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# Levosimendan vs. Milrinone: Early Renal and Hemodynamic Outcomes after Infant Cardiac Surgery

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## Avhandlingen baseras på följande delarbeten

I. Elin M. Thorlacius; Pertti K. Suominen; Håkan Wåhlander; Juho Keski-Nisula; Maria Vistnes; Sven-Erik Ricksten; Mats Synnergren; Birgitta S. Romlin; Albert Castellheim. **The effect of levosimendan versus milrinone on the occurrence rate of acute kidney injury following congenital heart surgery in infants: a randomized clinical trial.** *Pediatr Crit Care Med 2019;20:947-956*

II. Elin M. Thorlacius; Håkan Wåhlander; Tiina Ojala; Kaisa Ylänen; Juho Keski-Nisula; Mats Synnergren; Birgitta S. Romlin; Sven-Erik Ricksten; Albert Castellheim. **Levosimendan versus milrinone for inotropic support in pediatric cardiac surgery: results from a randomized trial.** *J Cardiothor Vasc Anesth 2020; 34:2072–2080*

*III.* Elin M. Thorlacius; Maria Vistnes; Tiina Ojala; Juho Keski-Nisula; Mattias Molin; Birgitta S. Romlin; Mats Synnergren; Sven-Erik Ricksten; Håkan Wåhlander; Albert Castellheim. **Levosimendan versus milrinone and release of myocardial biomarkers after pediatric cardiac surgery: post hoc analysis of clinical trial data.** *Pediatr Crit Care Med 2021;22(7):e402-e409*

IV. Elin M. Thorlacius; Juho Keski-Nisula; Maria Vistnes; Tiina Ojala; Mattias Molin; Mats Synnergren; Birgitta S. Romlin; Sven-Erik Ricksten; Håkan Wåhlander; Albert Castellheim **High-sensitive troponin T and interleukin-8 may serve as postoperative risk differentiators in infants undergoing congenital heart surgery.** *Manuscript*

**SAHLGRENSKA AKADEMIN**
**INSTITUTIONEN FÖR KLINISKA VETENSKAPER**

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# Levosimendan vs. Milrinone: Early Renal and Hemodynamic Outcomes after Infant Cardiac Surgery

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## Abstract

**Background:** Myocardial and renal dysfunctions are common after cardiac surgery in young children, which increases risk of complications and delayed recovery. Inodilators, such as milrinone and levosimendan, are frequently used to reduce the risk of low cardiac output syndrome in infants after cardiac surgery. Levosimendan has been demonstrated to increase renal blood flow and glomerular filtration rate in adult cardiac surgery, however there is a lack of infant studies. In the present thesis, the ability of levosimendan compared to milrinone in reducing renal and myocardial injuries after cardiac surgery in infants was investigated.

**Methods:** Two Nordic pediatric heart centers, Gothenburg and Helsinki, performed a double-blinded, randomized clinical trial (MiLe-1). Seventy infants, scheduled for total corrective cardiac surgery with cardiopulmonary bypass (CPB), received either levosimendan or milrinone. We performed the following comparisons between the two study groups: 1) the incidence of postoperative acute kidney injury (AKI), 2) the myocardial function with echocardiography, 3) changes in the plasma concentrations of myocardial biomarkers over time, and 4) in the whole study population, the associations between biomarkers of inflammation, renal, and myocardial dysfunction, with early clinical outcomes after cardiac surgery.

**Results**: The postoperative incidence of AKI was 39.5% in the milrinone group and 46.9% in the levosimendan group. The difference was not statistically significant. Neither was there a significant difference between the study groups regarding hemodynamic parameters, echocardiographic measurements, or the cardiac biomarkers. The peak plasma concentrations of the cardiac injury and inflammatory biomarkers were strong predictors of the development of severe AKI. In the patients with the lowest and highest quartile of the cardiac injury biomarker hs-cTnT and the proinflammatory biomarker IL-8 (measured at 2 hours post-CPB), we observed a strong association with the postoperative duration of ventilatory support, and the need of vasopressors.

**Conclusion:** We could not detect any significant differences in the incidence of AKI, myocardial function, or in the myocardial biomarkers after cardiac surgery in infants who received either levosimendan or milrinone. Plasma hs-cTnT and IL-8, measured 2 hours post-CPB, may have clinical value in infants after cardiac surgery, including early weaning of ventilatory support.

**Keywords:** cardiac surgery, infants, congenital heart lesions, levosimendan, milrinone, acute kidney injury, myocardial function, biomarkers

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