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Title

Reply to “Complications in DIEP flap breast reconstruction after mastectomy for breast cancer: A prospective cohort study comparing unilateral versus bilateral reconstructions”

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Competing Interests

None declared.

We thank Schaverien and Butler[1], and McInerney et al[2] for their compliments of our prospective cohort study investigating adverse outcomes in unilateral versus DIEP flap breast reconstruction[3] and we are equally delighted to provide our perspective on some of their comments.

In response to the request from McInerney et al[2] for our algorithm for perforator selection, here is our standard practice. Preoperatively, all patients undergo a Duplex scan by experienced radiologist, apart from those with a history of abdominal surgery, who undergo a CT angiogram. Both the investigations provide useful information on the perforating arteries including their diameters and course within the abdomen, whilst Duplex scan also images veins; locations of dominant vessel(s) are then marked by the radiologist on the abdomen. We always base our flap on the best (largest calibre) venous perforator, as explained in our previous publication, which is located by the Duplex[4]. We routinely check the perfusion of the DIEP vessels on the table and perform all preventive actions to avoid venous congestion as described by Galanis and colleagues[5]; additionally, we anastomose the SIEV with the cranial branch of the DIEV if congestion is visible before flap transfer[6]. We have never had to convert a DIEP to a TRAM flap and we still feel that this is not required. We do agree that free TRAMs have a two-fold lower relative risk (RR) of total flap failure than DIEPs[7] but we must point out that the absolute risk difference is very small (~2% for DIEPs vs ~1% for TRAMs). Similarly, the absolute difference in total flap failure rates for DIEPs and ms-TRAMs is <1% (1.7% for DIEPs vs 0.4% for ms-TRAMs)[8]. These minimal gains in flap survival are at the substantial cost of abdominal wall morbidity because 4% of TRAM flap patients developing abdominal hernias and 6% develope bulges, whilst <1% of DIEP patients experience such complications. The disparate gains in flap survival for a substantially higher risk of donor site morbidity is perhaps why cost-effectiveness analyses have consistently shown DIEPs to be superior to ms-TRAMs[8] for breast reconstruction. Whilst we agree with McInerney et al[2] that flap survival may be slightly better for TRAM variants, we suggest that the absolute gains are very small and must be balanced against the greater risk of abdominal wall morbidity.

We thank the responding authors[1,2] and agree that a robust understanding of the vascularity of the abdominal wall and an objective assessment of its vascular anatomy via preoperative perforator imaging is vital to improve outcomes. CTA perforator mapping is a cost-effective[9] method of perforator mapping which is associated with reduced morbidity[10], a shorter hospital stay[11], may save operative time and provides the opportunity to detect incidentalomas or occult recurrence[12]. Given these attributes and the diagnostic accuracy of CTA perforator location, we are planning to incorporate perforator mapping by axial imaging into standard practice.

McInerney et al[2] questioned the validity of the risk ratio quoted in our meta-analysis[13] and in the updated meta-analysis by Schaverien and Butler[1], both of which show that bilateral DIEP flap breast reconstruction carries a three-fold increased risk of total flap failure, compared to unilateral reconstruction. McInerney et al[2] suggested that by including a single study by their senior author[14], the pooled risk was disproportionately affected by their single flap failure. This allegation is incorrect for many reasons and we are pleased to take the opportunity to expand upon some of the mechanics 'under-the-hood' which generate meta-statistics and their interpretation. All systematic reviews and meta-analyses should be preceded by a robust protocol and development phase that undergoes peer review before commencement. The report of a systematic review should contain explicit details of methodology, a results section accompanied by summaries of study characteristics, risk of bias assessments and quality grading according to preordained criteria. This process is fundamental to the creation and interpretation of systematic review and meta-analysis according to the PRISMA statement[15], Cochrane Collaboration[16] and GRADE approach[17]. Hastening to the inference (comfortable in the knowledge that our group has produced the aforementioned material elsewhere[13]), we are confident in the pooled risks for many reasons. Firstly, the confidence intervals of all individual studies contain the mean for every study, i.e. there are no outliers disproportionately affecting the estimate. This is important because we also observe that the direction of effect is constantly in favour of unilateral reconstruction (i.e. there are no deviant studies). The measure of statistical heterogeneity (I^2) simply confirms these observations, showing that all data are in agreement – bilateral reconstruction appears to be more risky. Now,

consider how much weight is assigned to each study in the meta-analysis and how this influences the confidence in the estimate. The weight assigned to a study depends on whether a fixed or random effects approach is chosen; the latter incorporates the study level variation (Tau) into the estimate as well as between study variations. Both we[13] and Schaverien and Butler[1] assumed sufficient clinical heterogeneity to warrant random effects models which typically provide more conservative estimates adjusting for both within and between study variations. Meta-analysis of dichotomous outcomes by Mantel-Haenszel methods using the DerSimonian and Laird random effects weighting calculates weights (basically) from the sample size and number of positive events (in this case, flap failures), adjusted for the variance. The weighting given to Hofer et al was 6.1% in our original review[13] and 2.7% in the updated version[1]. This is not a "considerable contribution" as suggested and actually, Hofer et al[14] provided the lowest contribution of all included studies. Finally, to prove that McInerney et al[2] are mistaken in their assertion, we provide a sensitivity meta-analysis (Figure 1) with Hofer et al[14] removed which shows that bilateral DIEP flap breast reconstruction still carries a three-fold increased risk of total flap failure (95% CI 1.8, 5.1), compared to unilateral reconstruction. Although this contravenes best review methodology, we hope that this reassures readers of the confidence that we have in our analyses and that our explanation has helped to clarify some of the steps involved in reaching this conclusion.

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