Evidence Summary: Non-contact low-frequency ultrasound in wound management

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QUESTION

What is the best available evidence on the effectiveness of non-contact, low-frequency ultrasound (NCLFUS) in wound management?

Note: NCLFUS is a different therapy to contact low-frequency ultrasound therapy used for wound debridement.

SUMMARY

Non-contact, low-frequency ultrasound (NCLFUS) is an intervention that delivers ultrasound at a low-frequency range via a saline mist without direct contact with the wound[1]. The evidence for effectiveness of NCLFUS comes from a small volume of evidence. While low and very low quality studies demonstrate some improvement in wound healing rates when NCLFUS is used in conjunction with debridement and moist wound healing principles[2] (Level 1.b evidence), comparative studies (including a good quality randomised controlled trial)[3] found no improvement in wound healing that could be attributed to the use of NCLFUS (Level 1.c evidence). The evidence (as presented below) on the efficacy of NCLFUS in treating infection is conflicting.

BACKGROUND

NCLFUS is an intervention that delivers ultrasound at a low-frequency range via a saline mist. There is no direct contact with the wound; recommended use is 0.5–2 cm above the wound surface. The ultrasound is thought to stimulate vasodilation and blood flow to the wound, increase angiogenesis, promote release of growth factors and increase collagen in the wound[1] (Level 5.c evidence). It is also thought to have a role in reducing inflammation, bio-burden and biofilm[1] (Level 5.c evidence). However, studies that included before/after measurement of pro-inflammatory cytokines have contradictory findings[4,5] (Levels 1.c and 4.c evidence). Although NCLFUS is sometimes discussed as a method of wound debridement, there is no evidence it is effective for this outcome and the manufacturer does not promote the intervention for this use[1] (Level 5.c evidence).

In all the identified studies, NCLFUS was delivered at a frequency of 40 kHz and at a low intensity (0.2 to 0.6 W/cm^2) with the transducer held 0.5–2 cm from the wound bed. Treatment duration is based on wound size and ranges from three to 20 minutes per session. In most studies, treatment was delivered three times per week[2] (Level 1.b evidence). In most of the studies the wound was debrided as required (method unstated) before NCLFUS was administered. A wound dressing selected to promote moist wound healing was applied after the NCLFUS therapy and other interventions where appropriate were also used to promote healing (for example, pressure redistribution in pressure injuries, compression to manage venous vascular aetiologies)[2] (Level 1.b evidence).

CLINICAL BOTTOM LINE

Effectiveness in promoting healing in chronic wounds

- Eight studies (most are presented below) were included in a meta-analysis that found a mean wound area reduction of 85.2% (95% confidence interval [CI] 64.7% to 97.6%) after seven weeks of treatment with NCLFUS (n=4 studies, 188 participants). This compared to a mean wound area reduction of 62% for historical controls (n=218) receiving standard moist wound healing treatments[2] (Level 1.b evidence). It is unclear if this represented a significant result for NCLFUS as there was no between-group comparison and participants receiving NCLFUS also received standard wound care[3].
- A prospective randomised controlled trial (RCT) compared NCLFUS plus standard wound care (n=19) to standard wound care alone (n=17) for participants with hard to heal venous leg ulcers (VLUs) that had persisted for at least 10 weeks. In this trial standard wound care consisted of debridement, weekly wound cleansing and application of a non-adherent dressing and compression therapy. After eight weeks of treatment, there was no significant difference between groups for mean percentage change in wound area (NCLFUS –46.6% versus standard care alone –39.2%, p=0.565). There were also no significant differences between groups for secondary wound healing outcome measures[3] (Level 1.c evidence).
- A prospective RCT compared NCLFUS to treatment with sham ultrasound for healing shallow diabetic foot ulcers. All wounds were treated with a basic dressing (moistened gauze) and received baseline sharp/surgical debridement. After 12 weeks, there was no significant difference in complete healing rate in the intention-to-treat population (n=133, 26% versus 22%, p=0.69). There was a significant difference in complete healing rate favouring NCLFUS in the population of people who completed their assigned treatment course (that is, per-protocol population; 40.7% versus 14.3%, p=0.036). Mean time to healing also favoured the NCLFUS (p<0.014)[6] (Level 1.c evidence).
- In a second RCT participants with chronic ulcers associated with critical limb ischaemia (n=70) were treated with NCLFUS or daily debridement (method not stated) and standard wound management. More wounds in the NCLFUS group achieved greater than 50% wound healing by 12 weeks (63% versus 29%, p<0.01). The number of wounds achieving complete healing was not reported[7] (Level 1.c evidence).
- In a very small, underpowered RCT (n=12), participants with small (maximum 2.1 cm^2) chronic diabetic foot ulcers were assigned to three treatment groups: a

control group receiving standard care (n=4), a group receiving standard care plus weekly NCLFU (n=4) and a group receiving standard care plus three times weekly NCLFUS. The group receiving three times weekly NCLFUS achieved a significantly greater reduction in wound surface area by week five compared to the other groups (85% versus 25% versus 39% (control), p<0.05). The control group achieved greater healing than the group receiving once weekly NCLFUS[5], although there was no statistically significant differences between these two groups over time (Level 1.c evidence).

- In a prospective cohort study, 23 patients with 29 wounds of mixed aetiology were treated with NCLFUS. Over half of the wounds also received other treatments (primarily the application of a biological dressing — bioengineered tissue replacement) after reaching a healing plateau or demonstrating no healing after two–four weeks with NCLFUS treatment alone. When indicated, sharp/surgical debridement was also performed. Nine wounds (31%) achieved total healing with NCLFUS alone. Eleven wounds (37.9%) achieved healing when additional treatments were added to the NCLFUS regimen. Healing rate was comparable to that demonstrated by an historical control group (68.9% versus 72.02%)[8] (Level 3.c evidence).
- In a case series report participants with Category/Stage III pressure injuries (n=13, n=11 completed study) received NCLFUS daily for six days. A mean wound area reduction of 26% and a mean wound volume reduction of 20% were reported (p value not reported)[9] (Level 4.c evidence).
- In an uncontrolled prospective study, participants with VLUs (n=10) achieved a mean reduction in wound surface area of 42% (p=0.004) after receiving NCLFUS for four weeks. One patient achieved complete wound closure[4] (Level 4.c evidence).
- A retrospective chart review that identified 48 patients who received NCLFUS for VLUs, arterial post-surgical and trauma wounds, and other wound types found that 24% of wounds had achieved complete closure in a mean period of 4.3 weeks. There was median wound size reduction of 92% (p<0.0001) and significant improvement in documented wound exudate levels (p=0.03)[10] (Level 4.c evidence).
- In another retrospective record review, 41 patients were identified as receiving treatment with NCLFUS for surgical, trauma or chronic wounds. After between three and 16 weeks treatment, 38% of wounds achieved complete healing. Mean percentage reduction in wound area and wound mean reduction in wound volume after NCLFUS treatment (three to 16 weeks) were both 60% (p<0.0001)[11] (Level 4.c evidence).

Effectiveness in promoting healing in suspected deep tissue injury

- In a retrospective study, 127 cases of suspected deep tissue injury (SDTI) were reviewed and classified as cases or controls based on whether NCLFUS was administered. An SDTI assessment tool developed for this study was applied retrospectively to photographs to assess severity based on skin integrity, wound colour and total surface area. The groups were equivalent for SDTI severity at baseline, but the NCLFUS group had larger mean wound surface area (p value not reported) at baseline. The NCLFUS group achieved a significant reduction in SDTI severity scored, compared with the control group (p<0.00). The NCLFUS group also had greater spontaneous resolution (18% versus 2%)[12] (Level 3.c evidence).

Effectiveness in managing infection in chronic wounds

- An RCT exploring treatment of chronic wounds of mixed aetiology (n=133) found no significant difference in bacteria levels between wounds treated with NCLFUS compared with sham ultrasound[6] (Level 1.c evidence).
- In a case series report, 13 participants (n=11 completed study) with Category/Stage III pressure injuries with a baseline bacterial count of >105 CFU/g of tissue received NCLFUS daily for six days. A comparison of cultures taken via wound biopsy at baseline and at two weeks indicated there was a mean reduction of bio-burden from 4 x 107 to 2 x 107 CFU/g of tissue (p value not reported)[9] (Level 4.c evidence).
- In an uncontrolled prospective study, chronic venous leg ulcers (n=10) did not demonstrate any significant reduction in *S. aureus*, *P. aeruginosa* or *K. kristinae* after four weeks of NCLFUS treatment[4] (Level 4.c evidence).
- A retrospective chart review identified five chronic wounds with clinical signs of infection (confirmed via wound swab) that received NCLFUS. After four weeks of treatment with NCLFUS, 80% of wounds were infection-free[10] (Level 4.c evidence).

CHARACTERISTICS OF THE EVIDENCE

This evidence summary is based on a structured database search using the search term non-contact low frequency ultrasound. The evidence comes from:

- A systematic review of studies of various design[2] (Level 1.b evidence).
- Randomised controlled trials[5-7] (Level 1.c evidence).
- A prospective cohort study with an historic control[8] (Level 3.c evidence).
- A retrospective cohort study[12] (Level 3.c evidence).
- Retrospective case series reports[4,9-12] (Level 4.c evidence).
- Expert opinion[1] (Level 5.c evidence).

BEST PRACTICE RECOMMENDATIONS

The best quality evidence suggests that wounds treated with non-contact low frequency ultrasound for at least three times per week for up to 16 weeks in conjunction with standard care (debridement and contemporary moist wound healing strategies) do not heal significantly faster than wounds receiving standard care alone. (Grade B)

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