Wound drainage following groin dissection for malignant disease in adults (Protocol)

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[Intervention Protocol]

Wound drainage following groin dissection for malignant disease in adults

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the current level of evidence regarding whether placement of a drain is beneficial after groin dissection in terms of reducing haematoma, seroma, wound dehiscence and wound infection rates. If it is, the optimal type and duration of drainage following groin dissection will also be determined.

BACKGROUND

Description of the condition

Groin dissection, also known as inguinal lymphadenectomy or inguinal lymph node dissection, is commonly performed as part of the treatment for some tumours, including melanoma, and squamous cell carcinoma of the skin, penis or vulva, as well as other less common tumours (Gaarenstroom 2003; Swan 2003; Margulis 2010). It involves removal of all of the lymph nodes in the anatomical area known as the femoral triangle, at the upper inner part of the thigh. When groin dissection is performed because of confirmed spread (metastasis) of cancer to a lymph node, this procedure is known as a therapeutic lymph node dissection (TLND), and when it is performed because there is a high risk that a cancer might have spread to a lymph node, it is known as a prophylactic lymph node dissection (PLND). Recently the development of sentinel lymph node biopsy (SLNB) has allowed the detection of clinically occult micrometastases in the inguinal lymph nodes via a microscope, which could not be detected by examining the patient. In these cases if the SLNB is positive for metastatic disease a completion lymph node dissection (CLND) may be performed (Hakim 2006; Morton 2006; Yeung 2013). According to Hospital Episode Statistics, 688 inguinal lymph node dissections were performed in England in the year 2011-2012 (www.hesonline.nhs.uk).

Description of the intervention

At the end of the procedure, the surgeon usually places one or more drains in the wound (Ul-Mulk 2012). Commonly, closed suction drains are used, however it is possible that some surgeons

may use other drainage systems, such as epidermal vacuum therapy (Tauber 2013). Surgeons use either a volume-directed indication for removal of the drain(s), for example when drainage is less than 30 ml in 24 hours (Serpell 2003), or a time-directed indication for removal of the drain(s), for example on the seventh post-operative day irrespective of drain output (Coblentz 2002).

How the intervention might work

Standard surgical teaching suggests that a drain tube, connecting the cavity created by the surgery with the outside world, should be put in place at the end of the procedure in order to collapse dead space, and to prevent the accumulation of blood (haematoma) or serous fluid (seroma) in the cavity (Serpell 2003). It is thought that haematoma and seroma rates will be decreased by allowing fluid to drain from the wound. Conversely, complications such as wound infection may be increased by placement of a drain, as it provides bacteria with a potential portal for entry into the subcutaneous space (Samraj 2007; Carlson 2008).

Why it is important to do this review

It is not clear that drainage following inguinal lymph node dissection is beneficial. Furthermore, there is uncertainty regarding the correct time to remove drains, and whether to use a time- or volume-directed indication for removal. It is unclear whether insertion of a drain into the groin reduces, or increases, complication rates after this surgery. There have been no previous reviews addressing this question. We aim to use systematic review methodology to clarify this issue, define the quality of evidence supporting current practice, and if necessary, highlight the need for further high quality studies in this area.

OBJECTIVES

To assess the current level of evidence regarding whether placement of a drain is beneficial after groin dissection in terms of reducing haematoma, seroma, wound dehiscence and wound infection rates. If it is, the optimal type and duration of drainage following groin dissection will also be determined.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) only.

Types of participants

- There will be no restriction on country of origin.
- People having groin dissection for metastatic malignant disease, including - but not limited to - malignant melanoma, squamous cell carcinoma of the skin, penis, vulva or anus. The groin dissection may be therapeutic, prophylactic or completion (see Description of the condition).
- People over 18 years of age; there will be no restriction by gender.
- The setting for this surgery will be hospital inpatient care; adverse events may occur in the outpatient setting, and will be assessed, if recorded by the studies.

People having much more extensive surgery, where dissection includes higher lymph node groups including iliac, pelvic and para-aortic, will be excluded. Cloquet's node (the most superior inguinal node in the proximal groin) will be deemed the most superior limit for eligible studies.

Types of interventions

Studies reporting the following comparisons will be eligible for inclusion (all references below to the use of a surgical drain(s) allude to those inserted into the groin following inguinal lymph node dissection):

- Wound drainage compared with no wound drainage.
- One type of wound drain compared with another type of wound drain.
- Different timing of drain removal: to include removal according to fixed-time and fixed-volume protocols.

Types of outcome measures

Primary outcomes

- Wound complications by final follow-up (as defined by trial authors; including any or all of dehiscence (wound breakdown), haematoma, seroma).
- Wound infection, as defined by the Centers for Disease Control and Prevention (CDC) criteria (Horan 1992): that is, infection occurring within 30 days after groin dissection and the patient has at least one of the following:
    - purulent drainage from the superficial incision;
    - micro-organisms isolated from an aseptically-obtained culture of fluid or tissue from the superficial incision;
    - superficial incision that is deliberately opened by a surgeon and is culture-positive, or not cultured and the patient has at least one of the following signs or symptoms: pain or tenderness; localised swelling; redness; or heat;

- diagnosis of a superficial incisional surgical site infection by the surgeon or attending physician.

Secondary outcomes

- Length of hospital stay.
- Volume of fluid drained.
- Number of aspirations.
- Drain reinsertion.
- Lymphoedema.
- Quality of life outcomes including Patient-reported outcome measures, e.g. pain scores (using a validated scale).

Search methods for identification of studies

Electronic searches

We will search the following electronic databases to identify reports of relevant randomised clinical trials:

- The Cochrane Wounds Group Specialised Register;
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*) (Latest issue);
- Ovid MEDLINE (1946 to present);
- Ovid EMBASE (1974 to present);
- EBSCO CINAHL (1982 to present)

We will use the following provisional search strategy in The Cochrane Central Register of Controlled Trials (CENTRAL):
#1 MeSH descriptor: [Lymph Node Excision] explode all trees
#2 MeSH descriptor: [Lymph Nodes] explode all trees and with qualifiers: [Surgery - SU]
#3 ("inguinal lymph node dissection" or "inguinal lymphadenectomy" or (groin next dissect*) or (groin next surg*)):ti,ab,kw
#4 {or #1-#3}
#5 MeSH descriptor: [Drainage] explode all trees
#6 MeSH descriptor: [Suction] explode all trees
#7 drain*:ti,ab,kw
#8 #5 or #6 or #7
#9 #4 and #8
We will adapt this strategy to search Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL. We will combine the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) (Lefebvre 2011). We will combine the EMBASE search with the Ovid EMBASE filter developed by the UK Cochrane Centre (Lefebvre 2011). We will combine the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2011). We will not restrict studies with respect to language, date of publication or study setting.
We will search the following clinical trials registries:

- ClinicalTrials,gov (http://www.clinicaltrials.gov/)
- WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx)
- EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/)

Searching other resources

The reference lists of included studies will be checked independently by two review authors (DT, HS) for additional eligible trials.

Data collection and analysis

Selection of studies

Two review authors (DT, HS) will independently determine the eligibility of each study. These authors will analyse the titles and abstracts of all citations found through the search strategy previously described. They will obtain a copy of the full article for each citation reporting a potentially eligible trial. Independently, the two review authors will apply the eligibility criteria; any discrepancies will be resolved by consensus discussion with the third review author. Where necessary, and possible, additional information will be sought from the principal investigator of the trial concerned. Any exclusion of a potentially eligible trial from the review will be justified in the final report.

Data extraction and management

Independently, two review authors will extract the data for each included study using a pre-designed data extraction form. Data will be extracted according to the details of the trial (first author, year of publication, journal, publication status, period and country of study, sources of funding, study design, sample size); patient characteristics (age, sex, type of disease, stage of disease, type of surgery and prior treatment status); quality of the study; details of the surgery (PLND, TLND or CLND), number of nodes removed) details of the intervention; clinical variables related to patient well-being; duration of follow-up; and the outcomes. The third review author will be used to resolve any discrepancies regarding data extraction, and consensus will be reached. In the presence of multiple reports on an included trial, the most complete data-set feasible will be assembled for the trial.

Assessment of risk of bias in included studies

Independently, two review authors (DT, HS) will assess each study for risk of bias using the Cochrane Collaboration's 'Risk of bias' tool (Higgins 2011). We will consider selection bias, performance

bias, detection bias, attrition bias, and reporting bias for each individual study. Where there are unclear risks of bias due to inadequate descriptions within the trial report, we will attempt to contact the authors in order to clarify the risk. We will report all efforts we made to obtain additional information in the completed review. Any discrepancies will be resolved by consensus discussion with the third author. We will describe the support for our judgement on risk of bias within a study in the final review.

Measures of treatment effect

Dichotomous variables (wound complications, wound infection, drain re-insertion, lymphoedema) will be analysed as risk ratios (RR) with 95% confidence intervals (CI). Continuous variables (length of stay, volume of fluid drained, number of aspirations, total aspirate volume, total volume of drainage, patient-reported outcome measures) will be analysed as mean differences. Where different scales are used to assess continuous outcomes, analysis will be by standardised mean difference (SMD).

Unit of analysis issues

The clinically relevant time points reported in each study will be used to calculate complication rates. Wound infection, as defined by the CDC criteria, has to occur within 30 days of the procedure, therefore, this time point will be used as a cut-off for this outcome measure (see above). It is possible that cluster randomised trial designs will be encountered, for example randomisation by surgeon, or by operating list. Such trials will be analysed based on allocation, using summary values for reach cluster.

If bilateral groin dissections are performed with separate randomisation of each groin, we will analyse the results on a 'per groin' rather than a 'per participant' basis, as the outcomes of the two sides are likely to be independent, except for patient-reported outcome measures, which will not be analysed in these participants, as the effects of the two interventions will not be separable. We will conduct a sensitivity analysis using a 'per participant' basis to determine if there is an effect of bilateral groin dissections in the same patient.

Dealing with missing data

If the results of an RCT have been published, but information on the outcome of interest has not been reported, an attempt will be made, whenever possible, to contact the trial authors for the missing information. If continuous data are not presented as mean and standard deviation an attempt will be made, whenever possible, to contact the trial authors for the information in this format. All efforts made to obtain additional information will be reported in the completed review. Where possible, all analyses will be by intention-to-treat (Hollis 1999). If participants were allocated to one intervention (for example, no drain placement), but after randomisation underwent a different intervention (for example, the drain was actually placed), they will be analysed according to their randomisation allocation. If the results for dichotomous variables are not reported in some participants, we will base our analysis on both a worst possible outcome (for example, wound infection occurred in all non-reported cases), and a best possible outcome (for example, wound infection did not occur in all non-reported cases). Where participants are excluded from analysis without good cause we will conduct a sensitivity analysis to determine any effect of attrition bias.

Assessment of heterogeneity

We will explore heterogeneity using the Chi^2 test with significance set at P value 0.10, and measure the quantity of heterogeneity using the I^2 statistic (Higgins 2002).

Thresholds for the interpretation of the I^2 statistic can be misleading. A rough guide to interpretation is as follows:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

When interpreting the I^2 statistic, we will take factors such as clinical and methodological heterogeneity, along with whether the heterogeneity is in the magnitude of effect or in the direction of effect, into account, particularly where ranges overlap.

Assessment of reporting biases

We will compare the reported outcomes with those stated in the methods of the studies, and also those listed in clinical trials registries as both primary and secondary outcomes (for example http://www.clinicaltrials.gov/). If sufficient studies are identified (a minimum of 10), we will assess for publication bias by creating a funnel plot using software within Review Manager 5.2 using visual inspection to detect publication bias.

Data synthesis

We will present a narrative overview of the included trials. Where appropriate, we will present meta-analyses of outcome data using RevMan 5.2 (RevMan 2012). The decision to pool data in a meta-analysis will depend on the availability of outcome data and the assessment of between-trial heterogeneity. For comparisons where there is no apparent clinical heterogeneity and the I^2 value is less than, or equal to, 40%, we will apply a fixed-effect model. Where there is no apparent clinical heterogeneity and the I^2 value is greater than 40%, we will apply a random-effects model. However, we will not pool data where heterogeneity is very high (I^2 values of 75% or greater).

For the dichotomous outcomes we will present the summary estimate as a risk ratio (RR) with 95% confidence intervals (CI). Where continuous outcomes are measured in the same way across

trials, we will present a mean difference (MD) with 95% CI. We will present a standardised mean difference (SMD) where trials measure the same outcome using different methods.

Subgroup analysis and investigation of heterogeneity

If there are sufficient trials of adequate size it may be possible to conduct subgroup analyses. Ability to conduct the analyses will also depend on whether the required information is recorded in the trial publications. If data are not included, we will attempt to contact trial authors to obtain the data. The following will be considered for possible subgroup analysis.

- Effects of CLND or PLND versus TLND. These subgroups may behave differently, as those patients undergoing a TLND have macroscopic cancer in the lymph node basin, which, theoretically, may require a larger volume of tissue to be removed and create a larger dead space, thereby increasing the potential drainage after inguinal lymph node dissection. By contrast, some authors suggest that, when compared to TLND, CLND has an increased risk of wound infection owing to two procedures having been performed in the same anatomical location in rapid succession (de Vries 2006).
- Type of cancer, for example melanoma versus vulval cancer, versus anal cancer, versus penile cancer.
- Type of drain used, for example closed suction drainage versus gravity drainage.

Sensitivity analysis

A sensitivity analysis that includes, and then excludes, trials with a high risk of bias will be performed if sufficient trials at low risk of bias are identified to make this feasible. We acknowledge that there is no accepted definition of what constitutes a trial at high risk of bias, so we have decided to set a threshold so that trials assessed as having three or more of the seven elements of the Cochrane Collaboration 'Risk of bias' tool judged as being at high risk of bias will represent those studies at high risk of bias (Higgins 2011).

Presentation of results

We will present the main results of the review in 'Summary of findings' tables, which provide key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the main outcomes, as recommended by the Cochrane Collaboration (Schünemann 2011a). We plan to include the following main outcomes in the summary of findings tables.

- Wound complications (dehiscence, haematoma, seroma).
- Wound infection.

The 'Summary of findings' table includes an overall grading of the evidence related to each of the main outcomes, using the GRADE approach (Schünemann 2011b).

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* *Indicates the major publication for the study*

CONTRIBUTIONS OF AUTHORS

Dominic Furniss: Conceived the question, developed, co-ordinated and edited the protocol, performed part of the writing, made an intellectual contribution and approved the final version prior to submission and is guarantor for the protocol.

David Thomson: Conceived the question, developed, co-ordinated, completed the first draft, and edited the protocol, performed part of the writing, made an intellectual contribution and approved the final version prior to submission.

Hazim Sadideen: Conceived the question, developed, co-ordinated, completed the first draft, and edited the protocol, performed part of the writing, made an intellectual contribution and approved the final version prior to submission.

Contributions of editorial base:

Kurinchi Gurusamy: edited the protocol; advised on methodology, interpretation and protocol content. Approved the final protocol prior to submission.
Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the protocol.
Ruth Foxlee: designed the search strategy and edited the search methods section.

DECLARATIONS OF INTEREST

David R Thomson - none known

Hazim Sadideen - none known

Dominic Furniss - none known

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