Skeletonized internal thoracic artery harvest improves prognosis in high-risk population after coronary artery bypass surgery for good quality grafts

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CRD summary
The review concluded that, compared to pedicled harvesting, skeletonised internal thoracic artery harvesting provided superior quality grafts, less trauma, fewer complications and, in high risk patients, reduced mortality and adverse cardiac events. Given potential bias in the review process, unclear quality of the included studies and heterogeneity, these short-term conclusions should be treated with caution.

Authors' objectives
To determine the effectiveness and safety of different internal thoracic artery (ITA) harvesting techniques.

Searching
MEDLINE (from 1966), EMBASE (from 1974) and The Cochrane Library were searched up to July 2010 for relevant studies. Search terms were reported. There were no language restrictions. Abstract books and poster displays from major scientific meetings and references lists of retrieved studies and reviews were searched. Attempts were made to correspond with the authors of relevant trials.

Study selection
Clinical controlled trials that assessed ITA harvesting with different techniques (skeletonised versus pedicled harvesting) in coronary artery bypass grafting were eligible for the review. Eligible outcomes were mortality, postoperative cardiac-related events, blood loss, quality of graft harvested, sequelae involved with sternum and chest wall and respiratory function. Studies were excluded if they assessed the efficacy and safety of different techniques in mobilising the ITA in the same way.

Participants in the included studies ranged from 52 to 75 years of age and zero to 53% were women. Prevalence of diabetes mellitus ranged from zero to 100%. Studies were published between 1996 and 2010.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
Studies were assessed for quality using the Jadad scale and 2001 Cochrane Handbook criteria; these included randomisation procedure, use of intention-to-treat analysis, report of dropout rates, allocation concealment and extent to which valid outcomes were described. It appeared that only randomised controlled trials (RCTs) were appraised for quality. These studies were categorised for overall quality (high, moderate and low) using Cochrane criteria.

The authors did not state how many reviewers assessed the studies for quality.

Data extraction
Data were extracted on outcomes. Relative risks (RRs) were calculated for binary data and mean differences were calculated for continuous data, each with 95% confidence intervals (CIs). Data were extracted at the longest follow-up time. Where two studies from the same institution reported the same outcomes at similar follow-up times, the better quality or most informative publication was used for data extraction.

Two reviewers independently extracted data. Disagreements were resolved by re-review or consensus.

Methods of synthesis
Studies were pooled, where possible, and summary effect measures (RRs and weighted or standardised mean differences (WMDs, SMDs)) and their 95% confidence intervals were calculated using a fixed-effect model where no heterogeneity was evident; otherwise a random-effects model was used. Heterogeneity was assessed with $X^2$ and $I^2$. Publication bias was assessed by Begg's analysis of the funnel plot.
Results of the review
Twenty-two studies (5,184 participants, range 15 to 1,818) were included in the review. There were nine prospective randomised controlled trials (RCTs), four prospective non random controlled trials and nine case control studies. The authors stated that the RCTs had a composite score that indicated moderate quality, but few had adequate allocation concealment, blinding and specification of randomisation method. Follow-up ranged from the time of operation to 3.4 years; most studies had assessments either in hospital or within 30 days after surgery.

Quality of grafts: Compared to pedicled harvesting, skeletonised harvesting was associated with a significant increase in length of graft (WMD 1.99cm, 95% CI 0.87 to 3.11; five studies, significant heterogeneity), significantly larger calibre (WMD 0.13mm, 95% CI 0.07 to 0.20; three studies, no significant heterogeneity) and significantly higher flow capacity (WMD 23.24mL/min, 95% CI 7.52 to 38.96; seven studies, significant heterogeneity).

Postoperative sternal complications: Compared to pedicled harvesting, skeletonised harvesting was associated with significantly increased sternal perfusion (SMD 2.89, 95% CI 2.15 to 3.63; three studies, no significant heterogeneity) and significantly reduced internal wound infections (RR 0.68, 95% CI 0.50 to 0.93; sixteen studies, significant heterogeneity).

Pain: Compared to pedicled harvesting, skeletonised harvesting was associated with significantly lower present pain intensity scores on a visual analogue scale (SMD -1.05, 95% CI -2.02 to -0.09; three studies, significant heterogeneity). There was no evidence of a significant difference in chest wall pain or major dysaesthesia between groups (five studies).

Clinical outcomes: Compared to pedicled harvesting, skeletonised harvesting was associated with significantly reduced overall mortality (RR 0.70, 95% CI 0.50 to 0.98; 10 studies, no significant heterogeneity) and in a subgroup of participants at high risk (>70 years old or concomitant diabetes) (RR 0.57, 95% CI 0.33 to 0.98; five studies, no significant heterogeneity). There was a significantly reduced overall mortality within 30 days in participants with skeletonised harvesting compared to pedicled harvesting (RR 0.4, 95% CI 0.02 to 0.82; six studies, no significant heterogeneity). There was no evidence of a significant difference between groups in overall mortality in low risk patients (five studies) or in mortality over six months (four studies). In high-risk participants, compared to pedicled harvesting, skeletonised harvesting was associated with a significantly reduced risk of cardiac-related events (RR 0.38, 95% CI 0.14 to 0.99; four studies, no significant heterogeneity, but I²=53.1%). There was no evidence of significant differences in cardiac-related events in the overall population of participants (eight studies) or in participants at low risk (four studies).

Operative outcomes: Compared to pedicled harvesting, skeletonised harvesting was associated with significantly reduced blood loss (SMD -0.22, 95% CI -0.31 to -0.13; 10 studies, heterogeneity not reported), but significantly increased harvesting time (SMD 0.71, 95% CI 0.19 to 1.24; heterogeneity and number of studies not reported). There was no evidence of a difference in failure of the ITA (two studies) between groups.

Respiratory function: Compared with pedicled harvesting, skeletonised harvesting was associated with significantly less ventilation duration (SMD -0.15, 95% CI -0.27 to -0.04; six studies, no significant heterogeneity but I²=54.5%). There was no evidence of a difference in the incidence of acute respiratory failure between groups (three studies).

There was no evidence of publication bias from the funnel plot on sternal infection rates.

Authors' conclusions
When compared to pedicled harvesting, skeletonised internal thoracic artery harvesting provided superior quality grafts with additional advantages of less trauma, fewer postoperative complications and, in high-risk patients, reduced mortality and adverse cardiac events.

CRD commentary
The review addressed a clear research question. Broad inclusion criteria appeared appropriate. Several relevant sources were used to identify published and unpublished studies without language restrictions, so publication and language bias were unlikely. A discrepancy was noted in the reporting of the total number of included studies (22 versus 23 studies). Appropriate methods were used to extract data from the included studies. The authors did not state how many reviewers selected studies and assessed studies for quality, so reviewer error and bias from these processes could not be ruled out.
Various study designs were eligible and it appeared as though only the randomised controlled trials were assessed for quality. The authors stated that these studies were of moderate quality but only a small proportion had allocation concealment and blinding and only one study specified the randomisation method. Thus, the quality of all included studies was unclear and selection bias resulting from non-random allocation to groups could not be excluded.

The authors combined the results of RCTs and non randomised studies in meta-analyses. Given that the results of non-randomised studies are subject to a number of biases, pooling data in this way may not have been appropriate. Assessment of heterogeneity and publication bias were appropriate. Significant heterogeneity was identified in some analyses and attempts were made to explain how this might have occurred, but no sensitivity analyses were undertaken to assess the stability of the results. Variable follow-up and very few studies with greater than one year follow-up made long-term results unclear.

The conclusions should be considered short-term and should be treated with caution, due to potential bias in the review process, unclear quality of the included studies and heterogeneity between studies.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further research with an adequately designed prospective study and long-term follow-up were needed to confirm the review results.

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