Extended lymphadenectomy versus conventional surgery for rectal cancer: a meta-analysis


CRD summary
The authors concluded that extended compared with non-extended lymphadenectomy for rectal cancer did not confer any significant cancer-specific benefit, but was associated with increased urinary dysfunction. The review was generally well conducted and the authors’ conclusions appear to be appropriately cautious, given their reliance upon mainly non-randomised studies.

Authors’ objectives
To assess the value of extended compared with non-extended lymphadenectomy in the operative management of rectal cancer.

Searching
MEDLINE, EMBASE, and the Cochrane Library were searched for articles from 1965 to June 2009 and Google Scholar and Ovid were used to search the Internet. Search terms were reported and the related-articles feature was used to broaden the search. No language restrictions were imposed and the reference lists of relevant articles were consulted.

Study selection
Studies comparing extended with non-extended lymphadenectomy in patients undergoing surgery for rectal cancer were eligible for inclusion. Studies had to provide an accurate description of the surgical procedure. The review assessed five-year survival, five-year disease-free survival, local and distant recurrence, perioperative mortality and morbidity, length of operation, intra-operative blood loss, urinary dysfunction, sexual dysfunction, and defaecatory dysfunction. Most of the included studies were retrospective and most of the included patients had Dukes’ stage A to C rectal cancer. Some patients received radiotherapy, but this was not consistent across studies. The position of the tumour was mostly low or mid rectum.

The authors did not state how many authors performed the selection process.

Assessment of study quality
The quality of the observation studies was assessed using the Newcastle-Ottawa scale, which evaluated the method of patient selection, comparability of study groups, and number of outcomes reported, to give a score out of nine.

Two authors performed this validity assessment and, where required, consensus was reached by discussion.

Data extraction
The data on survival, cancer recurrence rates, perioperative outcomes, and functional outcomes were extracted and used to calculate odds ratios, weighted mean differences, or hazard ratios.

Two authors independently performed the data extraction and, where required, consensus was reached by discussion.

Methods of synthesis
The pooled odds ratios, hazard ratios, and weighted mean differences, together with 95% confidence intervals, were calculated using a fixed-effect meta-analysis, were possible, or if heterogeneity was present, a random-effects meta-analysis was used. Heterogeneity was assessed using the $I^2$ and $\chi^2$ statistics. Publication bias was assessed in funnel plots and the Begg test. Sensitivity analysis was undertaken by excluding older studies or poor-quality studies, matching for tumour stage and position, examining Dukes’ stage B and C only, and matching on radiotherapy use.

Results of the review
Twenty studies (n=5,502 patients) were included: one randomised controlled trial (n=45); three prospective non-
randomised studies (n=1,673); and 16 retrospective studies (n=3,784). Three studies had an overlapping population, but were included as they investigated different outcomes. The number of patients in each study ranged from 27 to 1,272. The quality of the studies was generally good; most of them scored at least seven out of nine. The main area where study quality was poor was matching between patient groups.

Survival: There was no significant benefit of extended compared with non-extended lymphadenectomy in five-year survival (six studies) and five-year disease-free survival (four studies). Heterogeneity was high (I^2 over 70%) in both analyses and a random-effects model was used. No publication bias was detected.

Cancer recurrence rates: There was no significant benefit of extended compared with non-extended lymphadenectomy in local recurrence (16 studies), distant recurrence (eight studies), and total recurrence rates (seven studies). Heterogeneity was low to moderate (I^2 0% to 54%) in all analyses and a fixed-effect model was used. No publication bias was detected for local recurrence, but it was detected for total recurrence (Begg test p=0.04).

Peri-operative outcomes: There was no significant difference between extended and non-extended lymphadenectomy in perioperative mortality (seven studies) and morbidity (four studies). Extended lymphadenectomy was associated with significantly longer operating times (OR 76.7 minutes, 95% CI 18.8 to 134.7; four studies) and significantly greater perioperative blood loss (WMD 536.5ml, 95% CI 353.7 to 719.2; three studies) compared with non-extended lymphadenectomy. Heterogeneity was low to high (I^2 0% to 94%) in all analyses and a random-effects model was used.

Functional outcomes: There was no difference between extended and non-extended lymphadenectomy for urinary incontinence (three studies), urinary retention (three studies), and defaecatory dysfunction (two studies). There was a significant increase in urinary dysfunction (three studies) in the extended group compared with the non-extended group (OR 3.73, 95% CI 1.7 to 8.2). Two out of three studies reported increased sexual dysfunction in the extended lymphadenectomy groups. Heterogeneity was low to moderate (I^2 0% to 50%) in all analyses and a fixed-effect model was used.

The results of the sensitivity analysis were also reported.

Authors' conclusions
Extended lymphadenectomy did not confer significant cancer-specific benefit for patients with rectal cancer, but was associated with longer operating times, greater intra-operative blood loss, increased urinary dysfunction, and possibly sexual dysfunction.

CRD commentary
The inclusion criteria were clearly defined and several relevant sources were searched. Publication bias was assessed and was not found to be a problem in most of the analyses. It was unclear how many reviewers selected studies, but validity assessment and data extraction were performed by two people, which reduced the chances of error and bias. A tool validated specifically for non-randomised studies was used to assess the quality of the included studies, which was appropriate for most of them. They were combined by meta-analysis, using a random-effects model where heterogeneity was present, and subgroups were explored in a sensitivity analysis.

The review was generally well conducted and the authors’ conclusions appear to be appropriately cautious given their reliance upon mainly non-randomised studies.

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

Research: The authors stated that a randomised trial comparing extended lymphadenectomy with neoadjuvant chemoradiotherapy might be desirable, but was unlikely to be ethical or technically feasible.

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