

## Original Contribution

# Effects of differential-phase remote ischemic preconditioning intervention in laparoscopic partial nephrectomy: A single blinded, randomized controlled trial in a parallel group design



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## ARTICLE INFO

## Article history:

Received 27 February 2017

Received in revised form 18 May 2017

Accepted 28 May 2017

Available online xxxx

## Keywords:

Remote ischemic preconditioning

Renal ischemia-reperfusion injury

Glomerular filtration rates

Neutrophil gelatinase-associated lipocalin

Cystatin C

## ABSTRACT

**Study Objective:** There are two windows of protection for remote ischemic preconditioning (RIPC), an early (ERIPC) and a late-phase (LRIPC). While ERIPC has been well studied, works on LRIPC are relatively scarce, especially for the kidneys. We aimed to compare the effects of early-phase versus late-phase RIPC in patients with laparoscopic partial nephrectomy (LPN).

**Design:** A randomized controlled study

**Setting:** The Second Affiliated Hospital of Anhui Medical University, 1 May 2012 to 30 October 2013

**Patients:** Sixty-five ASA 1 to 2 patients scheduled for LPN were located randomly to ERIPC group, LRIPC group and CON group (control).

**Interventions:** Three five-minute cycles of right upper limb ischaemia and reperfusion were performed after induction of anesthesia in ERIPC group. Patients in LRIPC group received similar treatment 24 h before surgery, while control patients were not subjected to preconditioning.

**Measurements:** Serum neutrophil gelatinase-associated lipocalin (NGAL) and serum cystatin C (CysC) were evaluated before the induction of anesthesia (0h), 2 h (2 h) and 6 h (6 h) after surgery. Unilateral glomerular filtration rates (GFR) were assessed before and after surgery to evaluate overall renal function.

**Main Results:** Serum NGAL and CysC were significantly lower in ERIPC and LRIPC groups at 2h post-operation ( $P < 0.001$ ), 6h post-operation ( $P < 0.001$ ). Additionally, The GFR were significantly lower in ERIPC and LRIPC groups than in CON group at the 3rd month after surgery ( $P = 0.019$ ;  $P < 0.001$ ). Moreover, compared to the ERIPC group, concentration of NGAL and CysC in LRIPC group decreased to a greater extent, while GFR and the percentage of decrement was significantly less in the LRIPC group ( $P = 0.016$ ;  $P < 0.001$ ).

**Conclusions:** Regardless of early-phase or late-phase intervention, limb remote ischemic preconditioning confers protection on renal ischemia-reperfusion injury in patients with laparoscopic partial nephrectomy, and the late-phase protection is more prominent.

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## 1. Introduction

Laparoscopic partial nephrectomy (LPN) has become the standard surgical treatment for Stage 1 (T1) renal cancer, with its merits of minimal invasion and rapid recovery [1]. Usually, temporary renal artery occlusion is required to facilitate surgery but this may result in renal ischemia reperfusion injury (IRI), one of the major reasons for decreased post-operational renal function [2]. Several surgical techniques

have been developed to reduce this functional damage during LPN but are relatively cumbersome or require surgical expertise [3,4]. Therefore, there is a need for a more reliable and universally applicable renal protective strategy.

Remote ischemic preconditioning (RIPC) is a simple and noninvasive technique to elicit endogenous protective mechanism against ischemia-reperfusion injury [5,6]. Huang J et al. reported that RIPC via transient lower limb ischaemia may reduce renal impairment in the short term, but failed in the long term despite a non-significant trend in favour of RIPC in patients undergoing LPN [7]. While Nicholson ML et al. performed a randomized trial of remote ischemic preconditioning in a series of live donor kidney transplants, they found that RIPC did not

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improve renal function after live donor kidney transplantation [8]. Studies have shown that there are two windows of protection for RIPC, an early (ERIPC) and a late-phase (LRIPC) [9]. Although ERIPC has been further studied, the work on LRIPC is relatively scarce, especially for the kidneys. Thus, the aim of this study is to assess and compare the protective effects of LRIPC with ERIPC against renal ischemia-reperfusion injury in patients undergoing LPN. The outcomes assessed include pre- and post-operative glomerular filtration rates (GFR) of the operative kidney and peri-operational serum concentrations of NGAL and cystatin C (CysC).

## 2. Materials and methods

### 2.1. Study subjects, protocol, measurements

Ethical approval for this study (NO. KY201204) was provided by the Ethical Committee of the Second Affiliated Hospital of Anhui Medical University, Anhui, China and registered at <http://www.chictr.org> (ChiCTR-TRC-14004610), and written informed consent was obtained from each subject. Patients diagnosed with renal tumors who were scheduled for LPN were recruited for this randomized, prospective, clinical trial from May 2012 to October 2013 in the hospital. Inclusion criteria included American Society of Anesthesiologists (ASA) physical

status I or II patients aged between 35 and 65 years, with stage 1 renal tumor diameter of <7 cm and normal renal function of the unaffected kidney assessed with the technetium ( $^{99m}\text{Tc}$ )-diethylene triamine pentacetic acid (DTPA) renal scintigraphy. They must also agree to long-time follow-up. The diuretics and antibiotics were not used perioperatively, and no chemotherapy was given in the postoperative period. Exclusion criteria included patient refusal, history of cardiac, pulmonary or other renal diseases, peripheral vascular disease that may compromise upper limb perfusion and obvious systemic inflammation as indicated by preoperative image data, blood routine test and temperature. Eligible patients were simple randomly assigned into three groups according to a computer-generated sequence: ERIPC group (early preconditioning just prior to LPN), LRIPC group (late preconditioning 24 h prior to LPN) and CON group (control; no preconditioning prior to LPN).

Remote ischemic preconditioning was achieved by a 3 cycles of tourniquet-induced occlusion of blood flow to the right upper extremity with a pressure of 200 mmHg for 5 min and intermitted with no pressure for 5 min [7,10]. This maneuver was performed at 24 h before surgery in the LRIPC group, while the patients in the ERIPC and CON groups had a non-inflated cuff applied on the right upper limb for 30 min. The patients in the ERIPC group received the treatment of remote ischemic preconditioning at 5 min after intubation, whereas in LRIPC and CON

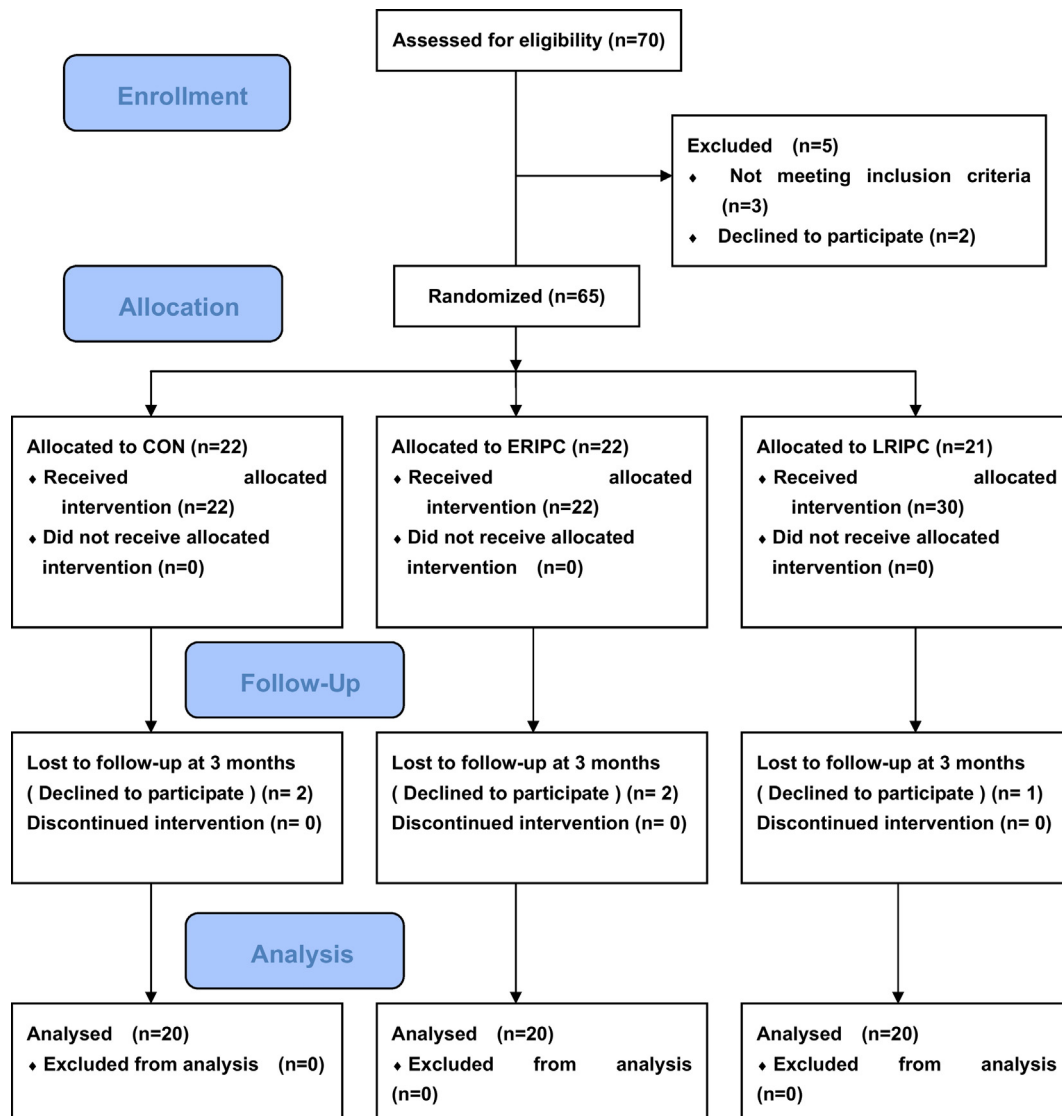


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

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