Systematic review of sentinel lymph node mapping procedure in colorectal cancer

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CRD summary
The authors concluded that overall sensitivity for sentinel node mapping was 70% in patients with colorectal cancer. The increased accuracy rate found in patients with early-stage colon cancer could lead to refined staging. Given the diversity of included study characteristics, the authors advised caution in the interpretation of review findings, and this seems justified.

Authors' objectives
To assess the performance of sentinel lymph node mapping in patients with colorectal cancer.

Searching
PubMed, EMBASE and The Cochrane Library were searched up to July 2011 for studies published in English. Search terms were reported. The reference lists of included studies, reviews and editorials were scanned for further studies. Meeting abstracts were not reviewed.

Study selection
Eligible for inclusion were studies that evaluated lymphatic mapping, using the sentinel lymph node procedure, in patients with colorectal cancer. To be included, studies had to report sufficient data on the performance of the sentinel lymph node procedure. Studies that included the use of indocyanine green were excluded.

Most included studies contained patients with both colon and rectal cancer, and most used the in vivo technique to identify sentinel nodes. Tracer methods included blue dyes or radiolabeled tracers. Sentinel node analysis was carried out with haematoxylin and eosin staining, immunohistochemistry and real-time polymerase chain reaction. The mean number of harvested lymph nodes was 16.7 (range 7.5 to 30); the average number of identified sentinel nodes was 2.8 (range 1 to 7.1). In general, there was wide variation in the included population, sentinel node procedures and pathological analyses.

Two independent reviewers selected the studies. Discrepancies were resolved by discussion.

Assessment of study quality
Study quality was assessed in terms of patient selection; sufficient description of sentinel node criteria and detection procedures; valid reference test (histology); more than 20 sentinel node procedures per year; outcome parameters reduced to stage or location of disease; and use of additional immunohistochemistry or polymerase chain reaction technique with subclassification of upstaging.

It appears that two reviewers carried out the quality assessment. Where discrepancies occurred, the original article was re-analysed.

Data extraction
Data were extracted to enable the construction of 2x2 contingency tables, ultimately to present sensitivity and the upstaging rate. The upstaging rate (the proportion of sentinel nodes classified as not containing cancer on the index test, and subsequently classified as containing cancer by histology) with 95% confidence intervals were also extracted.

Data were extracted independently by two reviewers. Where discrepancies occurred, the original article was re-analysed.

Methods of synthesis
Where possible, a random-effects model with an exact likelihood approach was used to calculate summary sentinel node accuracy data. Correlations between sensitivity and the number and method of sentinel node assessment were investigated with linear regression. Logistic regression was used in subgroup analyses to explore the relative influences of vivo and ex vivo detection; use of blue dye or colloid; less than four, or four or more sentinel nodes; colon or rectal...
carcinoma; early or advanced carcinoma; and high or low validity studies. Cut-off values for continuous variables were selected in advance according to clinical relevance or reporting convention.

**Results of the review**

Fifty-seven articles (3,934 patients; 3,944 sentinel node procedures) were included in the review. Sample sizes ranged from 8 to 500, with 10 studies containing more than 100 patients. All studies were prospective, with a valid reference test (histology), and clear sentinel node criteria and detection protocols. Twenty articles met at least three of the five remaining quality criteria.

The identification rate using the sentinel node procedure was 92.4% (94.6% in studies with more than 100 patients) and this was more successful in studies using *ex vivo* procedures (93.7% versus 89.2% in those using *in vivo* procedures; 18 studies). Pooled sensitivity was 69.6% (95% CI 64.7 to 74.6; 57 studies; 3,934 patients); the false negative rate was 30.4% (95% CI 25.5 to 35.3); and the overall pooled accuracy of the sentinel node procedure was 88.2% (95% CI 86 to 90.3).

Sensitivity was significantly higher: in patients when four or more sentinel nodes were identified (10 studies); in those with colon carcinomas (31 studies); and in those patients with early stage disease (six studies). Method of sentinel node detection (*in vivo/ex vivo*) when colloid was added to blue dye, type of tracer used, and presence of high quality studies did not show any statistically significant influence on the findings.

The mean upstaging rate was 18.9% ±11.8 (range 0 to 50%; 46 studies). Further results from subgroups of studies were also reported.

**Authors’ conclusions**

The overall sensitivity for sentinel node mapping was 70% in patients with colorectal cancer. The increased accuracy rate found in patients with early-stage colon cancer could lead to refined staging. Given the diversity amongst the included studies, the authors advised caution when interpreting the review findings.

**CRD commentary**

The review question and inclusion criteria were clearly reported. Credible data sources were searched, but the restricted search meant that language and publication biases could not be ruled out (acknowledged by the authors), and this suggested that relevant studies may have been overlooked. The review process appeared to be conducted with sufficient attempts to minimise error and bias.

Appropriate quality assessment criteria were used, although limited by the lack of assessment of test interpreters., and the results of this were summarised adequately (although full results were not presented). There was no reported assessment of statistical heterogeneity, and clinical variation was evident. However, potential sources of heterogeneity were explored, and the chosen method of synthesis seemed appropriate.

Given some potential threats to the reliability of findings from this review, the authors' cautious conclusion seems justified.

**Implications of the review for practice and research**

**Practice:** The authors stated that the *ex vivo* sentinel node procedure could be recommended in patients with colon cancer in addition to conventional resection, on the basis that *ex vivo* sentinel node mapping was an easy technique.

**Research:** The authors did not state any implications for research.

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**Bibliographic details**


**PubMedID**
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.