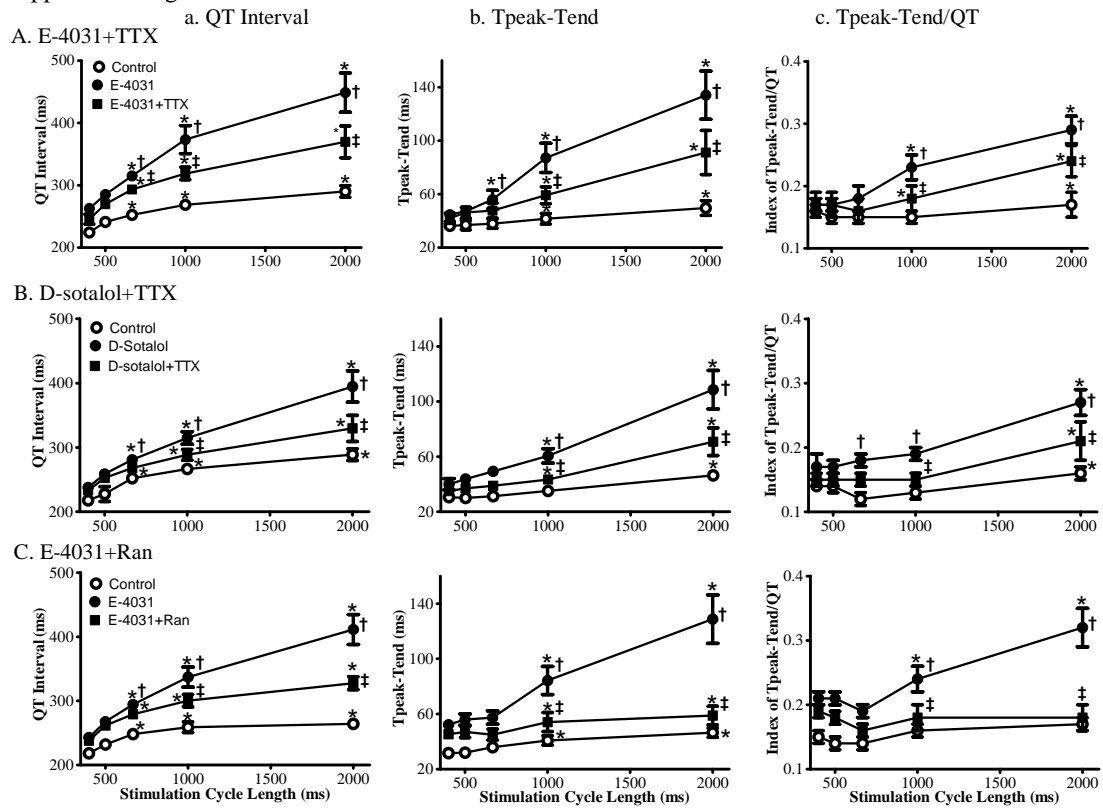


## **Supplemental material**

Supplemental figure.



**Supplemental figure legend.** Effect of TTX (A and B) and ranolazine (Ran, C) on the reverse rate-dependent changes of QT interval (a), Tpeak-Tend (b) and index of Tpeak-Tend/QT interval (c) caused by  $I_{K_r}$  inhibitors. QT interval, Tpeak-Tend and index of Tpeak-Tend/QT interval were measured in the absence (control) and presence of either E-4031 (20 nmol/L) or d-sotalol (10  $\mu$ mol/L) alone or E-4031 plus either TTX (1  $\mu$ mol/L, A) and d-sotalol (10  $\mu$ mol/L) plus TTX (B), E-4031 plus Ran (10  $\mu$ mol/L, C). Each point indicates a mean of 7, 11 and 11 hearts, respectively. \*, compared to the value at CL of 400 ms,  $p < 0.05-0.001$ ; †, Compared to control at the same CL;  $p < 0.05-0.001$ ; ‡, compared to either E-4031 (A and C) or d-sotalol (B) alone at same CL;  $p < 0.05-0.001$ .