Lab manual: processing perioperative swabs

'PERi-operative Selective Decontamination of the Digestive tract to prevent severe infectious complications after Esophagectomy: a Randomized multicenter clinical trial in patients with primary resectable esophageal carcinoma (cT1-4, N0-3, M0)'

Sponsor: Radboud university medical center, the Netherlands
Eu trial number: 2023-504144-33
Subject: Two perioperative eSWABS of the resection specimen
Manual created: 19.11.2023 - Version 1.0
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Abbreviations

SDD	Selective decontamination of the digestive tract

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General Information

Scope

This Lab Manual outlines the practical details for ordering, preparing, executing, handling, and processing the two peroperative microbiological swabs of the esophageal resection specimen in the PERSuaDER-trial.

Trial synopsis

Rationale: Esophagectomy is a complex surgical procedure, associated with significant morbidity and mortality rates. Most postoperative complications are caused by infections (10– 30%). These are thought to arise from (micro-)aspiration of bacteria residing in the oropharyngeal and gastrointestinal (GI) tract, leading to (respiratory) infections. Selective decontamination of the digestive tract (SDD) is a prophylactic antibiotic strategy that aims to prevent postoperative infections. Pathogenic aerobic gram-negative rods and yeasts tract are reduced, while anaerobic, protective microbiota are preserved. SDD has been shown to lower the risk for respiratory infections in an intensive care setting. Establishing SDD as effective addition to the standard care of esophagectomy patients is expected to increase their chance of survival.

Objective: Robust and prospective evaluation of SDD after esophagectomy as a protective strategy reducing postoperative pneumonia and other infectious complications, anastomotic leakage and mortality.

Study design and population: A randomized, controlled, open-label, multicenter trial, including 854 patients with primary resectable esophageal carcinoma ((y)cT1-4a N0-3 M0) planned for transthoracic esophagectomy.

Intervention: The intervention group receives SDD treatment additional to standard care, comprising two distinct liquids for oral administration: first the 5 ml amphotericin B suspension (100 mg/ml) and subsequently the 5 ml “SDD base for suspension”, containing both colistin sulphate (20 mg/ml) and tobramycin sulphate (16 mg/ml). Patients take the 5 ml amphotericin B, followed by the 5 ml “SDD base for suspension”, four times daily for one week, starting three days prior to the surgery. On the day of surgery, intake is limited to an early morning and a late evening dose. All other aspects of care are equal to the control group (standard care without SDD). All participants will be asked to keep a diary during the week around the surgery.

Swabs: Aiming to estimate the patient compliance, and to analyze pathogens causing infectious complications two swabs will be taken during surgery, in both intervention- and control group. One at the proximal site and one at the distal site of the resected specimen.

Main study parameters/endpoints: The cumulative incidence of postoperative pneumonia within 30 days after surgery.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients undergoing standard care do not experience any added risks due to participating in this study. The intraoperative esophageal sample which will be taken from all subjects to determine the microbial effect of SDD will be taken ex vivo from the surgical specimen and consequently provides no additional risk for the patient. Potential benefits of the SDD treatment are a lower incidence of infectious complications, such as pneumonia, and as a result shorter hospitalization and ICU stays, less re-operations, less readmissions and lower mortality. SDD can cause (mild) side effects such as vomiting/nausea, diarrhea, bloating, abdominal pain and loss of appetite.

Responsibilities

Taking the microbiological swab should always be carried out by or under direct supervision of a medical doctor with good knowledge of the PERSuaDER trial and this lab manual.
Ordering, preparing and transferring of the swabs can be carried out by a designated team member with sufficient access to and knowledge of local standard operating procedures, under supervision of a medical doctor familiar with the PERSuaDER trial and this lab manual.
Analysis of the swabs in the lab should be carried out by a facility that is compliant with the protocol requirements.

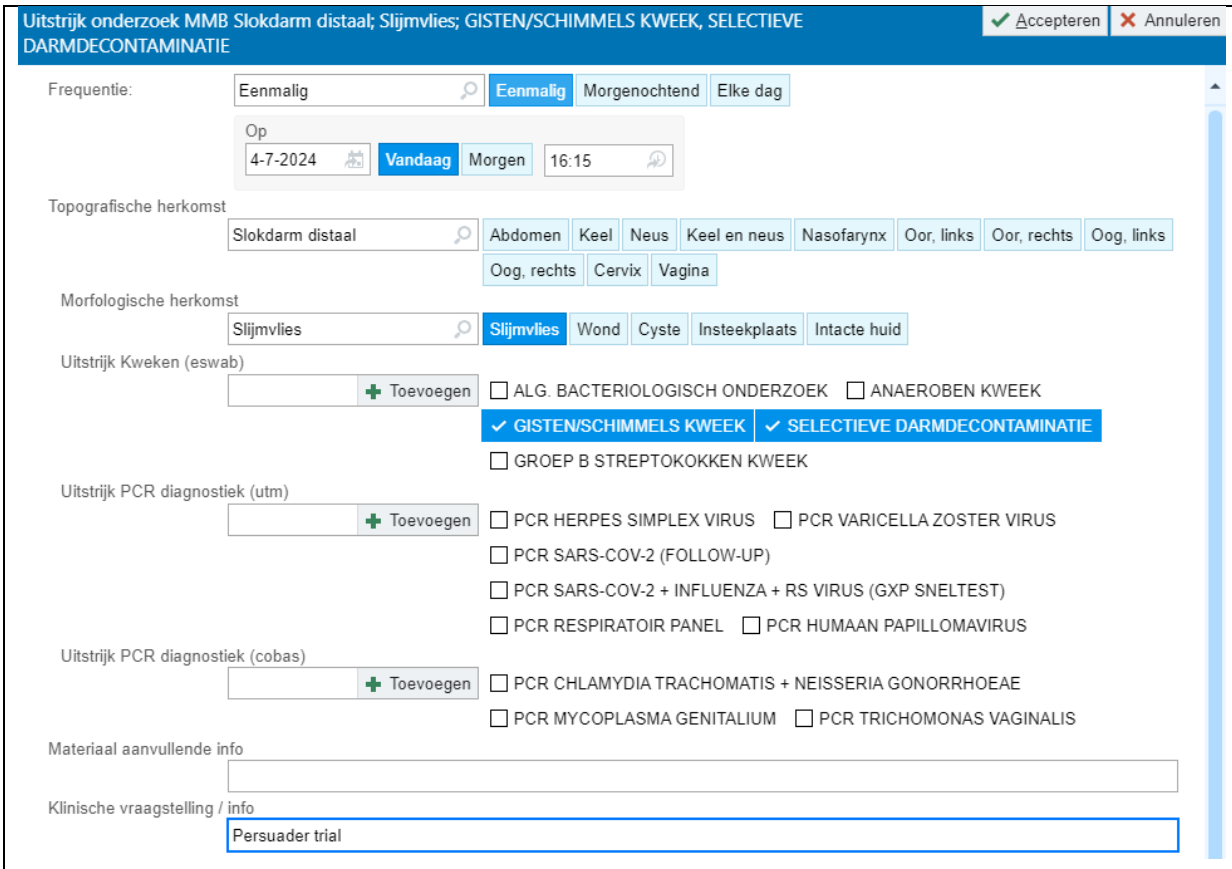
Ordering the swab

Two microbiological swabs need to be ordered in your hospital's electronic medical record (EMR) system. Make sure this is done on the correct patient profile with correct date and times.

For example, In UZ Leuven:
In Klinisch Werkstation (KWS) ordering the swab can be carried out by using DEAL or a paper-based request form.

- In DEAL, the swab can be ordered by typing the following string "cultuur (andere monsters)" or by typing the request number "1824". Indicate the target zones of the swabs (eg. esophagus and stomach), the setting (PERSuaDER trial, peroperative) and the correct date and time
- If using a paper-based method, please use request form 3030. Make sure to apply the patient identification information (label or written) and obtain a doctor's stamp and signature. Indicate the target zones of the swabs (eg. esophagus and stomach), the setting (PERSuaDER trial, peroperative) and the correct date and time

For example, in Radboudumc:
Place order in EPIC: see image below



- Select “SDD kweek voor Persuader trial”, which includes: yeasts, and gram negative rods.
- Use E-swab with pink cap

- Indicate the target zones of the swabs
    - Slokdarm Proximaal
    - Slokdarm Distaal

For other hospitals, we refer to local standard operating procedures for ordering the microbiological swabs.

Preparing the swab

During the time-out process at the start of the operation, the patient identity should be verified, and the microbiological swabs discussed. Make sure the following items are discussed: reason (ie. PERSuaDER trial), number of swabs (ie. 2), material (ie. eSwab®, actor (ie. surgeon). Double-check the swab requests for correct patient identity, correct date, time, number and target zone.
Two eSwabs® can then be opened and handed over to the operating team in a sterile fashion.

Executing the swab

Per protocol we will require two mucosal swabs: one at the proximal site and one at the distal site of the resection specimen. Take care not to disinfect the target areas before the swab is taken.

How to take the swab:

- Use the swab to collect the patient sample by gently rotating the swab across the target area. Avoid touching the swab applicator below the pink molded breakpoint as this could lead to contamination and incorrect test results.
- Remove the screw cap from the recipient and insert the swab all the way to the bottom of the tube.
- Holding the end of the swab shaft, bend it at a 180 degrees angle to break at the marked breakpoint. If needed, gently twist the shaft between thumb and forefinger to completely remove it.
- Screw the cap on tightly to prevent leakage.

Where to take the swab:
The purpose is to have an idea of the potential pathogens at the to-be-made anastomosis.

- Proximal site:
    - On the resection specimen: Open resection specimen proximally and swab the mucosa that was in the proximity of the area of the to-be-made anastomosis

    OR
    - On the proximal esophagus: After resecting the esophagus, endoluminally swab the distal end of the esophageal remnant.
- Distal site:

- On the resection specimen: Open the resection specimen distal to the tumor on an area adjacent to the to-be-made anastomosis and swab the mucosa.

OR

- On the candycane: After having made the anastomosis and the candy cane is resected; open the candycane and swab the mucosa

OR

- On the conduit: Before making the anastomosis, endoluminally swab the proximal part of the conduit.

Please make sure to mark the samples according to the target area (eg. proximal/esophagus, distal/stomach).

When both swabs are taken, the marked recipients can be handed over to the non-operating team.
There, a patient identification label should immediately be applied on the tube label. Including study name and subject number. If no patient identification labels are available, patient information should be written clearly on the tube label.

Transferring the swab to the lab

Please follow standard operating procedures of transport to the microbiology lab for your facility.

For example, in UZ Leuven:

At UZ Leuven, one of the following procedures can be followed: the pneumatic transport system (PTS / buizenpost), drop off at a delivery point, bring to the laboratory.
The PTS system is the preferred method of transport. For this procedure, please direct towards a PTS point.

- Place the tubes in a secondary recipient (plastic jar with metal screw lid) with the cap of the tube facing upwards.
- Fill the PTS cartridge with two secondary recipients, one or both containing the swabs. These secondary recipients serve to fixate the samples as much as possible during the transport.
- Place the request forms around the secondary recipients.
- When closing the cartridge, make sure there is no residual opening.
- On the PTS, make sure that LAG is programmed as destination. Wait until the light turns green, place the cartridge in the system.
- Wait until the cartridge is sent off to make sure that the sending is successful.

If the PTS system is not available, you can utilize the delivery points. For this, please locate the nearest LAG delivery point and drop off the samples with their associated request forms.

An employee of the service laboratory medicine (LAG) will collect it on weekdays at 10h00, 12h30, 15h00 and 17h00; and in weekends or holidays at 09h30 and 12h00.

At all times, the samples can also be taken manually to the service of laboratory medicine (LAG) in the central service building (CDG), Bordeaux, 7th floor.

For example, in Radboudumc:

After collection until transport, store at 4 °C. Transport at room temperature. Hand over at RLD Front Office reception desk (route 815) as soon as possible via courier, research personnel or personally by department employee.

For more information regarding the use of the pneumatic tube system, please refer to the page: 'Pneumatic Tube, the use and maintenance of Pneumatic Tube 110 Lab-line for the transport of body material to the RLD (version 3)' on Q-portal.

Ensure that the time between sample collection and the arrival of the sample at the laboratory is as short as possible; therefore, transport the material to RLD (Radboudumc Laboratory for Diagnostics) , route 815!

Analyzing the swab in the lab

In the laboratory the following analyses should be performed by using; **Columbia Blood Agar Plates (CBP),** McConkey Plate (MACS), Sabouraud Plate (SAB), or a similar substitute.

Culture for aerobic bacteria

- Determination of: *Enterobacterales, Pseudomonas aeruginosa,* and *Acinetobacter baumannii/calcoaceticus* complex
- No resistance testing.

- Presence of yeasts (+/-)

No anaerobic culture needed.

After analyses the samples should be destroyed according to local laboratory protocols.

Displaying the results

Results of the culture and resistance patterns should be sent to the local PERSuaDER research personnel, or uploaded in the EMR. (This is source data, and needs to be stored for 25 years).

These results need then to be added to the eCRF at the 30-day postoperative timepoint.

For example, in Radboudumc:
Result can be mailed to persuader.heel@radboudumc.nl

Thank you, for your collaboration.
For any remaining questions, please contact our PERSuaDER study team:

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