How useful is thrombocytosis in predicting an underlying cancer in primary care?: systematic review protocol

Bailey SER[1], Ukoumunne OC[2], Shephard EA[1], Hamilton W[1].

1 Primary Care Diagnostics, University of Exeter Medical School, College House, St Luke's Campus, University of Exeter, Exeter, Devon, EX1 2LU.

2 PenCLAHRC, University of Exeter Medical School, South Cloisters, St Luke's Campus, University of Exeter, Exeter, Devon, EX1 2LU.

Corresponding author: Bailey SER s.e.r.bailey@exeter.ac.uk

Rationale and objective

Early diagnosis of cancer is imperative to reduce the cancer burden in the UK and improve cancer survival. Identifying early markers of cancer can help general practitioners to direct patients at the greatest risk of cancer to appropriate investigative services. A raised platelet count, or thrombocytosis, has been linked to malignancy[1,2] and identified as a marker of poor prognosis in secondary care[3-9], but there is little evidence around the importance of this marker in a primary care setting, within a diagnostic context. This review aims to identify and explore the body of evidence concerning the association between thrombocytosis and cancer in primary care. This protocol was produced using guidance from the PRISMA-P statement.[10]

Research questions

- Are adults aged over 40 with thrombocytosis at greater risk of cancer than those with normal platelet counts?
- Which cancer sites have been found to be associated with thrombocytosis in primary care, and which are not?

Inclusion criteria

- Any type of cancer or cancer site
- Studies that have investigated the association between cancer and platelets (using platelets as a diagnostic tool, not prognostic factor).
- Studies based in primary care.
- Includes adults $\geq$40y
- English language
- Any observational, cohort, case-control study or literature or systematic review (due to the nature of the research question, RCTs were excluded)
- The last 30 years

Exclusion criteria:

- Studies that have investigated thrombocytosis or platelet count as a prognostic tool or guide to therapy.

- Case studies and RCTs
    - Case studies are excluded as this review is interested in population-level or cohort based studies that can provide evidence on a large number of patients.
    - RCTs are excluded as the independent variable in this study cannot be randomised.

Search strategy

The search strategy will comprise the following elements to identify relevant papers:

- Searching of electronic bibliographies including:
    - EMBASE (OvidSP) 1996-2014 (week29)
    - Medline (OVIDpalt)
    - Web of Science
    - The Cochrane Library

- Scrutiny of reference lists of included studies
- Contact with experts in the field

Study selection criteria and procedures

References will be uploaded to reference management software (Endnote X5). Duplicates will be checked and removed. The abstracts and titles of references retrieved by the electronic searches will be screened for relevance by SB using the pre-defined inclusion and exclusion criteria. Hits will be double screened by ES. Any differences in opinion over paper to include or exclude will be resolved by discussion.

Full text copies of potentially relevant studies that appear to meet all inclusion criteria will be obtained. The retrieved articles will be assessed for inclusion by checking each article against the pre-specified inclusion and exclusion criteria. A flow chart will be produced which will outline the study selection process, and reasons for exclusion of full text papers will be detailed.

Quality assessment and data extraction strategy

Study quality will be assessed using QUADAS-2. Data will be extracted into custom made data extraction forms by SB and WH. Data concerning the number of patients with and without cancer who had pre-diagnosis thrombocytosis will be the main extracted values.

Evidence synthesis

The evidence will be presented and synthesised as appropriate using meta-analysis if appropriate, or a narrative synthesis if meta-analysis is not appropriate.

Search strategy - Embase

Thrombocytosis OR platelet* (as a key word) OR thrombocyte OR thrombocyte count OR thrombocyte volume (MeSH terms)

AND

neoplasm OR carcinoma (mesh terms) OR cancer, carcinoma or paraneoplastic as key words

AND*

primary medical care OR primary health care OR general practice OR family medicine (mesh terms)

Search strategy – Medline

Thrombocytosis OR platelet* (as key words) OR blood platelets OR thrombocytosis OR platelet count (MeSH terms)

AND

neoplasms OR carcinoma (mesh terms) OR cancer as a key word

AND*

primary health care OR family practice OR general practice (mesh terms) OR primary care, family medicine, primary medical care as key words

Search strategy – Web of Science & Cochrane Library

Thrombocytosis OR platelet* OR thrombocyte

AND

neoplasm OR carcinoma OR cancer

AND*

primary medical care OR primary health care OR general practice OR family medicine

*the search will be run with and without this final filter in the preliminary stages to see how the filter affects the results.

 Endnote labels

1=include

2=exclude – not cancer

3=exclude – not investigating association with thrombocytosis

4=exclude – not primary care

5=exclude – not >40y

6=exclude – case study

7=exclude - RCT

Contributions

Study design: SB. Search strategy and execution: SB. Title and abstract screening: SB and EA. Data extraction: SB and WH. Data interpretation and analysis: all authors.

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