INPLASY

Role of Non-invasive Heart Signals and Cancer Survival Characteristics- An Updated Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

INTRODUCTION

Review question / Objective Whether non-invasive heart signals (HRV indices) can predict the progression and survival in adult patients with solid organ cancer?

Rationale Cancer is the leading cause of morbidity and mortality globally. The recurrence and metastatic spread are two key challenges in the cancer management. Majority of research is limited to pathological, surgical, and oncological management of such patients. In the context of oncological research, the role of non-invasive heart signals such as heart rate variability (HRV) has been the newer area of interest. Its role in prognostication and overall well-being is addressed in few studies. Only two systematic reviews (Zhou et al. 2016 and Kloter et al. 2018) exploring on prognostication role of HRV on cancer progression and survival are published. These reviews are based on searches from 2-3 databases only, and incorporated studies till 2016. Majority of included studies are retrospective in nature. In addition, 2016 meta-analysis did not mention about adjusted effect sizes (effects of modifiers or confounders), thus limits the validity of findings. Authors of other systematic review (Kloter et al. 2018) did not perform the quantitative meta-analysis and lacks focused primary outcome. Therefore, this updated systematic review and meta-analysis is an attempt to fill the gap in comprehensive understanding between HRV prognostication and cancer survival characteristics.

Condition being studied In the context of oncological research, the role of non-invasive heart signals such as heart rate variability (HRV) has been the newer area of interest. This study is

conducted for adult patients with solid organ cancer.

METHODS

Search strategy Key concepts- There are three main concepts: Heart rate variability, Cancer, and Prognosis.
Search terms/keywords/subject headings related to these three concepts- Term 1, 2 and 3 will be utilized in various combinations.
Term 1- Neoplasm, Neoplasia, Cancer, Cancers, Malignant, Malignancy, Malignancies, Benign, Benign Neoplasm, Tumors,
Term 2-HRV, heart rate variability, vagal tone, Vagal activity,
Term 3- Prognosis, Progression free survival, mortality, morbidity, complications, dead, death.

Participant or population This is a systematic review and will be based on PRISMA guidelines.Population-Adult patients (18 years of age or more or either sex) with solid organ cancer.

Intervention Non-invasive heart signals monitoring (HRV-indices).

Comparator High HRV indices, if information is available in more than 50% of included articles (Low HRV indices vs. High HRV indices).

Study designs to be included All study types [RCTs, observational studies (prospective/retrospective/mixed, cross sectional etc.]will be considered.

Eligibility criteria Exclusions-1 - Non-English articles. 2 - Animal studies. 3- Duplicate reports and secondary research articles such as correspondents, letters, and post hoc analyses will be excluded. 4 - Case series, case reports. 5 - Articles investigating autonomic dysfunction not associated with defined outcomes by our study. 6 - Abstracts. 7. Non-solid organ cancers (e.g. blood cancer).

Information sources Search Strategies (Electronic searches)- The specific search strategy will be developed. Literature searches will be conducted from inception to July 2023, of the following databases:1. MEDLINE 2. Embase 3. CINAHL (Cumulative Index to Nursing & Allied Health Literature) 4. Web of Science 5. Scopus. 6. PubMed 7. Cochrane Database 8. Clinicaltrial.Gov Grey literature will also be searched on Open Grey search. If any relevant information is missing, corresponding authors will be contacted. The

reference lists from the retrieved studies will be manually searched for additional citations.

Main outcome(s) Primary outcome-Overall survival (as defined by article-commonly diagnosis of HRV and death or the last follow-up).

Additional outcome(s) secondary outcome-Progression characteristics (Progression-free-, recurrence-free-or disease-free survival).

Data management Initial title and abstract screening for eligibility will be performed by two independent reviewers. Full text for titles that passed the initial screening will be retrieved and screened for eligibility. Any disagreement in the initial or full-text eligibility review will be resolved by consensus or by consulting to third reviewer. We will extract study characteristics independently using a standard data collection form developed on excel sheet.

Quality assessment / Risk of bias analysis Cochrane bias assessment tool for RCTs and Newcastle Ottawa Scale will be utilized for non-RCTs./observational studies.

Strategy of data synthesis Data collection and management- A standardized form will be used for data extraction from the included studies. Each study's demographics and primary and secondary outcomes will be recorded and presented in tables to organize, summarize the information, and identify trends across the data. Data synthesis The number of papers included and excluded during the systematic review process will be clearly presented in a flowchart for clear transparency (PRISMA flowchart). Papers selected will be presented in a summary table. Risk of bias of the selected papers will be conducted using the Newcastle-Ottawa Scale. Limitations of the studies will be discussed in detail
Analytical Plan- Where outcome data are of sufficient quality and participants, comparisons and outcomes are judged to be sufficiently like ensure an answer that is clinically meaningful, a meta-analysis will be performed. Meta-analysis will be performed using Review Manager. Dichotomous and continuous outcome summary data from each individual study will be entered into the Review Manager. Forest plots, relative risk (95% confidence interval), mean difference (95% confidence interval) and heterogeneity (χ^2 and I^2) will be generated for the outcomes.

Subgroup analysis If complete information about these variables are available-
1.Age,

2. Sex
Any other potential modifier or confounders (therapy, co-morbidities) are available across more than 50% manuscripts.

Sensitivity analysis 1. Based on quality of studies (Low vs fair/good)
2. Based on Publication before or after 2016
Depending upon the information available after data extraction, other sensitivity analyses will be performed after discussing with reviewer team.

Language restriction English.

Country(ies) involved Canada.

Keywords Heart Rate Variability, Cancer, Progression, Survival, Prognosis.

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