Supplementary material

Remote ischemic preconditioning in non-cardiac surgery (PRINCE): a multinational, double blind, sham-controlled, randomized clinical trial

**Collaborators**

Alessandro Belletti1, Luigi Beretta1,2, Benedetta Chiodi1, Francesco Deni1, Marco De Santis1, Sara Fiorito1, Carola Galbiati1, Rosario Losiggio1, Giacomo Monti1,2, Anita Nutta1, Federico Mattia Oliva1, Davide Oreggia1, Domenico Pontillo1, Erica Ronca1, Marta Veneziano2, Simone Vietri1, Pavel Ryzhkov3, Natalia Beloborodova3, Elena Shirshova4, Polina Turina4, Benazir Azimova5, Nazerke Zhanarystan6, Xue Yang7, Ziyu Zheng7, Daniele Orso8, Simone Bressan8, Yamume Tshomba9, Lucia Scurto9, Pavel Bagdasarov10, Daria Yavorovskaya10, Kristina Kadantseva3,11, Alexander Tetenich11, Giulio Calgaro12,13, Andrea Pradella13, Paolo Maino14, Erika Taddei15, Francesco Forfori15, Stefano Romagnoli16,17, Gianluca Villa16,17, Augusta Danella18, Michela Villano18, Felix Ramon Montes19, Alessandra Besozzi20, Grazia Zaza20, Artem Kuzovlev3,21, Ekaterina Svetalkina21, Vladimir Lomivorotov22, Maria Vargas23, Pasquale Sansone24, Yuki Kotani25

1Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, 20132 Milan, Italy

2School of Medicine, Vita-Salute San Raffaele University, 20132 Milan, Italy

3Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology, 107031 Moscow, Russia

4Saint-Petersburg State University Hospital, 190103 Saint-Petersburg, Russia

5National Scientific Center of Traumatology and Orthopedia Named N.Batpenov, 010000 Astana, Kazakhstan

6Astana Medical University, 010000 Astana, Kazakhstan

7Department of Anesthesiology and Perioperative Medicine, Xijing Hospital, 710032 Xi’an, Shaanxi, China

8Department of Anesthesia and Intensive Care Medicine, ASUFC University-Hospital of Central Friuli, 33100 Udine, Italy

9Department of Vascular Surgery, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, 00168 Roma, Italy

10I.M. Sechenov First Moscow State Medical University of the Russian Ministry of Health, 119991 Moscow, Russia

11A. Loginov Moscow Clinical Scientific Center, 111123 Moscow, Russia

12Department of Biomedical Sciences, Humanitas University, 20072 Pieve Emanuele, MI, Italy

13Department of Anesthesiology and intensive Care, IRCCS Humanitas Research Hospital, 20089 Rozzano, MI, Italy

14Division of Anaesthesiology, Ospedale Regionale di Lugano, 6900 Lugano, TI, Switzerland

15Department of Surgical, Medical, Molecular Pathology and Critical Care Medicine, University of Pisa, 56126 Pisa, Italy

16Department of Anesthesia and Critical Care, Azienda Ospedaliero-Universitaria Careggi, 50134 Florence, Italy

17Department of Health Science, University of Florence, 50134 Florence, Italy

18Department of Cardiothoracic and vascular Anaesthesia and Intensive Care, Azienda Ospedaliero Universitaria Pisana, 56123 Pisa, Italy

19Department of Anesthesiology, Fundación Cardioinfantil-Instituto de Cardiología, 111321 Bogotá, Colombia

20Anesthesia and Intensive Care Unit, Emergency Department, Busto Arsizio Hospital, ASST Valle Olona, 21052 Varese, Italy

21Oncological Center No. 1 of the S. S. Yudin City Clinical Hospital of the Moscow Department of Health, 117152 Moscow, Russia

22Department of Anesthesiology and Perioperative Medicine, Penn State College of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, PA 17033, USA

23Department of Neurosciences, Reproductive and Odontostomatological Sciences, University of Naples Federico II, 80100 Naples, Italy

24Department of Woman, Child and General and Specialized Surgery, University of Campania “Luigi Vanvitelli”, 81100 Napoli, Italy

25Department of Intensive Care Medicine, Kameda Medical Center, 296-8602 Kamogawa, Japan

Supplementary Table 1. Staging of acute kidney injury (KDIGO criteria).

| Stage | Serum creatinine | Urine output |
| --- | --- | --- |
| 1 | 1.5 to 1.9 times baseline or ≥0.3 mg/dL (≥26.5 μmol/L) increase | <0.5 mL/kg/hour for 6 to 12 hours |
| 2 | 2.0 to 2.9 times baseline | <0.5 mL/kg/hour for ≥12 hours |
| 3 | 3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dL (≥353.6 μmol/L) or initiation of renal replacement therapy or in patients <18 years a decrease in eGFR to <35 mL/minute per 1.73 m2 | <0.3 mL/kg/hour for ≥24 hours or anuria for ≥12 hours |

eGFR, estimated glomerular filtration rate.

Supplementary Table 2. Randomized Controlled Trials on RIPC performed in non-cardiac surgery (modified from Lamidi *et al*. [43] 2021 J Surg Res).

|  |  |  |  |
| --- | --- | --- | --- |
| First Author | Year | No. Patients | Surgery |
| Pedersen | 2019 | 142 | Vascular |
| Kepler | 2019 | 90 | Vascular |
| Garcia | 2016 | 201 | Vascular |
| Thomas | 2016 | 85 | Vascular |
| Healy | 2015 | 198 | Vascular |
| Mouton | 2015 | 69 | Vascular |
| Li | 2013 | 62 | Vascular |
| Walsh | 2010 | 70 | Vascular |
| Walsh | 2009 | 40 | Vascular |
| Ekeloef | 2019 | 573 | Orthopedic |
| Oh | 2020 | 63 | Orthopedic |
| Oh | 2017 | 72 | Orthopedic |
| Memtsoudis | 2014 | 60 | Orthopedic |
| Murphy | 2010 | 20 | Orthopedic |
| Lin | 2010 | 30 | Orthopedic |
| Hu | 2010 | 40 | Neurosurgery |
| Teo | 2020 | 50 | Liver surgery |
| Liu | 2019 | 136 | Urology |
| Hou | 2017 | 65 | Urology |
| Sales | 2017 | 60 | Neurosurgery |
| He | 2017 | 90 | Colorectal |
| Kanoria | 2016 | 16 | Liver surgery |
| Krag | 2016 | 60 | Head and Neck |
| Huang | 2013 | 82 | Urology |
| Antonowicz | 2018 | 84 | Gastrointestinal |

Supplementary Table 3. Cardiac risk stratification for non-cardiac surgical procedures according to 2002 ACC/AHA guidelines.

|  |  |
| --- | --- |
| High Cardiac Risk (Reported cardiac risk often greater than 5%) | |
|  | Emergent major operation, particularly in the elderly |
| Aortic and other major vascular surgery |
| Peripheral vascular surgery |
| Anticipated prolonged surgical procedures associated with large fluid shifts and/or blood loss |
| Intermediate Cardiac Risk (reported cardiac risk generally less than 5%) | |
|  | Carotid endarterectomy |
| Head and neck surgery |
| Intraperitoneal and intrathoracic surgery |
| Orthopedic surgery |
| Prostate surgery |
| Low Cardiac Risk (reported cardiac risk generally less than 1%) | |
|  | Endoscopic procedures |
| Superficial procedure |
| Cataract surgery |
| Breast Surgery |