Study Protocol

Can a dedicated chronic limb-threatening ischaemia (CLTI) clinic improve patient self-reported quality of life?

Protocol v 1.6 Date: 14/11/2022
This protocol has regard for the HRA guidance.

1. Background

Chronic limb-threatening ischaemia (CLTI) is the most severe form of peripheral arterial disease (PAD). It affects 1% of the population and its incidence is expected to rise. It is a condition where the circulation to one, or both limbs is inadequate. It requires investigation and may require surgery in order to improve the blood flow to the affected limb(s). Without improvement in circulation, ulcers and gangrene set in, and the only cure is a major limb amputation.

Vascular surgery units in the United Kingdom have undergone centralisation into regional networks over the last decade in order to consolidate vascular surgery into 'high volume centres' to provide high quality care and better outcomes for patients.

However, national analysis of the performance of units has demonstrated that only 50% of CLTI patients are revascularised within the 'deliberately-challenging timeline' issued by the Vascular Society of Great Britain and Ireland (Birmpili et al., 2021; Vascular Society of Great Britain and Ireland, 2019).
CLTI already comprises more than 50% of vascular unit workload and the prevalence of CLTI is expected to rise, further increasing the burden on vascular services (Fowkes et al., 2016; Vascular Society of Great Britain and Ireland, 2018, 2021).

There is ample evidence demonstrating a strong inverse correlation between the provision of specialist outpatient clinics in the assessment and management of diabetic foot ulcers and major lower limb amputation (Joret et al., 2019; M Kerr, Rayman, & Jeffcoate, 2014; Marion Kerr, 2017; Monteiro-soares, Vale-lima, Martiniano, Dias, & Boyko, 2021; Paisey et al., 2017), Diabetic foot ulceration is a condition which has significant overlap with CLTI. It could therefore be inferred that a similar service for CLTI patients would also confer the same benefits.

As many as 50% of CLTI patients also suffer from a significant degree of frailty, which makes treating patients with the condition more perilous (Houghton et al., 2021). The current guidance from the Vascular Society of Great Britain and Ireland recommends that patients who suffer with frailty should have access to elderly medicine specialists who can help with optimisation, complex decision making or advanced care planning. There is growing evidence that these services have

tangible benefits for vascular patients (Gordon, Evans, & Dhesi, 2017; J. Partridge, Sbai, & Dhesi, 2018; J S L Partridge et al., 2017; Judith S L Partridge et al., 2015)

At the Leeds Vascular Institute, we have implemented a dedicated CLTI clinic to assess and manage patients with the condition. Whilst there is limited evidence that these rapid access clinics can facilitate review and management of the condition, thereby successfully preventing major amputation in CLTI patients, the results are typically from single centre data series (Khan et al., 2020; Nickinson et al., 2021). There is a paucity of evidence evaluating patient opinions of this type of service and non that demonstrate any impact on their quality of life.

Furthermore, we have integrated an elderly medicine service [Perioperative Medicine for the Older Person undergoing Surgery (POPS)] to facilitate clinic reviews, decision making, advanced care planning for elderly (aged > 65 years old), medically complex (1 or more seriously debilitating medical conditions) and/or frail (Rockwood Clinical Frailty Score > 5) vascular patients. The elderly medicine service exists as a separate entity from the CLTI clinic and sees vascular patients with any vascular pathology, including aneurysmal or carotid disease in addition to CLTI. However, a significant proportion of patients seen in the POPS clinic originate from the CLTI clinic. Our area of interest with this is specifically CLTI as evidence suggests that frailty is more prevalent amongst this cohort than aneurysmal patients.

2. Rationale.

As previously mentioned, there is good evidence to suggest that specialist outpatient clinics are associated with good limb salvage outcomes, both for diabetic and CLTI patients.
All of the evidence that supports the use of CLTI clinics has been focused on clinical outcomes, but to our knowledge, there is no study that exists which has evaluated the benefit of the service on patient self-reported quality of life.

Additionally, elderly and/or frail CLTI patients are referred into the POPS clinic to help with complex decision making and advanced care planning.

These services have been designed and implemented with patients in mind but there is no evidence which actually determines the impact of these services from the patient's perspective.

Patient reported outcomes are an important measurement of a quality service and it is seldom reported in surgery. There is some limited evidence to suggest that CLTI clinics will be favourably reviewed by patients (Khan et al., 2020), but no evidence at all to determine if they can improve quality of life.

3. Theoretical Framework

The aim with CLTI treatment is to achieve limb salvage, that is to prevent the leg from deteriorating to the point of necessitating amputation. Limb salvage is seen as the ultimate goal following CLTI intervention.

The assumption is that patients who have their leg successfully saved, and avoid amputation will have a better quality of life because of it. However this has not been formally identified.
The POPS service exists to improve care provided to the most complex and frail CLTI patients. An evaluation of the service in terms of its clinical impact is already underway, but again we lack any patient feedback on the service.

4. Research Question / Aim

4.1 Objectives

To evaluate the difference that CLTI clinic attendance and management has on patient-reported quality of life.
Additionally, we want to explore what CLTI patients referred into the POPS service feel about the service they have received, if it has been beneficial, helped them make complex decisions or provided more information on their condition.

4.2 Outcome

We hypothesise that patients will have a statistically significant improvement in self-reported quality life after CLTI clinic assessment management in comparison to before CLTI clinic assessment and management.
We propose that the POPS service will be favourably reviewed by patients when provided with a structured questionnaire.

5. Study Design and Methods of Data Collection and Data Analysis

This will be a prospective observational repeated measures study.
Patients who are referred into the CLTI clinic will be identified from the clinic register, which also distinguishes between new patients and patients who are being followed-up.
New patients who are attending the CLTI clinic will be approached to enrol into the study. Patients who consent to enrolment in the study will have their details recorded on a register which will enable the researchers to identify when the next appointments are due and can therefore determine when the next questionnaire can be delivered.

If patients consent to participate, they will be asked to complete:
- Their first EuroQol-5D questionnaire immediately prior to their first CLTI clinic appointment
- 1 feedback survey about their CLTI clinic experience after their first appointment
- A second EuroQol-5D questionnaire 6-12 weeks after their treatment is complete
- A third EuroQol-5D questionnaire at 12 months after the initial appointment

Separately, patients who are then referred from CLTI clinics to the POPS service at (based on the POPS referral criteria) will be asked if they wish to answer a structured questionnaire about the POPS service. If they agree, they will be asked to complete:

- 1 additional feedback survey about their POPS clinic experience immediately after their appointment

This is in addition to the 4 questionnaires and surveys they have completed / will be asked to complete as part of the CLTI clinic evaluation.

The anticipated study start date is 1st December 2022, with primary completion expected around 1st July 2023. The expected study completion date is 1st July 2024.

5.1 Data collection

Data will be collected using the standardised EuroQol-5D questionnaire. This is a validated patient reported outcome measure which has been widely used in studies evaluating self-reported quality of life.

A license to use the questionnaire has been authorised and granted. The EuroQol survey will be delivered electronically using LimeSurvey software. It can be completed by study participants, with or without promptin from their carers or relatives, or researchers on behalf of study participants.

Additionally a structured questionnaire evaluating the CLTI clinic and/or POPS service using a Likert scale and free text comments will be administered to participants. We plan to use an iPad or tablet to administer the surveys to patients.

Survey responses that are entered are stored electronically within LimeSurvey, both on an app and also on a website cache. The survey itself contains no identifiable information at all.

Identifiable data will only be kept on a study registry within a password protected cloud drive attached to an NHS.net account. NHS.net is Caldicott compliant and therefore adequate for handling patient identifiable data. The purpose of this registry to is to ensure that subsequent survey responses from the same patients are linked together (as it is a repeated measures design) and also to highlight when new appointments are due. This information is not contained within the EuroQol survey.

6. Study Setting

The study will take place in the outpatient suite waiting room. Patients who are attending their first CLTI appointment and have consented to participate will be given the questionnaires on a tablet computer to complete. Identifying patients from the clinic register targets the exact demographic cohort. It is a single centre study. The POPS service is also in an outpatient suite.

7. Sample and Recruitment

7.1.1 Inclusion Criteria

All CLTI patients seen and enrolled in the CLTI clinic are eligible.

7.1.2 Exclusion Criteria

Patients who have significant cognitive impairment and are unable to communicate will be excluded, as they will be unable to respond to the questions. Patients with mild cognitive impairment but still demonstrate capacity that may require prompting from carers or relatives in order to answer questions can still be included as the EuroQol-5D is validated for this purpose.

7.2 Sampling

We will adopt a convenience sampling strategy. The rationale for this strategy is the available pool of respondents who attend the CLTI clinic. We have chosen a sample size of between 50 – 100 patients. The CLTI clinic runs 3 times weekly and attempts to see 3-4 new patients per clinic, which means on average 9 – 12 patients per week. This would mean we should achieve our sample in around 10 weeks. However, pragmatically speaking, not every clinic will have the same number of new patients, not every patient will be suitable and some patients will be lost to follow-up. Hence we have a range of between 50 – 100 responses would be sufficient.

There is no set amount of structured feedback questionnaire responses required, either of the CLTI or POPS clinic.

7.3 Sample identification

The researchers will identify the participants from a list of patients due to attend CLTI clinic, by attending the clinic and receiving a copy of the appointment schedule. The research team consist of those who provide clinical care to those patients in clinic, and therefore have access to identifiable data as part of their routine clinical role. Patients who have been referred to the POPS clinic from the CLTI clinic and consented to participate will be known to the researchers directly

7.4 Consent

Consent will be obtained in clinic, prior to the patient's first appointment. One of the research team will approach the patient, explain the nature of the study and provide them with a patient information leaflet.
There will be the opportunity to ask questions prior to consenting.
Patients who have mild cognitive impairment can still be included if they demonstrate capacity and consent to enrolment, even if they require some guidance in answering. The EuroQol-5D survey can be administered to someone else on behalf of the intended study participant who can prompt the participant to respond.

8. Ethical and Regulatory Considerations

8.1 Assessment and management of risk

There won't be any additional risks or harm to patients as a result of participation in the study because they are only required to fill out questionnaires. If patients become distressed during the provision of routine care, they can raise their issues with the

researchers who are also care providers, or any of the care providers in the CLTI clinic. Our CLTI Vascular Nurse Specialist overseas patients seen in the clinic and acts as a point of contact for patients who have questions or issues during their treatment, whether that is attending appointments, or lack of communication or pain. Patients are given a card with her direct number (0113 392 0943) and can get in contact during office hours (Mon-Fri 0800-1700). If concerns can't be addressed at this level, patients will be signposted to the Patient Experience team (PALS) on 0113 206 6261 or patientexperience.leedsth@nhs.net. Any safeguarding issues that are incidentally identified during the study will be communicated to the patient's GP or the adult safeguarding team.

An REC opinion will be sought and a draft IRAS form has been written in the anticipation of submitting it. The study will not begin until the relevant REC has reviewed and approved the proposal.

Amendments to the study will require a valid notice of amendment to the REC for consideration. This will be discussed with the Chief Investigator first.

8.2 Patient and Public Involvement

A PPI initiative was undertaken at LGI with a focus on CLTI. Patients were consulted with their carers about the condition as a whole. The main findings were that the condition as a whole was generally not well understood by patients and any future initiatives that involve patients and/or relatives in redesigning the service would be welcome.

8.3 Protocol Compliance

Any protocol deviations that occur will be reported to the Chief Investigator

8.4 Data Protection and Patient Confidentiality

Personal information which could identify patients will be kept secure on a password secured registry contained on an NHS.net secure cloud drive. NHS.net is Caldicott compliant and is appropriate for handling sensitive data. The purpose of this is solely to identify patient appointments which allow for linking study responses as per the repeated measures study design.

The EuroQol-5D survey has no patient identifiable data at all, and the responses are stored on the LimeSurvey application.

The principal investigator will have access to the registry of patients with identifiable data. This will only be available to the Principal Investigator and Chief Investigator. Analysis can be performed by other members of the research team as it doesn't require any handling of sensitive data. Data will be stored for 5 years

8.5 Indemnity

Insurance is not required above and beyond the NHS indemnity scheme because the research will only be conducted on NHS sites at the time of other clinical (ie outpatient appointments).

Access to the Final Study Dataset

The Principal Investigator and Chief Investigators will have access to the final dataset.

9. Dissemination Policy

The data will be owned by the Chief Investigator and the Trust. On completion, a Final Study Report will be prepared. The intent of the investigators will be to disseminate this information at scientific meetings and for publication. Participants can contact the Principal Investigator regarding the results once the Final Study Report has been written or when the study has been published.

Authorship Eligibility

The chief investigator, principal investigator and other researchers who participate in data collection, extraction, analysis and write-up will be considered for authorship.

10. References

Birmpili, P., Johal, A., Q, L., Watson, S., Chetter, I., Boyle, J. R., & Cromwell, D. (2021). Factors associated with delays in revascularization in patients with chronic limb-threatening ischaemia : population-based cohort study. *British Journal of Surgery*, *00*(0), 1–9. https://doi.org/10.1093/bjs/znab039

Fowkes, F. G. R., Aboyans, V., Fowkes, F. J. I., McDermott, M. M., Sampson, U. K. A., & Criqui, M. H. (2016). Peripheral artery disease: epidemiology and global perspectives. *Nature Reviews Cardiology*, *14*(3), 156–170. https://doi.org/10.1038/nrcardio.2016.179

Gordon, A. L., Evans, B., & Dhesi, J. (2017). The physician's role in perioperative management of older patients undergoing surgery. *Clinical Medicine*, *17*(4), 357–359.

Houghton, J. S. M., Nickinson, A. T. O., Helm, J. R., Dimitrova, J., Dubkova, S., Rayt, H. S., … Haunton, V. J. (2021). Associations of clinical frailty with severity of limb threat and outcomes in chronic limb-threatening ischaemia. *Annals of Vascular Surgery*, *76*. https://doi.org/10.1016/j.avsg.2021.04.017

Joret, M. O., Hons, B., Osman, K., Dean, A., Cao, C., Werf, B. Van Der, & Bhamidipaty, V. (2019). Multidisciplinary clinics reduce treatment costs and improve patient outcomes in diabetic foot disease. *Journal of Vascular Surgery*, *70*(3), 806–814. https://doi.org/10.1016/j.jvs.2018.11.032

Kerr, M, Rayman, G., & Jeffcoate, W. J. (2014). Health Economics Cost of diabetic foot disease to the National Health Service in England. *Diabetic Medicine*, 1498–1505. https://doi.org/10.1111/dme.12545

Kerr, Marion. (2017). DIABETIC FOOT CARE IN ENGLAND : An Economic Study. *Insight Health Economics*, (January), 1–52.

Khan, A., Hughes, M., Ting, M., Riding, G., Simpson, J., Egun, A., & Banihani, M. (2020). A ' hot clinic ' for cold limbs : the benefit of urgent clinics for patients with critical limb ischaemia. *Annals of the Royal College of Surgeons of England*, 412–417. https://doi.org/10.1308/rcsann.2020.0068

Monteiro-soares, M., Vale-lima, J., Martiniano, J., Dias, V., & Boyko, E. J. (2021). A

systematic review with meta-analysis of the impact of access and quality of diabetic foot care delivery in preventing lower extremity amputation. *Journal of Diabetes and Its Complications*, *35*(107837), 1–21. https://doi.org/10.1016/j.jdiacomp.2020.107837

Nickinson, A. T. O., Dimitrova, J., Houghton, J. S. M., Rate, L., Dubkova, S., Lines, H., & Gray, L. J. (2021). Does the Introduction of a Vascular Limb Salvage Service Improve One Year Amputation Outcomes for Patients with Chronic Limb-Threatening. *European Journal of Vascular & Endovascular Surgery*, *61*(4), 612–619. https://doi.org/10.1016/j.ejvs.2020.12.007

Paisey, R. B., Abbott, A., Levenson, R., Harrington, A., Browne, D., & Moore, J. (2017). Diabetes-related major lower limb amputation incidence is strongly related to diabetic foot service provision and improves with enhancement of services : peer review of the South-West of England. *Diabetic Medicine*, *35*, 53–62. https://doi.org/10.1111/dme.13512

Partridge, J., Sbai, M., & Dhesi, J. (2018). Proactive care of older people undergoing surgery. *Aging Clinical and Experimental Research*, *30*(3), 253–257. https://doi.org/10.1007/s40520-017-0879-4

Partridge, J S L, Harari, D., Martin, F. C., Peacock, J. L., Bell, R., Mohammed, A., & Dhesi, J. K. (2017). Randomized clinical trial of comprehensive geriatric assessment and optimization in vascular surgery, 679–687. https://doi.org/10.1002/bjs.10459

Partridge, Judith S L, Fuller, M., Harari, D., Taylor, P. R., Martin, F. C., & Dhesi, J. K. (2015). Frailty and poor functional status are common in arterial vascular surgical patients and affect postoperative outcomes. *International Journal of Surgery*, *18*, 57–63. https://doi.org/10.1016/j.ijsu.2015.04.037

Vascular Society of Great Britain and Ireland. (2018). *'Top Tips' for Reconfiguring Vascular Services Section July 2018*.

Vascular Society of Great Britain and Ireland. (2019). *A Best Practice Clinical Care Pathway for Peripheral Arterial Disease*.

Vascular Society of Great Britain and Ireland. (2021). *Provision of Services for People with Vascular Disease 2021*.