ischemia (in order to avoid any effect on ischemic and/or early reperfusion injury) with an E2-releasing pellet (80 μg/kg/day). Coronary segments (internal diameter 180 to 220 μm) were removed distal to the site of occlusion and mounted in a wire myograph to study the relaxing response to acetylcholine (Ach).

At 24 hours reperfusion (i.e. immediately before the onset of E2 treatment), OVX mice displayed a marked endothelial dysfunction (maximal relaxation to Ach: sham 55±/−4; IR 31+/−4%; p=0.05). One month after reperfusion, untreated OVX mice showed a persistent decreased relaxation, whereas chronic E2 markedly increased the relaxing responses in IR mice (to a level similar to that of untreated sham mice) (Figure). E2 also slightly increased the relaxing responses in sham mice. In vitro NO Synthase inhibition abolished the differences between mice, suggesting that E2 restored the decreased NO production induced by IR.

We thus demonstrate for the first time a marked beneficial effect of E2 on coronary endothelial healing after chronic reperfusion, leading to a restoration of coronary endothelial function.

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**G001**

**INTERVENTRICULAR DELAY ASSESSED BY EQUILIBRIUM RADIONUCLIDE ANGIOGRAPHY AS A PREDICTOR OF CLINICAL RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY**

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**Objectives** — We aimed to determine whether mechanical dyssynchrony assessed by Equilibrium RadioNuclide Angiography (ERNA) may predict response to CRT.

**Methods** — 70 patients were consecutively enrolled. ERNA, echocardiography and electrocardiogram were performed before biventricular pacemaker implantation. Positive response to CRT was defined as an improvement in NYHA class in patients alive and not readmitted for HF within 6 months.

**Results** — Mean age was 65±9 years, 74% of patients were men, 84% were in NYHA class III or IV. Main HF aetiologies were ischemic (36%) or dilated (50%). ERNA left ventricular ejection fraction was 84% were in NYHA class III or IV. Main HF aetiologies were ischemic (36%) or dilated (50%). ERNA left ventricular ejection fraction was 59±39 ms and 57±46 ms, p = 0.005. QRS duration, interventricular and intraventricular delay assessed by echocardiography, intraventricular delay assessed by ERNA, were not significantly different between the two groups.

In conclusion, by contrast to other methods, interventricular delay assessed by ERNA before implantation may help to identify responders and non-responders to CRT.

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**G002**

**TRANSFER OF ROLF S3-S4 LINKER TO HERG ELIMINATES ACTIVATION GATING BUT SPARES INACTIVATION**

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A recent study in Shaker, a voltage-dependent potassium channel, suggests a coupling between activation and inactivation. This coupling is controversial in hERG, a fast-inactivating voltage-dependent potassium channel. To address this question, we transferred to hERG the S3-S4 linker of the voltage-independent channel, rolf, in order to selectively disrupt the activation process. This chimera shows an intact voltage-dependent inactivation process consistent with a weak coupling, if any, between both processes. Kinetic models suggest that the chimera presents only an open and an inactivated states, with identical transition rates as in hERG. The lower sensitivity of the chimera to BeKm-1, a hERG preferential closed-state inhibitor, confirms that the chimera exists only in open or inactivated conformations. This chimera allows determining the mechanism of action of hERG blockers, as exemplified by the test on ketoconazole.

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**G003**

**CHARACTERIZATION OF A NOVEL 7-AMINO-ACID DUPLICATION LOCATED IN THE PAS DOMAIN OF HERG FOUND IN A PATIENT WITH CONGENITAL LONG QT SYNDROME**

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**Background & Aim** — Reduced cardiac repolarizing K+ currents, mainly Ikr (hERG) and IKs, prolong the duration of the QT-interval, which is a hallmark of the congenital long QT syndrome (LQTS). In this study, a novel heterozygous mutation in the hERG gene was discovered in a 37-year-old woman with history of Torsades de pointes and prolonged QTc. Here, we characterized the 7 amino-acid duplication (343 363dup) located in the PAS domain at hERG N-terminus.

**Results** — Since the duplication is in the PAS domain, which is involved in deactivation of hERG, we first studied this process using the patch-clamp method in CHO cells expressing wild-type (WT) and mutant (Dpl) hERG channels. The main deactivation time constant was reduced by 1.4–1.8-fold for hERG Dpl compared to WT in tail currents recorded at -150 and -90mV, respectively. Deactivation-