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Remote ischemic per-conditioning did not modulate kidney Klotho expression in acute kidney injury induced by renal ischemia/reperfusion injury

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Abstract

Background Renal ischemia-reperfusion injury (I/RI) is a major medical problem related to high mortality and morbidity. Klotho plays a critical role in the kidney pathogenesis of I/RI. The current study aimed to investigate the effect of cyclic remote ischemic perconditioning (RIPerC) on renal downregulation of the Klotho protein in bilateral ischemic reperfusion (BIR).

Material and method Twenty-four Sprague-Dawley rats were divided into (I) sham group which was subjected to abdominal mid-line incision without ischemia; (II) BIR group which was exposed to 60 min ischemia followed by 24 h of reperfusion; and (III) The BIR + RIPerC group which was subjected to the same renal BIR and occlusion of the left femoral artery (cyclic 4*5′/5′). After 24-h, the blood and kidney samples were collected. Plasma creatinine (Cr) levels and blood urea nitrogen (BUN) were determined. Total antioxidant capacity (TAC); total oxidant status (TOS); oxidative stress index (OSI); mRNA levels of IL-6, TNF-α, NF-kβ, IL-10, and klotho; and pathological changes were evaluated in the renal tissues.

Results BIR resulted in renal dysfunction, as confirmed by higher plasma levels of Cr and BUN and structural changes. This was accompanied by increased TOS levels, OSI index, and decreased TAC levels. IL-6, TNF-α and NF-kβ upregulated, and klotho and IL-10 downregulated after renal ischemia. In the BIR + RIPerC group, RIPerC attenuated the destructive effects of BIR. RIPerC was effective in decreasing oxidative stress and inflammation. However, this procedure cannot upregulate the Klotho gene.

Conclusion Remote ischemic per-conditioning provides protection against renal ischemic reperfusion injury without the klotho pathway.

Keywords Klotho, Renal ischemic reperfusion injury, Remote ischemic per conditioning, Acute kidney injury, Inflammation, Oxidative stress

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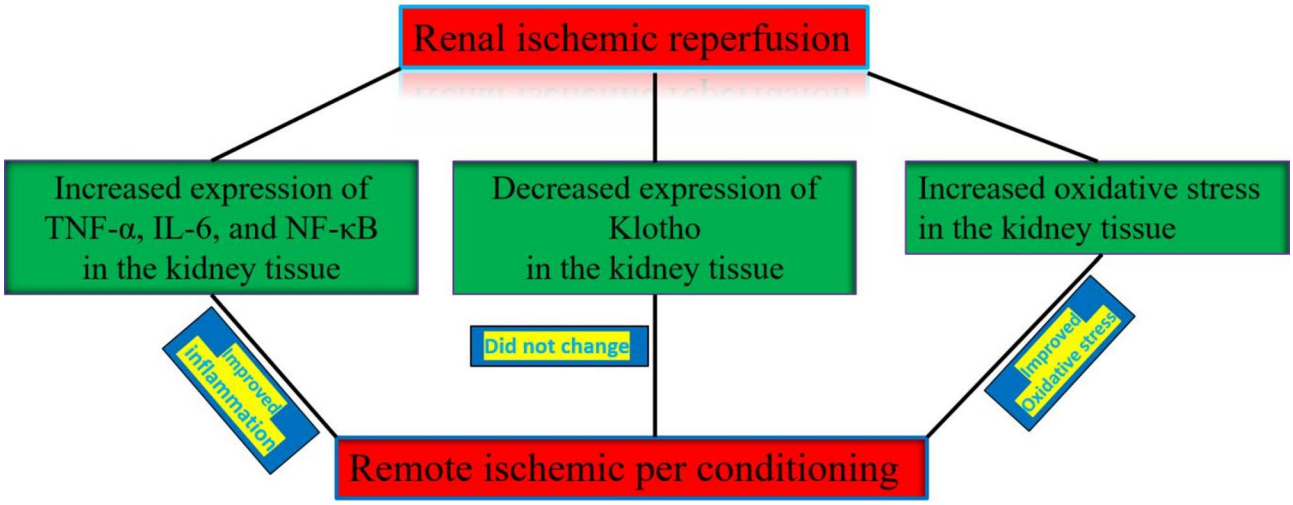

Diagram 1 Signaling pathway

Abbreviations

I/RI	Renal ischemia-reperfusion injury
RIPerC	cyclic remote ischemic perconditioning
BIR	bilateral ischemic reperfusion
TAC	total antioxidative capacity
TOS	total oxidative statuse

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Author contributions
Z.K. and V.Y. were responsible for designing and overseeing the project. P.Gh conducted the animal surgeries and collected samples. Z.K. and P.Gh analyzed the data, managed the database, performed statistical analyses, and prepared the manuscript. All authors participated in interpreting the data and reviewed and revised the final version of the manuscript.

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Data availability
The datasets generated and/or analyzed during the current study are not publicly available due to the need to keep them confidential but are available from the corresponding author on request.

Declarations

Ethical approval
This study was reviewed and approved by Shiraz University of Medical Sciences, with the approval number: [IR.SUMS.REC.1400.364]. This study was carried out in accordance with either the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, the European Communities Council Directive 2010/63/EU or the National Institutes of Health – Office of Laboratory Animal Welfare policies and principles. This study complies with the ARRIVE guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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