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Review

Circulating parathyroid hormone and risk of hypertension: A meta-analysis

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ABSTRACT

Objectives: To examine the relationship between circulating parathyroid hormone (PTH) level and risk of hypertension (HTN).
Methods: The electronic databases of PubMed, Web of Science and Embase were searched up to December 2017, for prospective cohort studies on the relationship between circulating PTH level and risk of HTN. The pooled relative risk (RR) of HTN for the highest versus lowest category of circulating PTH level as well as their corresponding 95% confidence interval (CI) were calculated.
Results: A total of six prospective cohort studies, which involved 18,994 participants and 5040 HTN cases, were included in this meta-analysis. The overall multi-variable adjusted RR showed a positive relationship between circulating PTH level and risk of HTN (RR = 1.35, 95%CI: 1.09 to 1.67; P = 0.006). A substantial level of heterogeneity was observed among the studies (P < 0.001, I^2 = 77.6%). No evidence of publication bias was observed among the studies according to Begg's rank-correlation test (P = 0.452).
Conclusions: The existing evidence suggests that an increase in circulating PTH level may be associated with a higher risk of HTN. However, due to the limited number of included studies, more well-designed prospective cohort studies are needed to further elaborate the issues examined in this study.

1. Introduction

Hypertension (HTN), one of the major causes of cardiovascular disease in aging populations [1], has led to global increases in morbidity and mortality [2]. As a result of nutritional transition and westernization, the prevalence of HTN is rising worldwide [3]. According to the data from the year 2000, over one fourth of adults were diagnosed with HTN, and this figure was predicted to increase by approximately 60% in 2025 [4]. Unfortunately, the specific pathogenesis of HTN has not yet been fully elucidated. A number of potential risk factors are considered to be associated with the development of HTN. Thus, the identification of these modifiable risk factors is an important step towards the prevention and management of HTN.

Parathyroid hormone (PTH), which is secreted by the parathyroid glands, plays a role in controlling calcium homeostasis. Excessive PTH level may adversely affect cardiovascular health beyond its role in the regulation of calcium and phosphate homeostasis [5]. Additionally, chronic elevation of serum PTH level may increase the osteoclast activity and urinary excretion of phosphorous, which exerts a negative impact on bone density [6,7]. In the kidney, PTH can trigger the hydroxylation of 25-hydroxyvitamin D to 1α-25-dihydroxy-vitamin D (active form), which enhances the intestinal absorption of calcium [6]. In addition, it has been shown that a lower concentration of blood 25-hydroxyvitamin D is associated with a higher risk of HTN [8]. Therefore, it is plausible that circulating PTH level is positively associated with risk of HTN. To the best of the authors' knowledge, although a number of prospective cohort studies have examined the relationship between circulating PTH level and risk of HTN [9–14], no final conclusion can be drawn. Thus, the present meta-analysis of prospective cohort studies aimed at further elaborating the relationship between circulating PTH level and risk of HTN. It was hypothesized that an increase in circulating PTH level was associated with a higher risk of HTN.

2. Materials and methods

2.1. Search strategy

This current meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [15]. We searched the electronic databases of PubMed, Web of Science and Embase up to December 2017, using a series of logic combinations of keywords and in-text words related to hypertension (“hypertension”, “hypertensive”, and “blood pressure”),

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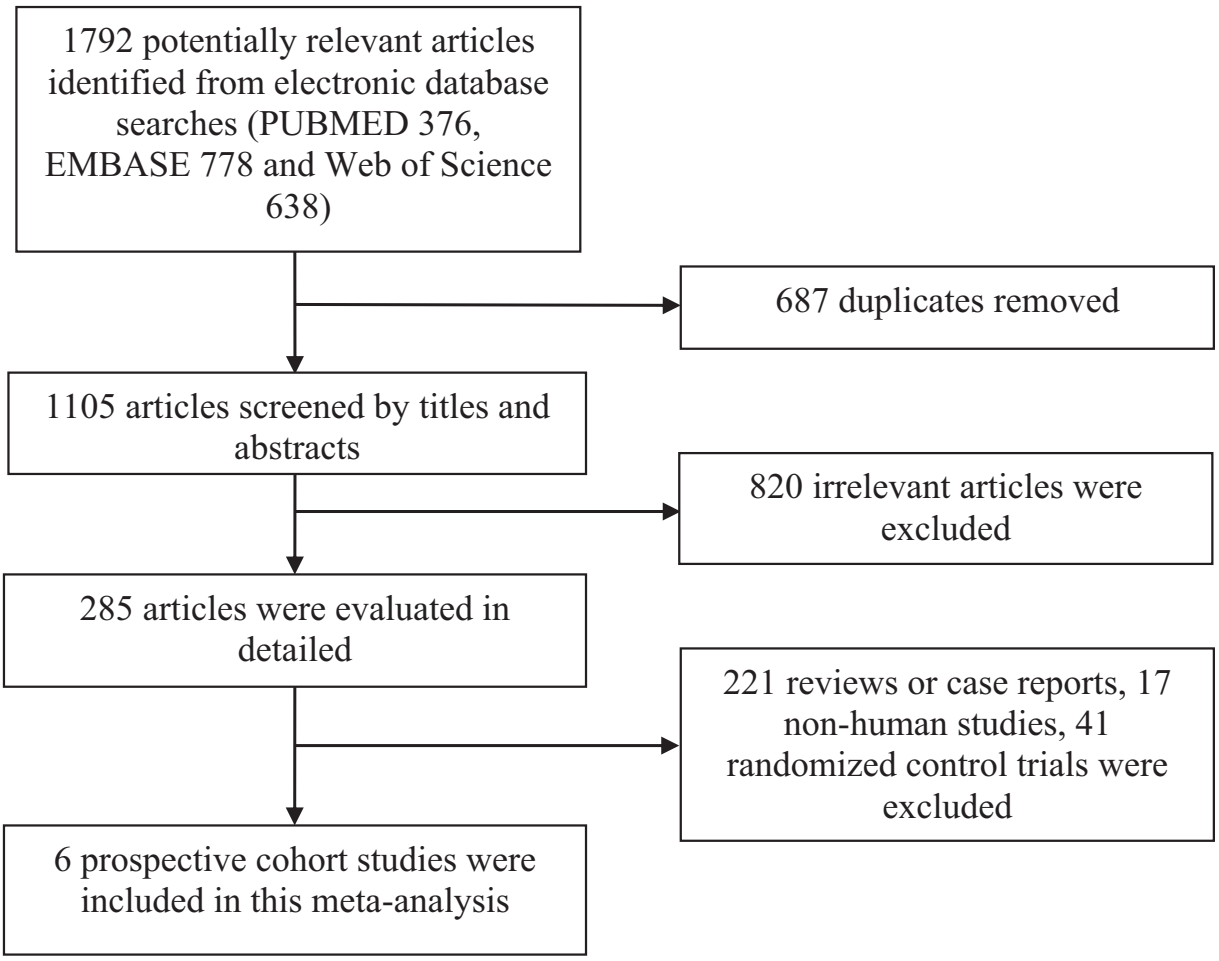

Fig. 1. Flow chart for the identification of prospective cohort studies that were included in this meta-analysis.

parathyroid hormone ("parathyroid hormone", "parathyrin", "parathormone", and "PTH"), prospective cohort ("cohort", "incident", "incidence", "prospective", "follow-up", "predict", "prognosis", and "prognostic"). No language restrictions were set in the search strategy. We first screened the titles and abstracts of all of the articles to identify eligible studies and then read the full articles to include eligible studies. Moreover, the reference lists from retrieved articles were reviewed to identify additional studies.

2.2. Study selection

The titles, abstracts and full texts of all retrieved studies were reviewed by two researchers (YZ and DZZ) independently. Disagreements were resolved by discussion and mutual agreement. The included studies were required to meet the following criteria: 1) prospective cohort studies that were in general population; 2) exposure of interest was circulating PTH level; 3) study outcome included the risk of HTN; and 4) hazard ratio (HR) or relative risk (RR) with 95% confidence interval (CI) were reported. The exclusion criteria were as follows: 1) duplicated or irrelevant articles; 2) reviews, letters or case reports; 3) randomized controlled trials; and 4) non-human studies.

2.3. Data extraction

Data extraction was conducted by 2 independent reviewers (YZ and DZZ); disagreements were resolved by consensus. The following information was collected: first author, year of publication, location, age at baseline, gender, number of participants and cases, follow-up years, adjustments, category and detection method of circulating PTH level, RR value and diagnostic criteria of HTN. The outcome of interest was the RR for the risk of HTN, for the highest versus lowest category of circulating PTH level.

2.4. Quality assessment

A quality assessment was conducted according to the Newcastle-Ottawa (NOS) criteria for non-randomized studies, which is based on three broad perspectives: the selection process of study cohorts, the comparability among different cohorts, and the identification of either the exposure or outcome of study cohorts. Disagreements with respect to the methodological quality were resolved through discussion and mutual agreement.

2.5. Statistical analyses

The outcome measures investigated in this meta-analysis was the RR of HTN (HR was transformed into RR directly). The pooled RR of HTN and its 95%CI were calculated. The most multivariable adjusted RR value reported in the original study was extracted for calculation if more than one was reported. The homogeneity of the effect size across trials was tested by Q statistics ($p < 0.05$ was considered heterogeneous). If significant heterogeneity was observed among the studies, the random effects model was used; otherwise, the fixed effects model was acceptable. The I^2 statistic, which measures the percentage of the total variation across studies due to heterogeneity, was also examined ($I^2 > 50\%$ was considered heterogeneous). Begg's test was performed