Protocol:

Study Title:

The effect of perineal wound infection on the anal sphincter

A prospective observational study evaluating the sonographic appearance of the anal sphincter in postpartum women with perineal wound infection.

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Clinical Investigation Plan Synopsis

Study Title	A prospective observational study evaluating the sonographic appearance of the anal sphincter in postpartum women with perineal wound infection.
IRAS Number	278466
Study Design	Prospective observational study
Study Participants	Women referred to the Croydon University Hospital perineal clinic with perineal wound infection following vaginal delivery
Planned Sample Size	80 (seen in year and patients agreeing to participate and exclusion criteria)
Planned Study Period	Until wound healed
	Objectives
Primary	To investigate the clinical progression of perineal wound infection
Secondary	1. To investigate whether perineal wound infection can extend to involve an intact anal sphincter 2. To investigate the integrity of the anal sphincter in women with a repaired obstetric anal sphincter injury and perineal wound infection.
Inclusion Criteria	- Women with childbirth related perineal injury/episiotomy and wound infection - Women over 18 years of age - Ability to understand and read the patient information sheet (in English) - Ability to give informed consent
Exclusion Criteria	- Vulnerable Adult - Fetal or neonatal death or poor neonatal outcome - Women who are in an immunosuppressive state (e.g human immunodeficiency virus or pharmacologically induced immunodeficiencies by chemotherapy or steroids) - Inability to give consent

TABLE OF CONTENTS

1. INTRODUCTION

In the United Kingdom (UK), 85% of women sustain perineal injury following a vaginal delivery, which accounts for over 350,000 women annually. Injury is either spontaneous, iatrogenic following episiotomy or a combination of the two, with 69% of these wounds subsequently requiring surgical repair (suturing)(1,2).

The perineum can be divided into two parts; the urogenital triangle which contains the external genital organs and the anal triangle containing the anal sphincter and canal(3). Spontaneous perineal injury can therefore be classified as shown below in Table 1. This differentiation to be made between injuries which involve external anal sphincter (EAS), internal anal sphincter (IAS) and anal mucosa(4).

Degree	**Injury**
First	Skin only
Second	Perineal muscles but not involving the anal sphincter
Third	Anal sphincter complex 3a- less than 50% of the external anal sphincter 3b- more than 50% of the external anal sphincter 3c- internal anal sphincter torn
Fourth	Anal sphincter complex and anal mucosa

Perineal injury following childbirth can however result in complications such as wound infection. Signs and symptoms associated with perineal wound infection including, increasing pain, swelling, erythema, excessive or offensive discharge, fever and wound dehiscence(5). Croydon Health Services has its own dedicated perineal clinic to manage women with perineal wound complications following childbirth. The incidence of perineal wound infection between January 2016 to September 2017 was 22.6%(6). In addition, in 2019, 120 women attended perineal clinic for review and management of symptoms suggesting perineal wound infection.

Endoanal ultrasound has been shown to be useful in the assessment of obstetric anal sphincter injury (OASI)(7). The anal sphincter can also be visualised using multiplanar transperineal ultrasound(three/four-dimensional)(8). However, the natural history and integrity of the anal sphincter in women with OASI and wound infection has never been evaluated.

In addition, wound infection can extend to affect deeper tissues (9). It is not known whether this infection can infiltrate an intact anal sphincter.

Understanding the natural history of perineal wound infections would enable appropriate interventions prior to the development of complications such as anal incontinence.

2. STUDY HYPOTHESIS, AIMS AND OBJECTIVES

Aim

To evaluate the sonographic appearance of the anal sphincter complex in women with perineal wound infections using three-dimensional (3D) endoanal ultrasound.

Objectives

Primary:

To investigate the clinical progression of perineal wound infection

Secondary:

3. To investigate whether perineal wound infection can extend to involve an intact anal sphincter
4. To investigate the integrity of the anal sphincter in women with repaired obstetric anal sphincter injury who sustain perineal wound infection.

3. CLINICAL INVESTIGATORS AND INVESTIGATION ADMINISTRATIVE STRUCTURE

3.1 Investigation Site Staff

CHIEF INVESTIGATOR	**Mr Abdul H Sultan**, MBChB, MD FRCOG Consultant Obstetrician & Gynaecologist Croydon Health Services 530 London Road, CR7 7YE Croydon, United Kingdom
INVESTIGATORS	**Miss Ranee Thakar,** MB.BS, MD, FRCOG Consultant Obstetrician and Gynaecologist, Subspecialist in Urogynaecology Croydon Health Services 530 London Road, CR7 7YE Croydon, United Kingdom
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4. METHODOLOGY

4.1 Overall Design

This is a single prospective observational study to assess the appearance of the anal sphincter complex in women with wound infection following childbirth related perineal injury using (3D) endoanal ultrasound or multi-planar transperineal ultrasound(3D/4D).

All patients who have been referred to the Croydon University Hospital dedicated perineal clinic with perineal wound infection will be invited to participate. All patients will be given a patient information sheet describing the study prior to consent. Patients will be given time to read the information included and time to discuss with relatives, colleagues and carers. In addition, time to ask the recruiter any questions that have arisen after reading the consent form. Informed consent will be obtained. Patients will be assessed at weekly intervals until the wound infection has resolved and the wound has clinically healed. At follow-up all patients will complete a case report form, have a vaginal, perineal and rectal examination. Following this, the wound will be photographed with the MolecuLight i:X Imaging Device: a portable, non-invasive, real-time camera used to depict the bacterial load of a wound. In addition, in perineal wounds that have superficially dehisced, wound healing progression will be mapped using the Silhouette® 3D camera: an imaging device that precisely and consistently measures the area, depth, volume of wounds and their healing progress. Finally, an endoanal ultrasound scan and/or transperineal ultrasound will be performed.

4.2 Procedures and Assessment

Patient data, history and physical examination:

As per standard procedure for the Croydon Health Services Perineal Clinic. Demographic and obstetric data will be collected prospectively from the maternity notes, including: maternal age, gestational age at delivery, parity, body mass index, duration of first and second stage of labour, indication for operative vaginal delivery, mode of delivery, mediolateral episiotomy, and neonatal weight. In addition, information in regards to the repair of the perineal injury including suture type, place of repair and grade of repairer. Presenting symptoms review, medical history, use of medications including antibiotics for wound infection will be obtained at baseline. Women will have a vaginal, perineal and rectal examination prior to ultrasound scan. This be recorded on the case report form.

All datasets will be coded and anonymised. The data will be stored in a secure room within the Trust. All electronic data will be stored within password protected IT system within the Trust, which is only accessible by the clinical and research team.

Endoanal Ultrasound

Endoanal ultrasound will be performed with the BK Flexfocus 400 (Gentofte, Denmark) fitted with a 12 - 16 MHz anorectal transducer (type 2050; focal point up to 20 mm and focal range 5 - 45 mm). Patients will be scanned in the left lateral position, with the endoanal probe along the axis of the anal canal.

Anal sphincter defects will be scored using a validated Starck score which accounts for depth, length and size of the defect for both internal and external anal sphincter, with a range from 0 being no defect to 16 being maximal defect.

Transperineal Ultrasound

If endoanal ultrasound is declined or not tolerated, the anal sphincter will also be assessed using three-/four-dimensional (3D/4D) transperineal ultrasound using a Voluson 730 Expert or Voluson S6 systems with a RAB 8–4-MHz transducer (GE Medical Systems, Zipf, Austria) with the probe placed externally on the area of the fourchette. Patients will be scanned in a dorsal lithotomy position with hips in a flexed and slightly abducted position. Advantages of this form of ultrasound include acceptability by patients as it is painless and non-intrusive(7,8).

Microbiological assessment:

If a wound swab has not been taken prior to referral or wound swab results are not available, one will be taken to detect the causative organisms. Appropriate antibiotics will then be given to cover the detected organism.

The Silhouette® 3D camera:

For wound that have superficially dehisced, the wound surface area, depth, volume and healing progress will be precisely measured using the Silhouette® 3D camera. This is a system that uses 3D laser technology to track wound healing progression.

The MolecuLight i:X:

The bacterial load of the perineal wound will be measured every week using the MolecuLight i:X. This is a system, which uses fluorescent illumination to capture and document the presence of bacteria. The fluorescence images obtained have distinct colours, which are associated with bacteria and other different wound aspects (Table 1). These findings will be supported by microbiological analysis of the wound with swab culture and sensitivity.

Table 1:

Red	Presence of potentially harmful levels of bacteria
Green	Connective tissues in skin
Dark/black areas	Blood, highly vascularized tissues, necrotic tissue, highly pigmented tissue (freckles, moles, etc.) or poorly illuminated areas
White	Materials in the field of view that are white (bed sheet, clothing, paper, wound measuring ruler, etc.) or oversaturation of color signal
Cyan	Presence of *Pseudomonas aeruginosa*

Statistical analysis

Statistical analysis will be performed using SPSS version 20.0 or higher.

4.3 Selection of Population for Investigation

4.3.1 Inclusion Criteria:

- Women with childbirth related perineal injury and wound infection
- Women over 18 years of age
- Ability to understand and read the patient information sheet (in English)
- Ability to give informed consent

4.3.2 Exclusion criteria:

- Vulnerable Adult
- Fetal or neonatal death or poor neonatal outcome
- Women who are in an immunosuppressive state (e.g human immunodeficiency virus or pharmacologically induced immunodeficiencies by chemotherapy or steroids)
- Inability to give consent

4.3.3 Participants Withdrawal from Treatment or Assessment

Participants are free to withdraw from the study at any time, and without any effect to their routine care.

4.4 Data Quality Assurance

4.4.1 Training of Staff

The chief investigator will ensure that the site staff has received appropriate training in the following:

- The Clinical Investigation Plan and execution of it
- Maintenance of the Investigator Site File

4.7.2 Data Management

Data entry will be completed by the research team on site. The data will be transferred to an electronic format and encrypted onto an external hard drive, which will be kept in a locked office cabinet.

As missing data has the potential to cause bias and so nullify study findings, every effort will be made by the site staff to will minimize and ensure there is no incomplete or missing data. All data collected will be inspected by site staff to identify missing data and outliers. If this problem however was to arise, the biostatistics team will also aid us with incomplete-data analysis strategies in order to come to appropriate, robust conclusions.

We will store research data generated by the study for 5 years.

Research findings will be disseminated for publications in peer- reviewed journals, presentations at professional meetings/conferences. If requested results will also be disseminated research participants and other interested groups or communities in a written format.

4.5 Statistical Methods and Determination of Sample Size

The sample size enrolled will be 80. This was calculated with reference to the number of women attending the Croydon University Hospital dedicated perineal clinic in 2019; 120 women. Taking into account women meeting the inclusion and exclusion criteria. In addition, women declining to participate.

5. STATEMENTS OF COMPLIANCE

5.1.1 Ethics and Regulatory Considerations

Declaration of Helsinki

The Investigators will ensure that this study is completed in compliance with the ethical principles of the Declaration of Helsinki.

Good Clinical Practice

The Investigator will ensure that this study is completed in compliance with Good Clinical Practice guidance and applicable regulatory requirement(s). The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

Participant Confidentiality

The Investigators will ensure that the participants' anonymity is maintained to protect their confidentiality and privacy. Data will be anonymised, in keeping with the Data Protection Act. Documents will be stored securely and only accessible by investigators and authorised personnel.

5.1.2 Patient Information and Consent Form

All patients will be given a patient information sheet describing the study prior to consent. This includes the study nature, purpose and possible risks and benefits. Patients will be given adequate time to read the information including and time to discuss with relatives, colleagues and carers. In addition, time to ask the recruiter any questions that have arisen after reading the consent form. Participants will be informed that they are free to withdraw from the study at any time, and without any effect to their routine care.

The participants signed consent form must be obtained before conduction of any investigation. A copy of the Patient Information Sheet including the signed Consent Form should be given to the subject.

5.2 Regulatory and standards

5.2.1 Standards and other

- Guideline for good clinical practice E6(R2)
- GDPR

5.2.2 Subject Data Protection

The written patient information sheet follows the GDPR requirements for transparency. It explains that health records will remain strictly confidential at all times in accordance with the Caldicott principles and the Data Protection Act 1998. All information collected will be coded for anonymisation with the link document locked and kept separately from the data. The coded data would be stored on NHS computers only and password protected with access to authorised researchers only.

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