–19:1000 thickness	80%
	Vagina	Skinning vulvectomy after Paget disease	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
	Vagina	Skinning vulvectomy after Paget disease IDDM HTN	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
	Vagina	Skinning vulvectomy post hydradenitis suppurativa	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
	Vagina	Skinning vulvectomy post hydradenitis suppurativa	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
	Vagina	Skinning vulvectomy post hydradenitis suppurativa	1	100	Intermittent	1.5:1; 13–19:1000 thickness	90%
Weinfeld et al[10]	Penis	Post excision of verrucous carcinoma	1	100	Continuous	15:1000 thickness	100%
	Penis and scrotum	Scrotal abscess	1	100	Continuous	15:1000 thickness	100%
	Penis	Scrotectomy post Fournier disease	1	100	Continuous	15:1000 thickness	100%
	Penis	Fournier disease, malnutrition	1	100	Continuous	15:1000 thickness	100%
Senchenkov et al[40]	Concealed penis	Post excision of scc	1	75	Continuous	1.5:1 unexpanded	100%
Stretter et al[41]	Leg	Chronic leg ulcer	1	125	Continuous	0.5 mm thick	100%
Scherer et al[42]	N/K	Burn injury	34	125	Continuous	0.3 mm thick meshed	96%
	N/K	Soft tissue loss		125	Continuous	0.3 mm thick meshed	96%
	N/K	Fasciotomy site coverage		125	Continuous	0.3 mm thick meshed	96%
Hallberg and Holmstrom[43]	Vagina	Mayer Rokitansky Kruster syndrome	1	125 then 75	N/K	Meshed	100%
Carson et al[44]	Lower extremities	Chronic wounds	50	125	Continuous	Meshed 1.5:1 expanded 1/12,000 in thick	100%
Statistics			101 n(t)	Range 75–125 average 105.8 mm Hg	mode: continuous	Range, 13–19/1000; range, 3–5 mm thick mode meshed	Mean take 95%

HIV indicates human immunodeficiency virus; HTN, hypertension; IDDM, insulin dependent diabetes mellitus; n, patient; NK, not known; n(t), total number of cases; SCC, squamous cell carcinoma.

multiple case and control wounds from the same model minimized confounding factors. The rigorous approach is underscored by the authors' attempts at objective data collection and interpretation through multiple skin biopsies which were interpreted blindly. Validity was also increased by repeated follow-up until day 11. Statistical analysis was performed with repeated measures 1-way analysis of variance, similarly to Scherer et al.[42]

Only 1 RCT addressing both qualitative and quantitative effects of TNP on STSG was retrieved. Moisidis et al[46] investigated "whether STSG take is improved with the application of TNP dressings as compared with bolster dressings." In this trial, 22 patients' wounds were divided into superior and inferior halves, and TNP or bolster dressings were randomized to a part of each wound separated by an intervening bridge. Moisidis et al[46] reported a significant qualitative difference in favor of TNP-dressed STSG but, surprisingly, no quantitative difference. The meticulously reported study-design inclusion criteria, randomization methods, and reportage loss to follow-up (<20%) underscore the rigorous approach taken in this elegant study. These factors increased the results' validity. The quantitative outcome ("percentage of epithelialization recorded by gross inspection") may have been subject to reporting bias: using a recording grid may have increased accuracy of data collection. This may have been mitigated by blinded data collection.

The main concern about this otherwise good RCT is whether the 2 treatments were truly independent. The same wound was partly treated with TNP and partly with bolster dressings, with an intervening bridge about which the authors did not comment. Topical negative pressure to a wound may alter microhemodynamics, a considerable distance away from the wound edge, especially in subcutaneous tissue which formed the main subcohort of wounds in this study. In their porcine models, Wackenfors et al[7] noted an increased blood flow up to 3 cm away from the wound edge with pressures of −75 mm Hg. Therefore, it may be possible that the bolstered area, which in Moisidis et al[46] was always adjacent to the TNP dressing, may have been subjected to the effects of TNP. If so, the variables compared would not be independent, raising concerns about the validity of the results. This study was therefore also classified at level 2b.[16]

The elegant double-masked RCT of Llanos et al[48] was performed on wounds 33 cm^2 average size, on typically mobile areas such as the hand and foot and mechanisms notorious for producing oozing wounds (eg, burns). In contrast to Moisidis et al[46] who reported a significant reduction of the lost graft area and shortened length of hospital stay. Reporting the methodology of randomization, the well-defined inclusion/exclusion criteria reduce risk of sample and reporting bias. Their method to replicate TNP substantially reduced operational costs, reducing resource allocation and small center bias. The choice of statistical tests was underpinned by an informed discussion. This study satisfied all the requirements of the CONSORT statement (2001),[49] underscoring a robust methodology and valid results. This exemplary RCT was therefore classified as level 1B.[16] However, 1 methodological difficulty was the use of wall suction, which can be subject to pressure drift.

TABLE 6. Evidence Supporting the Role of Perioperative Application of TNP to STSGs

Application of TNP to STSG may promote blood flow and microcirculation to the graft bed, and round the wound edges, stimulate angiogenesis and integrity of the basement membrane (grade C)
Chen et al,[18] level 2b; Morykwas et al,[5] level 4; Wackenfors et al,[7] level 4; Saxena et al,[19] level 5
Application of TNP may reduce graft loss due to lift off and shear, through reduction of edema exudates, and hematoma when compared to traditional dressings (grade B)
Llanos et al,[48] level 1b; Scherer et al,[42] level 3; Simman et al,[47] level 3b; Morykwas et al,[5] level 4; Blackburn et al[39]; Dainty et al[9]; Weinfeld et al[10]; Senchenkov et al[40]; Stretter et al[41]; Scherer et al[42]; Hallberg and Holmstrom[43]; Carson et al,[44] level 5 vs Moisidis et al,[46] level 2; no significant change
Application of TNP to STSG may result in significant qualitative improvement in split skin graft take compared to traditional bolster dressings
Moisidis et al,[46] level 2; Saxena et al,[19] level 5

DISCUSSION AND RECOMMENDATIONS

Literature published in the last 10 years suggests TNP influences active graft take and the rate of complications. Current best evidence suggests that the application of TNP to STSG may promote blood flow and microcirculation to the graft bed, around the wound edges, stimulate angiogenesis and integrity of the basement membrane (grade C). Complementing this effect, application of TNP may reduce graft loss due to lift off and shear, through reduction of edema, exudates, and hematomas when compared to traditional dressings (grade B). Application of TNP to STSG may result in significant qualitative improvement in split skin graft take compared to traditional bolster dressings. Data synthesis from Table 5 indicates that current best evidence suggests a highly successful take rate even at day 3. Furthermore, the case-series in Table 5 reports a 95% graft take in complicated cases. Naturally, case-series data are open to the possibility of reporting bias; however, these pooled data match the general outcome trends from other studies including Llanos et al.[48] Only 1 study suggested no significant difference[46] between TNP and traditional bolster dressings, and the validity of this study's qualitative findings may have been affected by nonindependent experimental conditions. Topical negative pressure is therefore proposed as the dressing of choice for STSG applied to complex, large, exuding, irregularly contoured wounds.

Evidence on the effect on TNP on quality of the graft take rests within level 2 to 5 evidence which demonstrated a positive albeit moderate effect. The evidence supporting these conclusions is summarized in Table 6. No study reported any deleterious effect arising from TNP application to graft take.

CONCLUSIONS

This systematic review suggests that TNP may impart a considerable advantage to split skin grafting over traditional dressings in quality and quantity of take. The current best-evidence recommendations provide a robust rationale for the continued use of TNP to STSG especially in complex, large, exuding, irregularly contoured wounds. Clinicians will be guided by this and future evidence, individual patient factors, and costs when deciding on the most appropriate application of TNP to skin grafts. The advantages in relation to graft take rates for complex procedures may offset any additional costs from TNP, and formal cost-effectiveness analyses would be a useful avenue for future study.

Well-conducted randomized clinical controlled trials in this area are sparse, and until a formal meta-analysis of randomized trials can be undertaken, herein lies the best consolidation of the evidence base that exists to date.

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