Supplementary Figure:

Supplementary Figure S1. *Dsg2*$^{mut/mut}$ time course of disease. [3]

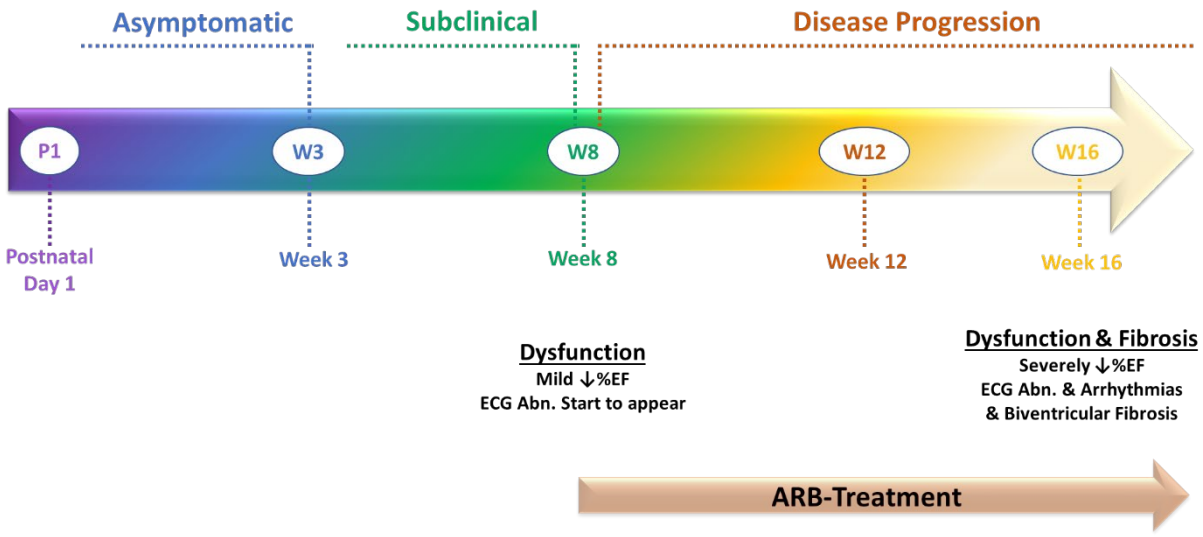
Supplementary Figure S2. mRNA transcription levels and echocardiography analysis of WT vehicle and *Dsg2*$^{mut/mut}$ mice treated with ARBs. (**A**) Percent left ventricular ejection fraction (%LVEF). (**B**) Percent fractional shortening (%FS). (**C**) RWT, relative wall thickness; **(D)** LVM, left ventricular mass. qPCR analysis of genes associated with **(E)** metabolism and **(F)** lipids and lipids carriers. Data presented as mean±SEM. *P<0.05 for any cohort vs WT Vehicle; †P<0.05 any Rosiglitazone-treated cohort vs vehicle-treated *Dsg2*$^{mut/mut}$ mice; #P<0.05 Rosiglitazone-treated WT vs Rosiglitazone-treated *Dsg2*$^{mut/mut}$ mice using One-way ANOVA with Tukey's post-hoc analysis.

Supplementary Tables:

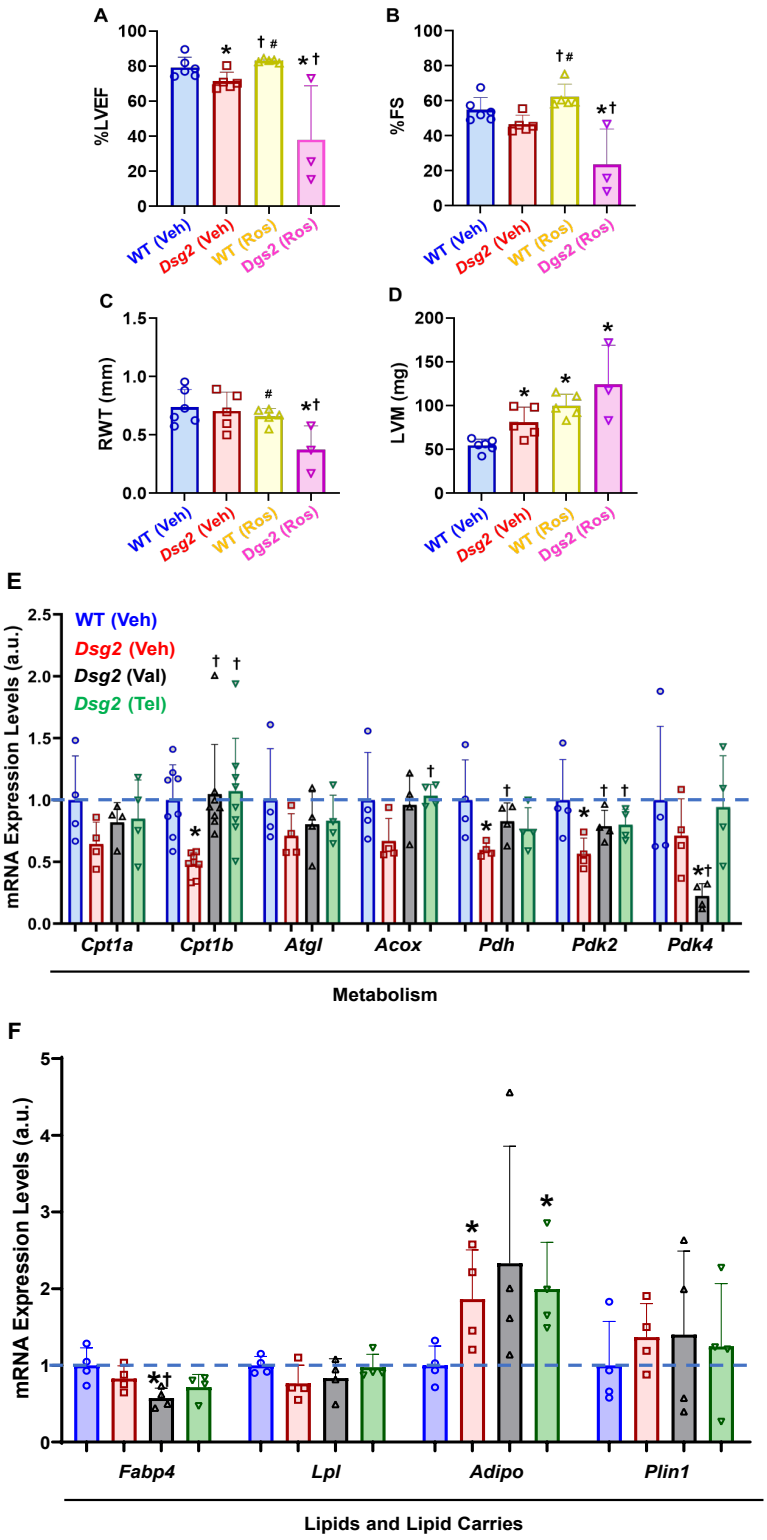
Supplementary Table S1. Echocardiographic, electrocardiographic, blood pressure plethysmography, and morphometric indices from Vehicle- and Drug-treated WT and *Dsg2*$^{mut/mut}$ mice at 8 weeks of age. IVSd, interventricular septal end-diastolic volume; IVSs, interventricular septal end-systolic volume; LVIDd, left ventricular internal diameter end-diastolic volume; LVIDs, left ventricular internal diameter end-systolic volume; LVPWd, left ventricular posterior wall end diastole; LVPWs, left ventricular posterior wall end systole; FS, fractional shortening; EF, ejection fraction; HR, heart rate; RR-I, R-R interval; PR-I, P-R interval; Pd, P-wave duration; QRSd, QRS duration interval; Q-Amp, Q-wave amplitude; S-Amp, S-wave amplitude; PVC, premature ventricular contraction; BPP, blood pressure plethysmography; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RWT, relative wall thickness; LVM, left ventricular mass. Data presented as mean±SEM, *P<0.05 for any cohort vs WT Vehicle; †P<0.05 any drug-treated *Dsg2*$^{mut/mut}$ cohort vs vehicle-treated *Dsg2*$^{mut/mut}$ mice; &P<0.05 for *Dsg2*$^{mut/mut}$ mice treated with Valsartan vs *Dsg2*$^{mut/mut}$ mice treated with Telmisartan using Student's t-test or One-way ANOVA with Tukey's post-hoc analysis.

Supplementary Table S2: Real-time PCR run protocol and forward and reverse primer sequences.

Supplementary Figure S1



Supplementary Figure S2



Supplementary Table S1

Parameters	Vehicle		Valsartan (30mg/kg/day)		Telmisartan (10mg/kg/day)	
	WT	*Dsg2*$^{mut/mut}$	WT	*Dsg2*$^{mut/mut}$	WT	*Dsg2*$^{mut/mut}$
Echo						
n	6	5	5	5	4	6
IVSd (mm)	0.85 ± 0.03	0.98 ± 0.06*	0.83 ± 0.04	0.82 ± 0.06	0.79 ± 0.15	0.79 ± 0.08*†
IVSs (mm)	1.44 ± 0.07	1.37 ± 0.11	1.28 ± 0.07*	1.21 ± 0.07*†	1.36 ± 0.12	1.21 ± 0.06
LVIDd (mm)	2.32 ± 0.12	2.66 ± 0.18*	2.15 ± 0.29	2.74 ± 0.31	2.44 ± 0.19	2.62 ± 0.23
LVIDs (mm)	1.05 ± 0.11	1.41 ± 0.05*	0.78 ± 0.14*	1.55 ± 0.31*	1.22 ± 0.19	1.24 ± 0.18
LVPWd (mm)	0.84 ± 0.05	0.92 ± 0.06	0.93 ± 0.09	0.81 ± 0.06&	0.81 ± 0.11	0.60 ± 0.04*†
LVPWs (mm)	0.97 ± 0.08	1.04 ± 0.04	1.20 ± 0.10*	1.06 ± 0.03&	0.90 ± 0.20	0.78 ± 0.10†
FS (%)	54.9 ± 3.1	46.7 ± 2.6*	64.1 ± 3.1*	44.9 ± 4.5*	50.1 ± 5.6	53.4 ± 4.0
EF (%)	79.3 ± 2.6	71.4 ± 2.6*	86.8 ± 2.1*	69.0 ± 5.4*	74.4 ± 5.3	77.7 ± 3.4
ECG						
HR (bpm)	433 ± 20	498 ± 14*	462 ± 6	506 ± 28*	468 ± 23	507 ± 10*
RR-I (ms)	139 ± 6.3	121 ± 3.9*	129 ± 2.0	120 ± 6.7*	129 ± 5.6	119 ± 2.4*
PR-I (ms)	36.4 ± 2.2	36.7 ± 0.5	39.3 ± 0.6	40.1 ± 1.9†	34.5 ± 3.4	36.0 ± 2.0
Pd (ms)	11.2 ± 0.8	8.3 ± 0.5*	11.5 ± 0.7	9.8 ± 0.8†	8.03 ± 0.2*	11.8 ± 1.0†
QRS-d (ms)	10.4 ± 0.6	10.3 ± 0.9	11.5 ± 0.4	12.7 ± 2.3	11.7 ± 3.3	18.3 ± 2.8*†
Q-Amp (mV)	-0.01 ± 0.01	-0.07 ± 0.05	-0.02 ± 0.0	-0.12 ± 0.06*	-0.00 ± 0.0	-0.21 ± 0.04*†
S-Amp (mV)	-0.14 ± 0.05	-0.11 ± 0.04	-0.21 ± 0.07	-0.01 ± 0.03*†	-0.16 ± 0.06	-0.04 ± 0.01*†
PVCs (%)	0.0 ± 0.0	0.34 ± 0.24	0.04 ± 0.05	0.22 ± 0.09*&	0.53 ± 0.22*	11.3 ± 4.2*†
BPP						
SBP (mmHg)	114 ± 7.7	132 ± 9.9	105 ± 2.6	114± 7.7†&	89.8 ± 5.9*	85.4 ± 2.5*†
DBP (mmHg)	64.6 ± 6.3	77.0 ± 10.1	58.4 ± 5.4	64.6 ± 10.2&	42.0 ± 1.8*	40.4 ± 1.5*†
MBP (mmHg)	81.2 ± 6.5	95.2 ± 10.0	74.0 ± 3.8	81.4 ± 9.2&	58.0 ± 2.4*	55.4 ± 1.0*†
Morphometric						
RWT (mm)	0.74 ± 0.07	0.71 ± 0.08	0.97 ± 0.26	0.62 ± 0.08&	0.69 ± 0.15	0.47 ± 0.04*†
LVM (mg)	54.6 ± 3.2	80.9 ± 8.7*	53.2 ± 7.3	68.0 ± 12.4	54.0 ± 7.8	49.9 ± 7.4†

Supplementary Table S2

mRNA gene Transcript	Forward Primer Sequence	Reverse Primer Sequence	qPCR Run Protocol
Cptb1a	GGCATAAACGCAGAGCATTCCTG	CAGTGTCCATCCTCTGAGTAGC	**Step 1:** 95°C for 3mins **Step 2:** 95°C for 10secs **Step 3:** 60°C **Step 4:** Go to Step 2 and repeat 60x
Cptb1b	CCAAGATCTGCTCCTACCACG	ACAGATAGCCGACGTTTGGAA	
Atgl	TCCGAGAGATGTGCAAACAG	TTGGTTCAGTAGGCCATTCC	
Acox	GCCATTCGATACAGTGCTGTGAG	CCCAGAAAGTGGAAGGCATAGG	
Pdh-E1α1	GGTGGTGTGGTCCTAGCTGT	ATTCCTGGTGGCTGCTACAC	
Pdk2	CTGGACCGCTTCTACCTCAG	GCCATCAAAGATGAGGGTGT	
Pdk4	GCCTTGGGAGAAATGTGTGT	TGCTTTGATTCCTTCCATCC	
PPARα	AGTTCACGCATGTGAAGGCT	AGCTCCGATCACACTTGTCG	
PPARδ	GGACCAGAACACACGCTTCCTT	CCGACATTCCATGTTGAGGCTG	
PPARγ	GTACTGTCGGTTTCAGAAGTGCC	ATCTCCGCCAACAGCTTCTCCT	
CEBPa	AGTCGGTGGACAAGAACAGC	ACGTTGCGTTGTTTGGCTTT	
CEBPb	CAAGCTGAGCGACGAGTACA	TCAGCTCCAGCACCTTGTG	
PGC1α	GAATCAAGCCACTACAGACACCG	CATCCCTCTTGAGCCTTTCGTG	
PGC1b	CAGCCTCAGTTCCAGAAGTCAG	CACCGAAGTGAGGTGCTTATGC	
Ctnnb1	GTTCGCCTTCATTATGGACTGCC	ATAGCACCCTGTTCCCGCAAAG	
Fabp4	TGAAATCACCGCAGACGACAGG	GCTTGTCACCATCTCGTTTTCTC	
Lpl	GCGTAGCAGGAAGTCTGACCAA	AGCGTCATCAGGAGAAAGGCGA	
Adipo	AGATGGCACTCCTGGAGAGAAG	ACATAAGCGGCTTCTCCAGGCT	
Plin1	GCCACTCCAACTCCAAATGT	GCACTGCTAGGCCAGTTTTC	
GAPDH	CATCACTGCCACCCAGAAGACTG	ATGCCAGTGAGCTTCCCGTTCAG	