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

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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 values ⩾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 ⩾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 ⩾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.[1,2] 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.[3] PAD-related ischaemia contributes to increased risk of ulcer, amputation and impaired wound healing in this population.[4] 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.[5,6] However, minor amputations have higher rates of complications such as non-healing and reported re-amputation rates of 20%–60%.[7–9]

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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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
5	1, 2, 3 and 4

It is possible that not all studies were identified as searches were restricted to English language only.

judgement of the surgical team supplemented by non-invasive clinical testing to assess the vascular status of the limb.[10] Although the ankle brachial pressure index (ABPI) is widely recommended as a non-invasive test for objectively assessing lower limb vascular status,[11] it can be falsely elevated in people with diabetes due to the effects of medial arterial wall calcification.[12] Furthermore ABPI does not detect lesions distal to the ankle which can also be a characteristic of diabetes-related PAD.[13] 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.[14] 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 ⩾30 mmHg were associated with a 25% higher chance of foot ulcer healing.[15] However, the literature relating to TSBP and TBPI thresholds required for successful healing post minor amputation is unclear. Consequently, the aim of this review was to systematically search the literature to determine whether the TBPI and TSBP can predict the likelihood of healing following minor amputations of the foot in persons with diabetes and to evaluate study findings by meta-analysis where possible.

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.[6] 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 ⩾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.[15,16] 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.[17,18]

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.[19] 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.

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)[20–29] and 7 were rejected (Supplemental Table 1)[30–36] 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,[20,23,26–28] and the other five articles between 2005 and 2015.[21,22,24,25,29] Indications for amputation included critical limb ischaemia (intolerable rest pain and tissue necrosis), neuropathic

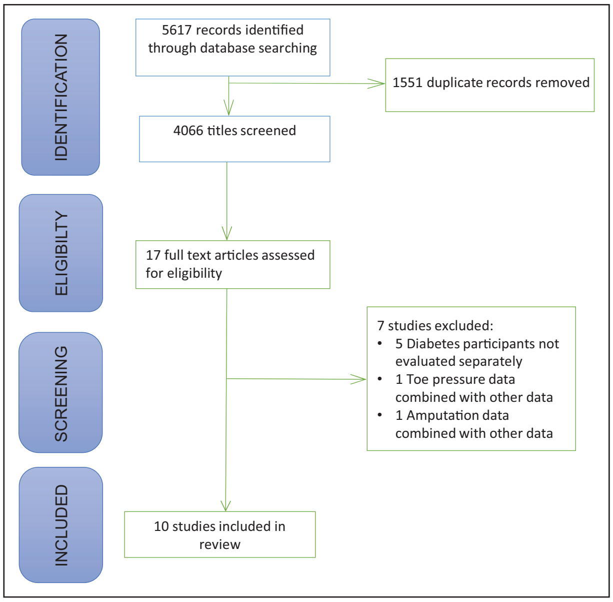

Figure 1. Prisma flow chart.

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 studies[27,28] 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 vasospastic 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 papers[26,28] 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 used[22,24,25,29] and the remaining four studies[20,21,26,27] reported using photoplethysmography (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 studied.[20,24,26,28] 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 studies[23,24,26,28,29] 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 interventions,[20,24,29] six did not report standardisation,[22,23,25–28] 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 outcomes [20,21,23,28,29] Larsson et al.[23] found that TSBP <15 mmHg resulted in an amputation healing rate of 6%, while Holstein[28] 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 TSBP and 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	Digit and ray amputataions were closed unless infection was present. TMA were closed with posterior flap technique.	No time period given. Healed or failed (incisional breakdown due to ischaemia, infection or necessitated re-ampuation 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 Pomajzl[26] 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	Primary closure	Average 10 months.	66.66% all	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	6 weeks Healed–skin cover complete (29.5%) Was healing–not complete but showed healthy granulation (34.1%) Having complications -wound breakdown requiring re amp. at a more proximal level (36.4%)	63.6%	Mean non-healed TSBP: 10.5 mmHg Mean healed TSBP: 31 mmHg Mean non-healed TBI: 0.21 Mean healed TBI: 0.85
Holstein[28] 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 24 TMA	Primary – 13	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
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 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)

Table 2. (Continued)

Study	Study type	Participant number	Age (years) Duration DM (years) Male (%)	TBI TSBP and method	Reason for amputation	Level of amputation	Method of closure	Review period for wound healing	Heal rate	Results
Mwipatayi et al.[29] Groote Schurr hospital, South Africa	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
Shaikh et al.[24] Addenbrooks hospital, UK	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	13 Hallux 25 Lesser toe 13 first Met 5 second to fourth met Seven 5th met 11 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
Stone et al.[22] Hospitals in Florida, USA	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
Vitti et al.[27] Hospital in Arkansas, USA	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
Wong et al.[25] National University Hospital, Singapore	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

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.[20]	Bone and Pomajzl[26]	Caruana et al.[21]	Holstein[28]	Larsson et al.[23]	Mwipatayi et al.[29]	Shaikh et al.[24]	Stone et al.[22]	Vitti et al.[27]	Wong et al.[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	Yes	Yes	Yes	Yes	Yes	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	Yes	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.

⩾30 mmHg; however, the TSBP thresholds reported by these studies varied considerably. Holstein et al.[28] reported an 81% healing rate post amputation where mean TSBP was ⩾30 mmHg, which is similar to Caruana et al.[21] who reported a mean TSBP of 31 mmHg in their healed participant group. Larsson et al.[23] reported a mean TSBP of 40 mmHg in their healed group, similar to Shaikh et al.[24] who only included participants with a TSBP >45 mmHg and reported initial healing of all participants. Five remaining studies reported a wide range of TSBP thresholds for successful healing outcomes including mean TSBPs of >50,[20,22] ⩾60,[29] 80.6,[27] and 83.6 mmHg.[26]

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.[21] and Larsson et al.,[23] reported mean TBPI >0.2 was associated with healing. However, Wong et al.[25] 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 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.[20,23,26,28] 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.[40] The meta-analysis showed that TSBP values <30 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 ⩾30 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 mmHg are associated with 2.09 times the RR of non-healing compared to TSBPs ⩾30 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.[25] 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,[22,24,25] smoking history,[22,25,27,29] sepsis,[25,26] poor nutrition and metabolic status[26] and presence of infection[25,29,41] are all known to affect healing outcomes independently of vascular status.[42,43] Complete surgical debridement of osteomyelitic bone is often difficult to achieve and residual bone infection following can further slow the progression of healing.[41]

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.[44] Four papers [22,23,24,29] 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.[23] 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[21] to 12 weeks,[22] other studies followed participants for up to 10 months,[26] 12 months[25,29] or 31 months,[24] and three other studies did not state their post-operative follow-up period.[23,27,28] 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.[45] Amputation levels in studies included in this review, while all classified as minor, varied from toe amputations[20,21,26–28] through to ray,[20,23,25] midfoot and TMAs.[20,21,23,24,26–29] While the initial amputation level is chosen to preserve as much of the foot as possible while still allowing healing,[46] more distal amputations have been associated with slower healing,[33,47] higher complication rates[48] and increased rates of revision amputations,[49] 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.[50] Other studies use secondary closure which involves leaving the tissue open after surgery and has the potential for a slower healing process.[5] Five of the included studies reported on the use of primary closure following amputation,[20,22,24,26,29] three studies described procedures which were a mixture of primary

Study or Subgroup	log[Risk Ratio]	SE	<30mmHg Total	=/>30mmHg Total	Weight	Risk Ratio IV, Random, 95% CI
Barnes et al 1981	2.6856	1.3748	5	7	1.2%	14.67 [0.99, 217.06]
Bone et al 1980	1.4351	0.4437	4	20	11.1%	4.20 [1.76, 10.02]
Holstein et al1984	1.7199	0.1824	31	53	65.9%	5.58 [3.91, 7.98]
Larsson et al 1993	1.7823	0.3173	65	51	21.8%	5.94 [3.19, 11.07]
Total (95% CI)			**105**	**131**	**100.0%**	**5.55 [4.15, 7.41]**

Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 3 (P = 0.82); I² = 0%
Test for overall effect: Z = 11.57 (P < 0.00001)

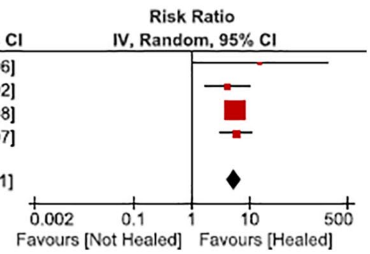

Figure 2. Forest plot of the association between post minor foot amputation healing outcomes and TSBP< 30 mm Hg.

and secondary skin closure[23,27,28] and two papers did not state the closure methods used in their study.[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[20,21,26,27] were associated with healed outcomes. Strandness and Sumner[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,[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.[38] This may partially explain the wide range of mean TSBP values reported by these trials.

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,[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.[53]

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 results of this study need to be interpreted in the context of a number of specific limitations. Although this review was designed to be comprehensive with a robust search on relevant databases, it is possible that not all studies were identified. The heterogeneity present in the vascular measurement methods, the amputation methods and follow-up periods, and the study participants reduce the strength of the current findings. The limited number of studies identified (n = 9) did not allow us to determine healing perfusion pressures for different levels of minor amputations.

Conclusion

TBPI or TSBP thresholds for prediction of healing post-minor amputations in the foot in people with diabetes 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.

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 $\geqslant 30$ 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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