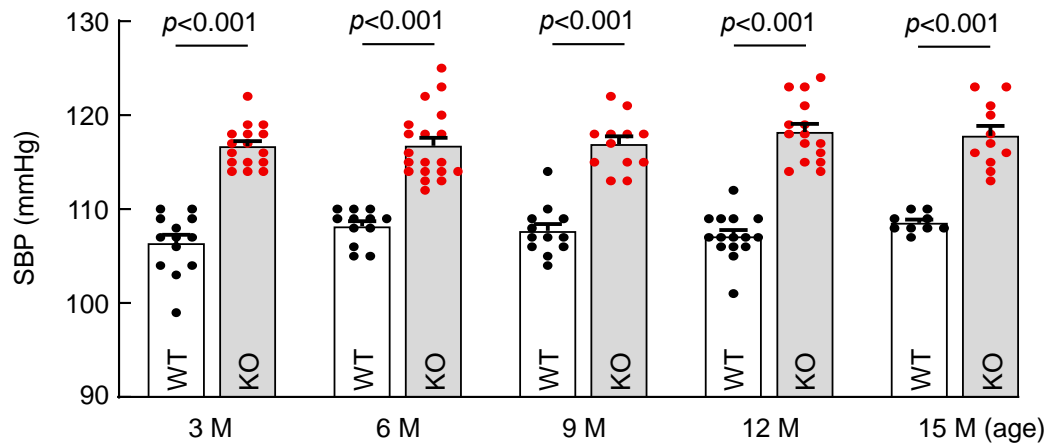
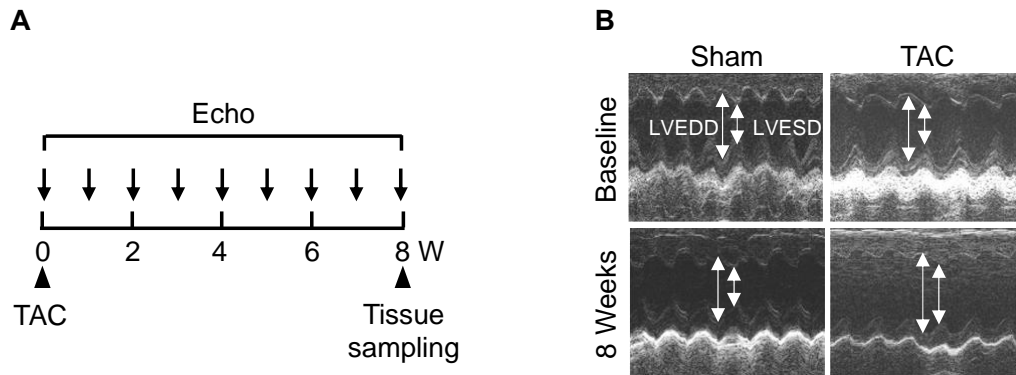


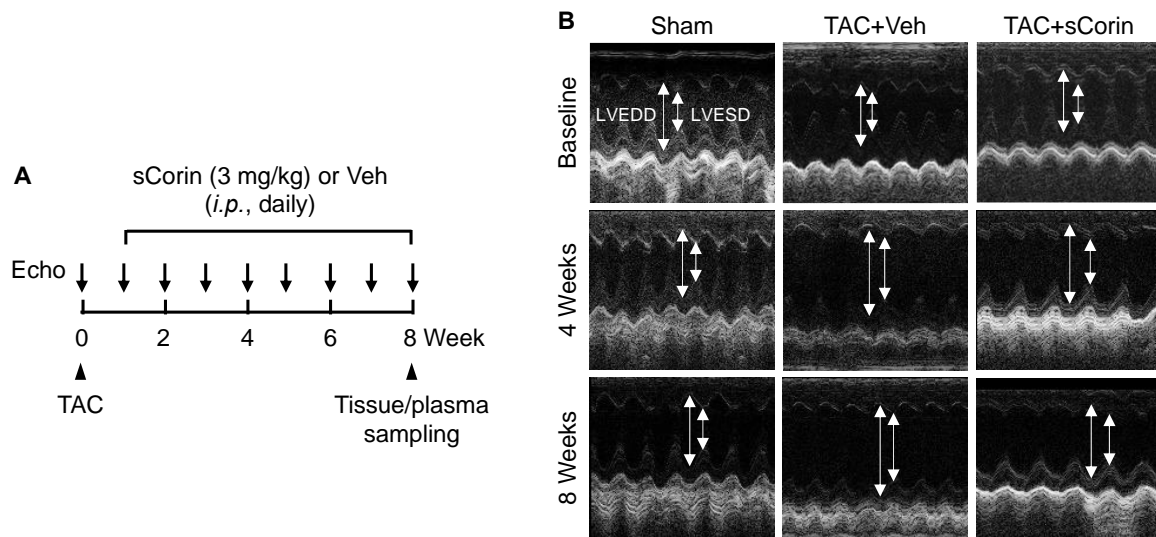
Supplementary Figures and Tables



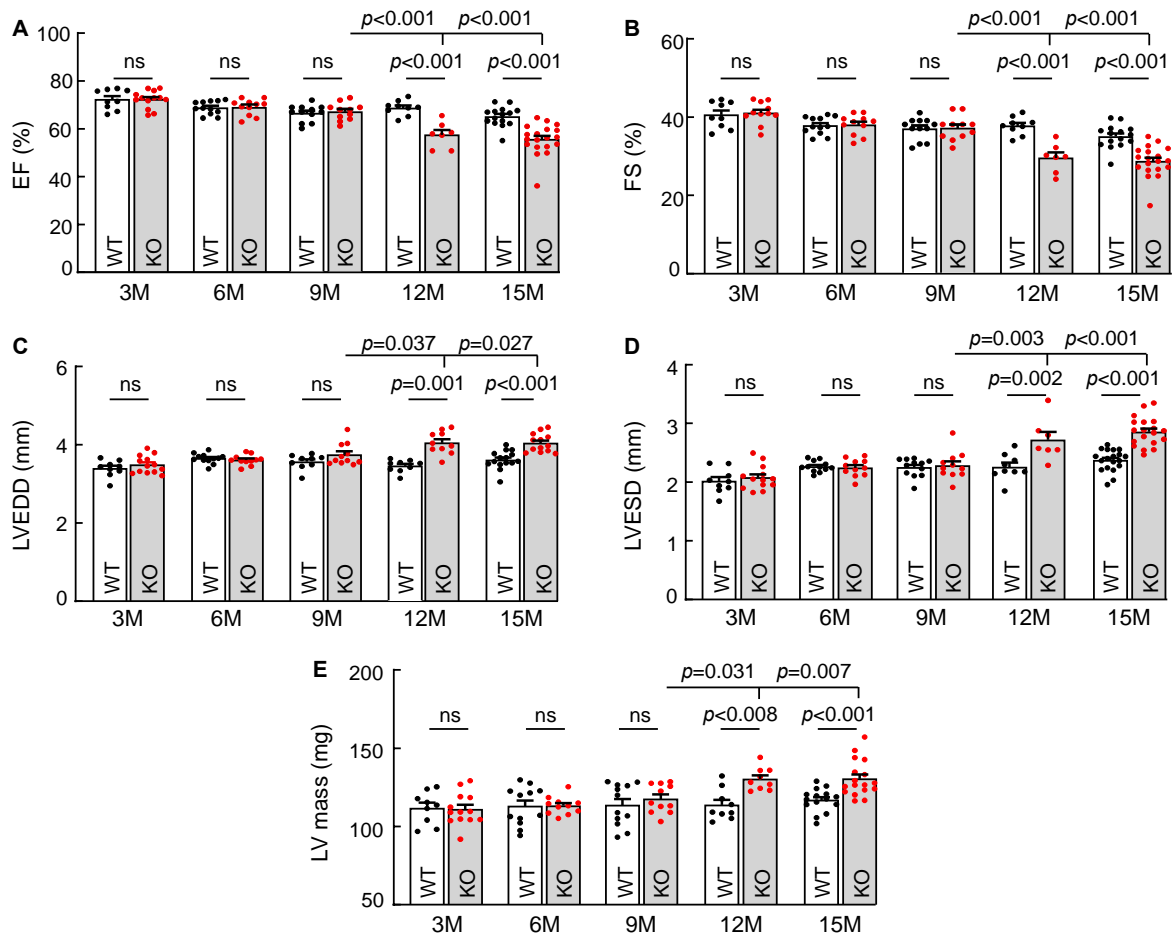
Supplementary Figure 1. Systolic blood pressure (SBP) in male WT and *Corin* KO mice at different months (M) of ages. Data are mean \pm SEM. $n = 9-19$ per group. P values were analyzed by one-way ANOVA.



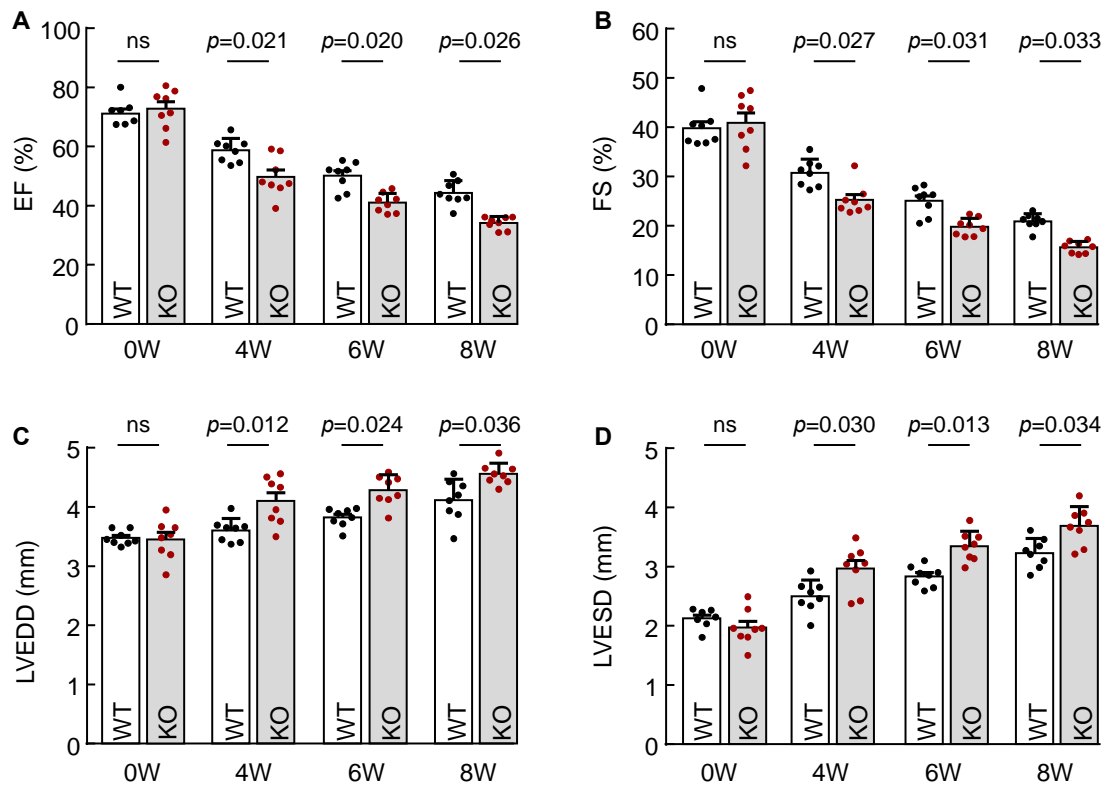
Supplementary Figure 2. Illustration of the TAC-induced heart failure model in mice. Sham or TAC operation was done in WT and *Corin* KO mice (male, 10-12 weeks old) (n = 8 per group). Echocardiography (Echo) was done weekly to assess cardiac function before (0 w) and up to eight weeks post-surgery, as illustrated in **(A)**. Representative echocardiographic images are shown in **(B)**.



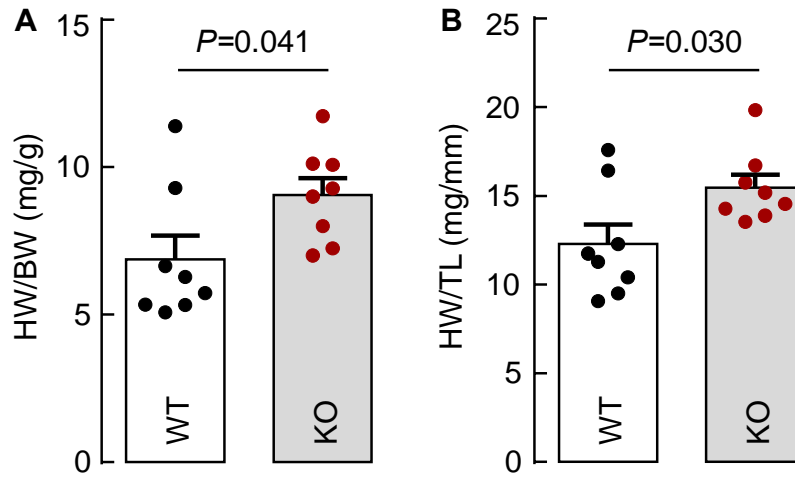
Supplementary Figure 3. Illustration of sCorin treatment in *Corin* KO mice subjected to TAC. **(A)** *Corin* KO mice (male, 10-12 weeks old) were subjected to the sham or TAC operation. One-week post-surgery, the TAC-operated *Corin* KO mice were treated with a vehicle (Veh) or sCorin (3 mg/kg) (i.p. daily). Echocardiography (Echo) was done weekly to assess cardiac function before (0 w) and up to eight weeks post-surgery. **(B)** Representative echocardiographic images from the sham- and TAC-operated *Corin* KO mice treated with vehicle or sCorin at 0- (baseline), 4-, and 8-weeks post-surgery.



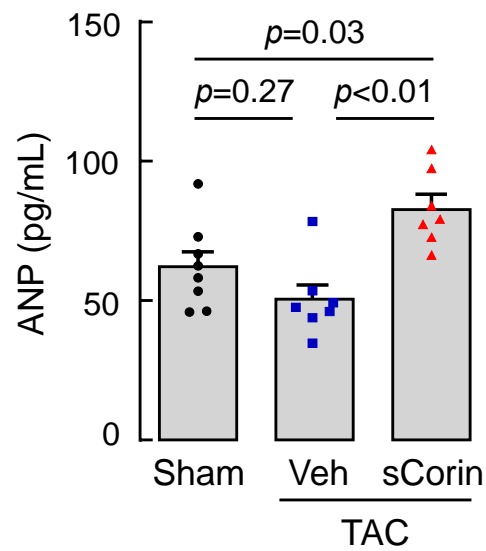
Supplementary Figure 4. Cardiac function in female WT and *Corin* KO mice at different ages. Echocardiography was conducted to examine ejection fraction (EF) (A), fractional shortening (FS) (B), left ventricular end diastolic dimension (LVEDD) (C), LV end systolic dimension (LVESD) (D), and LV mass (E) in female WT and *Corin* KO mice between 3-15 months (M) of age. Data are mean \pm SEM; n = 7-19 per group. P values were analyzed by one-way ANOVA. ns: not significant.



Supplementary Figure 5. Cardiac function in WT and *Corin* KO mice subjected to TAC. TAC was done in 10-12-week-old male WT and *Corin* KO mice. Cardiac function was assessed with echocardiography before (0 week) (W) and at 4, 6, and 8W post-surgery. The data of EF (**A**), FS (**B**), LVEDD (**C**), and LVESD (**D**) in the TAC-operated WT and *Corin* KO mice at different times were analyzed with two-way ANOVA. Data are mean \pm SEM; n = 8 per group. ns: not significant.



Supplementary Figure 6. Enhanced cardiac hypertrophy in *Corin* KO mice subjected to TAC. TAC was done in 10-12-week-old male WT and *Corin* KO mice. At 8 weeks post-TAC, hearts were isolated and weighed. Ratios of HW/BW (**A**) and HW/TL (**B**) in the WT and *Corin* KO mice were analyzed with Student's *t* test. Data are mean \pm SEM; n = 8 per group.



Supplementary Figure 7. Plasma ANP levels in sham- or TAC-operated *Corin* KO mice with vehicle or sCorin treatment. Plasma samples were isolated from the sham- or TAC-operated *Corin* KO mice with vehicle (TAC+Veh) or sCorin (TAC+sCorin) treatment at eight weeks post-surgery. Levels of ANP were measured by ELISA. Data are mean \pm SEM. $n = 7-8$ per group. Data were analyzed by one-way ANOVA.

Supplementary Table 1. Sequences of the oligonucleotide primers used in this study.

Gene	Locus	Primer	Sequence	Size (bp)
<i>Nppa</i>	NM_008725.3	forward reverse	CACAGATCTGATGGATTTCAGA CCTCATCTTCTACCGGCATC	68
<i>Nppb</i>	NM_001287348.2	forward reverse	GTCAGTCGTTTGGGCTGTAAC AGACCCAGGCAGAGTCAGAA	89
<i>Myh7</i>	NM_001361607.1	forward reverse	GGCAAGCTCACATATACACAGC ACAATCATGCCGTGCTGAC	111
<i>Ctgf</i>	NM_010217.2	forward reverse	TGACCTGGAGGAAAACATTAAGA AGCCCTGTATGTCTTCACACTG	112
<i>Gapdh</i>	NM_001289726.1	forward reverse	TGTTCCACCCCCAATGTGT GGTCCTCAGTGTAGCCCAAG	137

Supplementary Table 2. Cardiac hypertrophy in *Corin* KO mice

	WT	<i>Corin</i> KO
Heart weight (mg)	161.87 ± 4.39	178.00 ± 2.43**
Body weight (g)	35.42 ± 1.09	34.09 ± 0.68
Tibia length (mm)	18.83 ± 0.14	18.81 ± 0.11

Hearts from 15-month-old male WT and *Corin* KO mice were weighed. Data are mean ± SEM. n = 15-16 per group. ** $P < 0.01$ vs. WT, as analyzed by Student's *t* test.

Supplementary Table 3. Cardiac hypertrophy in TAC-operated *Corin* KO mice

	Sham	TAC
Heart weight (mg)	122.50 ± 4.53	225.00 ± 13.09**
Body weight (g)	25.66 ± 0.28	25.79 ± 0.27
Tibia length (mm)	16.40 ± 0.23	16.58 ± 0.69

Hearts from *Corin* KO mice at 8-weeks post sham or TAC operation were weighed. Data are mean ± SEM. n = 8 per group. ** $P < 0.01$ vs. sham, as analyzed by Student's t test.

Supplementary Table 4. Cardiac hypertrophy in TAC-operated *Corin* KO mice treated with sCorin

	Sham	Vehicle	sCorin
Heart weight (mg)	136.00 ± 4.96	258.50 ± 14.84**	202.90 ± 10.35***
Body weight (g)	26.34 ± 0.64	26.16 ± 0.48	25.83 ± 0.71
Tibia length (mm)	16.27 ± 0.14	15.84 ± 0.72	16.40 ± 0.56

Hearts from *Corin* KO mice at 8-weeks post sham or TAC with vehicle or sCorin treatment were weighed. Data are mean ± SEM. n = 13-15 per group. ** $P < 0.01$ vs. sham; *** $P < 0.01$ vs. vehicle, as analyzed by one-way ANOVA and Tukey's *post hoc* analysis.