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Original Research Paper

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PROGNOSTIC VALUE OF SERUM URIC ACID IN PATIENTS WITH ACUTE HEART FAILURE:A META-ANALYSIS

Dr.Mohit Desai — Assistant Professor, Department Of Medicine, Zmch, Dahod, Gujrat, Pin-389151.

Dr.Brajendra Kumar* — Professor, Department Of Medicine, Zmch,dahod,gujrat,pin-389151. *Corresponding Author

ABSTRACT Our meta-analysis aimed to determine the prognostic significance of SUA level in patients with AHF.We made a comprehensive search in databases from inception to April 6, 2018. All available observational studies that evaluated the prognostic value of SUA level in patients with AHF were eligible. Outcome of interests were all-cause mortality and the combined endpoint of death or readmission. Prognostic values of SUA level were summarized as higher vs lower SUA category or per 1 mg/ml SUA rise.Eleven studies involving 12,854 AHF patients were identified and analyzed. AHF patients with the highest SUA level had an increased risk of all-cause mortality (risk ratio [RR] 1.43; 95% confidence intervals [CI] 1.31–1.56) and combined endpoint of death or readmission (RR 1.68; 95% CI 1.33–2.13) after adjusting potential variables. In addition, per 1 mg/ml SUA rise significantly increased by 11% and 12% higher risk all-cause mortality and combined endpoint of death or readmission, respectively..This meta-analysis indicates that elevated SUA level independently predicts all-cause mortality and the combined endpoint of death or readmission in AHF patients. Measurement of SUA level may improve risk stratification of adverse outcomes in these patients.

KEYWORDS : all-cause mortality, major adverse cardiac events, meta-analysis, uric acid

INTRODUCTION

Uric acid as a Biomarkers can be used to refine the risk classification of AHF patients. Previous 2 meta-analyses have demonstrated that a higher level of SUA was a strong and independent predictor of all-cause mortality in patients with heart failure. However, this conclusion was mainly built on chronic heart failure patients and the strength of the prognostic value of SUA in AHF patients remains controversial..

MATERIAL AND METHODS

References of relevant articles were manually reviewed to ensure identification of any additional studies. No language restrictions were imposed.Two authors independently selected the eligible studies according to the following criteria:Original full-text observational studies or post hoc analyses of randomized controlled trials;reported the prognostic value of all-cause mortality or death combined readmission associated with SUA level in AHF patients;provided multivariate adjusted hazard ratios (HR), risk ratio (RR) or odds ratios (OR) with their corresponding 95% confidence intervals (CI) for the prognostic measures;follow-up duration no less than 3 months.The exclusion criteria were:enrollment of chronic heart failure patients;reported the unadjusted risk estimates;when multiple publications from the same studied patients, we selected the longest follow-up articles.Two authors independently extracted the following data from each study: first author's surname, publication year, study design, study location, sample size, patient age and gender, cutoff value of SUA, event number, duration of follow-up, multivariate adjusted risk estimate for prognostic outcomes, and adjustment for variables. The study quality of the selected studies was assessed using the Newcastle–Ottawa Scale for the cohort studies.Data analyses were performed using the most fully adjusted risk estimate for the higher vs the lower SUA level or each 1 mg/ml SUA rise. For analyzing SUA as continuous value, we recalculated risk estimate by 1 mg/ml SUA rise using the following formula: RR1 = exp(ln (RRSD)/SD). The pooled summary was expressed as RR and 95%CI. To explore the heterogeneity across studies, we applied the Cochran Q statistic (significance level of $P < .10$) and I^2 statistics (significance level of 50%).

RESULTS

Only 10 studies out of 732 finally met our predefined inclusion criteria.Total of 12,854 AHF patients were identified and analyzed. The mean/median age of the patients ranged from 68.2 to 82 years. All the selected studies were retrospective analysis. The sample size of the included studies ranged between 167 and 8246. The duration of follow-up ranged from 3 to 27.5 months. Of these studies, 2 reported the risk estimate by both categorical and continuous SUA level, 2 reported the risk estimate by categorical SUA level, and 5 reported data as continuous SUA level. For methodological quality assessment, the NOS of these studies ranged from 5 to 7 points.Three studies reported the combined endpoint of death or readmission events by categorical SUA level analysis and four studies reported this outcome by continuous SUA level analysis.The number of analyzed studies in the outcomes was small; therefore, we did not perform a funnel plot, Begg rank or Egger test to examine publication bias.

DISCUSSION

We find that high SUA level independently predicted all-cause mortality and the combined endpoint of death or readmission in AHF patients. AHF patients with hyperuricemia were associated with a 43% and 68% higher risk of all-cause mortality and the combined endpoint of death or readmission. Furthermore, per 1 mg/ml SUA rise significantly increased by 11% all-cause mortality and 12% combined endpoint of death or readmission risk.. In line with our meta-analysis, 2 previous meta-analyses have summarized that hyperuricaemia (SUA > 6.5 mg/dl) was associated with approximately 2.1-fold higher risk of all-cause mortality in both acute and chronic heart failure patients. AHF patients with hyperuricemia were associated with a 43% greater risk of all-cause mortality. Uric acid level at admission was an independent predictor of readmission or all-cause death during a 30 day period after discharge in acutely decompensated heart failure.Left ventricular ejection fraction (LVEF) of AHF may be an important confounder for the prognostic value of SUA. In patients with preserved LVEF, concomitant hyperuricemia was significantly associated with the combined endpoint of death or readmission but not in those with reduced LVEF.Patients admitted to hospital with heart failure commonly have some degree of renal dysfunction. Worsening renal function is one of the most important prognostic variables in heart failure patients. Despite the marked reduction of uric acid level, xanthine oxidase inhibitors (XOI) had no clear effect on

improving clinical outcomes in the OPT–CHF study and EXACT-HF trial. Our meta-analysis have few limitations. Like, our meta-analysis analyzed the retrospective study-level data but not individual patients's data and the inherent limitation of the original studies could not be avoided. Like. the number of the analyzed study in individual outcomes was small, which prevented us to conduct the subgroup analysis. In addition, different follow-up duration also may make the results less reliable.

CONCLUSION

We conclude that AHF patients with a higher level of SUA significantly increase risk of all-cause mortality and the combined endpoint of death or readmission, even after adjustment for conventional confounding factors. Determination of SUA level may improve risk stratification in patients with AHF.

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