



Amnion grafts for diabetic foot ulcers — yes or no?

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Welcome to the latest *Diabetes Digest* which, as ever, includes my commentary and some other publications that you might find interesting and useful in your daily practice. The paper that I have chosen to comment upon is a systematic review by Lakmal et al (2021) on the rationale for the use of amniotic membrane allografts in the treatment of diabetic foot ulcers (DFUs). The push to use amniotic membranes in the treatment of DFUs has been slow, but will surely become more prominent when considering claims of improved healing rates of hard-to-treat DFUs. This systematic review, as well as others in the literature, seeks to address the effectiveness of the use of these membranes. The authors used a standard methodology searching Pubmed, Cochrane library and Google scholar from January 1, 2000, and March 30, 2020, using the search terms “Amnion” OR “Placenta” AND “Diabetic foot” (MeSH terms) in the title or the abstract field. The authors searched for observational studies in terms of randomised controlled trials, prospective cohort studies, retrospective cohort studies and case series. In all, 64 citations were identified and all were from 2010 onwards.

Eligibility criteria included: full text papers, presence of diabetes type 1 and 2, and different preparation of amniotic allografts (dehydrated, cryopreserved and stem cell extractions). RCTs comparing amniotic membrane versus standard or conventional care were included. Studies designed with the aim of analysing the molecular basis without measuring clinical improvement of the ulcers were excluded, as were case studies. Data were extracted on trial design, study setting, amniotic membrane preparation methods used, control interventions, outcome measures and statistical analysis. Outcome

measure data regarding healing time, percentage healed, recurrences and adverse outcomes were extracted.

From 64 identified studies, only 12 met the inclusion criteria. Of these, eight were RCTs (5 multicentre) involving 454 patients (244 amnion, 210 control) with a mean ulcer size 5 cm², two were prospective studies (28 amnion treated) and two were retrospective studies (92 amnion treated) with a mean ulcer size ≥5 cm². All these studies except one (from Spain) were conducted in the USA. The DFU locations were varied with a mean duration of >28 days. The mean healing times for the amnion groups was very varied but significantly faster ranging from 3 to 26 weeks compared with the control groups.

In six RCTs, the follow-up duration was 12 weeks, while in the other two, it was 6 weeks. The prospective and retrospective studies included data until complete wound closure was achieved.

Just two of the studies examined ulcer recurrence rates, with one showing a recurrence rate in the amnion group of 14.3% versus 83.3% at 90 days, while the other found 5% recurrence versus 14% in the amnion and control group, respectively, at 112 days.

The different amniotic products used were Amnioband® (MTF Biologics), AmnioExcel® (Integra), EpiFix (MiMedx), Apligraf® (Organogenesis), Grafix® (Osiris), NEOX® CORD (Amnio Medical). The authors conclude that the current evidence suggests the use of amniotic membrane preparations for resistant DFUs may achieve relatively fast healing wound rates, but more evidence is required. In summary, I believe further research is needed, particularly in regards to ulcer relapse. ■

Lakmal K, Basnayake O, Hettiarachchi (2021) Systematic

JACC Cardiovasc Interv

Contemporary revascularisation strategies and outcomes among patients with diabetes with critical limb ischaemia: Insights from the National Inpatient sample

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓✓

1 Due to there being little in the literature regarding outcomes following revascularisation for critical limb ischaemia (CLI) in patients with diabetes, the authors set out to evaluate temporal trends in the frequency of revascularisation and associated outcomes in patients with diabetes and CLI.

2 The 2002-2015 National Inpatient Sample database was examined to determine temporal trends in hospitalisation for CLI. The central outcome of the study was in-hospital mortality.

3 A total of 1,222,324 hospitalisations in the US were covered by the study and it was found that the number of hospitalisations for CLI among patients with diabetes increased over time ($p < 0.001$). The use of lower-extremity revascularisation was found to increase, while in-hospital mortality decreased.

4 Revascularised patients had lower in-hospital mortality and major amputation compared with the individuals treated medically. The individuals who underwent surgical revascularisation had higher in-hospital mortality rates, but lower major amputation rates.

Ebadawi A, Elgendy IY, Saad M et al (2021) Contemporary revascularisation strategies and outcomes among patients with diabetes with critical limb ischaemia: Insights from the National Inpatient sample. *JACC Cardiovasc Interv* S1936–8798(20): 32311–6

Trials

Acupuncture in diabetic neuropathy - protocol for the randomised, multicentre ACUDPN trial

Readability ✓✓✓
 Applicability to practice ✓✓
 WOW! Factor ✓✓✓

1 Evidence in the literature is unclear about acupuncture's use when treating patients with diabetic peripheral neuropathy. The ACUpuncture in Diabetic Peripheral Neuropathy (ACUDPN) trial aimed to investigate the effectiveness of acupuncture for the treatment of diabetic peripheral neuropathy (DPN) symptoms.

2 A total of 110 type II patients will be treated with acupuncture treatment by clinicians in outpatient units in Germany, all of which had clinical symptoms of DPN in the feet and legs. Patients are to be randomised in a 1:1 ratio to receive either semi-standardised acupuncture plus routine care or just routine care alone. Twelve acupuncture treatments will take place per patient over the course of 8 weeks.

3 The primary outcome studied will be the overall DPN-related complaints in the extremities after 8 weeks as measured by the Visual Analog Scale (VAS). Other outcome measures include DPN-related pain, the Neuropathic Pain Symptom Inventory (NPSI) and Diabetic Peripheral Neuropathic Pain Impact (DPNPI) scores.

4 The results of this trial will be available in 2021 and it is hoped that they will help determine whether or not acupuncture can be considered effective for the treatment of DPN.

Dietzel J, Hörder S, Habermann IV et al (2021) Acupuncture in diabetic neuropathy -protocol for the randomised, multicentre ACUDPN trial. *Trials* 22(1): 164

Can J Diabetes

Prevalence and risk evaluation of diabetic complications of the foot among adults with type 1 and type 2 diabetes in a large Canadian population (PEDAL Study)

Readability ✓✓✓✓
 Applicability to practice ✓✓✓
 WOW! Factor ✓✓✓

1 This study aimed to determine the prevalence and types of early foot pathology in a large, Canadian, community care-based diabetes population, as awareness of, and screening for, modifiable early pathologies has to this point been inconsistent.

2 A retrospective, observational analysis of the LMC Diabetes & Endocrinology foot care program launched in 2017 to examine foot pathologies associated with vascular, nerve, nail, dermatologic complications and foot deformities was analysed.

3 A total of 5,084 individuals were assessed, 470 of which had type 1 diabetes and 3,903 with type 2 diabetes, with reduced pedal pulses, sensory neuropathy and onychomycosis reported in 8.9%, 16.7% and 14.5% in the type 1 diabetes group and 19.4%, 26.6% and 28.7% in the type 2 group, respectively. Across both groups, hyperkeratosis was present in 51% and foot deformities in 44.5%.

4 The importance of consistent screening was underlined by the findings of the study in order to effectively alleviate the morbidity and economic burden of lower-limb complications.

Aronson R, Chu L, Joseph N, Brown R (2020) Prevalence and risk evaluation of diabetic complications of the foot among adults with type 1 and type 2 diabetes in a large Canadian population (PEDAL Study). *Can J Diabetes* S1499–2671(20): 30466–4

J Wound Care

Expanded negative pressure wound therapy in healing foot ulcers: a prospective randomised study

Readability ✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓

1 The researchers set out to evaluate the benefits of treating diabetic foot ulcers (DFU) by negative pressure wound therapy (NPWT), in order to achieve reduced and more evenly distributed lateral tension lines across the wound.

2 Patients were randomly assigned into either the NPWT control group or the NPWT+ group. In terms of the former, patients were treated in a traditional manner, while in the NPWT+ group, foams were shaped to fit the wound exactly and then an additional foam was then wrapped around the foot.

3 Fifty-nine individuals were randomised into the two groups: 29 in the NPWT+ group and 30 in the NPWT group. Median healing time was the primary objective (NPWT+ 19 days, interquartile ratio (IQR) 7.5; NPWT 33 days, IQR 16; $p < 0.00001$) and complete wound healing at 3 weeks (NPWT+ 55.20% NPWT 26.70% $p = 0.02$). Secondary endpoints were the number of major amputations and the number of infections.

4 In conclusion, NPWT significantly reduced wound closure times and accelerated healing in the DFUs under observation.

Campitiello F, Mancone M, Della Corte A et al (2021) Expanded negative pressure wound therapy in healing foot ulcers: a prospective randomised study. *J Wound Care* 30(2): 121–9

“The push to use amniotic membranes in treating DFUs has been slow, but will surely become more prominent when considering claims of improved healing rates of hard-to-treat diabetic foot ulcers.”