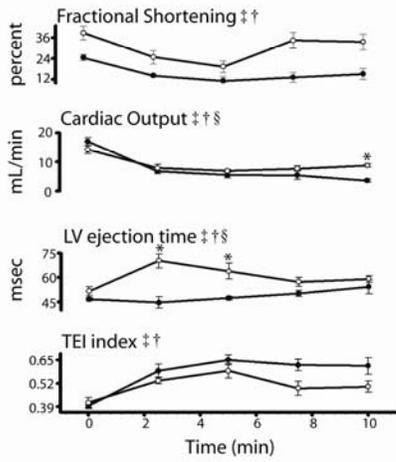
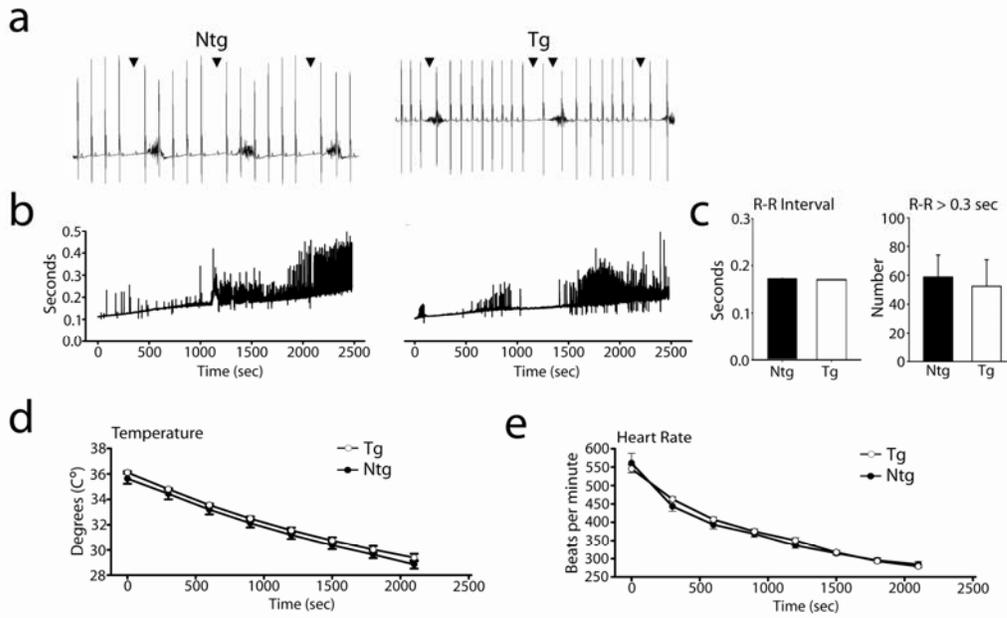


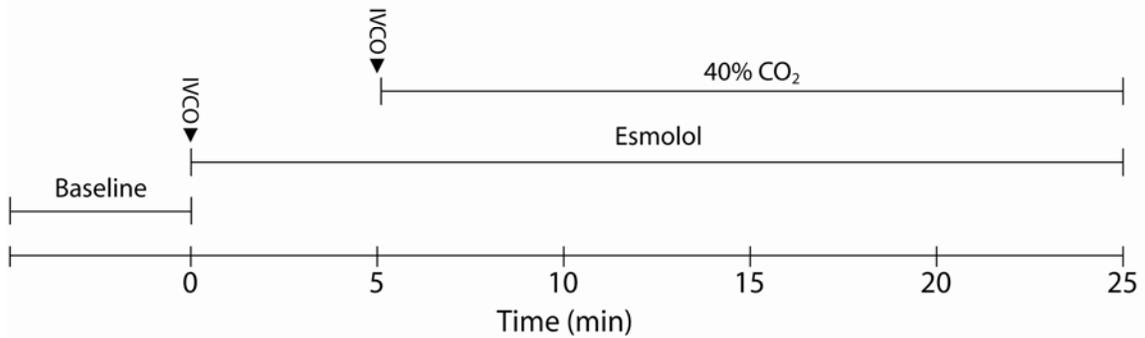
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



**Supplemental Figure 1.** Mean data showing cardiac function by echocardiography at baseline and during hypercapnia. Summarized mean data showing changes in cardiac functional parameters including fractional shortening, cardiac output, LV ejection time, and TEI Index between Ntg (●) and Tg (○) mice during the time course of hypercapnic acidosis. Values are expressed as mean ± SEM. 2 way repeated measures ANOVA main effects: time (§) and genotype (†)  $P < 0.05$ . 2 way repeated measures ANOVA interaction effects between time and genotype (§)  $P < 0.05$ . \*  $P < 0.05$  for Ntg vs. Tg. Ntg, nontransgenic (n=5); Tg, transgenic (n=7).

**Supplemental Figure 2.** Continuous *in vivo* radio-telemetry ECG measurements during a prolonged hypercapnic acidosis challenge. (a) Representative raw ECG tracings extracted during the final five minutes of the acidosis challenge showing arrhythmias in both Ntg and Tg mice. (b) Representative graphs showing the R-R interval as a measure of time during the forty minute acidosis challenge for Ntg and Tg mice. (c) Distribution and average R-R interval (left) and number of R-R intervals greater than 0.3 sec (right) during the acidosis challenge for Ntg (■) and Tg (□) mice. (d and e) The change in body temperature (d) and heart rate (e) during the time course of hypercapnic acidosis. Values are expressed as mean ± SEM. Ntg, nontransgenic (n=5); Tg, transgenic (n=5).

**Supplemental Figure 3.** Experimental design showing time points at which esmolol infusion and 40% CO<sub>2</sub> ventilation were initiated and the duration of the challenge. IVCO indicates time points where inferior vena cava occlusions were performed to acquire load independent measures of cardiac performance.