

INPLASY PROTOCOL

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Support: None.

Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None declared.

INTRODUCTION

Review question / Objective: Epidemiological studies discovered that the incidence of chronic kidney disease

Low testosterone levels and risk of adverse clinical events among male patients with chronic kidney disease: a systematic review and meta-analysis of cohort studies

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Review question / Objective: Epidemiological studies discovered that the incidence of chronic kidney disease (CKD) is higher in women than age-matched men, but male patients have a faster progression to end-stage renal disease (ESRD). On the other hand, CKD has a higher rate in women after menopause compared to premenopausal females, and the former present a more rapid progression. These facts suggest that sex hormones may play an important role in the development and progression of CKD. Testosterone, one of the primary male sex hormones, is not only responsible for the regulation of reproductive function, but also involved in numerous physiological processes. This meta-analysis aimed to systematically evaluate the prognostic significance of low testosterone levels in predicting the risk of adverse clinical events among male patients with CKD based on a pooled analysis.

Condition being studied: Previous studies have demonstrated that male CKD sufferers presented with decreased levels of endogenous testosterone which hold prognostic value in predicting adverse outcomes, but these findings have been inconsistent. Moreover, most of the findings were based on relatively small sample sizes.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 May 2022 and was last updated on 13 May 2022 (registration number INPLASY202250085).

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menopause compared to premenopausal females, and the former present a more rapid progression. These facts suggest that sex hormones may play an important role in the development and progression of CKD. Testosterone, one of the primary male sex hormones, is not only responsible for the regulation of reproductive function, but also involved in numerous physiological processes. This meta-analysis aimed to systematically evaluate the prognostic significance of low testosterone levels in predicting the risk of adverse clinical events among male patients with CKD based on a pooled analysis.

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METHODS

Participant or population: We will include CKD patients who had a minimum follow-up time of 1 year in cohort studies.

Intervention: Circulating testosterone levels will be main Exposure/Interventions.

Comparator: Per SD decrease in circulating testosterone levels at baseline associated the risk of adverse clinical events among male patients with CKD.

Study designs to be included: Prospective cohort studies, or retrospective cohort studies.

Eligibility criteria: Studies were eligible for inclusion if they: (1) were cohort studies irrespective of prospective or retrospective designs; (2) included subjects with CKD (hemodialysis, peritoneal dialysis or non-dialysis patients); (3) evaluated the prognostic value of endogenous testosterone levels for adverse clinical events, such as all-cause mortality, cardiovascular events. (4) reported an

adjusted hazard ratio (HR) and 95% confidence interval (CI); (5) had a minimum of 1 year of follow-up; (6) were available in English. The exclusion criteria were as follows: (1) reviews, conference abstracts, editorials, case reports, intervention studies, and non-human studies; (2) non-English language publications.

Information sources: The electronic databases including Pubmed, EMBASE, and Web of Science will be searched for the information sources.

Main outcome(s): Adjusted hazard ratio (HR) and 95% confidence interval (CI) will be pooled to estimate the association between per SD testosterone decrease and adverse clinical events.

Quality assessment / Risk of bias analysis: Study quality of the included studies will be assessed using the Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis: The effect estimates will be pooled using random-effects models or fixed-effects models depending on heterogeneity among studies.

Subgroup analysis: Subgroup analysis will be conducted based on study sites, design, patient types, age, mean follow-up duration, and adjusted confounders.

Sensitivity analysis: Sensitivity analyses will be conducted by omitting one study at a time to evaluate the stability of the pooled effect estimates.

Country(ies) involved: China.

Keywords: Chronic kidney disease; total testosterone; free testosterone; adverse clinical events; mortality; meta-analysis.

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