Lichen sclerosus diagnosis: which are the most important clinical diagnostic features?

Protocol for e-Delphi exercise to agree most important criteria

Abstract

Background: Vulval lichen sclerosus (LS) is an inflammatory skin condition is thought to affect at least 1% of women. Most patients have some degree of anatomical change due to scarring from inflammation caused by LS. In minor cases, this is subtle but in more severe instances, narrowing of the vaginal entrance occurs which is associated with functional difficulty such as passing urine and sexual intercourse. Around 3-5% go on to develop vulval malignancy and treatment may reduce this risk. LS impacts upon psychosocial and sexual well-being. Due to lack of awareness there are often delays in diagnosis which in turn delay the start of effective treatment and contributes towards the development of complications. This could be mitigated by raising awareness of LS and promoting disease recognition by using a validated set of diagnostic criteria.

Aims: To obtain international agreement on what clinical criteria are most important in identifying and diagnosing LS.

Methods: The project will be led by a multidisciplinary Steering Group including patient representation. A two-stage process will be used to establish the most important criteria in diagnosing LS: 1) Identification of potential diagnostic criteria that can be present in patients with LS: A long list of diagnostic criteria will be harvested through up to date systematic reviews and national/international guidelines for LS management 2) Expert agreement of the most important domains: international Electronic-Delphi consensus study involving different stakeholder groups including patient representation.

Impact and dissemination: The criteria agreed by consensus as the most important will tested in a multicentre diagnostic test accuracy clinical study. They will be used to create a tool to support patients and non-experts in identifying LS. Dissemination will be through existing and new networks with both patient and professional groups.

Introduction

Background

Genital skin conditions, particularly vulval conditions are common; a study of UK General Practitioners, demonstrated that over half saw more than 3 patients with vulval disease per month(1). A US community survey of 303 adult females reported one fifth with lower genital tract discomfort lasting longer than 3 months(2).

Lichen sclerosus (LS) is a commonly encountered non-infectious inflammatory genital skin condition in clinical practice(2). It probably affects at least 1% of women, although estimates of incidence and prevalence are not well defined and remain controversial (3-5). Anecdotal evidence suggests it is just as common in men and boys. An estimated 3-5% of vulval LS cases go on to develop malignancy (6-8). It has a significant impact on quality of life and affects psychosocial and sexual well-being. This negative impact has been shown to contribute towards self-harm or suicidal thoughts (9, 10).

In women and pre pubertal girls, LS primarily affects the vulva. A variety of symptoms, for example, intense itch, pain and splitting occur. The physical appearance of the vulva is affected. These symptoms of lichen sclerosus impact upon daily function. Delay in recognition of LS and late treatment/poor response to treatment leads to ongoing inflammation. Subsequent scarring can cause labial fusion, narrowing of the vaginal opening and burying of the clitoris. In girls, lichen sclerosus can result in an itchy vulva and often pain with defecation; medical treatment helps but cure is not expected in most and the disease will continue in adult life.

The anatomical changes that occur in lichen sclerosus are usually irreversible and can have a detrimental effect upon day-to-day function and psychological health of those affected. Men are at risk of serious urethral disease. People with lichen sclerosus also appear to have an increased risk of genital cancer.

Despite this, genital disease in general is a neglected area of health: it has received little attention from the research community and there is paucity of existing high-quality evidence to guide clinical practice.

There is lack of knowledge about clinical features and management of LS and genital skin conditions within the wider medical community. Patients describe delays in diagnosis, poor pathways of care and varying advice on how to treat their condition.

This project has been prioritised following the 'Lichen Sclerosus Priority Setting Partnership' which agreed internationally to the 'Top 10' future research priorities for genital LS (11) , of which one of the Top 10 future research questions was:

'What is the best way to diagnose lichen sclerosus (diagnostic criteria)?'

Furthermore, the themes of this work; prioritising women's health matters, reducing the burden of chronic conditions and addressing disease in older people, are outlined as priorities by the World Health Organisation(12) the NHS Five Year Forward View(13)..

This work is clinically relevant as improving care for patients with LS is vital to minimise the negative impact of the LS on physical, psychological and psychosexual wellbeing (10, 14). Particular priorities are reducing patients' symptoms, the risk of scarring, which might affect sexual relationships, leisure activities, and work, and risk of malignant transformation. There is some evidence that the risk of scarring and malignant transformation may be reduced by continuous long-term treatment (15).

Objectives

The objective of this project is to answer the following research question:

In vulval lichen sclerosus, what are the most important clinical criteria needed to make the diagnosis?

This project aims to engage stakeholders internationally to ensure widespread adoption of the results for implementation into patient care pathways.

Methods

Work plan and milestones

The project protocol will be prospectively registered on the Centre of Evidence based Dermatology website.

There will be two stages to this work:

1. Identification of possible diagnostic criteria: using up to date British Association of Dermatologists guidelines, European S3 guidelines and studies in the most recent Cochrane review for LS.

2. Provisional agreement of the most important domains: international Electronic-Delphi consensus study

Stakeholder involvement

Stakeholders for this project include a number of professional groups who are involved in the diagnosis and management of patients with LS, who have LS themselves and represent other patients with LS and researchers who plan/publish/research studies for LS interventions or who develop treatments for LS. The following groups are considered stakeholders to be involved as participants in the study to agree diagnostic criteria:

- Dermatologists
- Gynaecologists
- Specialist Nurses
- Urologists
- Oncologists
- Sexual Health Medicine practitioners
- Patients
- Clinical trialists
- Systematic reviewers
- Patient support group leads.

Health professionals will be identified through international specialist societies: the International Society for the Study of Vulvovaginal Disease (ISSVD), the British Society for the Study of Vulval Disease (BSSVD), the Australian and New Zealand Vulvovaginal Society (ANZVS), European College for the Study of Vulvar Disease (ECSVD), Indian Chapter of the ISSVD, the North American Chapter of the ISSVD, Latin American society in South America.

Patient representatives will be individuals who lead patient support groups as they will have a wider overview of the presenting features of LS. This is preferable to involving individual patients as they will only have their own experience.

International LS patient support group leads to be invited will be from several different groups:

- Danish group (https://www.lichensclerosus.dk)
- Swiss group
- Association for Lichen Sclerosus and Vulval Health (UK) (LSVCUKawareness.co.uk)
- Lichen Sclerosus; Beating it! Lichen Sclerosus Canada
- Lichen Sclerosus New Zealand and Australia (https://m.facebook.com/groups/lichen-sclerosis-new-zealand-and-australia-591123080903002/)

- Lichen Sclerosus support Network (https://www.lssupport.net)
- LS steunpunt (https://www.facebook.com/groups/992552784212187/?ref=br_rs)

Method for the identification of potential diagnostic criteria (Stage 1)

A list of possible outcome domains will be identified through the following sources:

1. Up to date reference literature of quantitative studies:
    a. British Association of Dermatologists Guidelines (2018): An in depth, robust systematic review has been performed by the British Association of Dermatologists lichen sclerosus guideline development group in preparation of the 2018 National Guidelines for the management of LS(16). This search was last performed on 17/7/17. It included randomised, non-randomised, non-controlled studies, case series and case reports. Outcomes have been listed in the supplementary material accompanying these guidelines
    b. European S3 guideline (2015)(5)
    c. Cochrane review (2011): In depth systematic review of randomised controlled trials(17)

Extraction of potential diagnostic criteria from each of these sources will be undertaken by the lead researcher. The list of diagnostic criteria will then be reviewed by all the Steering Group for members to add diagnostic criteria that they feel may have been missed.

Consensus Process and Definition, Method for the definition of core outcome domains (Stages 2 and 3)

Stage 2

A consensus study using electronic-Delphi (e-Delphi) methodology involving international stakeholders will be used to select the most important/relevant of the identified diagnostic criteria from Stage 1. The Welphi web-based system will be used for survey management (https://www.welphi.com/en/Home.html) Costs requested for this project include the use of software.

We have chosen web-based software to administrate the survey rather than paper based forms. Although they would increase the accessibility of the survey, paper based forms are impractical and require a large amount of resource and coordination. The survey will be run in English language.

The e-Delphi process is one in which a panel of participants answer a series of questionnaires over two or more rounds in an attempt to achieve consensus. In round 1 participants are asked to score the importance of including a particular diagnostic criteria in a core outcome set on a scale of 1-9 (1-3=not important, 4-6=important but not critical, 7-9=Critical). An option for 'unable to score' is also available. Participants will be able to provide feedback on individual items and suggest additional diagnostic criteria if they feel any are missing. Feedback will be collated and if necessary, rewording of the items will take place following discussion with the Steering Group. Following agreement with the Steering Group, the diagnostic criteria that have been missed will be added to the list in the second round of the Delphi survey.

Definition of consensus will be determined a priori. Criteria for a diagnostic criteria to be taken through to the next stage (diagnostic test accuracy study):

- at least 70% of participants score an outcome as 7, 8, or 9

And

- 15% or less of participants score it as 1, 2, or 3.

After a maximum of three rounds, if there are more than 8 diagnostic criteria that have met consensus, participants will be asked to organise by rank order to rationalise the number of criteria that go into the future study.

The survey instrument will be amended following round one and additional outcome domain items suggested by participants will be included in the subsequent round.

In subsequent rounds participants will receive feedback; they will be shown the distribution of scores from other participants, grouped by stakeholder, along with the score that they attributed to the individual outcomes. They will be asked to reflect, and rescore if they want to, having been shown the views of the other participants.

The e-Delphi will be concluded after a maximum of 3 rounds (plus ranking round if needed). Rounds will be held approximately 1 month apart. Participants will be given 2 weeks to complete each individual round.

Reminder emails will be sent to participants at key stages of the process to ensure maximum return of the Delphi survey questionnaire.

Participants will be encouraged to vote on all items within the Delphi survey and the option of 'unable to score' will be available. Therefore, missing data should not be experienced. If people do not participate in a round of the survey, they will not be invited to participate in the subsequent rounds.

This e-Delphi process will ultimately result in a shortlist of outcome domains to be taken through to the next stage of the project, which is a multicentre diagnostic test accuracy study (protocol and ethics application to be submitted separately).

Ethics and consent

Ethical approval will be sought from the University Of Nottingham School Of Medicine Ethics Committee. This Ethics Committee has been chosen as it is linked to where the project administration is taking place. Consent will be sought at the time of entry to the study by asking participants to complete check boxes to confirm their consent.

Results

Presentation of results is planned at key clinical meetings.

Dissemination and publication

Dissemination to healthcare professionals will be through presentations at clinical conferences and via publication in a peer reviewed journal.

All participants involved in the research will be informed of the study outcomes via a newsletter and through study updates on the Centre of Evidence Based Dermatology website.

Future research plan for developing LS diagnostic criteria.

The results from this study will inform the next stage of this project to develop Ls diagnostic criteria. They will be tested and in a multicentre diagnostic test accuracy study for their ability to accurately diagnose patients with LS compared to the gold standard clinician diagnosis.

Funding, Conflict of interest

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Dr Rosalind Simpson has no conflicts of interest to declare

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