

ABSTRACT NO. 01

**NITRIC OXIDE IS INEFFECTIVE AT INHIBITING NEOINTIMAL HYPERPLASIA IN TYPE I DIABETES**

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**INTRODUCTION:** Recently, we demonstrated that nitric oxide (NO) decreased neointimal hyperplasia more in type-II diabetes mellitus (DM) animals versus controls. This novel finding led us to question the effect of NO in a type-I DM model since this remains unknown. The aim of this study is to determine the efficacy of NO at inhibiting neointimal hyperplasia after arterial injury in vivo and its effects on vascular smooth muscle cell (VSMC) proliferation in vitro in a rodent model of type-I DM. We hypothesize that NO will inhibit neointimal hyperplasia more effectively in a type-I DM animal model versus control.

**METHODS:** Type-I DM was induced in Lean Zucker (LZ) rodents with streptozotocin. Neointimal hyperplasia was assessed using the rat carotid artery injury model. Morphometric analysis was performed at 14 days. VSMC from LZ and Zucker Diabetic Fatty (ZDF) rodents were harvested and exposed to NO with varying glucose concentrations (5-25mM). Proliferation was assessed using [3H]-thymidine incorporation.

**RESULTS:** Cholesterol, triglyceride, insulin and glucose levels were measured confirming the type-I DM model. Following arterial injury, baseline neointimal hyperplasia was significantly lower in type-I DM rodents versus controls (0.584 versus 0.784,  $P = .042$ ). Surprisingly, type-I DM animals had no significant reduction in neointimal hyperplasia with the NO donor PROLI/NO (19%,  $P = 0.133$ ), but PROLI/NO did inhibit neointimal hyperplasia in control animals (46%,  $P < 0.001$ ). The NO donor DETA/NO (500mM) inhibited proliferation greatest in euglycemic (5mM) LZ VSMC (63%,  $P = .002$ ) compared to hyperglycemic (25mM) LZ VSMC (24%,  $P = .073$ ). This same trend was seen in ZDF VSMC [type-II DM] (euglycemic, 41% reduction versus hyperglycemic, 23% reduction,  $P < 0.05$ ).

**CONCLUSION:** NO did not inhibit neointimal hyperplasia following arterial injury in an animal model of type-I DM. This data shows differential effects of NO in the two diabetic populations and suggests an alternative route is needed to combat restenosis in type-I DM.