Triggers of Thyroid Cancer Diagnosis: a Systematic Review and Meta-Analysis Protocol

Research question

The proportion of incidental thyroid cancer diagnosis is high and the majority of these cancers are found through the use of imaging studies.

Searches

Based on our research question, an experienced librarian will design and conduct a search strategy in the following databases: Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, and Scopus. Databases will be searched from inception to September, 2018. The language will be restricted to English, Spanish and Portuguese. This search strategy will be discussed with evidence-based medicine experts for thoroughness. Discussions and modifications will continue until agreement is reached among the librarian, experts and authors.

Types of study to be included

We will include observational studies, including case-control, cohorts, and cross-sectional. Studies must report a palpable nodule group and at least one incidental pathways of thyroid cancer detection (incidental diagnosis by imaging, and incidental histological findings). We will exclude letters, editorials, consensus statements, guidelines and review articles.

Condition or domain being studied

The incidence of thyroid cancer has increased worldwide. In the United States, it increased from a 4.9 to 14.2 per 100,000 person-years over the last two decades, while in South Korea, thyroid cancer increased by more than seven fold, from 6.3 per 100,000 person year in 1999 to 47.5 per 100,000 population in 2009. This difference in thyroid cancer trends reflects underlying different mechanisms of thyroid cancer detection. In South Korea, 90% of the new thyroid cancers were detected by screening with neck ultrasound. In other countries, however, the mechanism of detection of thyroid cancer is unclear. Understanding the method of thyroid cancer detection has potential implications on interpreting incidence rates, the diagnosis and management of thyroid cancer. The aim of this study is to summarize the available evidence to assess the frequency of incidental thyroid cancer and examine the triggers that lead to diagnosis with comparison across multiple cohorts.

Participants/population:

Inclusion criteria:

- Patient older than 18 years old with thyroid cancer confirmed histologically.

Exclusion:

- Patients enrolled in screening program (e.g. thyroid cancer screening, lung cancer screening).
- Patients exposed to radiation like Chernobyl.
- Patients with an underlying disease (e.g. familial adenomatosis poliposis)

Intervention: Not applicable.

Comparator: Not applicable.

Outcomes:

- Frequency of thyroid cancer cases attributed to each trigger of diagnosis.

- Studies must report a palpable nodule group and at least one incidental pathways of thyroid cancer detection (incidental diagnosis by imaging, and incidental histological findings):

    - Palpable nodule (symptomatic): When a thyroid nodule harboring thyroid cancer was found because a clinician or patient noted an abnormality on physical examination possibly related to the thyroid mass, or patient presented with neck compression symptoms including dysphagia, dysphonia, and neck-pain.
    - Incidental diagnosis by imaging: When a thyroid nodule harboring thyroid cancer was found during the use of imaging test requested for reasons unrelated to a thyroid nodular disorder or symptoms (ultrasound, TC, PET).
    - Incidental histological: When thyroid cancer was found incidentally in the histological examination of the thyroid gland removed for a benign condition (e.g., goiter, Graves' disease).

Data extraction

Reviewers, working independently and in duplicate, will assess each study title and abstract for eligibility. At commencement, we will calibrate our abstract screening eligibility criteria with 20 articles until agreement and understanding among reviewers is reached. These articles will be selected by the principal investigators. If necessary, inclusion criteria will be modified for clarity. Further, reviewers working independently, and in duplicate will consider all available full text reports for eligibility. We will pilot our full-text screening phase with 10 articles until understanding and agreement is reached. Subsequently, disagreements will be harmonized between the reviewers. Agreement for full-text screening will be measured using kappa test. For this phase, studies need to meet the full eligibility criteria to be included.

Risk of bias

Study quality will be assessed by two independent reviewers based on the nine-star Newcastle Ottawa Scale for cohorts and cross-sectional studies.

Strategy for data synthesis

We will calculate the overall proportion estimates and their confidence intervals (95% CI), by using the number of people with an incidental diagnosis and the total number of people in each study. This will be determined with the Freeman-Turkey double arcsine transformation. The random-effects model will be performed with the Dersimonian and Laird method. Moreover using generalized linear mixed models, we will conduct a sensitivity analysis, since we estimated that we could encounter studies with proportions close to 0 or 1. Heterogeneity

across studies will be assessed with the I2 statistic and visually, considering that I2 < 25% reflected low inconsistency and I2 > 75% reflected high inconsistency. All statistical analyses will be performed using Stata v15.0 (StataCorp, College Station, TX).

Analysis of subgroups

Comparisons based on age, sex, and tumor size will be performed: > 45 years vs. ≤ 45 years, female vs. male, and tumor size > 10mm vs. tumor size ≤ 10mm.