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Acute Kidney Injury Biomarkers in Marathon Runners: Systematic Review and Meta-analysis. Research Protocol

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Abstract

The objectives of this review are: to measure changes in renal biomarker levels before, immediately after, and 24 hours post-marathon; to identify promising biomarkers for the diagnosis of acute kidney injury; and to describe the temporal patterns of biomarker dynamics in relation to the marathon.
Materials and Methods: Inclusion criteria: studies of marathon runners reporting AKI-related biomarkers. Search in the following databases: PubMed, EMBASE, Web of Science, LILACS. Collected data: study design, participant characteristics, and biomarker values (pre-, post-, and 24 h post-race). Meta-analysis using random effects model. Risk of bias assessment: the National Heart, Lung, and Blood Institute pre–post tool.

Troubleshooting

1 Eligibility criteria

1 Include prospective and retrospective observational studies of individuals who participated in running a marathon, with primary outcomes being changes in urinary, serum, or plasma biomarkers indicative of AKI (e.g., serum creatinine, urinary creatinine, BUN-to-creatinine ratio, serum urea, TIMP-2, IGFBP-7, TIMP-2*IGFBP, urinary L-FABP, uNGAL, pNGAL, serum cystatin C, pKIM-1, uKIM-1, plasma/urinary TNF-alpha, plasma/urinary MCP-1, plasma/urinary YKL-40). Secondary outcomes include sCRP, copeptin, and sCK.

2 Information Sources

2 Search four databases to identify eligible studies: PubMed, EMBASE, Web of Science, and LILACS; additionally examine the reference lists of selected articles and reviews to identify further relevant studies.

3 Search Strategy

3 Construct and run search strategies using terms including “acute kidney injury”, “marathon”, and the relevant biomarkers; include MeSH terms, synonyms, singular/plural forms, and abbreviations. Conduct the searches from database inception until May 29, 2024, with no language restrictions.

4 Selection Process

4 Perform an initial semi-automated removal of duplicate records using Zotero (Corporation for Digital Scholarship).

4.1 Manually screen titles and abstracts to exclude articles that do not meet the eligibility criteria and to remove any remaining duplicates.

4.2 Have two authors manually review full-text versions of remaining articles and exclude irrelevant studies, non-eligible article types, and duplicates.

5 Data Collection Process

5 Manually extract data from each selected study by several authors.

5.1 Extract the following information from each study: study characteristics (country, region, marathon location, study design), participant demographics (age, % female), body mass

index, marathon event details (previous marathons completed, weekly running distance, running history in years), AKI criteria and AKI stage 1 reporting, and biomarker values measured in urine, serum, or plasma (and other indicators of acute kidney injury).

6 Effect Size

6 For each outcome, extract the mean and standard deviation. When mean/SD are unavailable, estimate values from median and interquartile range using formulas from the Cochrane Handbook.

6.1 Represent the effect size of interest by the mean values of the biomarkers. Collect measurements at three time points: before the marathon, immediately after the marathon, and 24 hours post-marathon.

7 Risk of bias assessment

7 Assess methodological quality of selected articles using the NHLBI quality assessment tool for before-after (pre-post) studies with no control group.

7.1 In addition to the NHLBI tool, apply four supplementary questions addressing: (1) clear exclusion criteria for alcohol/food abstinence 12 h before baseline measurement; (2) exclusion of comorbidities that could alter measurements; (3) exclusion of medication that could alter measurements; (4) reporting the use of water, electrolytes, or food during the marathon.

8 Synthesis Methods

8 Enter extracted means and standard deviations into meta-analyses using the meta package in R.

8.1 Use a random-effects model due to clinical heterogeneity among studies; present results as forest plots; assess statistical heterogeneity with the chi-squared Q test and the I^2 statistic; define statistical significance as $p < 0.05$. Perform all analyses using R version 4.3.2.

9 Assessment of Publication Bias

9 Assess publication bias using Egger's test.

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Conflicts of Interest: The authors declare no conflicts of interest.