Sentinel node detection in patients with thyroid carcinoma: a meta-analysis

Raijmakers P G, Paul M A, Lips P

CRD summary
There were significant weaknesses in the review methodology, reporting and data analysis. Given these limitations and the paucity of data, the authors’ conclusion that sentinel lymph node biopsy using $^{99m}$Tc colloid radiotracers demonstrated a higher detection rate than techniques using blue dyes in patients with thyroid carcinoma, should be interpreted with considerable caution.

Authors' objectives
To assess and compare the diagnostic performance of the injection of a radiotracer or a blue dye for the identification of sentinel lymph nodes in patients with thyroid cancer.

Searching
MEDLINE was searched to December 2007 for published English language studies. Search terms were reported. The bibliographies of identified articles were scanned for additional studies.

Study selection
Studies of ten or more participants with suspected thyroid carcinoma, in whom a radioactive tracer and/or a blue dye were used to identify sentinel lymph nodes, were eligible for inclusion. Included studies were required to use histopathological evaluation of surgically resected samples as the reference standard, and to report sufficient data for the calculation of sensitivity or sentinel lymph node detection rate.

The mean age of participants, where reported, ranged from 37 to 53 years. Study populations were majority female (71% to 91%, where reported). The proportion of malignant thyroid nodules ranged from 33 to 100% (100% in half of the included studies). Included studies assessed the accuracy of isosulfan blue dye, patent blue dye, methylene blue dye and $^{99m}$Tc colloid radiotracer for the detection of sentinel lymph nodes.

Assessment of study quality
The authors did not report that they assessed the validity of included studies.

Data extraction
Tracer type, volume and dose used were extracted, and, where possible, the sensitivity with 95% confidence intervals for the detection of sentinel lymph nodes and the sentinel lymph node detection rate were calculated for each study.

The authors did not state how data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Between study heterogeneity was assessed using the $\chi^2$ test. Pooled estimates of sensitivity and sentinel lymph node detection rate, with 95% confidence intervals, were calculated using a random-effects model where there was evidence of heterogeneity; a fixed-effect model was used in the absence of evidence of heterogeneity. Sub-group analyses were conducted for different sentinel lymph node detection techniques and a Z-test was used to assess differences between sub-group.

Results of the review
Fourteen studies, with a total of 457 participants, were included in the review. The histopathological technique used to confirm diagnosis varied considerably between studies.

Four studies (n=128 participants) assessed a $^{99m}$Tc colloid technique and ten studies (n=329 participants) used a blue dye technique. Sentinel lymph node detection rates were significantly higher among studies of $^{99m}$Tc colloid
radiotracer technique (0.96, 95% confidence interval (CI): 0.91 to 0.99) than studies of blue dye technique (0.83, 95% CI: 0.79 to 0.87, p<0.05).

The pooled sensitivity of blue dye techniques, based on six studies, was 0.87 (95% CI: 0.79 to 0.93).

One study of $^{99m}$Tc colloid technique reported a false negative rate of 11.3%.

**Authors' conclusions**

In patients with suspected thyroid carcinoma, sentinel lymph node biopsy using $^{99m}$Tc colloid radiotracers demonstrated a higher detection rate than techniques using blue dyes.

**CRD commentary**

The review addressed a clearly stated question, defined by appropriate inclusion criteria. The search strategy was limited to one bibliographic database and a review of the references of included studies, making the analysis vulnerable to the omission of relevant data. This problem was compounded by restriction to published English language studies, leaving open the possibility of both language and publication biases. No assessment of the methodological quality of included studies was reported. No methods to minimise error and/or bias were reported for the review process. Therefore, the vulnerability of the review to error and/or bias introduced by poor quality studies or in the review process cannot be assessed.

The results of the heterogeneity assessment, for studies included in the meta-analyses, were not reported. Simple pooling of sensitivity across heterogeneous studies is not generally recommended and the pooled estimates presented may be of limited value. The authors did not define sentinel lymph node detection rate the main result reported. As highlighted by the authors, the absence of data on the false negative rates of these tests was a significant factor hindering interpretation of their clinical value.

Given the limitations described, the authors' conclusion that sentinel lymph node biopsy using $^{99m}$Tc colloid tracers demonstrated a higher detection rate than techniques using blue dyes, in patients with thyroid carcinoma, should be interpreted with considerable caution.

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

Practice: The authors stated that sentinel lymph node detection is possible in patients with thyroid cancer, and the use of $^{99m}$Tc colloid techniques may be associated with higher detection rates.

Research: The authors stated that further clinical studies are required to assess the advantages of sentinel lymph node detection techniques and to determine the optimum technique (particularly with regard to false negative rates). The clinical impact of sentinel lymph node detection, on prognosis and treatment, requires further assessment.

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