Do toe blood pressures predict healing after minor lower limb amputation in people with diabetes? A systematic review and meta-analysis

Clare Linton, Angela Searle, Fiona Hawke, Peta Ellen Tehan, Mathew Sebastian and Vivienne Chuter

Abstract

**Purpose of study:** To investigate toe systolic blood pressure and/or toe-brachial pressure index in predicting healing post minor diabetic foot amputations.

**Key methods:** A systematic search of EMBASE and PubMed (including Medline and The Cochrane Library) was conducted from database inception to 9 March 2020. Two authors independently reviewed and selected relevant studies. Quality was assessed with a modified Critical Appraisal Skill Programme checklist.

**Main results:** Ten studies met the inclusion criteria. Nine studies investigating toe systolic blood pressure reported healing occurred at mean toe systolic blood pressure $\geq 30$ mmHg, ranging between 30 and 83.6 mmHg. The meta-analysis (four studies) found toe systolic blood pressure $<30$ mmHg had 2.09 times the relative risk of non-healing post amputation, compared to toe systolic blood pressure $\geq 30$ mmHg (relative risk = 2.09, 95% confidence interval: 1.37–3.20, $p = 0.001$). Two studies investigating toe-brachial pressure index report successful healing where toe-brachial pressure index $>0.2$, with one study reporting a higher value of 0.8.

**Main conclusions:** Successful post-amputation healing outcomes were reported at mean toe systolic blood pressure $\geq 30$ mmHg, and the results varied considerably between the studies. Further research should identify whether variables, including amputation level, method of wound closure and length of post-operative follow-up periods, affect the values of toe systolic blood pressure and toe-brachial pressure index observed in this review.

Keywords

Diabetes, amputation, foot, healing, toe systolic blood pressure, toe-brachial pressure index

Introduction

Diabetes and peripheral arterial disease (PAD) are the major conditions associated with lower limb amputations. The effects of PAD are particularly pronounced in people with diabetes as they have higher rates of PAD than the general population, which occurs at younger ages, progresses more rapidly and has a preference for arteries below the popliteal trifurcation. PAD-related ischaemia contributes to increased risk of ulcer, amputation and impaired wound healing in this population. Current literature suggests that, where possible, minor amputations (toe and partial foot amputations) are preferred over major amputations (above and below knee) as they result in better mobility and have significantly lower mortality rates compared to major amputations. However, minor amputations have higher rates of complications such as non-healing and reported re-amputation rates of 20%–60%.

Currently, there is no widely accepted clinical algorithm for predicting healing outcomes following minor amputation, with the level commonly determined by the

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judgement of the surgical team supplemented by non-invasive clinical testing to assess the vascular status of the limb. Although the ankle brachial pressure index (ABPI) is widely recommended as a non-invasive test for objectively assessing lower limb vascular status, it can be falsely elevated in people with diabetes due to the effects of medial arterial wall calcification. Furthermore ABPI does not detect lesions distal to the ankle which can also be a characteristic of diabetes-related PAD. Toe systolic blood pressure (TSBP) and toe-brachial pressure index (TBPI) are recommended as alternative non-invasive vascular assessments and have been shown to be reliable and accurate for the detection of PAD in people with diabetes. A recent systematic review that investigated the prediction of wound healing or the likelihood of major amputation in people with diabetes reported that TSBP values $\geq 30$ mmHg compared to $< 30$ mmHg. This threshold was chosen as it is the most widely cited threshold for healing capacity in chronic foot wounds and foot wounds in people with diabetes and foot ulcer. All data analyses were performed using Review Manager (RevMan) Version 5.3 software. A random effects model was used as it is considered more suitable for combining the results of studies where treatment effect may vary across studies due to factors such as differences in study population, interventions received and follow-up periods.

Assessment of the methodological and reporting quality of the included studies was conducted independently by C.L. and A.S. using an adapted version of the Critical Appraisal Skill Programme (CASP) Checklist for Cohort and Diagnostic studies. This checklist was designed for critical appraisal of a variety of research styles, and an adapted version of the checklist was used in this review due to the variety of study types expected to be identified in the search. The adapted checklist was pilot tested prior to the review by two authors (C.L. and V.C.). The checklist questions (Table 3) are designed to assess the quality of the study design including selection and measurement bias, blinding, confounding and reporting.

### Methods

Two reviewers (C.L. and A.S.) independently searched the electronic databases EMBASE and PubMed (including Medline and The Cochrane Database of Systematic Reviews) from inception to 9 March 2020. The search strategy for the PubMed database is reported in Table 1 and was modified for EMBASE as required. Reference lists of all retrieved papers, clinical guidelines and review articles were manually searched for additional studies. All original research study designs were included with no limitations on sample size. Published research evaluating people with diabetes (type 1 or 2) who underwent minor, non-traumatic foot amputation where non-invasive TSBP testing was performed at the time of or immediately prior to amputation were eligible for this review. Minor amputations were defined as any amputation where the tibial weight-bearing stump is preserved as per the classification of Nather and Wong. Studies were excluded if they reported on acute traumatic amputation, major amputation (above and below knee), amputation not related to diabetes or if revascularisation was determined to have occurred post measurement of TSBP.

Duplicate articles were removed and the remaining abstracts were independently screened for potential eligibility by C.L. and A.S. Full texts of all potentially eligible papers were retrieved and were independently assessed for eligibility by C.L., A.S. and V.C. Disagreements were resolved by discussion between C.L., A.S. and V.C. Where data were available, meta-analysis was performed to compare the risk of non-healing post minor amputation where TSBP $< 30$ mmHg compared to $\geq 30$ mmHg. This threshold was chosen as it is the most widely cited threshold for healing capacity in chronic foot wounds and foot wounds in people with diabetes and foot ulcer.

### Results

The initial database search resulted in a total of 4066 citations. A final 17 were deemed appropriate for full-text review (Figure 1). Following assessment, 10 studies were included in the review (Table 2) and 7 were rejected (Supplemental Table 1) on the basis of exclusion criteria.

Details of the 10 included articles, with a total of 965 participants, are reported in Table 2. Five of the articles were published between 1981 and 1994, and the other five articles between 2005 and 2015. Indications for amputation included critical limb ischaemia (intolerable rest pain and tissue necrosis), neuropathic

### Table 1. Search strategy for the PubMed database.

| Search strategy PubMed via Ovid |
|---------------------------------|
| 1 Amputatio*                   |
| 2 [Minor or (lower AND limb) or foot OR toe or forefoot or transmetatarsal or TMA] |
| 3 Heal* OR predict* OR outcome* OR success |
| 4 Pressur* OR index OR doppler OR pulse OR waveform OR oximetry OR microscopy OR perfusion OR transcutaneous OR TcPO2 OR TCOM OR ABI OR TBI OR PVR OR DWA OR PRT OR SPP |

It is possible that not all studies were identified as searches were restricted to English language only.
and ischaemic ulceration, non-healing ulceration, gangrene, deep infection and osteomyelitis. The mean age of the population group was 64.2 years, with one paper, Bone and Pomajzl,26 not providing data on age. All studies [except Wong et al. (25)] reported on the use of TSBPs. Two of the studies — Caruana et al.21 and Larsson et al.23 — also reported on the use of the TBPI, while Wong et al.25 reported on TBPI use only. Four studies used predetermined amputation levels with two including transmetatarsal amputation (TMA) only,22,29 ray amputations only,25 and one including all minor amputations in a set time period.24 Another three studies used clinical criteria which were not defined to determine amputation level.20,21,26 Larsson et al.23 stated that they used a non-detailed ‘specifically designed protocol’ to determine amputation level. The final two studies27,28 failed to provide any data on factors determining amputation level. The reported time periods where healing had occurred were between 6 weeks and 77 months and amputation site healing was reported as complete in a range between 43% and 84.3% of cases.

Methods of conducting vascular testing were varied between studies. Test conditions known to affect TSBP and TBPI measurements such as length of pre-test rest time, ambient room temperature, avoidance of prior caffeine intake or exercise and presence of vasoactive disorders and medications were inconsistently reported.37–39 Three papers failed to report on any pre-test or vascular testing methods.23–25 Ambient room temperatures were attained to reduce the risk of vasoconstriction in two papers26,28 and two papers reported on placing participants in a supine position prior to testing to allow a level circulatory flow.21,28 Similarly, equipment used for testing varied between studies, two reported using strain gauge and/or Doppler techniques to measure TSBP,23,28 four did not provide details of the testing method used22,24,25,29 and the remaining four studies20,21,26,27 reported using plethysmography (PPG).

**Methodological quality**

The methodological quality assessment is detailed in Table 3. All of the studies provided clear aims and outcome measures linking TSBP and TBPI variables to minor foot amputation healing outcomes. All of the studies reported dose-related healing outcomes associated with TSBP and/or TBPI. Reporting regarding the population studied, vascular testing methods and healing assessment was inconsistent. Four of the (mainly older) studies did not provide full details of the population studied20,24,26,28 Details of vascular testing procedures were not supplied by four studies.22,24,25,29 Wound healing definitions and timeframes were not defined by five studies21,24,26,28,29 and none of the included studies reported blinding with relation to healing outcomes. It is unknown if all likely effects of the amputations could be seen in the timeframes of the studies. In part this is due to the different review timeframes used, with the shortest being 6 weeks and the longest a 3-year follow-up of healed and unhealed wounds. Furthermore, definitions of healing were not consistent across the articles. In addition, complications and re-amputations are common after minor amputations and may not be related to the vascular factors assessed in these studies. Three of the included studies reported standardised surgical interventions20,24,29 six did not report standardisation22,23,25,28 and one did not report on surgical technique.21 In three studies, it could not be conclusively determined that revascularisation had not occurred post-TSBP measurement.22,26,29

**TSBP and amputation healing**

There was no agreement on a specific TSBP threshold that was predictive of healing between the nine studies that reported on TSBP and amputation healing. Nonetheless, lower mean TSBP values were associated with poorer amputation healing outcomes than higher mean TSBP values. Five studies found that TSBP values of <20 mmHg were associated with poorer healing outcomes20,21,23,28,29 Larsson et al.23 found that TSBP < 15 mmHg resulted in an amputation healing rate of 6%, while Holstein28 reported a TSBP < 20 mmHg had an 18.7% amputation healing rate. Similarly, Mwipatayi et al.29 reported a mean TSBP of 19 mmHg, in a group of non-healed participants, while both Barnes et al.20 and Caruana et al.21 reported mean TSBPs of 13 and 10.5 mmHg, respectively, in their non-healed participant groups.

In comparison, studies reported higher rates of healing post-minor amputation with higher TSBP values. All nine studies reported improved healing rates with mean TSBPs...
### Table 2. Characteristics of included studies.

| Study | Study type | Participant number | Age (years) | Duration DM (years) | Male (%) | TBI and TSBP method | Reason for amputation | Level of amputation | Method of closure | Review period for wound healing | Heal rate | Results |
|-------|------------|---------------------|-------------|---------------------|----------|---------------------|---------------------|---------------------|------------------|-----------------------------|-----------|---------|
| Barnes et al.²⁰ Medical centres in Richmond, USA | Prospective cohort | 113 total DM: 40 (35%) | Age: 65 | DM Duration: NS | Male: NS | TSBP by PPG | Intolerable rest pain, ischaemic ulceration or gangrene, tissue necrosis and functional status of the patient. | 40 ray | 12 TMA | No time period given. Healed or failed (incisional breakdown due to ischaemia, infection or necessitated re-ampputation at a more proximal level) | 67% all foot amputations with and without DM | Mean non-healed TSBP DM#: 13 mmHg Mean healed TSBP DM#: 51 mmHg Healing TSBP in DM > 25 mmHg |
| Bone and Pomajzl³⁰ Hospital surgery department in Texas, USA | Prospective cohort | 27 total DM: 24 (89%) | Age: NS | DM Duration: NS | Male: NS | TSBP by PPG | Gangrene Non-healing ulcerated lesion | 26 one or more toes | 4 TMA | 6 weeks | Healed–skin cover complete (29.5%) \nWas healing–not complete but showed healthy granulation (34.1%) \nHaving complications -wound breakdown requiring re amp. at a more proximal level | 63.6% | Mean non-healed TSBP DM#: 28.5 mmHg Mean healed TSBP DM#: 83.6 mmHg Healing TSBP in DM > 60 mmHg |
| Caruana et al.²¹ Tertiary referral hospital, Malta | Prospective cohort | 50 total DM: 50 (100%) | Age: 67.4 | DM duration: 15.6 | Male: 30 (60%) | TBI and TSBP by PPG | Ischaemic Neuropathic Neuroischaemic ulcerations | 44 toe | 6 TMA | NS | 68% secondary intention 14% skin grafts | Healed: intact skin for at least 6 months or at time of death. | 84.3% | Mean TSBP DM < 20 mmHg: 18.7% heal Mean TSBP DM 20–29 mmHg: 46.6% heal Mean TSBP DM > 30 mmHg: 81% heal Mean healed TSBP: 40 mmHg Mean TSBP < 15 mmHg: 6% heal Mean TSBP >= 15 mmHg: 51% heal Mean healed TBI: 0.24 Mean TBI <= 0.10: 5% heal Mean TBI > 0.20: 62% heal |
| Holstein²² Bispebjerg hospital, Denmark | Retrospective cohort | 134 total DM: 102 cases | Age: 65 | DM Duration: NS | Male: 89 (66.7%) | TSBP by strain gauge | Ischaemia Necrotic tissue drainage of pus | 32 Hallux 27 second to fourth toes | 49 Other toes 2 Tarsal 49 TMA | 5 months median heal time for DM | 44% in DM | Mean TSBP DM #<20 mmHg: 18.7% heal Mean TSBP DM 20–29 mmHg: 46.6% heal Mean TSBP DM > 30 mmHg: 81% heal Mean healed TSBP: 40 mmHg Mean TSBP < 15 mmHg: 6% heal Mean TSBP >= 15 mmHg: 51% heal Mean healed TBI: 0.24 Mean TBI <= 0.10: 5% heal Mean TBI > 0.20: 62% heal |
| Larsson et al.²³ Department of internal medicine, Sweden | Prospective cohort | 159 total DM: 159 (100%) | Age: 70 ± 13 | DM Duration: 18 ± 12 | Male: 86 (54%) | TSBP ad TBI by Strain gauge and Doppler NA in 24 patients | Foot ulcers | 11 toe 22 single ray 17 multiple ray 13 TMA | 7 atypical midfoot | 68% secondary intention 14% skin grafts | Healed: intact skin for at least 6 months or at time of death. | 84.3% | Mean TSBP DM < 20 mmHg: 18.7% heal Mean TSBP DM 20–29 mmHg: 46.6% heal Mean TSBP DM > 30 mmHg: 81% heal Mean healed TSBP: 40 mmHg Mean TSBP < 15 mmHg: 6% heal Mean TSBP >= 15 mmHg: 51% heal Mean healed TBI: 0.24 Mean TBI <= 0.10: 5% heal Mean TBI > 0.20: 62% heal |

(Continued)
| Study | Study type | Participant number | Age (years) | TBI or TBI | Reason for amputation | Level of amputation | Method of closure | Review period for wound healing | Heal rate | Results |
|-------|------------|---------------------|-------------|-------------|-----------------------|--------------------|------------------|-----------------------------|-----------|---------|
| Mwipatayi et al. | Retrospective case-control | 43 total DM: 27 (62.8%) | Age: 55 DM Duration: NS Male: 16 (59.3%) | TSBP by UK | gangrene, ischaemia in the toes and distal forefoot | TMA | Primary with plantar flap | Reviewed from 1 to 11 months for DM | 63% | Mean non-healed TSBP DM: 19 mmHg Mean healed TSBP DM: 60 mmHg |
| Groote Schurr hospital, South Africa | | | | | | | | | |
| Shaikh et al. | Retrospective cohort | 74 total DM: 74 (100%) | Age: 68 DM Duration: NS Male: 48 (64.9%) | TSBP by UK or palpable pulse | Foot ulcers Grade 3 Wagner's classification TP < 45 mmHg | TMA | Primary closure | 1–77 months (mean 31 months) Healed: intact wound skin edges after suture removal Re-ulcerated: breakdown of epithelialised skin or re-amputation Died | 61% | All had TSBP > 45 mmHg |
| Addenbrooks hospital, UK | | | | | | | | | |
| Stone et al. | Retrospective cohort | 74 total DM: 74 (100%) | Mean age: 64 DM Duration: NS Male: 64 (%) | TSBP in at least 50% by UK | Forefoot infection, gangrene | TMA | Primary flaps where possible. | Healing within 90 days with or without revisions. | 43% | Mean TSBP < 50 mmHg; 50% heal Mean TSBP > 50 mmHg: 91% heal |
| Hospitals in Florida, USA | | | | | | | | | |
| Vitti et al. | Retrospective cohort | 136 total DM: 110 (81%) | Mean age: 64.8 Duration: NS Male: 136 (100%) | TSBP by PPG | Severe infection, gangrene | Toe TMA | 55 open 81 closed | No time period given. | 57.3% for DM | Mean non-healed TSBP all DM: 46.5 mmHg Mean healed TSBP all DM: 80.6 mmHg TSBP no revascularisation DM < 38 mmHg: 0% heal Mean non-healed TBI: 0.5 |
| Hospital in Arkansas, USA | | | | | | | | | |
| Wong et al. | Prospective cohort | 150 total DM: 150 (100%) | Age: 56 DM Duration: NS Male: 100 66.7% | TBI by UK | Wet gangrene of the toe. Osteomyelitis of the proximal or distal phalanx. Soft tissue infection of the whole toe. | 150 Ray | Not stated | Good outcome: healed and does not develop any complications within 1 year. Poor outcome: proximal level reamputation and/or additional ray amputation on the same foot, and/or suffered mortality within 1 year after operation | 70.7% | Mean non-healed TBI: 0.5 Mean healed TBI: 0.8 |
| National University Hospital, Singapore | | | | | | | | | |

DM: diabetes mellitus; M: male; TMA: transmetatarsal; NS: not stated; TP: toe pressure; TBI or TBI: toe-brachial pressure index or toe-brachial index; PPG: photoplethysmography; NA: not available; PPV: positive predictive pressure; UK: unknown method; #: values calculated from figures provided in the article.
Table 3. Quality appraisal of included studies.

|                          | Barnes et al.\textsuperscript{20} | Bone and Pomajzl\textsuperscript{26} | Caruana et al.\textsuperscript{21} | Holstein\textsuperscript{28} | Larsson et al.\textsuperscript{23} | Mwipatayi et al.\textsuperscript{29} | Shaikh et al.\textsuperscript{24} | Stone et al.\textsuperscript{22} | Vitti et al.\textsuperscript{27} | Wong et al.\textsuperscript{25} |
|--------------------------|----------------------------------|-------------------------------------|----------------------------------|------------------------------|----------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-----------------------------|
| Are the aims of the investigation clearly defined? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Is the population clearly stated? | No | No | Yes | No | Yes | Yes | No | Yes | Yes | Yes |
| Are the outcomes measured clearly stated? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the vascular assessment method adequately described? | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes | No |
| Was the vascular assessment method appropriate? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Was the wound healing assessment method adequately described? | Yes | No | Yes | No | No | No | No | Yes | Yes | Yes |
| Was the wound healing assessment method appropriate? | Yes | UK | Yes | UK | UK | UK | UK | Yes | Yes | Yes |
| Were the inclusions and exclusions criteria appropriate for the aims of the study? | UK | UK | Yes | UK | UK | UK | UK | UK | Yes | UK |
| Was the assessor; at follow-up, aware of baseline results that may predict risk of healing? | UK | UK | UK | UK | UK | UK | Yes | Yes | UK | Yes |
| Would rates and reasons given for drop out affect the results of the study? | No | No | Yes | Yes | Yes | No | No | No | No | No |
| Could all likely effects have appeared in the time scale? | UK | UK | UK | UK | UK | UK | UK | UK | UK | UK |
| Could the effect be transitory? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Could a dose response be demonstrated? | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

UK: unknown.
was an 81% healing rate post amputation where mean TSBP was $\geq 30\, \text{mmHg}$, which is similar to Caruana et al. who reported a mean TSBP of $31\, \text{mmHg}$ in their healed participant group. Larsson et al. reported a mean TSBP of $40\, \text{mmHg}$ in their healed group, similar to Shaikh et al. who only included participants with a TSBP $>45\, \text{mmHg}$ and reported initial healing of all participants. Five remaining studies reported a wide range of TSBP values for successful healing outcomes including mean TSBPs of $>50$, $60$, $80.6$, and $83.6\, \text{mmHg}$.

**Toe-brachial index and healing post-minor amputation**

There was no consensus across the three studies that reported on the association between TBPI values and post-amputation wound healing. Two of the studies, Caruana et al. and Larsson et al., reported mean TBPI $>0.2$ was associated with healing. However, Wong et al. reported that a higher mean TBPI value of 0.5 was associated with poor healing outcomes in their cohort and that positive healing outcomes occurred when mean TBPI value is 0.8.

**Meta-analysis results for the effect of TSBP $<30\, \text{mmHg}$ on relative risk (RR) of healing post-minor foot amputation**

Four studies provided data that identified the number of participants ($n=104$) with non-healed/healed outcomes post-minor amputation and corresponding TSBP values and therefore could be included in the meta-analysis. Statistical analysis to assess the risk of publication bias was not used as fewer than 10 studies were included in the meta-analysis, in which case test power has been reported to be too low to distinguish chance from actual asymmetry. The meta-analysis showed that TSBP values $<30\, \text{mmHg}$ are associated with $2.09$ times the RR of non-healing [RR $= 2.09$, 95% confidence interval (CI): 1.37 to $3.20$, $p=0.001$] with substantial heterogeneity present ($I^2 = 52\%$, $p = 0.10$), compared to TSBP values $\geq 30\, \text{mmHg}$ (Figure 2).

**Discussion**

The aim of this review was to determine whether TSBPs and TBPIs could be used to predict the likelihood of healing following minor foot amputation in people with diabetes. This value is supported by the results of the meta-analysis which found that TSBPs $<30\, \text{mmHg}$ are associated with $2.09$ times the RR of non-healing compared to TSBPs $\geq 30\, \text{mmHg}$. Only one study investigated the relationship between TBPI and post-minor amputation healing and identified a TBPI of 0.5 as being associated with poor healing outcomes. A number of factors including disparate surgical cohorts and surgical methods, non-standard vascular testing methods and varied post-operative care and follow-up periods are likely to have resulted in the range of healing values reported by the studies.

Participant-specific factors including co-morbidities such as end-stage renal failure, smoking history, sepsis, poor nutrition and metabolic status and presence of infection are all known to affect healing outcomes independently of vascular status. Complete surgical debridement of osteomyelitic bone is often difficult to achieve and residual bone infection following can further slow the progression of healing.

Post-operative care including non-weight-bearing periods, offloading and footwear also affect wound healing, and if these are not standardized, then toe pressure thresholds required for healing may be misleading. Four papers report post-operative non-weight-bearing periods of between 3 weeks and 6 months, while offloading footwear or total contact casting was used by only one paper. Varied post-operative follow-up timeframes may also have affected the healing outcomes reported by the included studies. While some studies reported post-amputation healing outcomes after relatively short periods, such as 6 weeks to 12 weeks, other studies followed participants for up to 10 months, 12 months or 31 months, and three other studies did not state their post-operative follow-up period. Healing not occurring in the short term may have been captured by the studies that followed participants for longer time frames. In addition, the definition of healing varied between the studies which made comparisons of outcomes difficult. A standardised definition of healing outcomes is needed for future research to allow for accurate comparison of results between studies in wound healing.

Differing amputation levels are likely to further explain the variable healing outcomes reported, as both can have a significant impact on wound healing. Amputation levels in studies included in this review, while all classified as minor, varied from toe amputations through to ray, midfoot and TMAs. While the initial amputation level is chosen to preserve as much of the foot as possible while still allowing healing, more distal amputations have been associated with slower healing, a higher complication rates and increased rates of revision amputations, compared to more proximal amputations.

The different closure methods reported by the studies included in this review may also have influenced the post-surgical healing outcomes. Some studies used primary closure which approximates and aligns the skin prior to closure with sutures or staples under sterile conditions at the time of surgery. Other studies use secondary closure which involves leaving the tissue open after surgery and has the potential for a slower healing process. Five of the included studies reported the use of primary closure following amputation, three studies described procedures which were a mixture of primary
and secondary skin closure\textsuperscript{23,27,28} and two papers did not state the closure methods used in their study.\textsuperscript{21,25} The level of amputation was not linked to the type of closure in the majority of studies, making it difficult to interpret the association between level of amputation, skin closure method and the likelihood of predicting healing via TSBP or TBPI.

Method of measurement of TSBP, where reported, was also variable across the included studies and included strain gauge, Doppler and PPG and may have contributed to the inconsistent mean TSBP associated with healing across the included studies. Reported mean TSBPs of 51, 31, 83.6 and 80.6 mmHg\textsuperscript{20,21,26,27} were associated with healed outcomes. Strandness and Sumner\textsuperscript{51} compared the strain gauge and the PPG and found a small but consistent difference with the PPG measuring an average of 9.4% higher; therefore, the different techniques are likely to introduce variability. Similarly, the reliability of TSBPs and TBPIs obtained by PPG can be affected in participants with low systolic pressures,\textsuperscript{38} which is particularly relevant for the cohorts examined in this review. A TSBP measurement error of greater than ±25 mmHg has been reported by one trial investigating the intra and inter-tester reliability of TSBP and TBPI measurement in people with diabetes.\textsuperscript{38} This may partially explain the wide range of mean TSBP values reported by these trials.

The relationship between healing outcomes post minor amputation and pre-amputation TSBP and TBPI values could be more conclusively established by more consistent reporting in future investigations. This would include the use of standardised methods of vascular assessment, detailed reporting of post-surgical complications and any revascularisation techniques and full descriptions of the surgical cohorts including co-morbidities and lifestyle-related factors known to affect healing. In addition, a common definition of wound healing, including consistent evaluation and follow-up time frames, is needed. Further research, specific to the different types and levels of minor amputations, may also identify differences in TSBP and TBPI values associated with healing.

The strength of the conclusions that can be drawn from the current available data is limited by population cohorts and testing methods and level of detail in reporting of included studies, for example, timing of vascular assessments and revascularisation procedures, varying levels of minor amputation and lack of standardisation of healing outcomes. Nevertheless, all of the nine studies investigating TSBP found that healing occurred at mean TSBP values ≥30 mmHg in a range between 30 and 83.6 mmHg. A minimum TSBP value of 30 mmHg is supported by the wound ischaemia and foot infection (WIfI)-threatened limb classification system, which classifies TSBPs <30 mmHg as severe ischaemia,\textsuperscript{52} a condition that would be expected to impair wound healing. This level is also highlighted by the International Working Group on the Diabetic Foot, who recommend urgent vascular imaging and revascularisation in people with diabetes and a foot ulcer where the toe pressure is <30 mmHg.\textsuperscript{53}

The relationship between healing outcomes post minor amputation and pre-amputation TSBP and TBPI values varied considerably between the studies. However, all of the nine studies investigating TSBPs reported improved healing outcomes where mean TSBPs ≥30 mmHg, with a range of 30–83.6 mmHg. Meta-analysis results showed a RR of non-healing post amputation of 2.09 (95% CI: 1.37–3.20, \(p=0.001\)) with TSBPs <30 mmHg compared to TSBPs ≥30 mmHg. As only one study was identified that investigated the capacity for TBPI to predict post-amputation healing, no firm conclusions could be drawn. Identification of definite TSBP or TBPI thresholds associated with positive healing outcomes post minor foot amputation was complicated by heterogeneity present in the surgical cohorts and surgical techniques, vascular measurement methods and follow-up time periods.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|c|c|c|}
\hline
Study or Subgroup & log(Risk Ratio) & SE & Total & Total & Weight & Risk Ratio & Risk Ratio IV, Random, 95% CI \[0.002\] \[0.1\] \[1\] \[10\] \[500\] \\
\hline
Barnes et al 1981 & 2.6856 & 1.3748 & 5 & 7 & 1.2% & 14.67 (0.99, 217.06) & \\
Bone et al 1980 & 1.4351 & 0.4447 & 4 & 20 & 11.1% & 4.20 (1.76, 10.02) & \\
Holstoen et al 1984 & 1.7199 & 0.1824 & 31 & 53 & 65.9% & 5.59 (3.91, 7.98) & \\
Larsson et al 1993 & 1.7823 & 0.3173 & 65 & 51 & 21.6% & 5.94 (3.19, 11.07) & \\
Total (95% CI) & & & 105 & 131 & 100.0% & 5.55 (4.15, 7.41) & \\
\hline
\end{tabular}
\caption{Forest plot of the association between post minor foot amputation healing outcomes and TSBP< 30 mm Hg.}
\end{table}
Key messages

- While TSBP and TBPI testing are used as adjuncts in determining the vascular status of the lower limb, a specific level associated with post-amputation healing has not been clearly identified.
- Meta-analysis revealed a RR of 2.09 of non-healing post amputation with a TSBP <30 mmHg.
- A TSBP value of ≥30 mmHg may be included in the clinical decision-making process when assessing the healing potential of minor foot amputations in people with diabetes.

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Supplemental material

Supplemental material for this article is available online.

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