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Literature search parameters marginally improved the pooled estimate accuracy for ultrasound in detecting deep venous thrombosis

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Abstract

Background and Objectives—Data collection remains of utmost importance to avoid publication bias in systematic reviews. Our objectives were to compare search strategies with and without methodological terms in Medline, to find out how other databases complement Medline, and how these strategies affect the pooled estimates of the accuracy.

Study Design and Setting—A study was eligible if it prospectively compared ultrasound to venography for the diagnosis of deep venous thrombosis in the lower limbs. All relevant articles found with all databases, searched from 1966 through 2003, constitute the reference standard. Sensitivity was defined as the proportion of relevant studies found by Medline searches divided by the total number of articles in the reference standard.

Results—Of a total of 1,473 citations, 237 abstracts were included. The sensitivity of strategies without methodological terms was higher (96%) than those with (95%, 76%, and 95%). Searches of multiple databases found seven articles not found with Medline. Searches of congress proceedings (International Society of Thrombosis and Haemostasis) found three abstracts not published in full. The diagnostic odds ratio OR was 5.66 (95% confidence interval CI = 4.84-6.48) when multiple databases were searched and 5.57 (95% CI = 3.49-7.65) when only English-language articles in Medline were identified.

Conclusion—Medline searches combining free text and MeSH terms were more sensitive. Single Medline search affects only marginally the pooled estimate accuracy.

Keywords

Sensitivity; Specificity; Literature search; Diagnostic studies; Venous thrombosis

1. Introduction

The lack of a specific publication type and limited information on the rigor of indexing subheadings prove challenging for data collection in systematic review of diagnostic studies. There is not yet any designated Medline publication type for the evaluation of diagnostic

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studies. Randomized clinical trials have indexing terms available, but even then the sensitivity of Medline searches for randomized clinical trials is very low [1].

Search strategies have been developed to identify relevant diagnostic studies in Medline. Haynes et al. [2] and Devillé et al. [3] developed two general strategies in Medline not related to a specific disease. Van der Weijden et al. [4] proposed strategies to find sound diagnostic studies evaluating erythrocyte sedimentation rate and dipstick. They suggest that combinations of free text and MeSH (Medline Subject Heading) terms are more sensitive in the scope of a specific disease. McKibbin et al. [5] suggest some useful MeSH and text terms to harness Medline for diagnostic problems, and Haynes and Wilczynski [6] developed optimal search strategies for retrieving scientifically strong studies. Notably, Vincent et al. [7] have proposed a strategy with 98.8% sensitivity in retrieving diagnostic studies for deep venous thrombosis (DVT). Their results show that most of the systematic reviews on diagnosing a DVT have omitted a number of high quality articles.

Few authors have shown that searching Embase and Pascal Biomed could complement Medline in the field of randomized clinical trials [8-13]. Topfer [9] has compared literature searches for devices in Embase and Medline, however, all devices included in this study had therapeutic uses. We are not aware of any comparative literature search on multiple databases for diagnostic studies and it is not clear whether such an effort is necessary. Moreover, we lack evidence on whether search strategies and the number of databases searched affects the pooled estimates in systematic reviews of diagnostic tests.

Our study had three objectives:

1. To evaluate the sensitivity of search strategies with MeSH and free text terms referring to specific diseases, symptoms or tests, and those combining the latter with methodological terms in Medline;
2. To compare single Medline with multiple databases searches; and
3. To measure in which way different search strategies, number of databases searched, published short communications and the language of published articles affect the pooled estimates of the accuracy.

To achieve these objectives we comprehensively reviewed evaluations of ultrasonography for the diagnosis of DVT in asymptomatic patients.

2. Materials and methods

We used the PubMed interface to search Medline from 1966 through 2002. Science Citation Index, Embase, and Pascal Biomed were searched through 2002. Published short communications and abstracts were identified by searching Science Citation Index from 1979 through 2000 (the last date available) and by inspecting the proceedings of the 13th through 18th congresses of the International Society of Thrombosis and Haemostasis (ISTH), published 1993 through 2001.

We identified all relevant articles using search strategies with terms (MeSH and free text for Medline) related to venous thrombosis, venography, and ultrasonography in all databases. These articles constitute the reference standard.

Medline was then searched with strategies that combined specific disease and test terms with methodological terms (sensitivity, specificity, and so forth). The sensitivity of these strategies was defined as the proportion of relevant studies found, divided by the total number of articles in the reference standard.

The number of overlap articles in Medline and other databases allowed us to compare single vs. multiple databases search.

Two authors (B.K. and S.S.) independently reviewed all articles abstracts and included studies comparing ultrasonography to venography. A study was eligible if it prospectively compared ultrasound to venography for the diagnosis of DVT in the lower limbs of patients. A study was excluded if venography was not the reference standard or if lower limbs were not evaluated. Eligibility was independently assessed by two authors (B.K. and S.S.) from the abstracts when possible, or otherwise from the complete article. Differences were resolved by consensus.

Unweighted least squares linear regression was used to estimate a summary diagnostic odds ratio (OR) in asymptomatic patients [14,15]. We also summarized diagnostic ORs separately in level 1 studies (which included consecutive patients, blindly evaluated the two techniques, and verified the diagnosis with venography in all patients) and in level 2 studies (in which one or more of the level 1 characteristics were missing or not clearly present).

Moreover, we used the capture-recapture technique to evaluate the overlap between Medline and hand searching for the year 1998 and to estimate the number of potentially missed articles [16]. To perform the capture-recapture technique, 57 of 96 journals that had appeared at least once in the first Medline search and were available at our local library (University of California, Los Angeles) were selected for hand searching (B.K., S.S.). The Chapman's method was used to estimate the total population size as $N = \{[(M + 1)(n + 1)] / (m + 1)\} - 1$, where M is the number of publication identified by Medline, n is the number identified by hand searching, and m is the number identified by both sources.

3. Results

Of a total of 1,473 articles, 237 compared ultrasound to venography, 180 examined symptomatic, and 53 examined asymptomatic patients.

Table 1 shows the sensitivity of different literature search strategies used to search Medline. Sensitivities of strategies with methodological terms included were lower (94.5%, 75.5%, and 94.9%) than those without (95.8%). Science Citation Index, Pascal Biomed, Embase, and proceedings of ISTH congresses included 10 articles not found in Medline searches. From these, six studies [17-22] were in symptomatic patients and four studies (one article and three abstracts not published in full) were in asymptomatic patients [23-26]. Table 2 shows the overlaps between databases.

In asymptomatic patients, 50 articles and 3 abstracts not published in full were identified in the reference standard search; 42 articles and 3 abstracts were included for calculating the summary diagnostic OR. The eight remaining articles were excluded because four were considered multiple publications [27-30], two examined only superficial veins in preoperative patients [31,32], one was retrospective [33], and in one study it was not possible to distinguish data for symptomatic vs. asymptomatic patients [34]. Of the 45 studies, 42 were published in English, 2 in French [35,36], and 1 in Italian [37]. Detailed results of this meta-analysis are published elsewhere [38]. One article was missed when only the Medline database was searched, and one level 1 and three level 2 studies were missed when the Medline search was limited to English-language articles. Three abstracts were not published in full, and so could not be retrieved with Medline. Figure 1 shows the summary diagnostic OR when searches were limited to Medline or to English-language articles in Medline. In level 1 studies (i.e., with blind evaluation of the two techniques, absence of verification bias, and consecutive enrollment of patients), the diagnostic OR was 5.66 (95% CI = 4.84-6.48) when multiple databases were searched with no limitation to the language of publication and 5.57 (95% CI = 3.49-7.65) when only English-language articles in Medline were identified.

Out of a total of 16 articles, 14 were found with hand searching and 12 with Medline for the year 1998. The capture-recapture technique estimated that one article (95% confidence interval = 0-5) was probably left unidentified either by hand searching or by Medline for the year 1998.

4. Conclusion

To minimize publication bias, it is essential to identify all relevant studies for a systematic review, including published and unpublished studies. Because no regulatory requirement is necessary for evaluation of diagnostic tests, unpublished studies are likely to be more frequent and more problematic to retrieve than for randomized trials. Publication bias could also arise from literature search [39]. Consequently, sensitivities are likely to be overestimated, because the reference standard does not include all relevant published and unpublished studies. Searching all databases, references of selected studies, hand searching, and contacting experts are the techniques used for an exhaustive search [40,41]. With this approach, we found >1,000 articles to review. When our search was limited to Medline, however, seven articles and three abstracts not published in full were missed. Of these articles, three were indexed but not found with our strategy and four were not indexed in Medline (Table 2). Therefore, our results confirm that a comprehensive search of Medline is a difficult task and that strategies combining free text and MeSH terms are more sensitive in the scope of a specific disease for finding evaluations of diagnostic tests. The sensitivity of this strategy for ultrasonography in the diagnosis of DVT (96%) is close to the sensitivity estimated by van der Weijden [4] for dipstick (97%) for the diagnosis of urinary tract infection in general practice patients.

A few studies have shown that conclusions drawn by meta-analyses can differ when the search is limited to English-language articles [42,43]. It is not clear, however, whether a search limited to Medline might bias estimates of treatment benefit [13], provided the rest of the search is comprehensive. From our results in asymptomatic patients, the diagnostic OR is very little or marginally influenced by the number of databases searched. Nevertheless, finding four non-English articles (one level 1 article, three level 2 articles) and three abstracts (two level 1 and one level 2) not published in full shows that a comprehensive search might be necessary to minimize publication bias and to obtain a more comprehensive review.

We used the summary receiver operating characteristic method to summarize the accuracy of selected studies, and our results depend on the validity and limitations of this method. Future research should define the suitability of new methods for summarizing results of evaluation of diagnostic tests [44].

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Fig. 1. Search strategies for identifying relevant diagnostic studies for systematic reviews and their influence on summary diagnostic odds ratio.

Table 1
Sensitivity of Medline search strategies compared to the reference standard

Search strategies	Total articles found, no.	Relevant articles, no. (%)	Sensitivity, %
Reference standard: Medline A + Embase + Science Citation Index + Pascal Biomed	1,473	237 (16)	
Medline A	926	227 (24.5)	95.8
Medline A + Haynes et al. [2]	865	224 (25.9)	94.5
Medline A + Devillé et al. [3]	384	179 (46.6)	75.5
Medline A + McKibbon et al. [5]	895	225 (25.1)	94.9

For all four databases, search terms were related to venous thrombosis, venography, and ultrasonography; Medline searches included both MeSH and free text.

Table 2

Number of relevant articles retrieved by Medline, compared with other databases

Database	Found by Medline, no.	Not found by Medline, no.		
		Indexed	Not indexed	Total, no.
Embase	60	2	2	64
Science Citation Index	100	1	2	103
Pascal Biomed	31	0	2	33