


Efficiency of free thyroxine in predicting severity and mortality of patients with acute pancreatitis

A protocol for systematic review and meta-analysis

Tao Cheng, MBBS^{a,b,c} , Bo-Jie Xiao, BS^a, Bo-Fu Liu, MBBS^{a,b,c}, Tian-Yong Han, MBBS^a, Hai-Fang Yu, MD^{a,b,c,*}

Abstract

Background: Previous studies suggest that free thyroxine may be used as a severity indicator of patients with acute pancreatitis (AP) in emergency department, helping determine the differential care of AP. However, there are no systematic reviews and the association between free thyroxine and AP is still not completely understood. Therefore, we will undertake a systematic review of the literature to summarize previous evidence regarding this topic, in order to clarify whether free thyroxine can help us pick out the mild AP cases.

Methods: We will search the EMBASE, Web of Knowledge, PubMed, ClinicalTrials.gov, and Cochrane Library from inception to Mar 2021 to retrieve relevant studies using the search strategy: ("free thyroxine") AND (pancreatitis OR pancreatitides). Two authors independently judged study eligibility and extracted data. Heterogeneity will be examined by computing the Q statistic and I^2 statistic.

Results: This study proved the efficiency of free thyroxine in predicting the severity of patients with AP.

Conclusions: This study will provide reliable evidence-based evidence for the clinical application of free thyroxine predicting the severity of patients with AP.

Ethics and dissemination: Ethical approval is unnecessary as this protocol is only for systematic review and does not involve privacy data. The findings of this study will be disseminated electronically through a peer-review publication or presented at a relevant conference.

Abbreviations: AP = acute pancreatitis, APACHE II = Acute Physiology and Chronic Health Evaluation II, NOS = Newcastle-Ottawa Scale, SAP = severe acute pancreatitis.

Keywords: acute pancreatitis, free thyroxine, mortality, prognosis, severity

1. Introduction

Acute pancreatitis (AP) is a sudden inflammatory process in the pancreas^[1] and it is a common reason for hospitalization costing

TC and B-JX contributed equally to this work.

This work was supported financially by grants from the Science Foundation of Science and Technology Department of Sichuan (No. 2018SZ0390).

The authors have no conflicts of interests to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

^a Emergency Department, ^b Laboratory of Emergency Medicine, West China Hospital, ^c Disaster Medical Center, Sichuan University, Chengdu, Sichuan, China.

* Correspondence: Hai-Fang Yu, Department of Emergency Medicine and Laboratory of Emergency Medicine, West China Hospital, Sichuan University, 37 Guoxue Road, Chengdu 610041, Sichuan, China (e-mail: yuhaifang@wchscu.cn).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Cheng T, Xiao BJ, Liu BF, Han TY, Yu HF. Efficiency of free thyroxine in predicting severity and mortality of patients with acute pancreatitis: a protocol for systematic review and meta-analysis. *Medicine* 2021;100:7(e24809).

Received: 28 January 2021 / Accepted: 29 January 2021

<http://dx.doi.org/10.1097/MD.00000000000024809>

lots of resources annually.^[2] Severe AP cases are often associated with severe complications and high mortality,^[3,4] although mild AP cases can be successfully improved quickly but have unnecessarily long hospital stays.^[5] Therefore, it is necessary to predict the severity of AP earlier, for it is critical for determining early triage, aggressive resuscitation, and improving clinical outcomes of AP in high-risk patients. However, all prognostic systems in current use, such as Ranson criteria,^[6] Acute Physiology and Chronic Health Evaluation II (APACHE II),^[7] and Balthazar grade,^[8,9] involve many tests and are not convenient for clinical practice.^[10,11]

Previous studies suggest that free thyroxine may be used as a severity indicator of patients with AP in emergency department, helping determine the differential care of AP.^[12-14] To explore whether free thyroxine can help us pick out the mild AP cases who can be successfully improved quickly and unnecessarily long hospital stays, we will undertake the systematic review and meta-analysis.

2. Methods and analysis

2.1. Registration

This meta-analysis protocol is based on the Preferred Reporting Items for Systematic Reviews and meta-analysis Protocols (PRISMA-P) statement guidelines. The PRISMA-P checklist for

the protocol is provided in the PRISMA-checklist. This protocol has been registered on International Prospective Register of Systematic Reviews database. The registration number was INPLASY202110088.

2.2. Eligibility criteria

The inclusion criteria for the study will include:

1. studies with patient age ≥ 18 years old, a minimum hospital stay of 24 hours, and a diagnosis of AP;
2. conference abstracts were only included when they provided adequate relevant information for assessment;
3. free thyroxine was used for the prediction of severity or mortality of patients with AP.

Exclusion criteria will include: age < 18 years old, patients with chronic pancreatitis, pancreas carcinoma, thyroid disorders or history of thyroid surgery, and patients with incomplete data.

2.3. Searching strategy

We will search the EMBASE, Web of Knowledge, PubMed, ClinicalTrials.gov, and Cochrane Library from inception to Mar 2021 to retrieve relevant studies using the search strategy: (“free thyroxine”) AND (pancreatitis OR pancreatitides). No language restrictions will be applied. We will also search citations of relevant primary and review. Authors of abstract in the meeting will be further searched in PubMed for potential full articles. To minimize the risk of publication bias, we will conduct a comprehensive search that included strategies to find published and unpublished studies. The research summary of the screening flow chart is shown in Figure 1.

2.4. Data extraction and risk of bias

Two reviewers will be employed the searching strategy respectively, by reading the papers and scoring them according to the QUADAS-2 checklist^[15] and Newcastle–Ottawa Quality Assessment Scale^[16]; disagreement will be settled by a third opinion. Important information will be abstracted from the included articles in a standardized form by 2 reviewers. Important information include the name of the first author, publication year, publication country, type of study, study population, sample size, defined criteria of severe acute pancreatitis, outcomes studied (severity and mortality rate), and free thyroxine level. Risk of bias assessment will be carried out according to the Newcastle-Ottawa Scale (NOS) to rate the internal validity of the individual studies, and funnel plots will be constructed to assess the risk of publication bias.

2.5. Statistical analysis

All pairwise meta-analytic calculations will be performed with Review Manager software (RevMan) version 5.3 (Cochrane collaboration). Heterogeneity will be examined by computing the Q statistic and I^2 statistic, and presence of reporting bias by visual inspection of funnel plots. Statistical significance was considered when the P value $< .05$.

3. Discussion

It is well known that severe AP cases are often associated with severe complications and high mortality.^[4,14,17] However, mild acute pancreatitis cases do not need long hospitalization,^[5] and even can be treated out of hospital to recover quickly, which

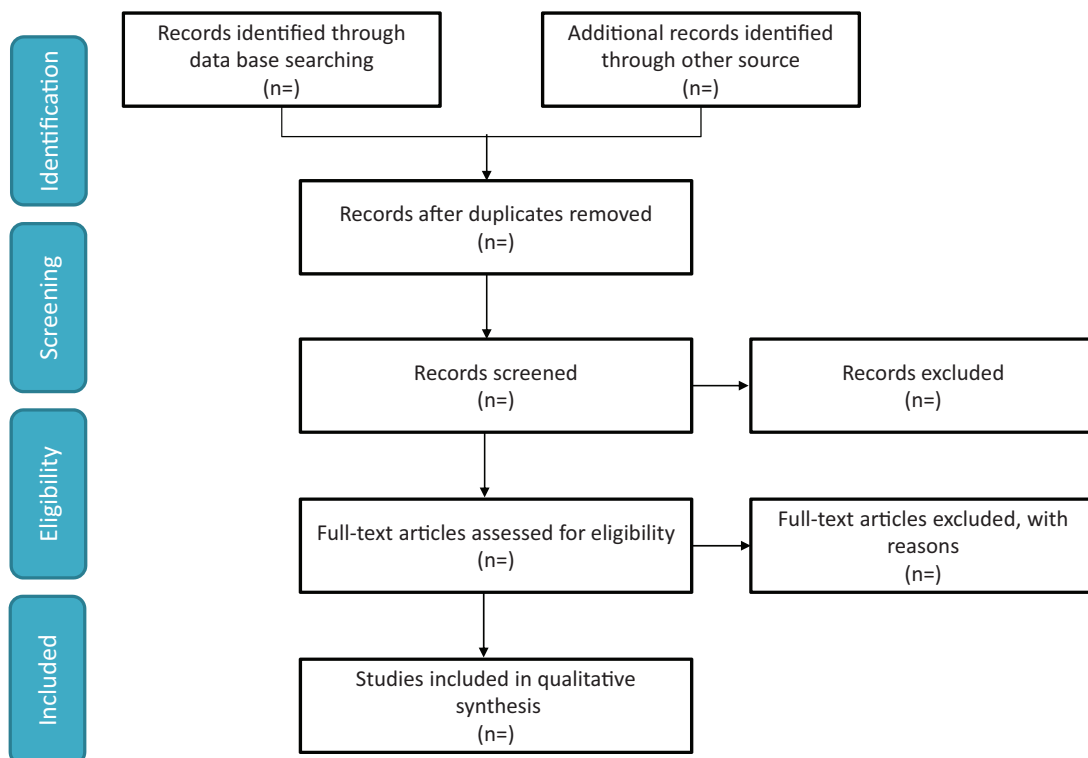


Figure 1. A flow diagram demonstrating the search strategy and study selection process for this study.

could reduce the proportion of hospitalizations and therefore save more costs. All prognostic systems in current use, such as Ranson criteria,^[6] APACHE II,^[7] and Balthazar grade,^[8,9] have significant weaknesses for involving many tests and are not convenient. Abnormalities in thyroid function parameters have been described in different pathologies, including AP, where significant changes in serum levels of thyroid hormones have been demonstrated. Some studies have reported that free thyroxine can predict the severity of patients with AP, but the conclusion is controversial.^[12–14,18]

To identify whether free thyroxine can predict the severity and mortality of AP, we will conduct the systematic review and meta-analysis. And this article is a protocol of the systematic review and meta-analysis, which presents the detailed description of review implement. The results of our review will be reported strictly following the PRISMA criteria and the review will add to the existing literature by showing compelling evidence and improved guidance in clinic settings.

Acknowledgments

The authors would like to acknowledge the participants and their families for taking part in the study.

Author contributions

Conceptualization: Tao Cheng, Bo-Jie Xiao, Bo-Fu Liu, Hai-Fang Yu.

Data curation: Tao Cheng, Bo-Fu Liu, Tian-Yong Han.

Formal analysis: Tao Cheng, Bo-Jie Xiao, Hai-Fang Yu, Tian-Yong Han.

Funding acquisition: Hai-Fang Yu.

Investigation: Tao Cheng, Bo-Jie Xiao, Bo-Fu Liu, Tian-Yong Han.

Methodology: Tao Cheng, Bo-Jie Xiao, Bo-Fu Liu, Hai-Fang Yu, Tian-Yong Han.

Project administration: Tao Cheng, Hai-Fang Yu, Bo-Fu Liu.

Resources: Tao Cheng, Bo-Jie Xiao, Tian-Yong Han.

Software: Tao Cheng, Bo-Jie Xiao, Tian-Yong Han, Hai-Fang Yu.

Supervision: Tao Cheng, Bo-Fu Liu, Hai-Fang Yu.

Validation: Tao Cheng, Bo-Jie Xiao, Tian-Yong Han, Bo-Fu Liu.

Visualization: Tao Cheng, Bo-Jie Xiao, Bo-Fu Liu, Hai-Fang Yu.

Writing – original draft: Tao Cheng, Bo-Jie Xiao, Tian-Yong Han, Bo-Fu Liu.

Writing – review & editing: Tao Cheng, Hai-Fang Yu.

References

- [1] Charalabopoulos A, Davakis S, Lambropoulou M, et al. Apigenin exerts anti-inflammatory effects in an experimental model of acute pancreatitis by down-regulating TNF- α . *In Vivo* 2019;33:1133–41.
- [2] Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology* 2012;143: 1179–1187. e1173.
- [3] Gapp J, Hall AG, Walters RW, et al. Trends and outcomes of hospitalizations related to acute pancreatitis: epidemiology from 2001 to 2014 in the United States. *Pancreas* 2019;48:548–54.
- [4] Yasuda H, Horibe M, Sanui M, et al. Etiology and mortality in severe acute pancreatitis: a multicenter study in Japan. *Pancreatol* 2020; 20:307–17.
- [5] Kothari D, Babineau M, Hall M, et al. Preventing hospitalization in mild acute pancreatitis using a clinical pathway in the emergency department. *J Clin Gastroenterol* 2018;52:734–41.
- [6] Ranson JH, Pasternack BS. Statistical methods for quantifying the severity of clinical acute pancreatitis. *J Surg Res* 1977;22:79–91.
- [7] Larvin M, McMahon M. Apache-II score for assessment and monitoring of acute pancreatitis. *Lancet* 1989;334:201–5.
- [8] Casas JD, Diaz R, Valderas G, et al. Prognostic value of CT in the early assessment of patients with acute pancreatitis. *AJR Am J Roentgenol* 2004;182:569–74.
- [9] Balthazar EJ, Ranson JH, Naidich DP, et al. Acute pancreatitis: prognostic value of CT. *Radiology* 1985;156:767–72.
- [10] Taylor SL, Morgan DL, Denson KD, et al. A comparison of the Ranson, Glasgow, and APACHE II scoring systems to a multiple organ system score in predicting patient outcome in pancreatitis. *Am J Surg* 2005; 189:219–22.
- [11] Gravito-Soares M, Gravito-Soares E, Gomes D, et al. Red cell distribution width and red cell distribution width to total serum calcium ratio as major predictors of severity and mortality in acute pancreatitis. *BMC Gastroenterol* 2018;18:1–9.
- [12] Yang WQ, Yang Q, Chen WJ, et al. Low FT3 is a valuable predictor of severe acute pancreatitis in the emergency department. *J Dig Dis* 2018; 19:431–8.
- [13] Yang N, Zhang D-L, Hao J-Y, et al. Serum levels of thyroid hormones and thyroid stimulating hormone in patients with biliogenic and hyperlipidaemic acute pancreatitis: difference and value in predicting disease severity. *J Int Med Res* 2016;44:267–77.
- [14] Zhang D, Hao J, Yang N. Relationship of thyroid hormone, thyroid stimulating hormone and blood calcium in patients with hyperlipidemic acute pancreatitis. *Chin J Postgrad Med* 2016;39:358–61.
- [15] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529–36.
- [16] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- [17] Pintado MC, Trascasa M, Arenillas C, et al. New Atlanta classification of acute pancreatitis in intensive care unit: complications and prognosis. *Eur J Intern Med* 2016;30:82–7.
- [18] Callejón G, Redondo E, Garcia-Aranda M, et al. Free thyroxine determination in the emergency department is a predictor of acute pancreatitis evolution. *Pancreas* 2018;47:1322–7.