## Pharmacological preconditioning with gemfibrozil preserves cardiac function after heart transplantation

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**Background:** The incidence of terminal heart failure is continuously growing, thereby increasing the clinical importance of its definitive treatment, heart transplantation. Pharmacological activation of soluble guanylate cyclase (sGC), thus increasing cGMP-signalling has been reported to have cardioprotective effects, however, potent sGC activator compounds are still under development thus they are not available for the clinical setting. Gemfibrozil, a widely used lipid-lowering fibrate has recently been shown to exert sGC activating properties in vitro. The aim of the present study was to investigate whether pharmacological preconditioning of donor hearts with gemfibrozil could protect against ischemia/reperfusion injury and preserve myocardial function in a heterotopic rat heart transplantation model.

**Methods:** Donor Lewis rats received p.o. gemfibrozil (150mg/kg BW) or vehicle for 2 days. The hearts were explanted, stored for 1h in cold preservation solution, and heterotopically transplanted. 1h after starting reperfusion, left ventricular (LV) pressure-volume relations and coronary blood flow were assessed to evaluate early post-transplant graft function. Additional histological and molecular biological measurements were performed.

**Results:** After 1h reperfusion, LV contractility (LV systolic pressure: 178±10 vs. 87±7 mmHg, $p<0.001$; dP/dtmax: 4595±472 vs. 2348±306 mmHg, $p<0.001$ at 180µl LV volume, active relaxation (dP/dtmin: −2473±216 vs. −1273±138 mmHg, $p<0.001$ at 180 µl LV volume) and coronary blood flow (2,7±0,2 vs. 2,1±0,2 ml/min/g, $p=0.02$) were significantly improved in the gemfibrozil pretreated hearts when compared to controls.

**Conclusion:** Pharmacological preconditioning with gemfibrozil reduces reperfusion injury and preserves graft function after heart transplantation, which could be the consequence of enhanced myocardial cGMP-signalling. Gemfibrozil might represent a useful tool for cardioprotection in the clinical setting of heart transplantation surgery in the future.