INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Diagnosis of Intrahepatic Cholangiocarcinoma by Raman Spectroscopy Provides High Efficiency: Protocol for A Systematic Review and Meta-Analysis

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Review question / Objective: **What is the pooled sensitivity, specificity and diagnostic accuracy of Raman spectroscopy on the diagnosis of intrahepatic cholangiocarcinoma?**
Condition being studied: **Following hepatocellular carcinoma, intrahepatic cholangiocarcinoma (ICC) is acknowledged as the second most common primary liver malignancy with an obviously increasing morbidity and mortality worldwide during the last decade. Statistically, the United States has seen an increase of ICC incidence in the last several decades, and an approximate incidence rate of 1.6 per 100 000 every year has been noted since the 21st century. Compared with HCC, ICC is known to have a comparatively worse long-term survival outcome, in which a satisfactory 5-year disease-free survival only possible in complete radical resections in extremely early phases. However, because ICC often presents with no or mild symptoms during early periods, the disease has likely developed into late stage with low possibility of a radical resection when a patient first searches clinical consultation.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2020 and was last updated on 25 November 2020 (registration number INPLASY2020110110).

INTRODUCTION

Review question / Objective: **What is the pooled sensitivity, specificity and diagnostic accuracy of Raman spectroscopy on the diagnosis of intrahepatic cholangiocarcinoma?**

Rationale: **The pooled sensitivity, specificity and accuracy of Raman spectroscopy will be calculated based on the extracted**

values of true positive, true negative, false positive and false negative values in the clinical trials. The aforementioned data can be extracted based on the charts that contain the primary data in the clinical trials.

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METHODS

Search strategy: Strictly conforming to the guidelines for performing meta-analysis, we intend to search extensively acknowledged authenticated databases including PubMed/Medline, Web of Science, Cochrane Library, ClinicalTirals.gov (http://www.ClinicalTrials.gov), China National Knowledge Infrastructure (CNKI) for related articles published from January 2008 to November 2020. Articles we primarily searched and identified will be subsequently screened for their quality, relevancy and availability. No language restriction will be used. The keywords (query) of our primary search will be as follows: ((((((intrahepatic cholangiocarcinoma) OR (ICC)) OR (liver tumor)) OR (liver mass)) OR (hepatocellular mass)) AND (Raman)) OR (Raman spectroscopy)) OR (RS).

Participant or population: We include patients pathologically diagnosed with ICC who simultaneously went through both the golden comparator (by liver puncture or biopsy after a radical surgery) and Raman spectroscopy.

Intervention: As far as we are concerned, our research is a diagnostic test. Therefore, the only intervention will be that the patients should undergo at least once Raman spectroscopy examination.

Comparator: The control will be those people who are disease-free or patients with other kinds of diseases other than ICC.

Study designs to be included: Randomized controlled trial or applying any kind of observational designs, including cross-sectional, case-control and cohort designs.

Eligibility criteria: Inclusion criteria: 1) reported the use of RS in ICC diagnosis; 2) being a registered randomized controlled trial or applying any kind of observational designs, including cross-sectional, case-control and cohort designs; 3) reported at least the diagnostic sensitivity, specificity value, or other important parameters like true positive (TP), false positive (FP), true negative (TN) and false negative (FN) values, based on which sensitivity and spe.

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Main outcome(s): The diagnostic sensitivity, specificity and accuracy.

Additional outcome(s): The positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio.

Data management: Two experienced investigators will independently analyze the included studies for original parameters which indicate the diagnostic efficiency as well as basic information concerning this article itself. During the process, unexpected discrepancies will be carefully discussed and resolved. More specifically, diagnostic sensitivity, specificity, accuracy, TP, TN, FP, FN values as well as spectra values will be extracted. In addition, the title, first author, nationality, department, ethnicity, study design, sex and median age of the patients and enrollment year will also carefully be extracted.

Quality assessment / Risk of bias analysis: Quality assessment will be performed based on the Quadas-2 tool [13]. In addition, the risk of bias will be obtained by RevMan 5.3 (The Cochrane Collaboration). The articles will be evaluated in the following processes: sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and others.

Strategy of data synthesis: The forest plots will be generated to display sensitivity and specificity estimates using Meta-Disc version 1.4 (Clinical Biostatistics Unit, UK). The bivariate model and the hierarchical summary receiver operating characteristic (HSROC) model will be used to summarize test performance. We intend to use these methods to respect the binomial structure of diagnostic accuracy data, thus jointly summarizing paired measures simultaneously, e.g. sensitivity and specificity or, positive and negative likelihood ratios (LRs). Meanwhile, as a random effects approach, the bivariate/ HSROC meta-analysis allow pooling results in view of knowing that heterogeneity is commonplace across included studies due to different or implicit thresholds. The said approach will be carried out by metandi (Meta-analysis of diagnostic accuracy using hierarchical logistic regression) command in STATA 14.2 (StataCorp, USA).Additionally, summary receiver operator characteristics (SROC) curves will be generated to assess the relationship between sensitivity and specificity. Meanwhile, the area under curve (AUC) will be simultaneously calculated to evaluate the overall performance of RS. The SROC curved is made through Meta-Disc version 1.4 (Clinical Biostatistics Unit, UK).

Subgroup analysis: None.

Sensibility analysis: Not intend to do the sensitivity analysis.

Language: English.

Country(ies) involved: China.

Other relevant information: None.

Keywords: Intrahepatic cholangiocarcinoma.

Dissemination plans: We intend to publish the protocol, which will be the mian dissemination plan.

Contributions of each author:

Author 1 - Hongyu Jin - The author came up with the plans of the research and did preliminary research. In the meantime, Hongyu Jin took charge of writing the original draft. Additionally, Hongyu Jin assisted Man Zhang in data processing and cross check the data extracted.
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