Methods

LV hemodynamics. LV end-systolic and end-diastolic pressures, slopes of LV end-systolic and end-diastolic pressure-volume relations) were measured or calculated, as previously described[1], from LV pressure-volume curves obtained in anesthetized (sodium methohexital, 60 $mg.kg^{-1}$, IP) animals at the end of the different protocols.

Echocardiographic studies. LV diastolic and systolic diameters, as well as LV fractional shortening were measured or calculated, as described previously[2, 3], from transthoracic Doppler echocardiographic tracings obtained in anesthetized rats (sodium methohexital; 60 $mg.kg^{-1}$, IP) at different time-points during the 90-day or at the end of the 2- and 7-day protocols, using an echocardiographic system (Vivid 7, GE, France) equipped with a 10 MHz transducer.

LV tissue perfusion. Myocardial tissue perfusion in the 'viable' part of the LV was evaluated in anesthetized rats (sodium methohexital; 50 $mg.kg^{-1}$, IP) using an MRI (Bruker Biospec 4.7 Tesla, France) by Arterial Spin Labeling acquisition sequence, as previously described.[4, 5]

Left ventricular histomorphology. After assessment of LV hemodynamics, the heart was dissected, the atria as well as right and left ventricle weighted separately, and sections of the LV were either immersed in fixative solution or snap frozen in liquid nitrogen for subsequent assessment of LV collagen or LV immunohistochemistry and enzymatic activities.

LV collagen density was determined as described previously[6], while infarct size was measured by planimetry either on triphenyltetrazolium-stained fresh tissue slices in the 2-day protocol[7], or on Sirius-red stained slices in the 7- and 90-days protocols as described previously.[2, 3]

Cardiac oxidative stress. Reactive oxygen species production in the 'viable' part of the LV was evaluated by electron paramagnetic resonance spectroscopy, as previously described.[6]

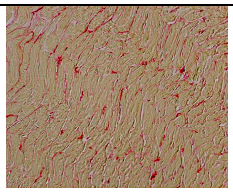
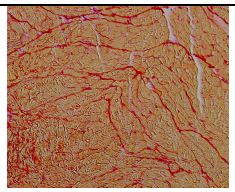
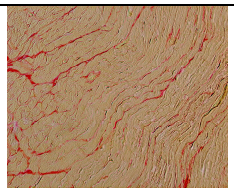
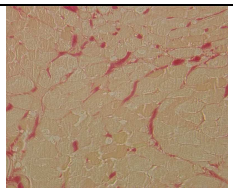
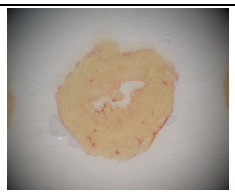
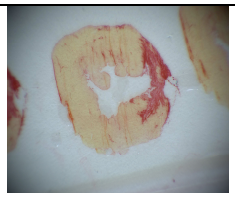
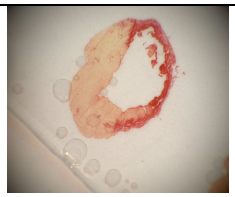
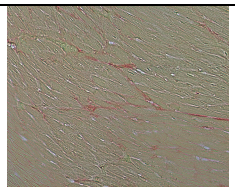
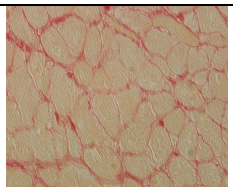
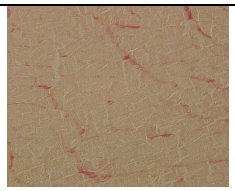
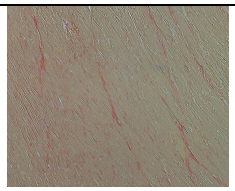
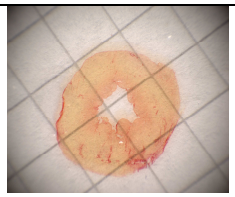
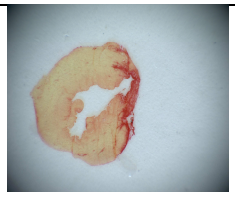
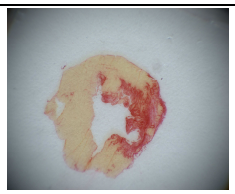
Cytosolic and mitochondrial superoxide dismutase (SOD), cytosolic catalase, and selenium-dependent glutathione peroxidase activities were measured spectrophotometrically as previously described.[8-10]

Coronary vascular function. Coronary endothelium-dependent vasorelaxation and the role of NO, NADPH oxidase-originating reactive oxygen species, and superoxide anions were assessed *ex vivo* by obtaining concentration–relaxing response curves to acetylcholine, as described previously[1, 11], before and after incubation of the coronary vessel for 20 min with the NO-synthase inhibitor L-NNA (10^{-4} M) [12], the NADPH oxidase inhibitor apocynin (10^{-4} M), or superoxide dismutase, SOD (200 U/mL). Endothelium-independent relaxation responses to increasing concentrations of sodium nitroprusside (SNP) were also examined in serotonin pre-contracted arteries.[11]

References

1. Fang Y, Nicol L, Harouki N, Monteil C, Wecker D, Debunne M, Bauer F, Lallemand F, Richard V, Thuillez C, Mulder P. Improvement of left ventricular diastolic function induced by beta-blockade a comparison between nebivolol and metoprolol. *J Mol Cell Cardiol*. 2011;51:168-176
2. Litwin SE, Katz SE, Morgan JP, Douglas PS. Serial echocardiographic assessment of left ventricular geometry and function after large myocardial infarction in the rat. *Circulation*. 1994;89:345-354
3. Mulder P, Compagnon P, Devaux B, Richard V, Henry JP, Elfertak L, Wimart MC, Thibout E, Comoy E, Mace B, Thuillez C. Response of large and small vessels to alpha and beta adrenoceptor stimulation in heart failure: Effect of angiotensin converting enzyme inhibition. *Fundam.Clin.Pharmacol.* 1997;11:221-230
4. Waller C, Hiller KH, Voll S, Haase A, Ertl G, Bauer WR. Myocardial perfusion imaging using a non-contrast agent mr imaging technique. *Int J Cardiovasc Imaging*. 2001;17:123-132
5. Kober F, Iltis I, Cozzone PJ, Bernard M. Myocardial blood flow mapping in mice using high-resolution spin labeling magnetic resonance imaging: Influence of ketamine/xylazine and isoflurane anesthesia. *Magn Reson Med*. 2005;53:601-606
6. Mulder P, Mellin V, Favre J, Vercauteren M, Remy-Jouet I, Monteil C, Richard V, Renet S, Henry JP, Jeng AY, Webb RL, Thuillez C. Aldosterone synthase inhibition improves cardiovascular function and structure in rats with heart failure: A comparison with spironolactone. *Eur Heart J*. 2008;29:2171-2179.

7. Vivaldi MT, Kloner RA, Schoen FJ. Triphenyltetrazolium staining of irreversible ischemic injury following coronary artery occlusion in rats. *Am J Pathol*. 1985;121:522-530
8. Crapo JD, McCord JM, Fridovich I. Preparation and assay of superoxide dismutases. *Methods Enzymol*. 1978;53:382-393
9. Aebi H. Catalase in vitro. *Methods Enzymol*. 1984;105:121-126
10. Isabelle M, Vergeade A, Moritz F, Dautreaux B, Henry JP, Lallemand F, Richard V, Mulder P, Thuillez C, Monteil C. Nadph oxidase inhibition prevents cocaine-induced up-regulation of xanthine oxidoreductase and cardiac dysfunction. *J Mol Cell Cardiol*. 2007;42:326-332
11. Richard V, Kaeffer N, Tron C, Thuillez C. Ischemic preconditioning protects against coronary endothelial dysfunction induced by ischemia and reperfusion. *Circulation*. 1994;89:1254-1261
12. Lorthioir A, Joannides R, Remy-Jouet I, Freguin-Bouilland C, Iacob M, Roche C, Monteil C, Lucas D, Renet S, Audrezet MP, Godin M, Richard V, Thuillez C, Guerrot D, Bellien J. Polycystin deficiency induces dopamine-reversible alterations in flow-mediated dilatation and vascular nitric oxide release in humans. *Kidney Int*. 2015;87:465-472

		Wistar		
	Sham	I/R	I/R Early Gevo	I/R Delayed Gevo
Collagen density				
Infarct Size				
		GK		
	Sham	I/R	I/R Early Gevo	I/Delayed Gevo
Collagen density				
Infarct Size				

Representative photos for interstitial collagen and infarct size in sham operated, I/R early and delayed gevokizumab-treated Wistar or GK ratsat the end of a 90 days treatment period.