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Comparative effectiveness of extracorporeal shock wave, ultrasound, low-level laser therapy, noninvasive interactive neurostimulation, and pulsed radiofrequency treatment for treating plantar fasciitis

A systematic review and network meta-analysis

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Abstract

Background: Plantar fasciitis is one of the most common causes of adult heel pain. The aim of this study is to comprehensively compare the effectiveness of various therapies for plantar fasciitis using network meta-analysis.

Methods: Studies were comprehensively searched on Embase, MEDLINE via PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and the Physiotherapy Evidence Database (PEDro) up to December 4, 2017. Randomized controlled trials that used extracorporeal shock wave therapy, ultrasound, ultrasound-guided pulsed radiofrequency treatment (UG-PRF), intracorporeal pneumatic shock therapy (IPST), low-level laser therapy (LLLT), and noninvasive interactive neurostimulation (NIN) for the treatment of plantar fasciitis were included. The primary outcome is change in pain relief. Risk of bias was assessed using the Cochrane risk of bias tool. Quality assessment was performed using the GRADE system.

Results: Nineteen trials with 1676 patients with plantar fasciitis plantar fasciitis were included. In the pair-wise meta-analysis, radial extracorporeal shock wave therapy (RSW), LLLT, and IPST showed a significant pooled reduction in the visual analogue scale (VAS) compared with placebo at 0 to 6 weeks [mean difference (MD)=6.60, 95% confidence interval (CI): (6.04, −7.16); MD=2.34, 95% CI: (1.60, 3.08); MD=2.24, 95% CI: (1.44, 3.04), respectively]. Compared with placebo, UG-PRF [MD=2.31, 95% CI: (1.26, 3.36)] and high-intensity focused extracorporeal shock wave (H-FSW) [MD=0.82, 95% CI: (0.20, 1.45)] showed superior pain-relieving effects at 2 to 4 months; UG-PRF [MD=1.11, 95% CI: (0.07, 2.15)] and IPST [MD=4.92, 95% CI: (4.11, 5.73)] showed superior effects at 6 to 12 months. In the network meta-analysis, only RSW induced significant pain reduction compared with placebo at 0 to 6 weeks [MD=3.67, 95% CI: (0.31, 6.9)]. No significant differences were found for the 2 to 4-month and 6 to 12-month periods because of the wide 95% CIs.

Conclusions: We recommend treating plantar fasciitis with RSW. The commonly used ultrasound and focused extracorporeal shock wave (FSW) therapies can be considered as alternative treatment candidates. IPST, NIN, and LLLT may potentially be better alternatives, although their superiority should be confirmed by additional comprehensive evidence.

PROSPERO registration number: PROSPERO (CRD42015017353).

Abbreviations: CI = confidence interval, CrI = credible interval, FSW = focused extracorporeal shock wave, H-FSW = high-intensity focused extracorporeal shock wave, IPST = intracorporeal pneumatic shock therapy, L-FSW = low-intensity focused extracorporeal shock wave, LLLT = low-level laser therapy, M-FSW = medium-intensity focused extracorporeal shock wave, NIN =

1. Introduction

Plantar fasciitis is one of the most common causes of adult heel pain, occurring in an estimated 10% of the population. Several treatment options are available to relieve plantar heel pain including rest, stretching,[1] foot orthotics,[2] night splinting,[3] and invasive therapies. For the majority of patients, plantar fasciitis is a self-limiting condition and can be treated effectively by nonsurgical treatments.[4,5] Nevertheless, in recalcitrant cases, surgery is suggested.[6–8]

Focused extracorporeal shock wave therapy has become a popular alternative to traditional surgical approaches.[4] A pneumatic generator produces focused extracorporeal shock waves that travel from the point of contact on the skin's surface to the affected area. Its exact treatment mechanism is unknown; however, this therapy likely promotes tissue healing and neovascularization.[9] Notably, other therapies that apply different energy forms for treating plantar fasciitis are available and have demonstrated favorable results.[10] These include ultrasound therapy[11,12] and the recently developed ultrasound-guided pulsed radiofrequency (UG-PRF) treatment for the gastrocnemius,[13] low-level laser therapy (LLLT),[14] radiotherapy (i.e., radiation therapy),[15] noninvasive interactive neurostimulation (NIN)[16] and intracorporeal pneumatic shock therapy (IPST).[17] In contrast to surgical approaches or injection therapy, these interventions treat plantar fasciitis with different types of energy output that can propagate through a medium, such as sonic waves, mechanical oscillations, heat, or light. Their effects on tissue are dependent on stimulus intensity, stimulus frequency, pulse interval, treatment duration, and application method (e.g., minimally invasive).[10]

A previous systematic review and network meta-analysis[18,19] revealed that extracorporeal shock wave therapy is clinically effective for relieving chronic recalcitrant plantar fasciitis. Additionally, radial extracorporeal shock wave therapy (RSW) is advantageous over focused extracorporeal shock wave therapy (FSW) in terms of pain relief. However, Chang et al[18] only reported outcomes at 6 months or at the follow-up closest to 6 months for analysis because the follow-up duration varied among included studies. Furthermore, until now, no systematic reviews on LLLT, IPST, UG-PRF, and NIN for plantar fasciitis treatment have been reported. Thus, although all 7 treatment options appear to be more effective than placebo in alleviating plantar heel pain, the most effective treatment is currently unknown. Therefore, we conducted a Bayesian network meta-analysis to compare the therapeutic effectiveness among these 6 therapies for treating plantar fasciitis across different time intervals.

2. Methods

2.1. Protocol and registration

We prospectively registered this systematic review and network meta-analysis with PROSPERO (CRD42015017353) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for network meta-analyses.[20]

2.2. Search strategy

We comprehensively searched Embase *via embase.com*, MEDLINE via PubMed, CENTRAL (Cochrane Central Register of Controlled Trials) and the Physiotherapy Evidence Database (PEDro) up to December 4, 2017, without language or date restrictions. Only randomized controlled trials (RCTs) were included. The search terms used in Embase are presented as an example in Appendix 1, http://links.lww.com/MD/C549. To avoid the potential omission of studies, we searched additional databases, such as opengrey.eu for gray literature. We also manually screened reference lists of previous systematic reviews and meta-analyses of plantar fasciitis. Two reviewers (XL and LZ) independently reviewed the titles and abstracts of all of the studies retrieved by the search. Duplicates were removed using Endnote X7 (Thomson Reuters Co, New York). Full-text articles were obtained and examined if necessary. Then, the reviewers selected potentially relevant studies according to the eligibility criteria. If a disagreement occurred regarding the inclusion or exclusion of a study, then a third reviewer (JY) was consulted.

2.3. Eligibility criteria

2.3.1. Types of studies.
We included randomized controlled clinical trials for treating plantar fasciitis. Studies should evaluate at least 2 modalities, including sham therapy. Trials were excluded if they did not provide validated therapeutic protocols; did not report the results of pain relief; did not provide a specific range of treatment intensity of the intervention group; or compared different methods of focused extracorporeal shock wave therapy application within the same range of energy output.

2.3.2. Types of participants.
Participants in the included studies were adults (older than 18 years) diagnosed with plantar fasciitis. Studies were excluded if they included participants belonging to specific populations such as athletes or those who had suffered from fracture or underwent surgery on the involved heels.

2.3.3. Types of interventions.
Interventions included shock wave therapy (focused extracorporeal shock wave therapy and radial extracorporeal shock wave therapy). Additionally, low-level laser therapy, ultrasound therapy, intracorporeal pneumatic shock therapy, and ultrasound-guided pulsed radiofrequency treatment were included. The therapies were compared with each other or with a sham group. We also divided the treatment intensity of FSW into 3 levels according to Chang method[18]: low intensity (energy flux density $\leq 0.08 \, mJ/mm^2$), medium intensity (energy flux density $= 0.08$–$0.28 \, mJ/mm^2$), and high intensity (energy flux density $\geq 0.28 \, mJ/mm^2$).

2.3.4. Types of outcomes.
We chose pain relief as the outcome because pain is the predominant symptom in participants with plantar fasciitis. Validated measures of the change in pain relief included the visual analogue scale (VAS), the numerical rating scale pain score, the pain subscale of the validated Foot Function Index, or other indices of pain relief outcomes. All pain data were transformed to a range of 0 to 10. The postinterventional

follow-up time points were defined as following: short-term (0–6 weeks), intermediate-term (2–4 months), and medium-term (6–12 months). If the data from more than 1 follow-up result were available for 1 period, then the time points closest to 4 weeks, 3 months, and 6 months were adopted. In addition, if several states of pain were present, then we applied the following priority levels: morning pain,[21,22] first-step pain,[11–14,23] daily activity pain,[24,25] overall pain,[26,27] night pain,[28] rest pain, and pressure pain.

2.4. Data extraction and quality assessment

Two reviewers (XL and LZ) independently extracted the data using a predesigned extraction form. The extracted information included the participant characteristics, interventions, treatment method, dose/schedule, proportion of patients who were female, average age of the patients, duration of condition, outcome measures, funding, and conflicts of interest. Next, the data were integrated. Discrepancies within the data abstracted were typically resolved through discussions; however, a third reviewer was consulted when an agreement could not be reached. Two reviewers (XL and LZ) independently assessed the risk of bias. The Cochrane Collaboration Risk of Bias Tool (Review Manager, V.5.2; Revman, Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration) was used. This tool covers the following domains: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases. We also assessed the risk of bias across trials. If more than 50% of the information was from trials at a low risk of bias, the domain was judged to be at a low risk of bias. Similarly, if most information was from RCTs had an unclear/high risk of bias, the domain was considered to be at an unclear/high risk of bias.

After all the outcomes were evaluated, a summary of findings table was created using the GRADE system,[29] following the 4-step approach to rate the quality of evidence in each of the direct and mixed estimates based on methods developed by the GRADE working group.[30,31]

2.5. Statistical analysis

First, a pair-wise meta-analysis was performed using random-effects models. Every pair of studies with the same treatment was determined. Next, the results were reported as the mean difference (MD) with corresponding 95% confidence intervals (CIs), in addition to the number of pairs of studies. These statistical analyses were performed using STATA via the Metan

package (Version 14.0; STATA Corporation, College Station, TX). Statistical heterogeneity across studies was quantified using the χ^2 test and by calculating the inconsistency (I^2).

Second, random-effects network models were developed within the Bayesian framework using the Markov Chain Monte Carlo algorithm in WinBUGS (Bayesian inference Using Gibbs Sampling for Windows, Version 1.4.3; Imperial College and MRC, UK).[32] The model was based on 3 Markov chains for 100,000 iterations after a burn-in of 50,000. A thinning interval of 10 was applied, which collected 1 sample every 10 iterations. Consequently, 30,000 samples were gained for each parameter. Through this process, the Brooks–Gelman–Rubin method was used to assess the convergence between the direct and indirect variances.[33] According to the theory of Brooks and Gelman,[33] if the result of the potential scale reduction factor (PSRF) approximates or is equal to 1, then convergence has been reached. This result was also presented via the MD with 95% CrIs. If the null value was not included in the 95% CrIs of the MD, then a significant difference was indicated. The rank probability for each treatment was estimated using WinBUGS, and the data were then imported into STATA. Next, plots of the surface under the cumulative ranking curves (SUCRA) were generated.[34] The value of SUCRA was presented as the percentage of the area under the curve, where 100% indicates the best treatment, and 0% indicates the worst treatment. Placebo compared with other treatments was always considered; therefore, the comparisons between placebo and other treatments are also presented. The network order in STATA was used to plot the MDs and 95% CrIs over these 3 follow-up durations.

2.6. Inconsistency analysis

If a "loop" (e.g., A-B-C) was present in the network, then each comparison in the loop (e.g., A-B) might be an indirect result of the other comparisons (e.g., A-C and C-B); consequently, the direct and indirect results might differ. Model inconsistency was assessed using the node-splitting method.[35] If the P value was smaller than .05, then an inconsistency was considered as detected. The node-splitting models were generated via the Gemtc package (version 0.6–1, http://cran.r-project.org/package=gemtc) within R (version 3.2.3, http://www.r-project.org).

2.7. Sensitivity analysis and meta-regression

To test the influence of low-quality studies, a sensitivity analysis was conducted after excluding the low-quality studies. We recalculated the network result via the rank probability. If no

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Table 1

The result of inconsistency analysis and meta-regression.

Inconsistency	0–6 wk		2–4 mo		6–12 mo	
	Comparison	P value	Comparison	P value	Comparison	P value
	PLA vs L-FSW	.31	PLA vs L-FSW	.54	NA	NA
	PLA vs M-FSW	.66	PLA vs M-FSW	.96		
	PLA vs RSW	.003475	PLA vs H-FSW	.96		
	PLA vs LLLT	.56	PLA vs RSW	.54		
	L-FSW vs M-FSW	.67	L-FSW vs RSW	.54		
	L-FSW vs RSW	.06	M-FSW vs H-FSW	.96		
	L-FSW vs ULT	.56				
	LLLT vs ULT	.57				
DIC	Without the covariate	With the covariate	Without the covariate	With the covariate	Without the covariate	With the covariate
	39.15	39.09	27.02	24.82	21.15	21.23
Regression coefficient	0.01138 (−0.019516,0.04053)		0.02457 (0.01292,0.03494)		0.02301 (−0.00537,0.05158)	

DIC = deviance information criterion, H-FSW = high-intensity focused extracorporeal shock wave, L-FSW = low-intensity focused extracorporeal shock wave, LLLT = low-level laser therapy, M-FSW = medium-intensity focused extracorporeal shock wave, PLA = placebo, RSW = radial extracorporeal shock wave therapy, ULT = ultrasound therapy.

significant difference occurred, then the results were considered credible.

A meta-regression was performed to assess the relationship between the sample size and the treatment effect (Table 1). As recommended by the UK's National Institute for Health and Care Excellence, a single interaction term was used as the covariate.[36] No significant change in the deviance information criterion (DIC)[36] was observed. The covariate did not include a null in the 2 to 4 months result, indicating that the sample size of the study at 2 to 4 months was associated with the treatment effectiveness.

2.8. Ethical approval

This systematic review does not require ethical assessment because only indirect literature will be included and evaluated.

3. Result

3.1. Eligible studies

Our search strategy yielded 1699 potentially relevant articles. After carefully screening the titles and abstracts, 87 potentially eligible articles were obtained. After a careful full-text screening, 68 articles were discarded for the reasons listed in Fig. 1. Twenty-four RCTs met the inclusion criteria.[11,13–15,17,21–28,37–43]

However, 3 articles[15,42,43] on radiotherapy, 1 on radio-frequency[44] and 1 on cryotherapy[37] could not be used to construct a comprehensive network with other studies because of self-contrast and were therefore excluded. Finally, 19 RCTs that mentioned ultrasound therapy, UG-PRF, L-FSW, M-FSW, H-FSW, RSW, LLLT, IPST, and NIN were included in the quantitative analysis. The characteristics of the included trials are presented in Table 2.
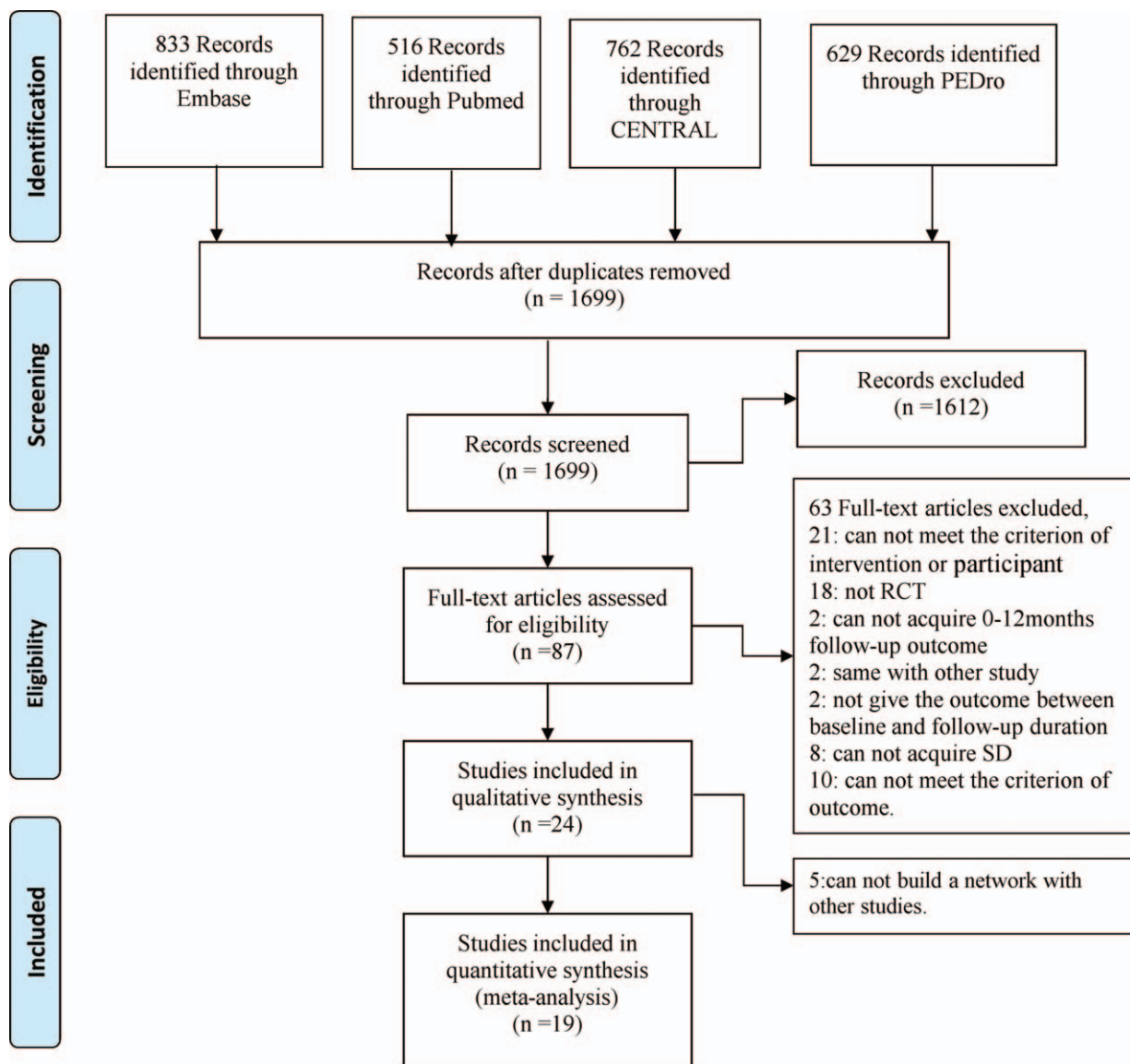
Figure 1. PRISMA 2009 flow diagram. Flowchart for literature search selection. Note: 19 studies that met the inclusion criteria were included in this network meta-analysis. N = numbers.

Table 2

Characteristics of the included studies.

Author	Publication year	Duration of condition	Intervention	Method	Schedule (Treatment Dose)	Average age (y)	Number of patients	Company Funding	Conflicts of interest	Female patients	Outcomes (mean±SD) 0–6wks	Outcomes (mean±SD) 2–4mo	Outcomes (mean±SD) 6–12mo
Ye et al	2015	>1mo	UG-PRF	The PRF treatment was carried out by at 42C for 5 min	once a week for 3 wk	49	50	No	No	31 (62%)	NA	-3.42±2.73	-2.81±2.80
Konjen et al	2015	>3mo	PLA	without radiofrequency energy	2000 impulses, once a week for 6 wk	51.8	50	No	No	31 (62%)	NA	-1.11±2.50	-1.70±2.34
			RSW	NA		45.6	15			11 (73.3%)	-4.27±0.90	-6.59±1.03	-6.99±1.17
Macias et al	2015	>3mo	ULT	3MHz,0.5–1watt/cm², for 10min	3 sessions/week for 6 wk	45	15	Yes	Yes	13 (86.7%)	-2.97±0.92	-4.19±1.25	-3.93±1.40
			LLLT	635-nm (red) laser light generating a 17-mW output	10 minutes,2 sessions/week for 3 weeks	56.70	37			24 (64.9%)	-2.96±2.42	NA	NA
Lee et al	2013	>3mo	PLA	placebo light-emitting diodes	1,000 shocks/session and week,3sessions	55.81	32	NA	No	18 (56.3%)	-0.53±1.60	NA	NA
			L-FSW	0.08mJ/mm²		55.28	30			5 (16.7%)	-1.67±1.23	NA	NA
Ibrahim et al	2010	>6mo	M-FSW	0.16mJ/mm²	2000 pulses,2 sections	51.2	30	NA	No	2 (13.3%)	-2.70±1.10	NA	NA
			RSW	0.17mJ/mm²		56.6	25			18 (72.0%)	-7.90±1.37	-7.40±0.30	-8.00±0.26
Dogramaci et al	2009	>6mo	PLA	Heel clasp blocked the wave	1,000 shock, 1 session	49.1	25	NA	NA	14 (56.0%)	-1.30±0.35	-1.20±0.20	-1.50±0.44
			IPST	a rigid probe was directly introduced into the calcaneal spur		51.76	25			10 (40.0%)	-6.32±1.7222	NA	-6.88±1.50
Kiritsi et al	2009	>6weeks	PLA	inactive	3 times weekly for 6 wk	52.68	25	NA	NA	12 (48.0%)	-4.08±1.10	NA	-1.96±1.43
			LLLT	an infrared wave length of 904nm with four infrared diodes		41	15			6 (40.0%)	-4.00±2.03	NA	NA
Gerdesmeyer et al	2008	>6mo	PLA	inactive	2000 pulses/2 weeks,3 sections	41	15	NA	No	6 (40.0%)	-1.80±0.89	NA	NA
			RSW	0.16mJ/mm²		52.4	125			87 (69.6%)	NA	-5.60±3.93	-6.19±4.36
Liang et al	2007	>6months	PLA	placebo handpiece	2000 pulses/section and week, 3 sections	52	118	NA	NA	79 (66.95%)	NA	-4.41±4.18	-4.65±4.55
			H-FSW	0.56mJ/mm²		52.1	28			19 (67.9%)	NA	-2.57±2.14	-2.37±2.41
Kudo et al	2004	>6months	M-FSW	0.12mJ/mm²	Total 3800 pulses (2330mJ/mm²)	47	25	Yes	NA	18 (72.0%)	NA	-2.43±2.52	-2.65±2.57
			H-FSW	0.64mJ/mm²		51.1	58			40 (67.0%)	NA	-3.60±2.77	NA
Theodore et al	2004	>3months	PLA	Foam cushion	Total 1300mJ/mm2	48.8	56	Yes	NA	33 (58.9%)	NA	-2.60±2.34	NA
			H-FSW	0.36mJ/mm²		50	76			62 (81.6%)	NA	-4.30±2.34	NA
C.A. Speed et al	2003	>3months	PLA	Air cushion	1500 pulses, 3sections	53	74	No	NA	47 (63.5%)	-3.10±2.69	-3.60±2.69	-3.89±2.91
			M-FSW	0.12mJ/mm²		51.7	46			26 (56.5%)	-2.70±2.60	-3.22±2.46	-4.10±2.65
Haake et al	2003	>9months	L-FSW	without contact	4000 pulses, 3sections	52.5	42	No	No	25 (59.5%)	-1.11±2.19	-2.29±2.76	-6.30±2.35
			PLA	0.08mJ/mm²		53.1	135			98 (72.6%)	-0.63±2.10	-3.80±2.88	-6.00±2.35
Rompe et al	2002	>6months	L-FSW	Polyethylene foil	Total 3000 pulses	52.9	136	No	NA	106 (77.9%)	-2.60±2.82	-3.20±3.01	-2.50±0.92
			PLA	0.08mJ/mm²		44	50			21 (42.0%)	-2.80±2.79	NA	0.20±0.95
Hawamdeh et al	2016	>1month	PLA	30 pulses per treatment	2000 shocks/session and week, 3weeks	49	50	NA	NA	20 (40.0%)	NA	NA	NA
			M-FSW	0.25mJ/mm²		NA	15			8 (53.3%)	-3.64±2.01	NA	NA
Krukowska et al	2016	>1month	PLA	a clasp on heel	2 weeks in a series of ten treatments	NA	19	NA	No	13 (68.4%)	-2.63±3.04	NA	NA
			ULT	1.5watt/cm²	2 weeks in a series of four treatments	51.1	20			NA	-4.51±1.24	NA	NA
			RSW	NA		51.4	27			NA	-4.82±1.05	NA	NA
Ulusoy et al	2017	≥6months	LLLT	830nm of laser light with 50mW	5 sessions each week during a consecutive 3-week period	53.4	20	No	No	16 (80%)	-4.34±1.70	NA	NA
			ULT	2 W/cm²	5 sessions each week during a consecutive 3-week period	50.95	20			17 (85%)	-3.37±2.13	NA	NA
Razzano	2017	>6months	NIN	electrical paresthesia for the first 10 minutes	3 sessions weekly for 20 minutes,a total of 10 sessions	53	55	No	No	25 (45.5%)	-4.40±1.06	-5.50±0.80	NA
			M-FSW	0.15 mJ/mm²	3 consecutive weeks, 2000 shockwave impulses	50.6	49			26 (54%)	-1.40±1.56	-2.50±1.11	NA
Król	2016	>3months	L-FSW	0.4 mJ/mm²	5 procedures at weekly intervals.	53.05	21	No	No	11 (52.4%)	-4.10±2.49	-4.60±2.52	NA
			RSW	2000 pulses applied to the identified site, 2000 pulses delivered to the heel and sole of the foot	5 procedures at weekly intervals	52.09	22			7 (31.8%)	-4.20±2.12	-5.20±2.10	NA

H-FSW = high-intensity focused extracorporeal shock wave, IPST = intracorporeal pneumatic shock therapy, L-FSW = low-intensity focused extracorporeal shock wave, LLLT = low-level laser therapy, M-FSW = medium-intensity focused extracorporeal shock wave, NIN = noninvasive interactive neurostimulation, PLA = placebo, RSW = radial extracorporeal shock wave therapy, UG-PRF = ultrasound-guided pulsed radiofrequency treatment, ULT = ultrasound therapy.
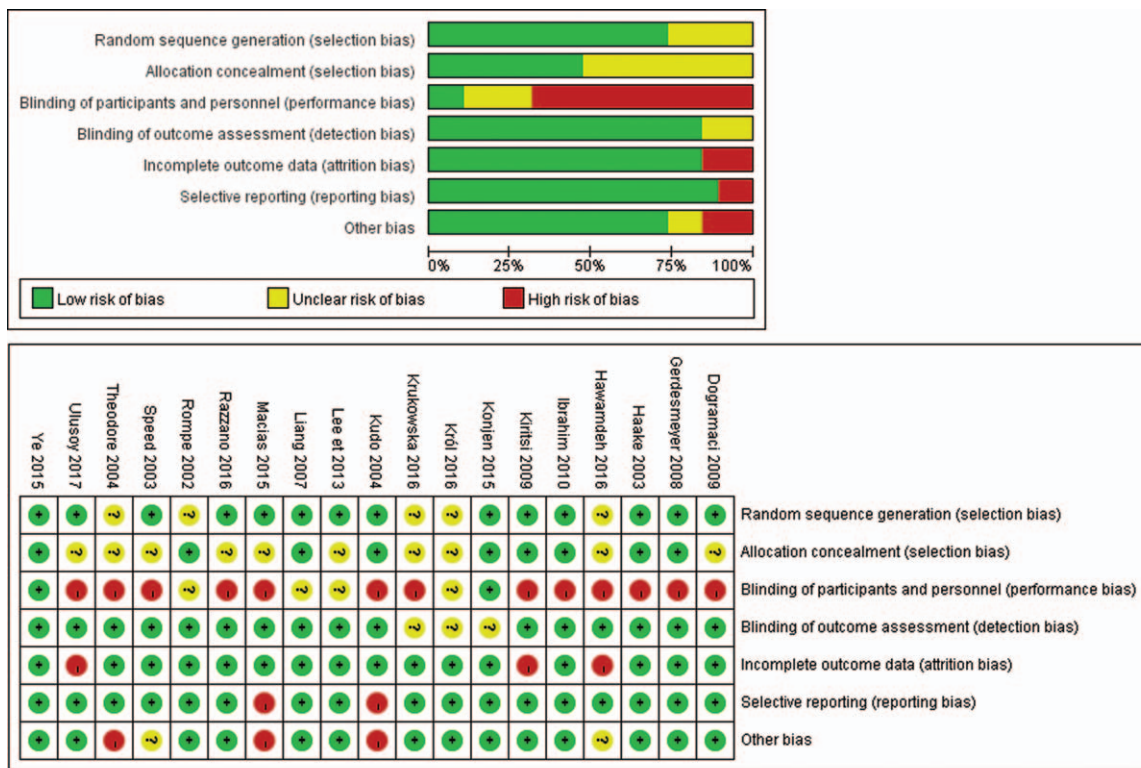
Figure 2. Risk of bias graph (upper) and summary (lower).

Nineteen trials with 1676 patients were included. The network for the 0 to 6 week, 2 to 4 month, and 6 to 12 month follow-up durations included 14, 11, and 9 studies, respectively. The total numbers of participants in these studies were 1027, 1213, and 932 respectively.

3.2. Risk of bias and quality assessment

Quantification of the risk of bias assessment is presented in Fig. 2. A random sequence was adequately generated in 14 trials, and the risk of bias in the domain of randomization was judged to be low. We considered that the risk of bias was unclear for the domain of allocation concealment because more than half of the studies had unclear information about the methods used to conceal the allocation (n=10, 52.6%). For the incomplete outcome data element, there was a low risk of bias because most information stemmed from studies with a low risk of bias (n=16, 84.2%). There was also a low risk of selective outcome reporting because 17 of the studies had a low risk of bias in this domain (89.5%). In addition, the risk of other biases was also low (n=14, 73.7%). The outcome assessors were successfully blinded in most trials (n=16, 84.2%), and the risk of bias in these domains was judged to be low. The participants and personnel were unsuccessfully blinded in most trials (n=13, 68.4%), and the risk of bias in this domain was judged to be high.

The results of the GRADE evaluation of interventions for plantar fasciitis are presented in Appendix 2, http://links.lww.com/MD/C550. All the reasons for downgrading are labeled. Because the design of inclusion criteria was rigid, there was no obvious nontransitivity. Due to the inconsistency and imprecision in the 2 to 4 month and 6 to 12 month results, the confidence of the evidence at the 2 follow-ups was low or very low.

3.3. Results of the pair-wise meta-analysis

All data were imported into STATA, and direct comparisons were made using metan with a random-effects model. The MDs and 95% CIs were calculated. The results are listed in the lower-left triangle of Table 3(A–C, respectively).

RSW, LLLT, and IPST therapy were associated with a significant pooled reduction in VAS compared with the placebo at 0 to 6 weeks [MD=6.60, 95% CI: (6.04, 7.16); MD=2.34, 95% CI: (1.60, 3.08,); MD=2.24, 95% CI: (1.44, 3.04); respectively]. Similarly, at 2 to 4 months, the MD in the VAS score reduction compared with placebo was 0.82 [95% CI: (0.2, 1.45)] for H-FSW and 2.31 [95% CI: (1.26, 3.36)] for UG-PRF. At 6 to 12 months, the MD was 1.11 [95% CI: (0.07, 2.15)] for UG-PRF and 4.92 [95% CI: (4.11, 5.73)] for IPST.

We found a significant improvement for M-FSW treatment compared with L-FSW [MD=1.03, 95% CI: (0.44, 1.62)]. No significant difference was found between RSW and ultrasound at 0 to 6 weeks. However, RSW conferred a greater pain reduction than ultrasound at 2 to 4 months [MD=2.39, 95% CI: (1.58, 3.21)] and 6 to 12 months [MD=3.06, 95% CI: (2.14, 3.98)]. In addition, NIN demonstrated better pain relief effectiveness than M-CSF at 0 to 6 weeks [MD=3.00, 95% CI: (2.48 3.52)] and 2 to 4 months [MD=3.00, 95% CI: (2.62, 3.38)].

There was significant heterogeneity across the groups when comparing RSW versus ULT at 0 to 6 weeks, PLA versus RSW at 2 to 4 months, and PLA versus L-FSW and PLA versus RSW at 6 to 12 months (I^2=76.3%, P=.040; I^2=98.9%, P=.000; I^2=97.6%, P=.000; I^2=98.6%, P=.000, respectively). All the heterogeneity results are presented in Appendix 3, http://links.lww.com/MD/C551.

Table 3

A. Results (mean difference, with 95% confidence interval) of the pair-wise meta-analysis and the network meta-analysis for 0 to 6 weeks.
B. Results (mean difference, with 95% confidence interval) of the pair-wise meta-analysis and the network meta-analysis for 2 to 4 months
C. Results (mean difference, with 95% confidence interval) of the pair-wise meta-analysis and the network meta-analysis for 6 to 12 months

A. 0 to 6 weeks

PLA	1.11 (-2.09,4.31)	1.24 (-1.89,4.29)	0.41 (-4.42,5.27)	**3.67 (0.31,6.9)**	2.7 (-0.42,5.77)	2.5 (-1.46,6.36)	2.22 (-2.6,7.01)	4.25 (-1.4,9.88)
N=1, -0.20 (-0.88, 0.48)	L-FSW	0.13 (-3.44,3.7)	-0.7 (-6.51,5.06)	2.56 (-1.07,6.14)	1.59 (-2.64,5.81)	1.39 (-3.07,5.75)	1.11 (-4.71,6.76)	3.14 (-2.82,9.03)
N=2, 0.56 (-0.26, 1.386)	**N=1, 1.03 (0.44, 1.62)**	M-FSW	-0.83 (-6.55,4.88)	2.43 (-1.88,6.53)	1.46 (-2.79,5.79)	1.26 (-3.48,6.03)	0.98 (-4.74,6.62)	3.01 (-1.72,7.77)
N=1, 0.40 (-0.47, 1.27)			H-FSW	3.26 (-2.72,9.03)	2.29 (-3.52,8.04)	2.09 (-4.18,8.3)	1.81 (-5.01,8.62)	3.84 (-3.47,11.28)
N=1, 6.60 (6.04, 7.16)	N=1, 0.10 (-1.28, 1.48)			RSW	-0.97 (-4.81,2.93)	-1.17 (-4.24,1.94)	-1.45 (-7.29,4.4)	0.58 (-5.73,6.98)
N=2, 2.34 (1.60, 3.08)					LLLT	-0.2 (-4.11,3.64)	-0.48 (-6.2,5.19)	1.55 (-4.87,8)
			N=2, -0.81 (-1.77, 0.16)	N=1, -0.97 (-2.27, 0.33)		ULT	-0.28 (-6.47,5.97)	1.75 (-4.9,8.51)
N=1, 2.24 (1.44, 3.04)							IPST	2.03 (-5.37,9.47)
		N=1, 3.00 (2.48, 3.52)						NIN

B. 2 to 4 months

PLA	1.60 (-2.76,5.98)	0.84 (-3.52,5.24)	0.89 (-2.63,4.5)	3.27 (-0.36,6.77)	2.34 (-3.24,7.99)	0.85 (-5.84,7.54)	3.84 (-3.21,10.94)
N=1, 0.60 (-0.12, 1.32)	L-FSW	-0.75 (-6.97,5.44)	-0.71 (-6.38,4.89)	1.67 (-2.85,6.01)	0.74 (-6.44,7.75)	-0.75 (-7.87,6.38)	2.25 (-6.11,10.57)
N=1, 0.93 (-0.17, 2.03)		M-FSW	0.05 (-4.34,4.34)	2.42 (-3.3,7.97)	1.49 (-5.65,8.63)	0.01 (-8,7.91)	3.00 (-2.47,8.52)
N=2, 0.82 (0.20,1.45)	N=1, 0.14 (-1.13, 1.41)		H-FSW	2.37 (-2.66,7.37)	1.45 (-5.19,8.01)	-0.04 (-7.61,7.45)	2.95 (-4.04,9.99)
N=2, 3.72 (-1.19, 8.63)	N=1, 0.60 (-0.79, 1.99)			RSW	-0.93 (-7.55,5.73)	-2.42 (-8.07,3.23)	0.58 (-7.27,8.51)
N=1, 2.31 (1.26, 3.36)					UG-PRF	-1.49 (-10.23,7.22)	1.51 (-7.5,10.73)
				N=1, -2.39 (-3.21, -1.58)		ULT	2.99 (-6.55,12.9)
		N=1, 3.00 (2.62, 3.38)					NIN

C. 6 to 12 months

PLA	1.52 (-3.25,6.34)	-0.23 (-7.1,6.57)	-0.50 (-10.16,9.26)	4.06 (-0.75,8.88)	1.07 (-5.80,7.95)	0.97 (-7.33,9.32)	4.92 (-1.81,11.78)
N=2, 1.51 (-0.84, 3.87)	L-FSW	-1.75 (-10.12,6.58)	-2.02 (-12.73,8.83)	2.54 (-4.29,9.27)	-0.45 (-8.84,7.96)	-0.55 (-10.10,9.01)	3.40 (-4.83,11.71)
N=1, -0.21 (-1.37, 0.95)		M-FSW	-0.27 (-7.13,6.60)	4.29 (-4.12,12.69)	1.30 (-8.32,11.03)	1.20 (-9.58,12.07)	5.15 (-4.44,14.87)
		N=1, -0.28 (-1.63, 1.07)	H-FSW	4.56 (-6.36,15.37)	1.57 (-10.30,13.43)	1.47 (-11.29,14.24)	5.42 (-6.26,17.13)
N=2, 4.05 (-0.81, 8.91)				RSW	-2.99 (-11.38,5.41)	-3.09 (-9.83,3.64)	0.86 (-7.43,9.24)
N=1, 1.11 (0.07, 2.15)					UG-PRF	-0.10 (-10.93,10.71)	3.85 (-5.73,13.46)
				N=1, -3.06 (-3.98, -2.14)		ULT	3.95 (-6.76,14.62)
N=1, 4.92 (4.11, 5.73)							ISPT

Upper-right triangle presents the findings (MD, with 95% CI) of the network meta-analysis conducted using WinBUGS 1.4.3.

Lower-left triangle presents the findings (MD, with 95% CI) of the pairwise meta-analyses conducted using STATA 14 and N refers to the numbers of RCTs which compared the 2 interventions directly.

A positive MD favors the lower-right intervention, a negative MD favors the upper-left intervention.

Statistically significant findings are shaded.

CI = confidence interval, H-FSW = high-intensity focused extracorporeal shock wave, IPST = intracorporeal pneumatic shock therapy, L-FSW = low-intensity focused extracorporeal shock wave, LLLT = low-level laser therapy, MD = mean difference, M-FSW = medium-intensity focused extracorporeal shock wave, NIN = noninvasive interactive neurostimulation, PLA = placebo, RSW = radial extracorporeal shock wave therapy, UG-PRF = ultrasound-guided pulsed radiofrequency treatment, ULT = ultrasound therapy.
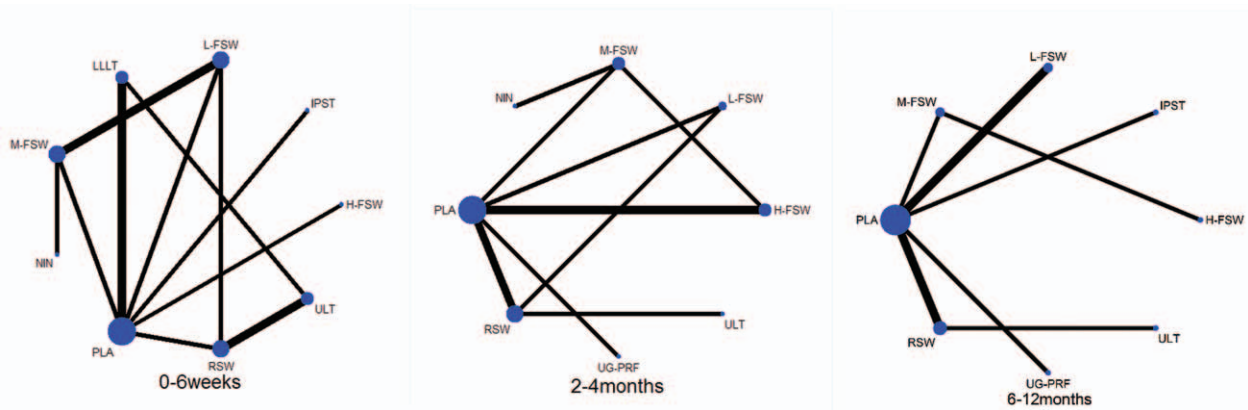
Figure 3. Network of comparisons of extracorporeal shock wave, ultrasound, low-level laser therapy, and pulsed radiofrequency treatment for Plantar Fasciitis (Left: 0–6 weeks; mid: 2–4 months; right: 6–12 months). Note: The size of the circle represents the number of patients, and the thickness of the edge represents the number of studies. H-FSW = high-intensity focused extracorporeal shock wave, IPST = intracorporeal pneumatic shock therapy, L-FSW = low-intensity focused extracorporeal shock wave, LLLT = low-level laser therapy, M-FSW = medium-intensity focused extracorporeal shock wave, NIN = noninvasive interactive neurostimulation, PLA = placebo, RSW = radial extracorporeal shock wave therapy, UG-PRF = ultrasound-guided pulsed radiofrequency treatment, ULT = ultrasound therapy.

3.4. Results of the network meta-analysis

Three comprehensive network graphs were built using STATA (Fig. 3; the size of the circle represents the number of participants, and the thickness of the edge represents the number of studies). All potential comparisons were calculated via WinBUGS and are presented as MDs and 95% CrIs. All of the PSRF parameters were approximately 1, indicating a strong convergence. The results are listed in the upper-right triangle of Table 3, and the significant differences are shaded.

RSW, ultrasound, LLLT, IPST, and NIN all corresponded to significant pain reduction compared with placebo at 0 to 6 weeks [MD = 6.61, 95% CrI: (5.05, 8.18) for RSW; MD = 5.8, 95% CrI: (3.86, 7.73) for ultrasound; MD = 2.33, 95% CrI: (1.10, 3.58) for LLLT; MD = 2.24, 95% CrI: (0.61, 3.84) for IPST; and MD = 3.00, 95% CrI: (2.48, 3.52) for NIN]. In contrast, statistical significance was observed only for RSW when compared with the placebo [MD = 3.67, 95% CrI: (0.31, 6.9)]. No significant differences were found for the 2- to 4-month and 6- to 12-month periods, as all the results had wide 95% CrIs.

Because placebo was the most commonly used control, comparisons with placebo across 3 different follow-up durations are shown in the plot. With regard to changes in pain scores, all of the treatments yielded better outcomes than placebo over the 3 time periods except for L-FSW at the short-term and M-FSW and H-FSW at the medium-term. However, only LLLT, ultrasound therapy, RSW, and IPST showed statistically significant superiority with regard to the short-term results. These results are presented in a forest plot (Fig. 4).

3.5. Rank probability based on SUCRA

The ranking probability of each treatment in terms of 3 follow-up durations is illustrated in Fig. 5. Larger areas under the SUCRA curve represent better effectiveness. NIN and IPST showed the highest probability of being the best treatment to relieve pain in the short (79.5%) and in the medium (81.1%) term, respectively, closely followed by RSW (79.4% and 78.6% respectively). RSW showed the highest probability of being the best treatment in the intermediate (83.9%) term.

3.6. Inconsistency analysis

Inconsistencies among the results are listed in Table 1. The P value for the inconsistency of PLA versus RSW at 0 to 6 weeks was .003475, indicating the detection of a significant inconsistency. The other P values were > .05, demonstrating that no inconsistencies were detected.

3.7. Sensitivity analysis and meta-regression

After excluding 1 low-quality study (Hawamdeh et al),[39] the SUCRA changed slightly, although no change occurred in the rank probabilities, indicating that the results of the network meta-analysis are robust.

A meta-regression did not reveal a significant change in the DIC; however, we found that the covariate (sample size) did not include a null result over the 2 to 4-month period. This finding suggests that the covariate was associated with the treatment effectiveness at 2 to 4 months. No significant change in DIC was observed (Table 1).

4. Discussion

The present meta-analysis compared the effectiveness of focused extracorporeal shock wave therapy, radial extracorporeal shock wave therapy, LLLT, NIN, pulsed radiofrequency treatment, and ultrasound therapy for the treatment of plantar fasciitis. The network meta-analysis indicated that RSW had the highest probability of providing the best outcome at 2 to 4 months (76.9%). NIN (79.5%) and IPST provided the best outcome (81.1%) at 0 to 6 weeks and 6 to 12 months, respectively, but were only slightly better than RSW (79.4% and 78.6%, respectively) at each time point.

We assessed 7 modalities in our network meta-analysis. These interventions treat plantar fasciitis with different types of energy output that can propagate through tissue, such as sonic waves, mechanical oscillations, heat, or light. These modalities are accompanied by processes involving energy generation and transformation, and effects on tissue are dependent on stimulus
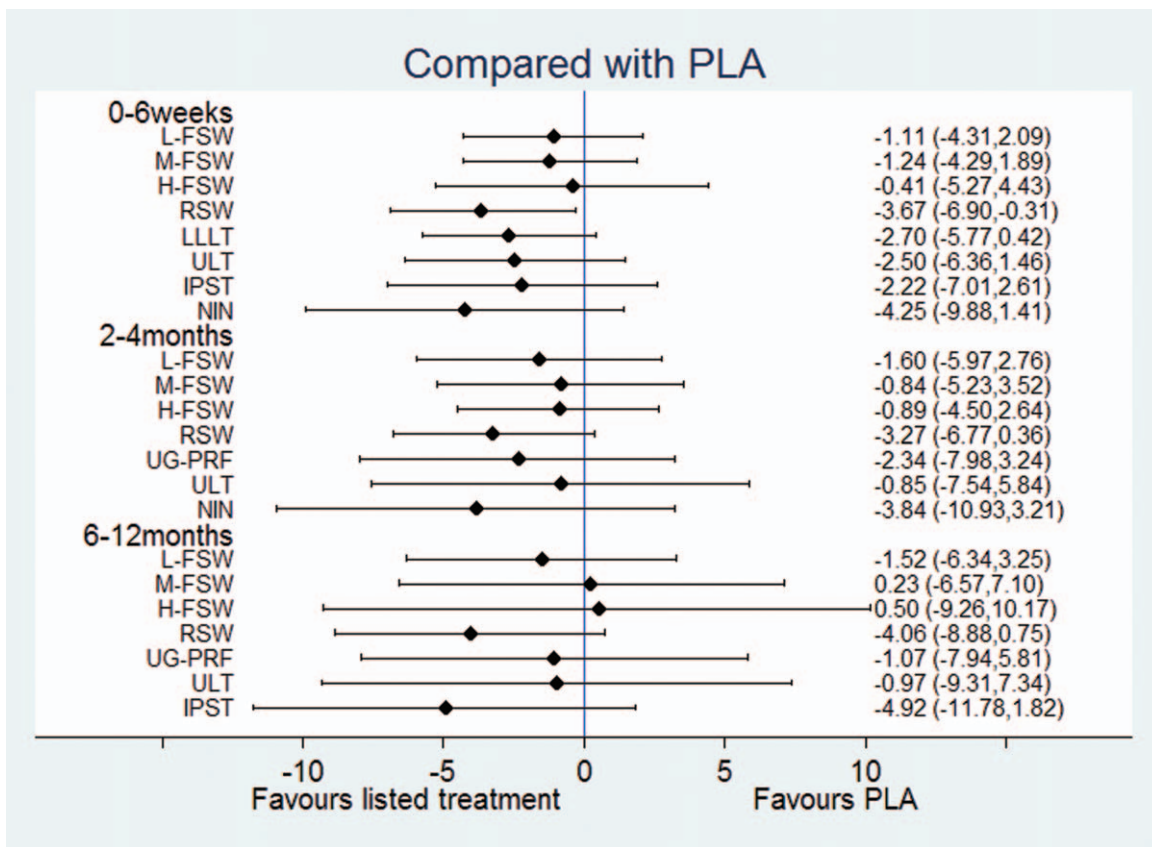
Figure 4. Treatment options compared with Placebo. H-FSW=high-intensity focused extracorporeal shock wave, IPST=intracorporeal pneumatic shock therapy, L-FSW=low-intensity focused extracorporeal shock wave, LLLT=low-level laser therapy, M-FSW=medium-intensity focused extracorporeal shock wave, NIN=noninvasive interactive neurostimulation, PLA=placebo, RSW=radial extracorporeal shock wave therapy, UG-PRF=ultrasound-guided pulsed radiofrequency treatment, ULT=ultrasound therapy.

intensity, stimulus frequency, pulse interval, treatment duration, and application method (e.g., minimally invasive).

Extracorporeal shock wave continuously transmits sonic waves at a frequency of 16 Hz to 20 MHz and has been harnessed and used for various applications in medical science. RSW is a recently developed alternative to FSW for managing plantar fasciitis, and its major advantages over FSW include better patient tolerance and not requiring adjunct local anesthesia during treatment.[45] In addition, RSW devices are cheaper, smaller, and easier to use.[46] Furthermore, the present study showed that RSW corresponded to the second-best short- (0–6 weeks) and medium-term (6–12 months) outcomes and the best intermediate-term (6–12 months) outcome, that is, pain relief effectiveness, among all the modalities. This efficacy is satisfactory and stable. Thus, we strongly recommend RSW for adults with plantar fasciitis who have had symptoms for over 6 months and in whom conservative therapies have been unsuccessful but before surgical treatments are considered.
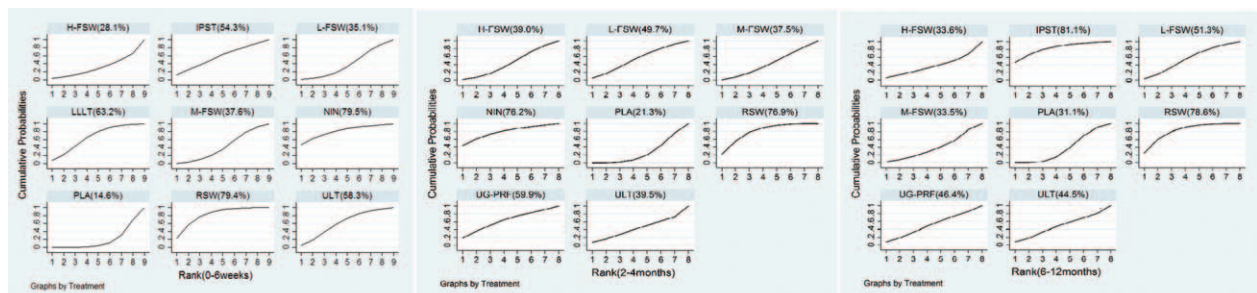

Figure 5. SUCRA of extracorporeal shock wave, ultrasound, low-level laser therapy, noninvasive interactive neurostimulation and pulsed radiofrequency treatment for Plantar Fasciitis (upper: 0–6 weeks' result; mid: 2–4 months' result; lower: 6–12 months' result). Note: The area under the curve represents the cumulative rank probability of each treatment. The larger the area, the better the cumulative rank probability. H-FSW=high-intensity focused extracorporeal shock wave, IPST=intracorporeal pneumatic shock therapy, L-FSW=low-intensity focused extracorporeal shock wave, LLLT=low-level laser therapy, M-FSW=medium-intensity focused extracorporeal shock wave, NIN=noninvasive interactive neurostimulation, PLA=placebo, RSW=radial extracorporeal shock wave therapy, SUCRA=surface under the cumulative ranking curves, UG-PRF=ultrasound-guided pulsed radiofrequency treatment, ULT=ultrasound therapy.

Regarding FSW, L-FSW showed the most significant pooled reduction in VAS over the 6 to 12-month period (treatment effectiveness compared with placebo), followed by M- and H-FSW. This finding is consistent with Chang's result at 6 months.[18] However, our data favor placebo treatment over M- or H-FSW, which may be in part due to the following reasons. We adopted 3 time points with different follow-up durations; however, the extracted data in Chang's meta-analysis corresponded to the follow-up assessment closest to 6 months (26 weeks), which is usually considered an intermediate-term assessment. Our work used different inclusion criteria than those in Chang's study. We included more recent RCTs and excluded RCTs of athletes.[47] Moreover, we did not include Marks's[48] work, which did not provide a baseline VAS score. (This author only provided changes in VAS scores at 1 and 6 months.) We included 6 other treatment types in our network meta-analysis (i.e., mixed treatment comparisons). Importantly, all of the 95% CIs regarding RSW in pain reduction included 0, and large 95% CIs including 0 were observed over the medium term. It should be noted that FSW was inferior to RSW at all time intervals, which may be because the shock wave energy of FSW may be weakened by disturbances (such as bone, calcifications, etc.) in the pathway to the target.[49] Additionally, in terms of H-FSW, this method demonstrated unsatisfactory results and may cause more pain during treatment.[45,50] Thus, our data suggest that FSW is a suboptimal choice for treatment of plantar fasciitis compared with RSW.

Ultrasound therapy is another commonly used treatment for plantar fasciitis. It involves piezoelectric crystals that use high-frequency alternative current to transform electrical energy into mechanical oscillation energy.[51] The pooled results of the network meta-analysis showed that ultrasound did not demonstrate significantly better outcomes than placebo over the short, intermediate, and medium terms due to the wide 95% CrIs. Thus, ultrasound therapy does not seem to be an optimal choice for reducing plantar fasciitis pain over the 3 time periods.

LLLT is a recently developed technology. It operates on the principles of photochemistry, using a discrete wavelength of light to initiate a signal transduction cascade by stimulating a protein capable of absorbing light energy, also known as a photoreceptor protein.[14] Compared with placebo, LLLT showed the third-best short-term treatment effect [MD=2.7, 95% CrI: (−0.42, 5.77)] in the network result, indicating its satisfactory short-term pain-relieving effects. Importantly, however, all studies included supported its short-term superiority; thus, long-term follow-up data are needed.

Only 1 study applied NIN. This method is a new form of electrotherapy that has already been shown to have positive results in treating myofascial syndrome and other musculoskeletal conditions. NIN might exert an anti-inflammatory effect in areas of local inflammation. Notably, this method demonstrated the best short-term [MD=4.25, 95% CrI: (−1.4, 9.88)] and intermediate-term [MD=3.84, 95% CrI: (−3.21, 10.94)] effectiveness. Thus, more relevant clinical RCTs of long-term results are required in the future.

Similarly, only 1 study applied IPST. This method showed promising results because it demonstrated the best medium-term effectiveness [MD=4.92, 95% CrI: (−1.81, 11.78)] and better short-term effectiveness [MD=2.22, 95% CrI: (−2.6, 7.01)] (ranked fifth) compared with placebo in the network result. This result may be due to the fact that it is typically used as a minimally invasive approach, which might engender superior effectiveness compared with noninvasive modalities. However, as an invasive approach, IPST may have a temporary lower efficacy compared with RSW because the VAS score is relatively higher at 0 to 6 weeks due to wound healing during that time. Although invasive, IPST is well tolerated under local anesthesia, imparts no weight bearing restrictions and allows participants to quickly return to work. Because a pneumatic lithotripter is much cheaper than commercially available shock wave machines and readily available in almost all hospitals, IPST may be a viable option to treat plantar fasciitis, especially in health centers where shock wave therapies are not available.

UG-PRF is a less neuro-destructive alternative than continuous radiofrequency heat lesions.[12] It uses high-frequency current at 500 kHz, called radiofrequency, to generate heat at the electrode tip to cause coagulation. According to Ye et al,[13] UG-PRF can inactivate the trigger points in the gastrocnemius, which can relieve muscle contracture and reduce plantar heel pain. During treatment, a needle is inserted into the gastrocnemius, rather than the heel, at trigger points. A traditional pair-wise meta-analysis associated UG-PRF with a significant pooled reduction in VAS compared with placebo over the intermediate and medium terms. The network result favored UG-PRF, although the trend was not significant.[44] The potential failure of accurate needle placement and the risk of nerve injury should be carefully considered even under ultrasound guidance. Only 1 RCT included this intervention with unsatisfactory effectiveness; thus, more relevant studies of short-term results are expected in the future.

Collectively, regarding clinical implications, in patients who have had symptoms for over 6 months and in whom conservative therapy has been unsuccessful, we recommend RSW before surgical treatments are considered. ULT and FSW therapies, which are commonly used in current clinical practice, can also be considered treatment candidates. The benefits of IPST, NIN, and LLLT need to be carefully tested in additional clinical trials.

This study has some advantages and strengths. It only included RCTs with a prospective design criterion. All potential treatments (e.g., rarely studied NIN and IPST) were included because the type of intervention was not limited in the database search. Furthermore, all P values regarding the inconsistencies were less than .05. The sensitivity analysis did not show a significant change in the cumulative probabilities rank, and no significant change in the DIC was found according to the meta-regression results. Therefore, the outcome of this meta-analysis is valid and reliable. We adopted 3 time points for the different follow-up durations. This strategy provided us certain insight with regard to time effectiveness. We also divided FSW therapies into 3 subgroups based on different energy intensity effluxes. In addition, unlike conventional meta-analyses techniques, Bayesian methodology advantageously enabled us to simultaneously compare every treatment. We calculated indirect comparisons via Bayesian statistics. Furthermore, this model was used to build inconsistency, sensitivity, and meta-regression tests.

We discuss 4 limitations here. First, some treatments were presented in only 1 study, including IPST and NIN, or without results for all 3 follow-up durations. The pooled results also showed that NIN and IPST had the highest probability of being the most effective treatment at 0 to 6 weeks and 6 to 12 months, respectively. Thus, we highlight the need for more high-quality RCTs in the future to corroborate these results. Second, this network meta-analysis did not include radiotherapy in its comparison because the 4 identified articles only used radiotherapy for self-comparison and, consequently, failed to form a network with another treatment. Thus, we suggest that more RCTs should focus on radiotherapy for comparison with other

modalities to further elucidate its pain-relieving efficacy. Third, the qualities of the included studies varied. Some studies were better designed RCTs with high patient numbers and adequate randomization; however, other studies had few participants or weak blinding/allocation. This limitation can be addressed after more high-quality studies are conducted in the future. Fourth, significant heterogeneity existed within particular subgroups because treatment schedules and dosages varied across studies, and our review ignored these differences. This uncertainty is magnified when integrating these factors in mixed-treatment comparisons, as evidenced by the enlarged 95% CrIs. Our meta-regression indicated that the sample size was associated with the treatment effectiveness over the 2 to 4-monthperiod. This finding might explain why most of the indirect comparisons were insignificant in the intermediate and medium terms. There is inconsistency between the direct and indirect comparisons for PLA versus RSW ($P = .003475$). Thus, network comparisons (mixed evidence) of PLA versus RSW were rated down in GRADE due to incoherence.

5. Conclusions

The present meta-analysis compared the effectiveness of 8 modalities for treating plantar fasciitis. Regarding the 3 follow-up effectiveness time points, RSW provided relatively more effective and stable pain relief compared with other interventions and is therefore a promising candidate for clinical applications. Ultrasound therapy and FSW therapies can also be considered treatment candidates. However, H-FSW and UG-PRF are not recommended. Regarding the 0- to 6-week and 6- to 12-month periods, NIN and IPST provided the greatest pain relief, respectively, and, thus, have the potential to be more effective alternatives. Randomized trials comparing NIN, IPST, UG-PRF, and LLLT are needed to obtain more precise estimates of their relative efficacy.

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Writing – review & editing: Xian Li, Li Zhang.

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