Protocol: A systematic review and meta-analysis of the outcomes and complications of using the Deep Inferior Epigastric Perforator (DIEP) flap for breast reconstruction in cancer patients.

Introduction

“The free abdominoplasty flap for breast reconstruction" was first described by Hans Holmstrom in 1979,\(^ {1,2}\) and the first DIEP breast reconstruction was performed by Allen and Treece in 1992.\(^ {1,2}\) Since then the DIEP flap has become increasingly popular and is currently the gold standard for autologous breast reconstruction.\(^ {3,4}\) It is associated with good aesthetic outcomes and low donor site morbidity,\(^ {5}\) but is associated with a comparatively higher expense than other forms of breast reconstruction.\(^ {3}\) Potential complications include fat necrosis (6-18%), vascular compromise which may lead to flap loss (1-4%), tumour recurrence (2.3%), haematoma or seroma formation and abdominal donor site pathology.\(^ {6}\)

A recent review by Cubitt et al of 141 patients who underwent 159 DIEP flap reconstructions by a single surgeon in the UK between 2003 and 2010 reported improvements in their complication rates through modification of operative technique and improvements in peri-operative care.\(^ {7}\) In this review 26% of patients experienced a complication, with 15% being re-admitted and 20% of all patients requiring further surgery.\(^ {7}\) The authors stated that improvements in operative technique over time such as shaping the flap after transfer to the chest rather than before transfer reduced complications including partial flap necrosis.\(^ {7}\) Moreover, the introduction of low molecular weight heparin, early ambulation and thrombo-embolic deterrent stockings prevented subsequent pulmonary emboli in their cohort, without increasing rates of haematoma.\(^ {7}\) This is supported by a study by Enajat et al who looked at the risk of pulmonary embolism in patients undergoing DIEP breast reconstruction; 4% of patients experienced PE with high BMI >25 and BRCA gene mutation being risk factors.\(^ {8}\) The authors designed a prediction model to identify high-risk patients who may benefit from more aggressive thrombo-prophylaxis.\(^ {8}\)

Moreover, a recent review article and meta-analysis of 2398 patients from 17 studies, has established that bilateral DIEP flap breast reconstruction is associated with significantly higher complication rates, including total flap failure (RR 3.31 p = 0.003) and breast seroma (RR 7.15 p = 0.03), in comparison to unilateral reconstruction.\(^ {9}\) A further recent review of 123 patients in America who underwent 179 flap reconstructions demonstrated that heavier flaps have an increased chance of developing fat necrosis compared to lighter flaps (OR 1.5 per 100g increase, P < 0.001) and flaps with more than one perforator had a lower incidence of fat necrosis.\(^ {10}\) There is much debate regarding pre-operative imaging as part of planning DIEP procedures with the use of either doppler ultrasonography, computed tomography angiography or magnetic resonance angiography, and a recent review suggests that magnetic resonance angiography is most effective.\(^ {11}\)

A vast amount of research has been undertaken into methods of improving operative outcomes and reducing complications, with the intended benefits of improving patient satisfaction and cost-effectiveness. A systematic review is therefore needed of the current outcomes including patient satisfaction and complication rates of DIEP flap breast reconstruction for breast cancer alongside a review of new methods to improve operative outcomes and peri-operative care.
**Hypothesis / Aims**

The primary aim of this systematic review is to evaluate success rates and patient satisfaction of the DIEP flap for breast reconstruction from current literature, alongside the incidence of complications (return to theatre, venous congestion, arterial thrombosis, partial/full flap loss, fat necrosis, infection, haematoma, seroma and donor site complications).

Secondary aims are to review advances in peri-operative care and operative techniques described in the current literature to see if they significantly reduce complication rates.

**Methodology**

A systematic review of all published literature in the last five years (from January 2010 onwards) relating to DIEP breast reconstruction will be undertaken, in accordance with PRISMA guidelines. Prior to commencing the review, details will be registered in PROSPERO. Studies will be identified using the search terms “deep inferior epigastric perforator flap”. Appropriate studies and reviews will be identified by searching the following databases: MEDLINE, EMBASE, CINAHL and the Central Register of Controlled Trials for all papers in the last five years relating to the DIEP flap. We will search the reference lists of previous studies and reviews for potentially relevant additional articles. The methodology is summarised in Figure 1. Records will be kept of all searches. All studies identified will be critically appraised and screened first for eligibility and then bias (using the Newcastle-Ottawa Quality Assessment Scale). The results of appropriate studies will be included for discussion in the systematic review. Studies which are not appropriate will be excluded, along with any duplicate studies identified and a record will be kept of the reasons for exclusion. The search will be restricted to English language papers and will be re-run just before the final analyses to include any new studies.

Eligibility Criteria: participants are expected to be patients undergoing DIEP flap breast reconstruction for breast cancer. Intervention is DIEP flap which may be primary or delayed, unilateral or bilateral. Outcomes as already mentioned will be success rates, patient satisfaction, complications, improvements to operative technique and peri-operative care. Case reports, cohort studies and review articles will all be included. Studies and study outcomes will be screened for bias. Outcomes from all studies will be included in the review and the Newcastle-Ottawa scale will be used to critically appraise the risk of bias across studies. Data will be analysed using appropriate statistical tests.

Abstracts of studies retrieved using the search strategy and those from additional sources (identified by searching reference lists of identified papers) will be screened independently by two review authors to identify studies that meet our inclusion criteria. The full text of these potentially eligible studies will be retrieved and independently assessed for eligibility by two review team members and screened for potential bias. Studies that are affected by bias along with duplicate studies will be excluded. A record of all studies excluded will be kept and reported on in the review. Any disagreement between the two review authors over the eligibility of particular studies will be resolved through discussion with a third reviewer.

A standardised, pre-piloted form will be used to extract data from the included studies for assessment of study quality and to synthesize evidence. Extracted information will include: study setting; study population; participant demographics; complication rates (return to theatre, venous congestion, arterial thrombosis,
partial/full flap loss, fat necrosis, infection, haematoma, seroma and donor site complications); any measures of patient satisfaction; success rates; study methodology; outcomes and times of measurement; any suggested advances in operative technique or care; information for assessment of the risk of bias. Two review authors will extract data independently; discrepancies will be identified and resolved through discussion with a third author. Missing data will be requested from study authors.

**Expected Outcomes**

The number of studies initially identified and assessed for eligibility will be stated and reasons for exclusion along with exclusion criteria will be clarified, for example duplicate studies and DIEP reconstruction not used for treatment of breast cancer. For each study included, the success rate of DIEP flaps along with complications and patient satisfaction, if commented on, will be listed. Individual study characteristics will be described alongside risk of bias and outcome bias for each study. Success rates and complication rates will be presented for each study. Suggested improvements in operative technique and peri-operative care from all studies identified will be critically appraised, their results described and discussed in detail.

We will provide a narrative synthesis of the findings from the included studies, describing assessment of patient satisfaction and success rates and evaluating the quality of evidence. The incidence of common complications will be calculated. We will go on to discuss types of interventions to improve operative technique and peri-operative care described in different studies and calculate risk ratios to see if they significantly reduced complication rates.

Outcomes of DIEP breast reconstructions will therefore be evaluated including success rates, patient satisfaction and complications. A discussion and analysis of advances in pre-operative planning and operative technique will provide a summary of the most recent advances in performing the DIEP breast reconstruction with the aim of reducing complications and their associated expense, alongside improving patient satisfaction.
Figure 1. Selection process of eligible trials for inclusion in review

- Articles identified through EMBASE search: Number
- Records identified through PUBMED search: Number
- Records identified through CENTRAL search: Number
- Records identified through CINAHL search: Number

- Articles after screening titles and abstracts: Number
- Articles after screening titles and abstracts: Number
- Articles after screening titles and abstracts: Number
- Articles after screening titles and abstracts: Number

- Additional articles identified through searching reference list of relevant articles: Number
- Search results combined: Number

- Duplicates removed: Number
- Full-text articles excluded: Number

- Full-text articles assessed for eligibility: Number
- Articles included in meta-analysis: Number
References


13) PROSPERO website. International Prospective Register of Systematic Reviews. Found online at http://www.crd.york.ac.uk/PROSPERO/

14) Wells GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [webpage on the Internet]. Ottawa, ON: Ottawa Hospital