

Title:

Risk factors for the development and evolution of deep tissue injuries: A systematic review

Abstract:**Aims:**

The aim of this systematic review is to identify the current epidemiological evidence indicating the unique risk factors for deep tissue injury (DTI) in addition to the proportion of DTI which evolve rather than resolve and the anatomical distribution of DTI.

Methods:

A systematic literature search was undertaken using the MEDLINE and CINAHL Plus databases using the search terms 'Deep tissue injury OR DTI [Title/abstract]'. A google scholar search was also conducted in addition to hand searches of relevant journals, websites and books which were identified from reference lists in retrieved articles. Only peer-reviewed English language articles published 2009-2021 were included, with full text available online.

Results:

The final qualitative analysis included nine articles. These included n=4 retrospective studies, n=4 prospective studies and n=1 animal study.

Conclusion:

The literature indicates that the majority of DTI occur at the heel and sacrum although in paediatric patients they are mainly associated with medical devices. Most DTI are reported to resolve, with between 9.3-27% deteriorating to full thickness tissue loss.

Risk factors unique to DTI appear to include anaemia, vasopressor use, haemodialysis and nicotine use although it is unclear if these factors are unique to DTI or are shared with grade I-IV PI. Factors associated with deterioration include cooler skin measured using infrared thermography and negative capillary refill. With 100% of DTI showing positive capillary refill in one study resolving without tissue loss ($p=0.02$) suggesting this may be an effective prognostic indicator.

Prospective studies of DTI's are challenging to conduct. Future longitudinal prospective studies are required with a focus on establishing potential causal links between risk factors identified in the earlier retrospective studies as baseline eligibility criteria across primary, secondary and tertiary care. Further work is also needed to establish reliable diagnostic criteria for DTI in addition to more studies in paediatric populations.

Keywords: DTI, deep tissue injury, pressure, risk factors

1. Introduction:

The risk factors for deep tissue injuries (DTI) are unclear and is further compounded by the terminology used which fails to encapsulate the deep tissue injury form (Oomens et al., 2019) and the classification systems used (EPUAP, 2019). Despite being widely recognised that deeper tissue damage mainly occurs at the bony prominences when there is high pressure in combination with shear forces, leading to tissue ischaemia and cell death (Gefen, 2009), variations in reporting of DTI have contributed towards the collection of low-quality prevalence data. In a systematic review by Tubaishat et al. (2018) the proportion of pressure ulcers by grade rates for those categorised as unstageable/suspected deep tissue injury was documented to be 0% - 14% globally in acute care settings. However, the authors note that a limitation of their findings was the lack of a consistent and standardised method across the appraised studies when conducting point prevalence. Within the UK, this lack of clarity has led to DTI being described by NHS Improvement (2019, p6.) as a 'hidden' category of pressure injury, alongside medical device related injuries. DTI are currently associated with similar pathophysiological processes as grade I-IV pressure injury including similarities in risk factors such as poor mobility, impaired sensation, and reduced blood flow (Fletcher et al., 2017). Adding to this discussion Kayser et al. (2018) in a retrospective analysis of the 2011–2016 International Pressure Ulcer Prevalence data also reported that alongside ambulatory status, incontinence management were substantial predictors of risk in acquiring severe pressure ulcers. Key differences however, between DTI and grade I-IV PI include the ability for DTI to 'resolve' (healing with no break in dermal tissues), or 'evolve' which can lead to significant tissue loss creating deep, chronic wounds (Fletcher et al., 2017).

There are no major studies investigating the economic burden of DTI however it is currently estimated to cost the NHS more than £3.8 million daily (NHS Improvement 2018). A study by Guest et al (2018) investigating the costs of PI management in community settings reported that costs increase with the severity of the ulcer and unhealed ulcers can cost up to 2.4 times more than managing healed ulcers. Notably, the authors reported that outcomes were not reached by all PI included with the study indicating that the true costs to patients and the NHS posed by large or

chronic wounds, such as evolved DTI, is still unknown. A recent study on the global burden of pressure injuries reported that the burden is highest among high-income countries, this may be due to the ageing populations or issues related to reporting (Zhang et al 2021). Compounding our current understanding of DTI and PI are the varied and changing grading systems used by clinicians to categorize these wounds. According to Levine (2019) clinical coding systems used in the US often utilise more codes for wounds related to pressure than there are grades in contemporary grading systems. This may negatively impact the value of retrospective data analyses to identify risk factors to help prevent these injuries in addition to limiting the comparability of data collected from different healthcare systems.

Deep tissue injury (DTI) became a distinct classification of pressure injury (PI) in 2009 following the recognition of the unique clinical presentation and pathogenesis of these injuries compared with normal PI (Fletcher et al 2017). DTI have since been defined as

“...purple or maroon localized area of discoloured intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue.”

(NPIAP/EPUAP/ PPPIA, 2019, p.3).

Variations across healthcare systems in requirements for reporting and data collection, has caused confusion regarding when and how DTI should be reported. Despite the recognition of the unique clinical appearance, and natural history of DTI compared to PI initially presenting as grade I-IV ulcers, there remains little data indicating the unique risk factors associated with DTI or what influences their outcomes. This review seeks to delineate current evidence showing the basic epidemiological characteristics of DTI. Determining the current risk factors for DTI may allow more focused study of unique risk factors associated with their development and subsequent evolution or resolution. Knowledge of the risk factors associated with DTI may help develop preventative interventions and contribute towards a more evidence-based approach to root cause analysis investigations for PI, the outcomes of which have been associated with notable increases in litigation

costs to the NHS in recent years (Stephenson 2019). DTI also remain a frequent source of litigation in the United States (Stewart et al 2022).

2. Methodology

This review was conducted following the PRISMA statement, to optimise the reporting within the review and reduce the risk of publication bias (Moher et al 2009).

Research Question:

What are the epidemiological features of deep tissue injuries?

Objectives:

1. Determine the anatomical distribution of DTI as reported in the literature.
2. Determine the proportion of DTI which evolve into full-thickness tissue loss as reported in the literature.
3. Identify potential risk factors for DTI that do not otherwise feature in current literature on pressure ulcers/injuries.

A simple search strategy was adopted to maximise the retrieval of primary studies. A PICO / PEO / SPIDER framework was not used to reduce the risk of excluding potentially relevant articles by including more restrictive search terms based on research methodology, specific patient populations or specific outcome data. The currently limited literature base providing clinical data on DTI made a simple search strategy viable, and more likely to yield relevant articles using the search terms 'deep tissue injury OR DTI'. Systematic searches of the Medline, CINAHL Plus databases were used as they are considered essential databases for questions related to nursing (Sibirana et al 2005). A GOOGLE scholar search was also conducted with hand searches of relevant journals, websites and books identified from reference lists in retrieved articles.

The inclusion criteria for the review consisted of articles published between 2009-2021, as 2009 was the year DTI were re-defined into the current (2021)

NPIAP/EPUAP/ PPPIA (2019) definition. This is to ensure consistency in definitions utilised within the studies and avoid erroneous inclusion of data related to what would now be considered non-DTI pathologies. Published and unpublished randomised controlled trials (RCTs), including cluster-RCTs, non-RCTs (NRCTs), prospective studies, pre–post-studies and interrupted-time-series (ITS) studies where the full text of the article was available and written in English. The types of

participants in the studies could include adults and paediatrics or animal studies which model the development or deterioration of DTI. The exclusion criteria consisted of articles written before 2009, not written in English and where full text was not available.

Search terms used: Deep tissue injury OR DTI [Title/abstract]

The literature search resulted in a set of 378 articles after duplicates were removed using Mendeley reference manager. Studies were screened by the first author for inclusion in the qualitative analysis resulting in 358 articles being excluded based on inclusion /exclusion criteria. Full-text screening of the remaining 20 articles identified 9 studies for inclusion in the final analysis (Richbourg et al 2011, Sullivan 2013, Sari et al 2015, Cox et al 2016, Hobson et al 2017, Kirkland-Khyn et al 2017, Pellegrino et al 2017, Tescher et al 2018, Bates-Jensen et al 2018). Notably, three studies were excluded due to changes to the definition of DTI mid-study (Kottner et al 2010, VanGilder et al 2010 and Honaker et al 2014). Kottner et al reported that no back-analysis was conducted to account for the change in definition of DTI mid-study and VanGilder et al (2010) reported a threefold increase in DTI reported within their study which was attributed to the change in definition. Honaker et al (2014) did not describe if/how the change in definition affected their results, it is therefore unclear how DTI were defined within this study. These three studies were excluded to avoid contamination of the analysis within this review from data related to non-DTI PI. Data analysis undertaken in all three studies was not stratified by year of diagnosis, so it is unclear how reliable risk factors for DTI development or evolution reported in these studies are. The pre-2009 definition included the term 'suspected' (Fletcher 2017), which indicates that in some cases there was either uncertainty over the diagnosis (by definition) or that the injury may be re-classified as non-DTI if no evolution into an open wound occurred. The change in definition may therefore have had an impact on both the inclusion of DTI in studies pre-dating the current definition and consequently impact on the analysis of potential risk factors for DTI, particularly for the evolution of DTI into open wounds.

Analysis of the quality of evidence from the included studies was undertaken using the Strengthening Reporting of Observational Studies in Epidemiology statement (STROBE) (Von Elm et al 2007). A quality assessment of the included cohort studies using the STROBE checklist (see table 1). The STROBE checklist is made up of twenty-two items, eighteen are usual to all the three observational designs, that is, cohort, cross-sectional, and case-control studies and include assessment of items such as title, abstract, introduction, methods, results, discussion, funding and sponsorship and a conclusion. The other four checklist items have specific variations according to the study design for example assessment of the participants, statistical methods, descriptive data and outcome data. On review, the studies were given a red, amber green (RAG) rating to indicate whether the STROBE criteria were met (green), unmet (red) or unclear (amber) (see table 2). For example, in relation to 'main results' the Bates-Jensen et al (2018) study reported relative risk ratios with a 95% confidence interval, so this was highlighted as green. Whereas, in the Sullivan (2013) study descriptive statistics were used only, so this was highlighted as red. This reflects the variations in methodological robustness between the studies.

Assessment of quality was undertaken by authors MW, MS and SP to reduce the risk of bias using Critical Appraisal Skills Programme (CASP) checklists. These are generic tools for appraising the strengths and limitations of any qualitative research methodology (CASP UK, 2021).

3. Results

The studies retrieved via the search included n=4 retrospective studies (Sullivan 2013, Hobson et al 2017, Kirkland-Khyn et al 2017, Tescher et al 2018). These studies involve retrospectively examining the case notes of patients with DTI or PI to yield data related to risk factors for the acquisition and/or deterioration of DTI in addition to other key epidemiological data. Retrospective studies are often quick and cheap to carry out and are therefore common in healthcare (Toftthagen 2012). However, they are limited by the data available in-patient case notes and an absence of control over historical factors affecting outcomes potentially threatens internal validity of the studies (Parahoo 2014). For this reason, retrospective studies cannot be used to determine cause-and-effect relationships (Toftthagen 2012).

Prospective studies providing data on risk factors for DTI evolution into open wounds and describing the demographics of patients with DTI were also identified (n=4) (Richbourg et al 2011, Cox et al 2016, Pellegrino et al 2017, Bates-Jensen et al 2018). These studies prospectively observe cohorts of patients with DTI/PI over a period to observe correlations between pre-defined factors and clinical outcomes. The prospective studies included in this review adopted various methodologies and included data on different and inconsistent risk factors making comparisons between them difficult. Often the studies were insufficient in length with around half of the included DTI not reaching final outcomes in some cases (Campbell et al 2010, Richbourg et al 2011, Bates-Jensen et al 2018). One murine model of DTI deterioration was also included (Sari et al 2015) which provided data on the potential implications of anatomical variation on DTI outcomes. It is interesting to note that most studies did not mention use of power analysis to calculate the number of participants in the study, this is therefore a limitation to the generalizability of the findings.

3.1. Anatomical distribution of DTI

Five of the nine studies reported data on the anatomical distribution of DTI (Richbourg et al 2011, Sullivan 2013, Cox et al 2016, Pellegrino et al 2017 and Tescher et al 2018). The anatomical distribution of PI is often reported in prevalence studies (Clark et al 2017, Jacq et al 2021). By understanding the distribution of

injuries, a more accurate risk profile can be developed for DTI. For example, it is frequently reported that more severe PI (grade III+) are present at the sacrum (Clark et al 2017). By understanding the most common sites that DTI occur the unique characteristics of these injuries may be determined, and potential intrinsic factors associated with their development identified. According to Smart (2013) stiff musculature present around the sacrum and heel may contribute towards a compartment-syndrome-effect following swelling caused by ischaemia and vascular occlusion and therefore suggests that DTI be re-named as 'hypoxic reperfusion ulcers' (p.58). This theory relies on an assumption that the physiological and metabolic state of the patient are more significant factors in DTI than the extrinsic pressure related factors commonly associated with grade I-IV PI.

Data from the included studies indicate that the majority of DTI are reported at the sacrum (41.9% - Richbourg et al 2011, 40%-Sullivan 2013, 26% coccyx – Tescher et al 2018). The study by Cox et al included anatomical distribution data which was not stratified by PI grade. Pellegrino et al (2017) was the only study to report data on paediatric patients reporting the majority of DTI at the heel (33%) followed by medical device related (27%). Overall, the studies broadly support the theory of Smart (2013) with the majority of DTI reported at the heel and sacrum which are areas associated with stiff musculature. The Pellegrino et al (2017) study however suggests a risk profile for DTI which is different in paediatric patients. Within this study the authors did not stratify the risk data by PI grade making it impossible to determine what the anatomical distribution of DTI may be in paediatric patients.

3.2. Risk factors for DTI

In total five of the included studies reported data relating to risk factors for DTI (Richbourg et al 2011, Sullivan 2013, Kirkland-Kyhn et al 2017, Tescher et al 2018, and Bates-Jensen et al 2018). Risk factors identified within the included studies can be seen in Table 4 below.

Table 4. Risk factors for DTI reported in the literature

Risk factor	Statistically significant	Supporting study
Anaemia	Unknown	Richbourg et al (2011)
Nicotine use		Richbourg et al (2011)
Undergoing surgical procedure during hospital admission		Richbourg et al (2011)
Reduced mobility		Richbourg et al (2011)
Incontinence		Richbourg et al (2011)
Post organ transplant		Richbourg et al (2011), Sullivan (2013)
Peripheral vascular disease		Tescher et al (2018)
Hypertension		Tescher et al (2018)
Increased length of time in surgery (6<hours)	P<0.001	Richbourg et al (2011), Kirkland-Kyhn et al (2017)
Use of haemodialysis	P<0.001	Kirkland-Kyhn et al (2017)
Shock	P<0.001	Kirkland-Kyhn et al (2017)
Low mean diastolic blood pressure (49mmHg)	P<0.001	Kirkland-Kyhn et al (2017)
Low sub-epidermal moisture scores	P<0.007	Bates-Jensen et al (2018)
Higher Braden score (mean 14.1)	P<0.01	Bates-Jensen et al (2018)

The earliest descriptive study by Richbourg et al (2011) based on prospective data, reported risk factors identified via comparison of multiple pressure ulcer risk factor variables using the Fisher exact test. Notably, peripheral arterial disease was not identified as a statistically significant risk factor suggesting nicotine use may not be a proxy indicator of arterial disease but an independent risk factor. However, this study utilised a small sample of n=40 subjects from a variety of settings including care homes, patients own homes, clinics, and inpatient settings. The sample size was not informed by a power calculation. The authors reported limitations of the study including poor consistency between nurses in classifying the lesions included in the study as DTI. It is also notable that anaemia is associated with skin manifestations of several dermatological conditions (Hunter et al 2013). It is therefore unclear if this is a true risk factor for DTI, it could also suggest that the DTI reviewed in this study could be the result of a non-DTI, dermatological aetiology.

Sullivan (2013) conducted a retrospective review including a sample of 77 patients with DTI drawn from an acute inpatient population. Data analysis in this study included only descriptive statistics. It is therefore unclear whether the factors identified within this study are statistically or clinically significant. It may be possible that the factors reported in this study are reflective of the participant demographics rather than potentially contributory factors associated with the development or evolution of DTI. A later retrospective study by Kirkland-Kyhn et al (2017) investigated risk factors for DTI development in critical care patients via a review of electronic medical records over a five-year period between 2010-2015. The authors utilised a control group of patients who did not develop a pressure injury to conduct statistical tests indicating the significance of risk factors for DTI. The authors reported that it appeared patient related factors are more statistically significant than extrinsic factors which supports data previously reported by Sullivan (2013). Kirkland-Kyhn et al (2017) only reviewed sacral DTI in critical care patients, it is therefore unclear if these risk factors are common across all patient groups or if they represent risk factors unique to DTI rather than PI as the control group used in this study were of patients with no pressure injuries. However, it could be argued that haemodialysis, shock and length of time in the operating theatre are proxy indicators of immobility which may be the more significant risk factor. The findings of both the

Richbourg et al (2011) and the Kirkland-Kyhn (2017) studies were supported by a retrospective descriptive analysis of hospital-acquired DTI by Tescher et al (2018). The authors reported that pre-DTI factors included peripheral vascular disease and hypertension, suggesting that intrinsic factors may play a greater role in the development of DTI than extrinsic factors. However, this study utilised a non-statistically powered sample and did not analyse the statistical significance of data related to factors associated with the development of DTI.

The studies by Richbourg et al (2011), Sullivan (2013), Tescher et al (2018) did not use control groups, comparing patients with DTI to patients with grade I-IV PI. It is therefore unclear if these factors are unique to DTI compared to other types of PI.

Bates-Jensen et al (2018) reported the only longitudinal prospective study investigating risk factors for the development of PI including DTI. The authors focused on the use of subepidermal moisture (SEM) scans using the Delfin MoistureMeter (Delfin Technologies, LTD, Greenwich, Connecticut). SEM scans are proposed to indicate the presence of tissue damage by measuring macroscopic changes in subdermal moisture (Smith 2019). Bates-Jensen et al (2018) reported that SEM values were significantly lower when DTI were observed ($p=0.007$) compared to patients with no visible damage. Compared to DTI, SEM values were significantly higher for erythema ($p=0.005$). However, SEM scans are still not considered a reliable indicator of PI risk and are not currently recommended by the National Institute for Health and Care Excellence (2020). The Bates-Jensen et al (2018) study utilised a sample of nursing home residents who may have had co-morbidities which may have contributed to the development of DTI such as, anaemia, (Richbourg et al 2011) peripheral vascular disease or hypertension (Tescher et al 2018). It is therefore likely that changes in subepidermal moisture levels may be predictive of DTI development or evolution but do not necessarily represent a risk factor unique to DTI compared to grade I-IV DTI.

3.3. Factors associated with evolution / resolution

Studies by Richbourg et al (2011), Tescher et al (2018), Bates-Jensen et al (2018) and Cox et al (2018) provided data on factors potentially associated with the

evolution or resolution of DTI as well as the acuity of the underlying illness. Risk factors for the evolution of DTI identified within the included studies can be seen in Table 5 below.

Table 5. Risk factors for the evolution of DTI

Risk Factor	Statistically significant	Supporting study
Higher concurrent SEM values	Not statistically significant	Bates-Jensen et al (2018)
Nicotine use	Unknown	Richbourg et al (2011)
Undergoing surgical procedures		Richbourg et al (2011)
Shape of underlying structures (e.g., bone)		Sari et al (2015)
Anaemia	P<0.005	Richbourg et al (2011), Tescher et al (2018)
Cooler skin temperature at the site of discoloration	P<0.08	Cox et al (2016)
Negative capillary refill	P<0.02	Cox et al (2016)
History of cerebrovascular accident	P<0.03	Tescher et al (2018)
Use of mechanical ventilation	P<0.01	Tescher et al (2018)
Increased critical care length of stay	P<0.03	Tescher et al (2018)
Vasopressor use post DTI diagnosis	P<0.003	Tescher et al (2018)
Low air loss mattress use post DTI diagnosis	P<0.002	Tescher et al (2018)
Use of medical devices	P<0.002	Tescher et al (2018)
Use of feeding tube	P<0.02	Tescher et al (2018)

To date the only prospective study primarily investigating the natural history of DTI in human subjects was conducted by Richbourg et al (2011). The results of this descriptive study indicated that risk factors for evolution of DTI into open wounds. The authors reported that 26% of DTI evolved into full thickness tissue loss. This is almost triple the evolution rate reported in later retrospective studies, although this may reflect improvements in preventative care or changes in reporting (Sullivan 2013, Tescher et al 2018). The Richbourg et al (2011) study reported that 48% of the DTI included showed no change within the trial follow up period, this in combination with the utilisation of a small sample size (n=40), may have skewed the data.

A later prospective study by Cox et al (2016) investigated relationships between skin temperature measured using infrared thermography and other factors associated with the progression of discoloured skin (grade I, II PI and DTI) into necrosis. This was the first study providing data on risk factors to be statistically powered and utilise multivariate analysis. Notably, 100% of lesions with a positive capillary refill did not progress into necrosis. The Cox et al (2016) study sample was drawn from six skilled nursing facilities and excluded patients with lesions 'suspected to be of other aetiologies'. It is unclear exactly how patient eligibility was assessed in this regard. Patients who were actively dying were also excluded. Notably, an audit of NHS inpatients in an hospital in England reported that 44% of patients passed away within eight weeks of an incident report being submitted (White 2017). This suggests that end-of-life patients may be at greater risk for poorer outcomes related to DTI, data related to this patient group is therefore likely to be valuable in establishing an accurate risk profile for DTI.

The study by Tescher et al (2018) study supported the earlier Sullivan (2013) study reporting that only a minority (11%) of DTI evolved to full thickness tissue loss. However, due to the retrospective design of the Tescher et al (2018) study and lack of comparison group it is unclear whether these risk factors represent the risk of deterioration of all pressure ulcers e.g., grade I to grade III or whether these factors are unique to the evolution of DTI.

Bates-Jensen et al (2018) reported SEM values for predicting deterioration in a small cohort of patients with DTI (n=40). Of these n=10 progressed to full thickness tissue loss. These patients showed higher concurrent SEM values than patients whose DTI did not evolve. However, this finding was not reported to be statistically significant, it is therefore unclear if it is clinically significant. Importantly, 55% (n=22) of the DTI observed within the Bates-Jensen et al (2018) did not resolve despite optimal care being provided including off-loading and repositioning. This supports the earlier Richbourg et al (2011) study which reported that 25% of DTI developed into full-thickness ulcers despite 'aggressive' preventative care. This may indicate that current management approaches for DTI may have limited efficacy, or that intrinsic factors may play a greater role in DTI outcomes. The latter possibility appears to be supported by data presented in early studies related to risk factors for DTI, showing

that patients co-morbidities (particularly cardiovascular and haematological pathologies) appear to be a statistically significant factor in both the development and evolution of DTI (Richbourg et al 2011, Kirkland-Kyhn 2017, Tescher et al 2018).

3.4. Animal model of DTI deterioration:

A murine model for deep tissue injury deterioration was developed by Sari et al (2015). The model utilised a prominence device (a solid object) placed subcutaneously with pressure applied over the skin. The study demonstrated via histological analysis that under the study conditions tissue damage starts in the deeper muscle tissue consistent with the current consensus on the 'bottom up' nature of DTI (Fletcher et al. 2017). The authors reported that the pressure within the tissues created by the shape of the subcutaneous prominence was crucial to the deterioration of the DTI rather than resolution. It is difficult to extrapolate the findings of this study to human subjects due to the inherent differences between animal and human tissue (Ansell, 2012). The Sari et al., (2015) only considered the shape of underlying structures and their interaction with external pressure and suggests that sufficient pressure applied to any patient with anatomy consistent with the test conditions should experience deterioration of the DTI regardless of other extrinsic / intrinsic factors. This is not observed in clinical practice however, DTI can occur due to medical devices (Tescher et al., 2018) which have various shapes and may create pressure over tissues inconsistent with the Sari et al. (2015) study. It also does not account for comorbidity which has been demonstrated to impact DTI outcomes (Kirkland-Kyhn et al., 2017).

4. Discussion

Retrospective studies of DTI have indicated key epidemiological features of DTI. Currently indicating the majority of DTI occur on the sacrum and heels (Sullivan 2013, Tescher et al 2018). It appears the majority of DTI do not evolve into open wounds with between 9.3-11% deteriorating to full thickness tissue loss (Sullivan 2013, Tescher et al 2018) however it is possible this is an underestimate with the

outcomes of many DTI being lost to follow up. Key factors for DTI development appear to include use of haemodialysis, shock, low diastolic blood pressure and increased length of time in surgery, which would increase immobility and pressure on the skin (Kirklan-Kyhn et al 2017). Factors associated with evolution into open wounds include a history of cerebrovascular accident, anaemia, mechanical ventilation, critical care length of stay, vasopressor use, low air loss mattress use post-DTI diagnosis and use of medical devices (Tescher et al 2018). It is also possible that the shape of underlying anatomical structures such as sub-dermal bones may influence DTI outcomes (Sari et al 2015).

Data indicating the relative importance of intrinsic factors in the development of DTI is supported by seminal work on the nature of hyperaemia by Bliss (1998) who reported that persistent erythema, like that seen in pressure injuries, is an indication of inflammation. The escape of fluid and protein into the interstitium creates discolouration of the skin as the concentration of immune cells in the tissues increases and thrombosis in the small vessels occurs. As such, factors such as neurological, vascular or haematological changes created by infection or pharmaceuticals may increase the risk persistent erythema (Bliss 1998). Crucially, determining the balance of intrinsic and extrinsic factors contributing to the development of DTI may be key to effective prevention and treatment strategies. The unusual discolouration of the skin in cases of DTI may be explained in part by these intrinsic micro-vascular level changes in concentrations of inflammatory cells due to intrinsic factors.

Clinical practice in pressure ulcer care is currently limited by factors including the ongoing lack of data indicating the value of preventative strategies, variations in care and clinimetric issues with current risk assessment tools (Wynn 2020). Current NICE (2014) guidance on the prevention and management strategies does not discriminate between DTI and grade I-IV PI (or between paediatric and adult patients) despite the observable differences in the clinical manifestations of these injuries. Risk factors identified by the studies included in this review indicate there may be targets for the prevention and management of DTI specifically, for example, identifying and treating anaemia (Sullivan 2013, Tescher et al 2018) and reviewing the use of vasopressor drugs (Tescher et al 2018) in patients at risk of DTI

development or deterioration. For example, those undergoing surgical procedures or who require haemodialysis (Kirklan-Kyhn et al 2017).

Routine reporting of DTI is recommended in the updated NHS improvement pressure ulcer definition and measurement framework (2018) and the Wounds UK (2017) consensus document on DTI recognition and management. However, a study by Coleman et al (2016) reviewing pressure ulcer reporting across 24 NHS trusts reported significant variations in monitoring systems sufficient to preclude trust-trust comparisons of data. It is unclear if this remains an issue. Consistency in reporting of data related to DTI is likely to assist with robust retrospective and prospective studies on risk factors unique to these wounds (Wynn 2021).

4.1. Limitations

The search for literature within this review did not include grey literature. No meta-analysis was performed on data from the included studies. Only studies published post-2009 were included due to changes in consensus over the definition of DTI in this year. This may have excluded data related to DTI in earlier studies however there is no pragmatic method to determine if this data would have been relevant to this review. Finally, studies focusing on grade I-IV PI were excluded, these studies may have included additional data on DTI. When interpreting the findings of this review, consideration must be given to the potential impact of factors affecting the development and natural history of DTI which were not investigated in the reviewed studies. This is due to the inherent limitations of retrospective data analysis, where data may be unavailable for all potential factors of interest, in addition to the limitations of prospective studies which may exclude data on factors that are currently not suspected to be relevant in the case of DTI. Only one study presented data on paediatric patients. It is therefore unclear if the findings of this review can be extrapolated to this population. This study also restricts the search terms to DTI only and, therefore, does not include studies reporting all grades of PI including DTI.

5. Conclusion:

The literature currently indicates that the majority of DTI occur at the heel and sacrum although in paediatric patients they are mainly associated with medical devices. Most DTI are reported to resolve with only between 9.3-27% deteriorating to

full thickness tissue loss although this may be an underestimate due to, in some cases, the majority of DTI in the included studies being lost to follow up. Risk factors unique to DTI appear to include anaemia, vasopressor use, haemodialysis, and nicotine use although it is unclear if these factors are unique to DTI or are shared with grade I-IV PI. Factors associated with deterioration include cooler skin measured using infrared thermography and negative capillary refill. With 100% of DTI showing positive capillary refill in one study resolving without tissue loss ($p=0.02$) (Cox et al 2016), suggesting this may be an effective prognostic indicator. Notably, one study reported that in 55% ($n=22$) of the DTI observed within did not resolve despite optimal care being provided including off-loading and repositioning (Bates-Jensen et al 2018).

Future longitudinal prospective studies are required with a focus on establishing potential causal links between risk factors identified in the earlier retrospective studies as baseline eligibility criteria.

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