
Article:
Jones, AD, De Siqueira, J orcid.org/0000-0002-1653-2832, Nixon, JE et al. (3 more authors) (2022) Plantar shear stress in the diabetic foot: A systematic review and meta-analysis. Diabetic Medicine, 39 (1). e14661. ISSN 0742-3071

https://doi.org/10.1111/dme.14661

Plantar Shear Stress in the Diabetic Foot: A Systematic review and Meta-analysis

Running title: Plantar Shear Stress in the Diabetic Foot

Alexander D Jones,[1] Jonathan De Siqueira,[1,2] Jane E Nixon,[3] Heidi J Siddle,[4] Peter R Culmer,[5] and David A Russell[1,3]

Affiliations:

1 – Leeds Vascular Institute, Leeds Teaching Hospitals NHS Trust, Leeds, LS9 7TF, UK

2 - Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds LS2 9JT, UK

3 – Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, LS2 9JT, UK

4 - Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, LS7 4SA UK

5 – Leeds School of Mechanical Engineering, University of Leeds, LS2 9JT, UK

Corresponding author:

Mr Alexander D. Jones, The Leeds Vascular Institute, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK (alexander.jones9@nhs.net)

Manuscript word count:

4294

Abstract word count:

254

Conflict of interest:

The authors declare no conflict of interest

What is already known?

- Shear stress has been implicated in the pathogenesis of diabetic foot ulcer formation.

What has this review found?

- Patients with diabetes and a current or previous ulcer exhibit greater shear stress than their ulcer-free counterparts.

What are the implications?

- This identifies shear stress as a potential risk factor for diabetic foot ulcer formation and provides the impetus to develop systems that utilise shear as part of foot ulcer prediction and prevention strategies.

Abstract

Aims

Diabetic foot ulceration (DFU) is a multifactorial process involving undetected, repetitive trauma resulting in inflammation and tissue breakdown. Shear stress forms a major part of plantar load, the aim of this review is to determine whether elevated shear stress results in ulceration.

Methods

A systematic review of the Ovid Medline, EMBASE, CINAHL and Cochrane library databases was performed. Studies involving patients with diabetes who underwent plantar shear stress assessment were included. The primary outcome was plantar shear stress in patients with diabetes who had a current/previous diabetic foot ulcer compared with those with no prior ulceration. Meta-analysis was performed comparing shear stress between those with a current or previous DFU and those without, and those with diabetes and healthy controls.

Results

The search strategy identified 1461 potentially relevant articles, sixteen studies met the inclusion criteria, involving a total of 597 patients. Comparing shear stress between the current/previous DFU group and those without: Standardised mean difference (SMD) 0.62 (95% CI -0.01 – 1.25), in favour of greater shear stress within the DFU group, $p = 0.05$. Comparing shear stress between people with diabetes and healthy controls: 0.36 (95% CI -0.31 – 1.03), in favour of greater shear stress within the diabetes group, $p = 0.29$.

Conclusion

This review suggests that that patients with diabetes and a history of ulceration exhibit greater shear stress than their ulcer free counterparts. This strengthens the premise that development of systems to measure shear stress may be helpful in DFU prediction and prevention.

Key words:

Diabetic Foot, Diabetic Foot Ulcer, Plantar Shear Stress, Pathophysiology

Introduction

Four hundred and sixty-three million adults live with diabetes globally, with prevalence expected to rise to 700 million by 2045.[1] Up to one quarter will develop a diabetic foot ulcer (DFU),[2] with 5-8% of these requiring a major amputation within 1-year.[3] Survival is poor, 5-year mortality following development of a DFU has been estimated at 30.5%, with half of patients undergoing a major amputation dead in 5 years.[4] As well as the human cost, there is also a significant financial burden. It is estimated that total expenditure on healthcare related to ulceration and amputation in diabetes in the UK to be in excess of £900 million per year, equivalent to 0.9% of total National Health Service spending.[5]

Ulceration is a multifactorial process with peripheral neuropathy and arterial disease playing central roles. Neuropathy leads to the loss of protective sensation and often development of abnormal foot architecture.[6] Loss of protective sensation results in undetected, repetitive trauma to the foot.[6] This effect is compounded by the development of structural abnormalities, which increases plantar stress leading to inflammation and tissue breakdown.[6] Plantar pressure forms the vertical component of the load experienced during normal gait. Sites of elevated plantar pressure have been demonstrated to be subject to greater risk of ulcer formation and pressure assessment is incorporated into the International Working Group on the Diabetic Foot (IWGDF) guidelines for ulcer prevention and management.[6] Shear stress, acting parallel to the foot, forms the tangential component of plantar load. Usually caused by friction between the foot-surface interface, it comprises antero-posterior (AP) and medio-lateral (ML) components which act perpendicular to the longitudinal axis of the foot.[7] Pollard et al., were the first to measure shear forces in healthy subjects.[8] They identified greatest levels of shear stress under the 1st metatarsal head (MTH), which were reduced by the use of a total contact cast.[8] It is suggested that the repetitive, multidirectional nature of shear stress, both at surface and subsurface levels is a significant contributor to ulcer formation.[7,9–13] Plantar tissue in patients with diabetes has been shown to be stiffer when shear is applied compared with patients without diabetes, making it less able to dissipate shear stress and thus more susceptible to tissue breakdown.[14] Callus formation, a significant predictor of ulceration, is also hypothesised to form as a result of shear forces.[15,16] Despite awareness of the pathogenic nature of shear, it has been less extensively investigated than direct plantar pressure. This is primarily due to the technical difficulties associated with its measurement.[17] As such, numerous methods, both barefoot and in-shoe, have been applied to attempt plantar shear stress assessment.[18] Focussing on biomechanical methods of shear assessment, the aims of this systematic review are to summarise the current evidence behind shear stress assessment in progressive risk categories of diabetic foot disease, to determine whether elevated shear stresses are associated with ulceration, and identify whether shear assessment as part of an offloading strategy has been implemented to reduce the risk of ulcer formation.

Methods

Search strategy

A detailed protocol for this review is available on the PROSPERO database.[19] A systematic review of the Ovid Medline (1946 – July 2020), (EMBASE 1947 – July 2020), CINAHL database (1961 – July 2020) and Cochrane library (1995 – July 2020) databases was performed. The search strategy included keywords, MESH headings and synonyms for ‘diabetic foot’, ‘mechanical stress’, ‘biomechanics’, ‘kinetics,’ ‘plantar shear’, ‘plantar pressure’ and ‘ground reaction force’ (GRF) (Appendix 1). Two reviewers independently performed abstract screening using a pre-defined protocol. Full texts of

identified studies were retrieved and assessed. Those meeting the eligibility criteria were included in the final analysis. When disagreement occurred, a third author was consulted. Forward and backward searching of included studies was performed to identify relevant articles that may meet the inclusion criteria.

Inclusion and exclusion criteria

English language randomised controlled trials, cohort, case-control, and cross-sectional studies were eligible for inclusion with no limitation on date of publication. Studies involving adult patients with diabetes who underwent plantar shear stress assessment, with or without healthy controls, both direct measurement and indirect estimation utilising other biomechanical parameters. Barefoot and in-shoe analyses were included; however, studies that measured only shod GRF were excluded as the shoe-ground interface does not reflect the stress of the plantar aspect of the foot. Studies were excluded that provided only analysis of peak pressure or utilised modelled data without in vivo measurements. Studies using temperature as a surrogate marker for shear were also excluded, as numerous factors other than shear result in a temperature rise.[20]

Outcomes

The primary outcome of interest was plantar whole foot peak shear stress in patients with diabetes who had a current or previous diabetic foot ulcer, compared with those without ulceration. This is defined as the peak shear stress recorded across the whole plantar aspect of the foot. Definition of DFU was according to study preference, however generally the accepted definition is any full thickness lesion (involving epidermis and dermis) below the malleoli in patients with diabetes.[21] Secondary outcomes of interest were regional peak shear stress, shear time integral, AP and ML GRF in patients with diabetes, with or without a history of diabetic peripheral neuropathy (DPN) compared with healthy controls. Regional peak shear stress was defined as the peak shear stress recorded within a pre-specified area of the plantar surface of the foot according to each study. Shear time integral was defined as the area under the shear-time curve. AP ground reaction force is defined as the anterior-posterior force at the foot-surface interface during gait, ML ground reaction force is defined as the medio-lateral force at the foot-surface interaction during gait. A further outcome of interest was the incidence of DFU formation in those that undergo plantar shear assessment to inform therapy, compared with standard therapy, delivered without knowledge of plantar shear measurement. Studies were included that reported one or more outcome in the population of interest.

Data extraction and synthesis

Data was extracted by the primary author using a standardised proforma and reviewed for accuracy by the second author. A third author in place to resolve disputes was not called upon. Descriptive data including study type, methodology, population characteristics as well as numerical data including mean and standard deviation for each shear variable was extracted. When absolute figures were not provided for key variables the authors were contacted to provide unpublished data. When this was not provided data was extracted from graphs using GraphGrabber 2.0 software (Quintessa). PRISMA reporting guidelines for systematic reviews were adhered to throughout. Risk of bias assessment was performed using the Newcastle-Ottawa Assessment scale for case-control studies, cohort studies and cross-sectional studies as appropriate.[22] Meta-analysis of relative risk/odds ratio was to be performed

between treatment arms (shear stress assessment and standard care). Meta-analysis was also planned to compare shear stress between patients with diabetes with a current or previous DFU and those without, and to compare those with diabetes (DPN and diabetes controls (DC)) and healthy controls. When groups were separated into those with DPN and those without, the results from the DPN group were chosen as these are at greater risk of developing DFU. Data appropriate for synthesis included whole foot peak shear stress, shear time integral, tangential GRF and regional measures of these outcomes. Meta-analysis was performed when three or more studies reported an outcome of interest. Results estimated from pressure data were not included within the meta-analysis. Standardised mean difference was calculated using the Review Manager 5.3 statistical software package (Cochrane collaboration). The Q and I^2 statistics were used to assess statistical heterogeneity between studies. The DerSimonian and Laird random effects model was used due to the heterogeneity present in patient selection and methods of assessment used.

Results

The search strategy identified 1461 potentially relevant articles, two rounds of screening found 16 studies that met the inclusion criteria, involving total of 597 patients (Figure 1). The methodologies of the included studies are displayed in table 1. No studies were identified that used shear assessment as part of risk stratification or management strategy. Furthermore, no prospective studies were identified investigating shear stress and ulcer formation. Four cross-sectional studies investigated the distribution of plantar shear in patients with diabetic foot disease. [7,11,12,23] Nine case-control studies compared shear stresses between patients with varying impacts of diabetic foot disease (including those with a current or previous ulcer, DPN without ulcer history and non-DPN diabetes controls) and healthy controls. [9,10,13,24–29] One case-control study compared patients with varying degrees of diabetic foot disease without the use of healthy controls.[30] One cohort study[15] and one cross-sectional study compared shear stress in patients with diabetes with and without the presence of callus.[17] Results from the risk of bias assessments are presented in table 2.

Significant heterogeneity was found in measurement of shear stress (table 1). Nine studies measured plantar shear pressure[7,9–12,15,16,24,30]. Of these, three were in-shoe[7,15,16] and 6 were barefoot assessments.[9–12,24,30] Three studies utilised commercially available force plates to measure vertical and tangential GRF.[13,25,26] One study presented measured force (Newtons)[13], two presented results as a percentage of bodyweight. Three studies derived peak shear stress and depth of shear stress from plantar pressure assessment using a potential function based upon the theory of elasticity to estimate subsurface shear stresses.[23,27,28] The final study used the Hertzian contact theory to calculate shear stresses based upon measurements of in-shoe plantar load and heel-pad thickness.[29] Studies also varied in location of shear assessment (table 1).

Shear stress in those with a current or history of diabetic foot ulceration

Three studies compared whole foot peak shear stress between patients with a current or previous DFU and patients with diabetes without a history of ulceration and were eligible for meta-analysis. This included 45 patients with a current or history of DFU and 104 patients with DPN or non-DPN diabetes controls without a history of ulceration. Baseline characteristics are shown in table 3. The standardised mean difference was 0.62 (95% CI -0.01 – 1.25), in favour of those with DFU measuring greater shear stress, p = 0.05 (Figure 2).

Yavuz et al.,[30] identified significantly greater whole foot peak shear stress in those with a previous DFU compared with patients with diabetes without a history of ulceration (135.3kPa versus 86.4kPa, p = 0.0465). No difference in peak pressure was noted between groups. Fernando et al.,[13] compared those with active ulceration with sex and age matched DPN or non-DPN diabetes controls. Significantly greater AP and vertical GRF were found within the DFU group compared with diabetic controls. These remained significant after adjusting for age, body mass index (BMI) and sex. However, there was no difference in the ML component of shear force between those with a history of ulceration and diabetic controls. Conversely, Uccioli et al., found no difference in AP GRF between patients with DPN, with or without a history of ulceration.[26]

Shear stress in patients with diabetes compared with healthy controls

Five studies compared plantar shear stresses in patients with diabetes, with and without DPN (DPN/DC group), and healthy controls and were eligible for meta-analysis.[9,10,13,25,26] Baseline characteristics are described in table 4. Two directly measured shear stress[9,10] and three measured tangential GRF.[13,25,26] The standardised mean difference was 0.36 (95% CI -0.31 – 1.03), in favour of greater shear stress within the diabetic group, p = 0.29 (Figure 3).

Yavuz et al., identified significantly greater whole foot peak shear stress in the DPN group compared with healthy controls (91.3kPa versus 64.6kPa, p = 0.035), however no difference between the DPN and non-DPN diabetes control groups.[9] Regional analysis (table 4) revealed significantly greater peak shear between DPN and both non-DPN diabetes and healthy controls at the hallux (p = 0.07 and p = 0.02 respectively) and DPN and healthy controls at the central forefoot (p 0.05). The shear time integral was significantly elevated at the hallux (p = 0.002), medial forefoot (p = 0.001) and central forefoot (p = 0.002) in the DPN group compared with non-DPN diabetes controls. [9] In 2008, Yavuz et al., performed a similar study comparing barefoot shear stress and pressure between 15 patients with DPN and controls and found the resultant shear (AP + ML shear) to be 31% greater in those with DPN (p 0.016).[10] Studies analysing GRF draw different conclusions. Sawacha et al., and Fernando et al., found whole foot and midfoot AP and ML forces to be significantly greater in those with diabetes compared with healthy controls.[13,25] Uccioli et al., however, found GRF in controls to be significantly greater than those with DPN.[26]

Shear stress and callus formation

Amemiya et al.,[15] investigated the relationship between pressure and shear stress and callus formation in 59 patients with DPN. Callus was present in 20 patients, all of which was removed prior to assessment, patients were re-examined after one month for callus formation. At the 1st, 2nd and 5th MTHs, patients were assigned to the 'callus formation group' if the callus was present at that MTH at pre-test assessment and re-occurred at that location. Peak pressure and peak shear did not differ between groups at either the 1st, 2nd or 5th MTHs. Significantly higher rates of foot deformity were present in the 'callus formation groups' of the 1st and 2nd MTHs, which suggests a difference in pressure or shear may have been present though was not detected. Hamatani et al., found no difference in peak pressure or shear between those with callus and those without, however those with callus experienced a higher peak-to-peak shear difference, 0.0500 kgf versus 0.0380 kgf (p = 0.031).

The distribution and magnitude of shear stress in patients with diabetic foot disease

Four studies described direct measures of shear stress and their distribution in patients with diabetic foot disease , two of these provide values,[7,12] and the data of two studies are extracted from graphs provided.[9,15]One further study describes regional tangential GRF. Measured peak maximal shear stress within the forefoot ranged between 18 and 158kPa (Table 5). Perry et al., recorded lowest levels of shear stress (18 kPa) at the toes and medial MTHs, however only initiation of gait was examined.[12] Yavuz et al., found the highest regional peak shear in the DPN group was seen at the hallux (77.9kPa), which was significantly greater than within non-DPN diabetes control and healthy control groups.[9] Highest regional peak shear within diabetic control and healthy groups occurred at the central forefoot (77.6kPa and 61.1kPa respectively).[9] Amemiya et al., did not perform significance tests between regions however their results suggest increased shear stress at the medial forefoot compared with the lateral, however shear stress was not recorded at the hallux or the heel.[15] Lord et al., also noted a trend towards reduced peak maximal shear stress moving laterally across the forefoot however significance tests were not performed between regions.[7]

Discussion

The prognosis of patients following development of diabetic foot ulceration is poor, with 5-year survival rates equivalent to that of colorectal cancer.[4] Improved methods of identifying those at risk of ulceration, and those at risk of re-ulceration are vital to prevent the cycle of tissue destruction which leads to major amputation and ultimately loss of life. This meta-analysis highlights shear stress as a factor of interest in the pathophysiology of ulcer formation, yet one which requires further investigation. The results suggest patients with diabetes with a previous/current DFU exhibit elevated levels of shear stress compared with their ulcer free counterparts. Whilst a trend towards significance was noted, the result was not significant. A similar trend towards increasing shear stress was identified in patients with diabetes compared with healthy controls; this difference did not reach significance despite the studies being adequately powered. However, all studies revealed significantly greater shear stress in patients with diabetes compared with controls bar those normalising GRF according to bodyweight. The exact relationship between shear stress and ulcer formation has not been determined. High levels of shear stress were identified at the hallux and first and second MTHs,[9] the most common sites for plantar ulcer formation.[31] However, whilst one study identified 50% of ulcers formed at the site of maximal shear,[11] no other longitudinal studies have described a causal relationship between peak shear and ulcer formation. An absence of prospective studies, with significant heterogeneity in both the study protocol and technique of measurement of shear stress, mean firm conclusions cannot be drawn. Prospective studies, identifying those exhibiting elevated plantar shear stress and with length of follow-up sufficient to identify ulcer formation are necessary to determine the true effect of shear on patients with diabetic foot disease.

Offloading strategies, guided by plantar pressure assessment, have been shown to reduce healing time and reduce recurrence of DFUs.[32] However, whilst it has been demonstrated that those who develop DFUs often sustain elevated levels of plantar pressure, many do not, and there is often disparity between location of peak pressure and ulcer formation. Ledoux et al., performed a prospective analysis of patients with diabetes, measured plantar pressures at baseline and followed up to assess ulcer formation.[33] When hazard ratios were estimated by site, a statistically significant elevation in risk was observed in relation to peak pressure under the MTHs, while the elevation in risk associated with peak pressure at other sites was not significant. Furthermore, the heel and hallux regions had higher peak pressures at non-ulcer sites,[33] suggesting that peak pressure predicts increased risk of ulceration at the MTHs though not elsewhere. These findings are similar to those found by Veres et al.,[34] and Yavuz et al.,[11] found only 38% of plantar ulcers developed at the site of peak pressure. This suggests

there are gaps in our understanding of the pathomechanics and the biomechanical risk factors of ulcer formation. Lazzarini et al., describe the concept of 'plantar tissue stress' – "the accumulation of all mechanical stresses on an area of plantar foot tissue from all weight bearing activity over time."[17] The contribution of vertical pressure to overall plantar tissue stress appears more significant than that of shear, and shear is dependent upon pressure to effect injury. However, the additional cyclical changes in direction of shear force may result in greater tissue fatigue than unidirectional vertical force alone. Analysing plantar load in patients who have and have not ulcerated allows comparisons to be drawn regarding the presence or absence of risk factors. The finding that patients who have a current or previous ulcer show evidence of greater shear stress than their ulcer free counterparts denotes shear a potential biomechanical risk factor for ulcer formation. It is in this context that further research should be directed.

This systematic review highlights the technical difficulty of shear assessment, demonstrated by the numerous methodologies implemented in its measurement. Amemiya et al., used a commercially available device,[16] all other centres use custom-made devices with significant variation in the technology used, including strain-gauge systems[9–12,30], piezoelectric transducers[16] and magnetic resistive transducers.[7] Further variation is introduced by those that utilise surrogate markers of shear, including the tangential components of GRF[13,25,26] and using algorithms to convert peak pressure gradients to shear stresses.[23,27,28] Other systems have been used to measure shear stress though have not been trialled on patients with diabetes and therefore were not included in this review, including optical methods,[35] microstrip antennas[36] and capacitive microsensors.[37] Commercially available platforms are available and widely used for pressure measurement. However, there is no reference standard against which the results of the custom-built shear devices can be validated. In the absence of a secondary pressure platform, pressure assessment is also simple to validate through a static loading device. However, controlled application of shear stress with which to validate against is challenging. Methods estimating shear stress with pressure measurements and contact modelling have also not been validated against in-vivo measurements.[23,27,28]

There are limitations to this meta-analysis. A significant limiting factor is the evidence base, comprising studies with small sample sizes, risk of bias in many areas and nil prospective studies. With regards to the three studies investigating shear stress in those with a previous or current ulcer, Yavuz et al., present the only study directly measuring shear stress, yet there is paucity of information with regards to the conduct of the study.[30] Fernando et al., use a control group that comprises patients with diabetes, both with and without DPN.[13] As such, including both of these groups will result in a cohort of patients with markedly different levels of foot pathology. However, the data was not provided to perform a separate analysis. It was felt that the additional information provided valuable insights, and therefore a decision was made to accept the heterogeneity rather than exclude the data. Uccioli et al., and Fernando et al., analyse the tangential GRF applied through the foot.[13,25] However, the mechanical insult to the foot is dependent upon the surface area through which the force is applied which remains an unmeasured variable. Furthermore, Uccioli et al., normalised GRF according to bodyweight, Fernando et al., analysed absolute values. Overall, the comparison between patients with and without a history of ulceration is based upon a small number of studies, with heterogenous patient cohorts and methods of shear assessment. The findings should therefore be interpreted with the acknowledgement of these caveats.

More broadly, the wide range of modalities makes standardisation and interpretation of results across studies challenging. This review has attempted to mitigate the difference in scales used by comparing standardised mean difference. This however cannot account for the wide variability in outcomes reported, nor only analysing isolated aspects of the plantar surface. Several studies focused only on

the forefoot[12,15] and many neglected the hallux,[12,15,16,38] thereby excluding areas of the plantar foot that ulcerate, and as Ledoux et al., identified, may be less susceptible to the effects of pressure, and shear stress may have more of an effect.[33] Biomechanical surrogate markers of shear stress were included within this review, though not within the analysis. Shear occurs at different spatiotemporal locations to pressure,[12,39] and the methods have not been validated against real-world data.[27] Therefore, those utilising only pressure measurements to derive shear may draw inaccurate conclusions.[23,27–29]. Shear time integral has been shown to be elevated in multiple plantar regions in patients with DPN compared with non-DPN diabetes controls.[9] The time exposed to elevated plantar shear may be as significant a contributor to tissue injury as peak shear. However, shear time integral was an inconsistently reported variable and the data is not available for meta-analysis. Adjustment for potential confounding variables was inconsistent. Fernando et al., matched for age and sex, despite this, significant differences in sex, age and BMI were noted between groups.[13] Results were however adjusted and remained significant after adjustment. Yavuz et al., (2014) also assessed for influence of age and BMI on outcomes though found neither accounted for a significant proportion of the variance.[9] The diagnosis of DPN varied, with some adopting the use of Semmes-Weinstein monofilament,[10,12,27,28] others vibration perception threshold[7,9,26,27] and a variety of screening tools.[25,26] Uniform use of a recommended method of diagnosing peripheral neuropathy (IWGDF) would produce a more homogenous comparator. Study design further affects the interpretation of these results. As stated previously, no prospective studies have investigated the relationship between shear stress and ulcer formation.

A significant factor in shear assessment becoming clinically useful is modifying the technology from barefoot to in-shoe. The cornerstone of management of patients with diabetic foot disease is ensuring plantar tissue stress reduction through all weight bearing activities by using appropriate offloading measures. Therefore, barefoot analysis does not reflect the typical shear stresses that are sustained during a normal day. Only three of the studies directly measuring shear stress performed in-shoe analysis,[7,15,16] and none of these systems had the capacity to measure shear stress of the whole plantar surface. Wang et al., presented evidence-based requirements for wearable systems to monitor plantar load in patients with diabetic foot disease.[40] They describe load measuring capabilities of >740kPa for pressure and >140 kPa for shear, distribution of sensors across the plantar surface, sensor maximum surface area of 10mm x 10mm and a sampling rate of no less than 50Hz. In addition, they are required to be low profile and robust to maintain structural integrity in an environment subjected to significant load, changes in pH and temperature.[40] The optimal sensing technology has not been determined, with advantages and drawbacks with each method.[40] Choice will in part be determined by the desired clinical application; whether for use within a gait laboratory, during clinical assessment or to be worn on a daily basis for long term assessment of plantar load. Irrespective of the method chosen, consideration must be given to the cohort of patients wearing the technology and the clinicians and healthcare systems who may implement it. Development should be informed by a multidisciplinary approach to ensure user friendly, cost effective systems that can play role in healthcare pathways. Failure to consider these aspects, will lead to systems that are of academic interest alone and not inform or improve patient care. The results of this review highlight that the technology and evidence base is far from this stage. The future direction of shear assessment must satisfy the basic requirements highlighted above. Following establishment of a reliable, repeatable and robust tool to measure shear, rigorous academic methods should be applied to determine its efficacy.

Conclusion

This review shows that there is significant heterogeneity in the methodology and technologies used to measure shear stress in patients with diabetic foot disease. With this caveat, the available evidence suggests that high risk patients with diabetes and a history of ulceration exhibit greater shear stress than their ulcer free counterparts. Therefore, shear stress is an identifiable and potentially modifiable risk factor in ulcer formation. However, progress is required in several areas before it can be considered for use in clinical practice. Crucially, the technology must advance to allow in-shoe measurement of shear stress. This may allow prospective studies to identify associations between shear stress and future ulcer formation and in turn suggest strategies to mitigate this effect.

Funding:

This research received no specific grant from any funding agency in the public, commercial or non-for-profit sectors.

Contribution statement:

All authors were responsible for the drafting of the article and making critical revisions for intellectual content. All authors have approved the version to be published.

References

1. International Diabetes Federation. IDF Diabetes Atlas, 9th edition. Brussels, Belgium: 2019. Available at: https://www.diabetesatlas.org.

2. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367-2375.

3. Lepäntalo M, Apelqvist J, Setacci C, Ricco JB, de Donato G, Becker F et al. Chapter V: Diabetic foot. *Eur J Vasc Endovasc Surg*. 2011;42(SUPPL. 2):60-74.

4. Armstrong DG, Swerdlow MA, Armstrong AA, Conte MS, Padula W V., Bus SA. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. *J Foot Ankle Res*. 2020;13(1):2-5

5. Kerr M, Barron E, Chadwick P, Evans T, Kong WM, Rayman G et al. The cost of diabetic foot ulcers and amputations to the National Health Service in England. *Diabet Med*. 2019;36(8):995-1002.

6. Bus SA, Lavery LA, Monteiro-Soares M, Rasmussen A, Raspovic A et al.Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev*. 2020;36(1):e3269.

7. Lord M, Hosein R, M. A study of in-shoe plantar shear in patients with diabetic neuropathy. *Clin Biomech*. 2000;15(4):278-283.

8. Pollard JP, Le Quesne LP, Tappin JW. Forces under the foot. *J Biomed Eng*. 1983;5(1):37-40

9. Yavuz M. American Society of Biomechanics Clinical Biomechanics Award 2012: Plantar shear stress distributions in diabetic patients with and without neuropathy. *Clin Biomech*. 2014;29(2):223-229.

10. Yavuz M, Tajaddini A, Botek G, Davies BL. Temporal characteristics of plantar shear distribution: relevance to diabetic patients. *J Biomech*. 2008;41(3):556-559.

11. Yavuz M, Master H, Garrett A, Lavery LA, Adams LS. Peak plantar shear and pressure and foot ulcer locations: A call to revisit ulceration pathomechanics. *Diabetes Care*. 2015;38(11):e184-e185.

12. Perry JE, Hall JO, Davis BL. Simultaneous measurement of plantar pressure and shear forces in diabetic individuals. *Gait Posture*. 2002;15(1):101-107.

13. Fernando ME, Crowther RG, Lazzarini PA, Sangla KS, Buttner P, Golledge J. Gait parameters of people with diabetes-related neuropathic plantar foot ulcers. *Clin Biomech (Bristol, Avon)*. 2016;37:98-107.

14. Pai S, Ledoux WR. The shear mechanical properties of diabetic and non-diabetic plantar soft tissue. *J Biomech*. 2012;45(2):364-370.

15. Amemiya A, Noguchi H, Oe M, Takehara K,Ohashi Y, Suzuki R et al. Shear Stress-Normal Stress (Pressure) Ratio Decides Forming Callus in Patients with Diabetic Neuropathy. *J Diabetes Res*. 2016;2016:3157123.

16. Hamatani M, Mori T, Oe M, H, Noguchi H, Takehara K, Amemiya A, et al. Factors Associated With Callus in Patients with Diabetes, Focused on Plantar Shear Stress During Gait. *J Diabetes Sci Technol*. 2016;10(6):1353-1359.

17. Lazzarini PA, Crews RT, van Netten JJ, Bus SA, Fernando ME, Chadwick PJ, Najafi B. Measuring Plantar Tissue Stress in People With Diabetic Peripheral Neuropathy: A Critical Concept in Diabetic Foot Management. *J Diabetes Sci Technol*. 2019;13(5):869-880.

18. Rajala S, Lekkala J. Plantar shear stress measurements - A review. *Clin Biomech*. 2014;29(5):475-483.

19. Jones, AD., De Siqueiria J., Siddle, H., Culmer, P., Russell D. The role of plantar shear assessment in the management of the diabetic foot: a systematic review. *PROSPERO Int Prospect Regist Syst Rev*. 2020;CRD4202020.

20. Yavuz M, Ersen A, Hartos J, Lavery La, Wukich DK, Hirschman GB et al. Temperature as a causative factor in diabetic foot ulcers: A call to revisit ulceration pathomechanics. *J Am Podiatr Med Assoc*. 2019;109(5):345-350.

21. van Netten JJ, Bus SA, Apelqvist J, Lipsky BA, Hinchcliffe RJ, Game F et al. Definitions and criteria for diabetic foot disease. *Diabetes Metab Res Rev*. 2020;36(S1):1-6.

22. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M TP. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2013.

23. Zou D, Mueller MJ, Lott DJ. Effect of peak pressure and pressure gradient on subsurface shear stresses in the neuropathic foot. *J Biomech*. 2007;40(4):883-890.

24. Berki V, Davis BL. Spatial frequency content of plantar pressure and shear profiles for diabetic and non-diabetic subjects. *J Biomech*. 2016;49(15):3746-3748.

25. Sawacha Z, Guarneri G, Cristoferi G, Guiotto A, Avogaro A, Cobelli C. Integrated kinematics-kinetics-plantar pressure data analysis: a useful tool for characterizing diabetic foot biomechanics. *Gait Posture*. 2012;36(1):20-26.

26. Uccioli L, Caselli A, Giacomozzi, Macellari V, Giurato L, Lardieri L, Menzinger G. Pattern of abnormal tangential forces in the diabetic neuropathic foot. *Clin Biomech*. 2001;16(5):446-454.

27. Lott DJ, Zou D, Mueller MJ. Pressure gradient and subsurface shear stress on the neuropathic forefoot. *Clin Biomech*. 2008;23(3):342-348. doi:http://dx.doi.org/10.1016/j.clinbiomech.2007.10.005

28. Mueller MJ, Zou D, Bohnert KL, Tuttle LJ, Sinacore DR. Plantar stresses on the neuropathic foot during barefoot walking. *Phys Ther*. 2008;88(11):1375-1384.

29. Atlas E, Yizhar Z, Khamis S, Slomka N, Hayek S, Gefen A. Utilization of the foot load monitor for evaluating deep plantar tissue stresses in patients with diabetes: proof-of-concept studies. *Gait Posture*. 2009;29(3):377-382.

30. Yavuz M, Ersen A, Hartos J, Schwarz B, Garrett AG, Lavery LA et al. Plantar Shear Stress in Individuals With a History of Diabetic Foot Ulcer: An Emerging Predictive Marker for Foot Ulceration. *Diabetes Care*. 2017;40(2):e14-e15.

31. Armstrong DG, Lavery LA, Harkless LB. Validation of a Diabetic Wound Classification System. *Diabetes Care*. 1998;21(5):855-859.

32. Hulshof CM, van Netten JJ, Pijnappels M, Bus SA. The Role of Foot-Loading Factors and Their Associations with Ulcer Development and Ulcer Healing in People with Diabetes: A Systematic Review. *J Clin Med*. 2020;9(11):3591.

33. Ledoux WR, Shofer JB, Cowley MS, Ahroni JH, Cohen V, Boyko EJ. Diabetic foot ulcer incidence in relation to plantar pressure magnitude and measurement location. *J Diabetes Complications*. 2013;27(6):621-626.

34. Veves A, Murrary HJ, Young MJ, Boulton AJM. The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. *Diabetologia*. 1992;35(7):660-663.

35. Tavares C, Domingues MF, Frizera-Neto A, Leite T, Leitao C, Alberto N et al. Gait Shear and Plantar Pressure Monitoring: A Non-Invasive OFS Based Solution for e-Health Architectures. *Sensors (Basel)*. 2018;18(5).

36. Mohammad I, Huang H. Pressure and shear sensing based on microstrip antennas. *Sensors Smart Struct Technol Civil, Mech Aerosp Syst 2012*. 2012;8345:83451D

37. Heywood E, Jeutter D, Harris G. Tri-axial plantar pressure sensor: design, calibration and characterization. *Conf Proc IEEE Eng Med Biol Soc*. 2004;3:2010-2013.

38. Atlas E, Yizhar Z, Gefen A. The diabetic foot load monitor: A portable device for real-time subject-specific measurements of deep plantar tissue stresses during gait. *J Med Devices, Trans ASME*. 2008;2(1):11005.

39. Stucke S, McFarland D, Goss L, Fonov S, McMillan GR, Tucker A et al. Spatial relationships between shearing stresses and pressure on the plantar skin surface during gait. *J Biomech*. 2012;45(3):619-622.

40. Wang L, Jones D, Chapman GJ, Siddle HJ, Russell DA, Alazmani A, Culmer P. A Review of Wearable Sensor Systems to Monitor Plantar Loading in the Assessment of Diabetic Foot Ulcers. *IEEE Trans Biomed Eng*. 2020;67(7):1989-2004.

Tables

Title	Authors	Year	Study type	Groups (n)	Outcome	Barefoot /in-shoe	Footwear	Region	Device	Sensor type	Number of sensors	Size of sensors	Method of walking trial
Plantar Shear Stress in Individuals With a History of Diabetic Foot Ulcer: An Emerging Predictive Marker for Foot Ulceration.	Yavuz et al.,	2017	Case control	DUHx (9), DPN (16)	Plantar shear (kPa)	Barefoot	NA	Whole foot	Custom-built Cleveland clinic shear plate	Strain gauge	NS	NS	NS
Shear Stress-Normal Stress (Pressure) Ratio Decides Forming Callus in Patients with Diabetic Neuropathy.	Amemiya et al.,	2016	Cohort study	DPN - callus/non-callus (59)	Plantar shear (kPa)	In-shoe	Usual shoe	1st, 2nd, 5th MTH	ShokacChip	Piezoelectric	4 per trial	1.0cm x 1.0 cm	15 m walk Mean of two walking trials
Factors Associated With Callus in Patients with Diabetes, Focused on Plantar Shear Stress During Gait	Hamatani et al.,	2016	Cross sectional	DPN - callus (9)/non-callus (41)	Plantar shear (kPa)	In-shoe	Trial shoe	1st, 2nd, 5th MTH and heel	Custom-built: F-scan pressure sensor sheet overlayed with two uniaxial sensor sheets (AP shear) in the metatarsal region, one biaxial sensor sheet (AP + ML) overlayed the calcaneal region	Piezoelectric	960 cells	0.5 x 0.5 cm	Three steps per foot, first step removed from analysis
Spatial frequency content of plantar pressure and shear profiles for diabetic and non-diabetic subjects.	Berki et al.,	2016	Case control	DPN (13), HC (13)	Plantar shear (kPa)	Barefoot	NA	Whole foot	Custom-built Shear and pressure evaluating camera system (SPECS)	Surface stress sensitive film mounted on a 6 component force plate that measures ground reaction forces	20,000	1.6 x 1.6 mm	Three steps with second step making contact with sensor sheet (Two step method) Mean of four trials
Gait parameters of people with diabetes-related neuropathic plantar foot ulcers.	Fernando et al.,	2016	Case control	DU (21), DPN (69), HC (56)	Plantar shear (AP and ML GRF N)	Barefoot	NA	Whole foot	OR-6 AMTI Force plate	Strain gauge	NS	NS	Mean of 10 walking trials
Peak plantar shear and pressure and foot ulcer locations: A call to revisit ulceration pathomechanics	M., Yavuz et al.,	2015	Cross sectional	DUHx (8)	Plantar shear (kPa), ulcer location	Barefoot	NA	Whole foot	Custom-built Cleveland clinic shear plate	Strain gauge	NS	NS	NS
Plantar shear stress distributions in diabetic patients with and without neuropathy.	Yavuz et al.,	2014	Case control	DPN (14), DC (14), HC (11)	Plantar shear (kPa)	Barefoot	NA	Whole foot	Custom-built Cleveland clinic shear plate	Strain gauge	80	1.25cm x 1.25cm	Two step method Mean of three walking trials
Integrated kinematics-kinetics-plantar pressure data analysis: a useful tool for characterizing diabetic foot biomechanics.	Sawacha et al.,	2012	Case control	DPN (12), HC (12)	Plantar shear (AP and ML GRF %BW)	Barefoot	NA	Whole foot	FP4060-10 Bertec Force plate, Imagortesi plantar pressure	Strain gauge	NS	NS	Patients walked at a self-selected speed along a walkway. At least three force-plate

									system fixed to force plate				strikes of each limb were recorded for each patient
Utilization of the foot load monitor for evaluating deep plantar tissue stresses in patients with diabetes: proof-of-concept studies.	Atlas et al.,	2009	Case control	DPN + DC (10), HC (6)	Peak cylindrical shear	In-shoe	Usual shoe	Calcaneus	Custom-built - flexiforce sensor (Tekscan)	Elastic modulus of tissue measured by indentation in vivo, with measurement of ground reaction forces. Herz solution to calculate internal stresses			Mobilise on flat surface for two minutes, followed by ascent and descent of 10 step staircase
Plantar Stresses on the Neuropathic Foot During Barefoot Walking	Mueller et al.,	2008	Case control	DU (12), HC (12)	Derived plantar shear (kPa)	Barefoot	NA	Whole foot	EMED ST P-2	Capacitive	NS	NS	Two step method, three trials per foot
Pressure gradient and subsurface shear stress on the neuropathic forefoot.	Lott et al.,	2008	Case control	DU (22), DPN (16), HC (16)	Derived plantar shear (kPa)	Barefoot	NA	Forefoot	F-scan	Resistive	960	0.5 x 0.5 cm	Two walking trials, mean of 3 consecutive steps in the middle portion of the trial
Temporal characteristics of plantar shear distribution: relevance to diabetic patients.	Yavuz et al.,	2008	Case control	DPN (15), HC (20)	Plantar shear (kPa)	Barefoot	NA	Whole foot	Custom-built Cleveland clinic shear plate	Strain gauge	80	1.25cm x 1.25cm	Two step method Mean of three walking trials
Effect of peak pressure and pressure gradient on subsurface shear stresses in the neuropathic foot.	Zou et al.,	2007	Cross sectional	DUHx (20)	Derived plantar shear (kPa)	In-shoe	Trial shoe	Whole foot	F-scan	Resistive	960	0.5 x 0.5 cm	Two walking trials, does not describe when data taken
Simultaneous measurement of plantar pressure and shear forces in diabetic individuals.	Perry et al.,	2002	Cross sectional	DPN (12)	Plantar shear (kPa)	Barefoot	NA	Forefoot	Custom-built Cleveland clinic shear plate	Strain gauge technology	16	2.5cm x 2.5 cm	Right foot on initiation of gait
Pattern of abnormal tangential forces in the diabetic neuropathic foot.	Uccioli et al.,	2001	Case control	DUHx (15), DPN (19), DC (27), HC (21)	Plantar shear (AP and ML GRF %BW + braking and propulsive)	Barefoot	NA	Whole foot	Custom-built Piezo-dynamometric platform overlaying a Bertec force plate	Piezoelectric, strain gauge	NS	NS	Patients walked across a 5.6 m walkway with platform embedded in the centre Mean of 6 walking trials per foot
A study of in-shoe plantar shear in patients with diabetic neuropathy.	Lord et al.,	2000	Cross sectional	DUHx (6)	Plantar shear (kPa)	In-shoe	Usual shoe with insole substituted for trial inlay accommodating sensors	Heel and 1st, 2nd, 3rd and 4th MTHs	3 transducers mounted flush to trial insole (F-scan - plantar pressure)	Magnetoresistive transducers	3	1.6cm x 1.6cm	Patients walked across a 10m walkway, data recorded for 5s over the central walk, left and right feet

Table 1: Methodology of included studies (DU – active diabetic foot ulceration, DUHx - previous diabetic foot ulceration, DPN – diabetic peripheral neuropathy, DC – non-DPN diabetes control, HC – healthy control, MTH – metatarsal head)

Case-control	Selection				Comparability	Exposure		
Study	Case definition	Representative of cases	Selection of Controls	Definition of Controls	Comparability of cases and controls on the basis of design/analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
Yavuz et al., 2017	*			*		*	*	*
Berki et al., 2016						*	*	*
Fernando et al., 2016	*	*	*	*	*	*	*	*
Yavuz et al., 2014	*	*		*	*	*	*	*
Sawacha et al., 2012	*	*		*		*	*	*
Atlas et al., 2009	*					*	*	*
Mueller et al., 2008	*	*			*	*	*	*
Lott et al., 2008	*			*	*	*	*	*
Yavuz et al., 2008	*			*	*	*	*	*
Uccioli et al., 2001		*		*	*	*	*	*

Cross-sectional	Selection				Comparability	Outcome	
Study	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of exposure	Comparability	Assessment of outcome	Statistical test
Hamatami et al., 2016	*			*		**	*
Yavuz et al., 2015				*		**	
Zou et al., 2007				*		**	
Perry et al., 2002				*		**	*
Lord et al., 2000	*			*		**	

Cohort	Selection				Comparability	Outcome		
Study	Representative of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Amemiya et al., 2016	*	*	*	*		*		*

Table 2: Newcastle-Ottawa risk of bias assessment for case-control, case series and cohort studies

	DFU					Non-DFU			
Study	n	Age	BMI	% Men	Active ulcer	N	Age	BMI	% Men
Yavuz et al., 2017	9	NS	NS	NS	0	16	NS	NS	NS
Fernando et al., 2016	21	63.1	34	71.4	21	69	63.4	31.8	66.7
Uccioli et al., 2001	15	57.3	27.5	66.7	0	19	53.7	27	52.6

Table 3: Baseline characteristics of subjects with a current or history of diabetic foot ulceration (DFU) compared with patients with diabetes without a history of ulceration (non-DFU)

	DPN/DC				HC			
Study	n	Age	BMI	% Men	n	Age	BMI	% Men
Fernando et al., 2016	69	63.4	31.8	66.7	56	57.6	26.1	42.9
Yavuz et al., 2014	14	52.4	28.9	35.6	11	65.5	27.8	36.4
Sawacha et al., 2012	12	62	25.2	66.7	12	60.3	24.1	83.3
Yavuz et al., 2008	15	60.5	29.2	80	20	45.8	24.9	60
Uccioli et al., 2001	19	53.7	27	52.6	21	56.6	25	61.9

Table 4: Baseline characteristics of subjects with DPN (+/- non-DPN diabetes controls if cohort does not specify) compared with healthy controls (HC).

Study			Hallux	Toes	Medial Forefoot	Central forefoot	Lateral forefoot	1st MTH	2nd MTH	3rd MTH	4th MTH	5th MTH	Heel	Forefoot	Rearfoot
Amemiya et al., 2016 (kPa)	DPN Non-Callus	-	-	-	-	-	-	120 (extracted)	118 (extracted)	-	-	62 (extracted)	-	-	-
	DPN Callus	-	-	-	-	-	-	127 (extracted)	158 (extracted)	-	-	83 (extracted)	-	-	-
Yavuz et al., 2014 (kPa)	DPN	14	77.9	35 (extracted)	54 (extracted)	72 (extracted)	51 (extracted)	-	-	-	-	-	-	-	-
	DC	14	50 (extracted)	27 (extracted)	49 (extracted)	77.6	61 (extracted)	-	-	-	-	-	-	-	-
	HC	11	46 (extracted)	28 (extracted)	44 (extracted)	61.1	46 (extracted)	-	-	-	-	-	-	-	-
Sawacha et al., 2012 (%B.W.)	DPN	12	-	-	-	-	-	-	-	-	-	-	-	14.94	10.42
	HC	12	-	-	-	-	-	-	-	-	-	-	-	13.25	12.69
Lott et al., 2008 (kPa)	DUHx	22	-	-	-	-	-	-	-	-	-	-	-	90	-
	DPN	16	-	-	-	-	-	-	-	-	-	-	-	79	-
Mueller et al., 2008 (kPa)	DU	12	-	-	-	-	-	-	-	-	-	-	-	230	93
	HC	12	-	-	-	-	-	-	-	-	-	-	-	170	70
Zou et al., 2007 (kPa)	DUHx	20	-	-	-	-	-	-	-	-	-	-	-	79	67
Perry et al., 2002 (kPa)	DPN	12	-	18	-	-	-	18			33		-	-	-
Uccioli et al., 2001 (kPa)	DUHx	15	3.1	-	-	-	-			16.6			12.8	-	-

Range (peak to peak of AP GRF) (%B.W)	DPN	19	3.5	-	-	-	-			15.4		13.4	-	-
	DC	27	4.3	-	-	-	-			15.8		15.2	-	-
	HC	21	5.7	-	-	-	-			16.6		15.8	-	-
Lord et al., 2000 (kPa)	DPN	6	-	-	-	-	-	72.7	63.6	50.5	39.4	41.0	-	

Table 5: Regional distribution of shear stress in the diabetic foot. (DU – active diabetic foot ulceration, DUHx - previous diabetic foot ulceration, DPN – diabetic peripheral neuropathy, DC – non-DPN diabetes control, HC – healthy control, MTH – metatarsal head)