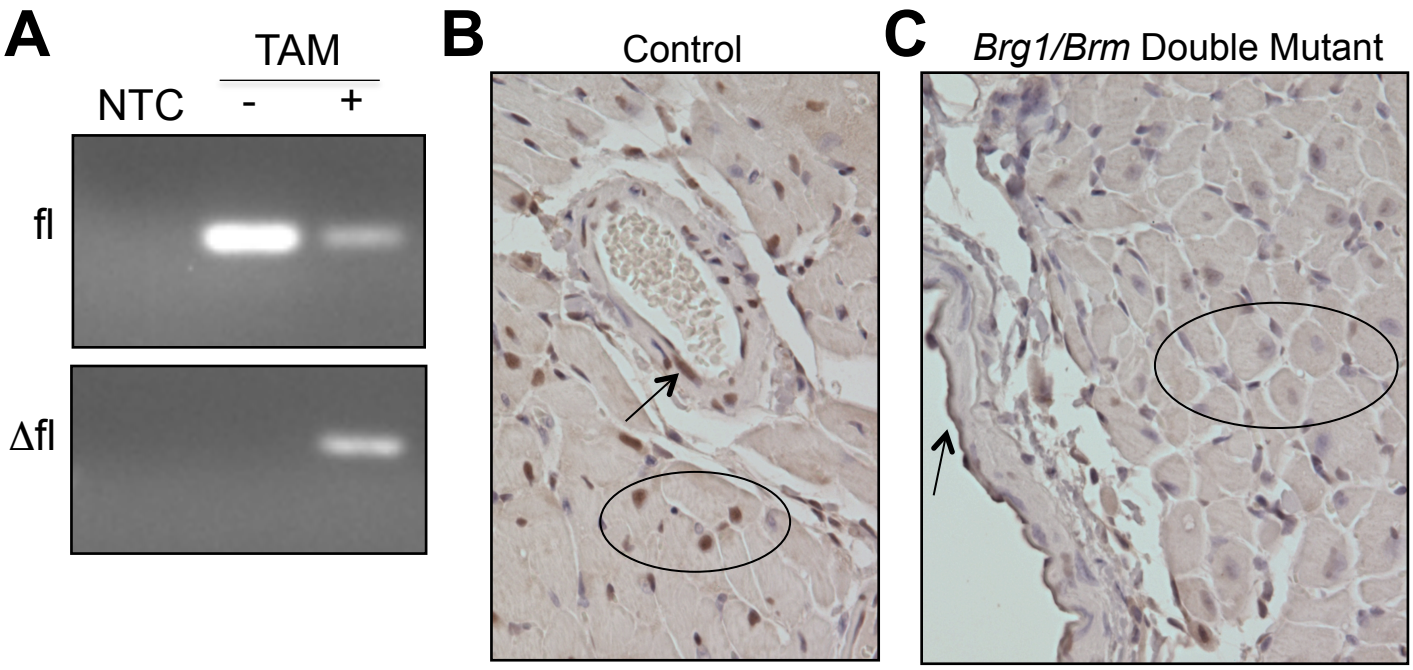
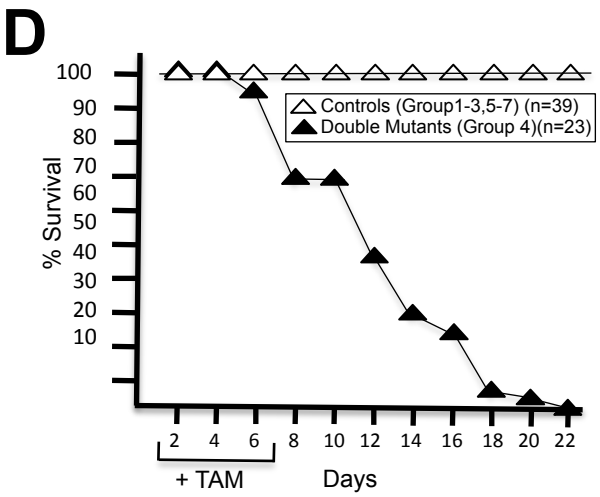



| Category | *Brg1* | MHC-Cre-ERT | *Brm* | TAM | # |
|---|---|---|---|---|---|
| Group 1 | fl/fl | - | -/- | - | 6 |
| Group 2 | fl/fl | - | -/- | + | 14 |
| Group 3 | fl/fl | + | -/- | - | 4 |
| ***Group 4**** | ***fl/fl*** | **+** | ***-/-*** | **+** | ***23*** |
| Group 5 | fl/+ | + | -/- | + | 7 |
| Group 6 | fl/fl | + | +/- | + | 5 |
| Group 7 | fl/fl | - | +/- | + | 3 |

**Figure S1. A combined requirement for BRG1 and BRM in cardiomyocytes for organismal survival.** (**A-C)** Tamoxifen-induced ablation of *Brg1* in cardiomyocytes. **(A)** PCR detection of the *Brg1* floxed (fl, top panel) and Δfloxed (Δfl, bottom panel) alleles in genomic DNA prepared from cardiac tissue of $Brg1^{fl/fl}$; MHC-Cre-ERT mice that were untreated (-) or treated (+) with tamoxifen (TAM). The floxed PCR product is diminished but still detected in TAM-treated mice because the Cre-mediated excision event does not occur in cell types other than cardiomyocytes such as vascular endothelial cells. NTC, no template control. **(B)** IHC showing BRG1 nuclear staining in cardiomyocytes (encircled region highlights one field of cells) and vascular endothelial cells (arrow) of cardiac tissue section from control mice (Group 2: $Brg1^{fl/fl}$; no MHC-Cre-ERT transgene but treated with TAM). **(C)** IHC showing lack of BRG1 staining in cardiomyocytes (encircled region highlights one field of cells) in cardiac tissue sections from *Brg1/Brm* double-mutant mice. Presence of BRG1 staining in vascular endothelial cells (arrow) at levels comparable to the control serves as an internal positive control. **(D)** Kaplan-Meier survival curve of mice after administration of tamoxifen (+ TAM) on days 1 through 7. The number of mice for each genotype and ± TAM treatment is listed below. *Brg1/Brm* double mutants are the experimental mice in Group 4 (enclosed by box), whereas the other 6 groups are controls.

**Figure S2.** Longitudinal analysis of cardiac function in individual *Brg1/Brm* double-mutant (red text) and control mice (blue text) following the loss of BRG1 via TAM feeding. Echocardiogram data for each numbered animal is shown in a separate panel on pages that follow. The sex of each animal is designated as M (male) or F (female) next to the animal number.

# →*Brg1/Brm* double mutants

## Grp4

18, 19, 23, 24, 33, 37, 38, 39, 41, 43
44, 55, 56, 57, 58, 59, 60, 65, 66, 70

***Key:***
***Grp 1 Brm-- /flx/flx No Tg Chow Diet***
***Grp 2 Brm-/- flx/flx No Tg +TAM***
***Grp 3 Brm-/- flx/flx Brg1 Tg+ Chow***
***Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM***
***Grp 5 Brm-/- flx/+ Brg1 Tg+ Chow***
***Grp 6 Brm-/- flx/+ Brg1 Tg+ Tam***

# →Controls

## Grp1 42, 45, 48, 49, 50

## Grp2 20, 21, 26, 28, 32, 34, 35, 36, 40

## Grp3 29, 47

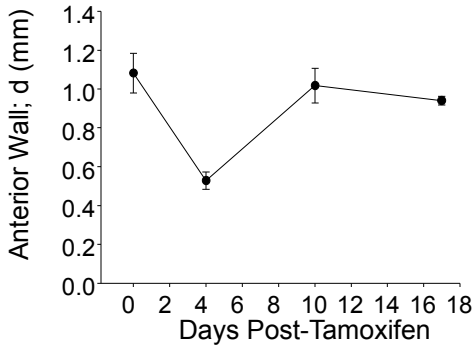
## Grp5 25, 46

## Grp6 71, 72, 73, 75, 80, 83, 85

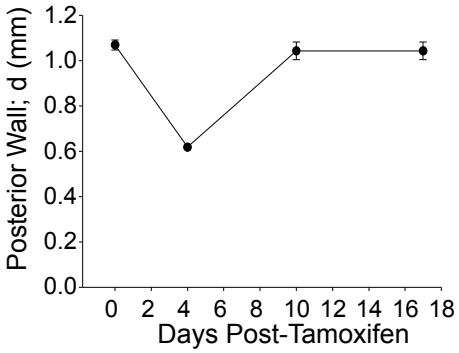
## Mouse 42 F

# Grp 1 Brm-- /flx/flx No Tg Chow Diet

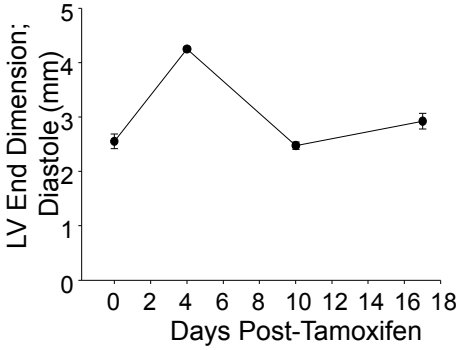
### Anterior Wall; Diastole



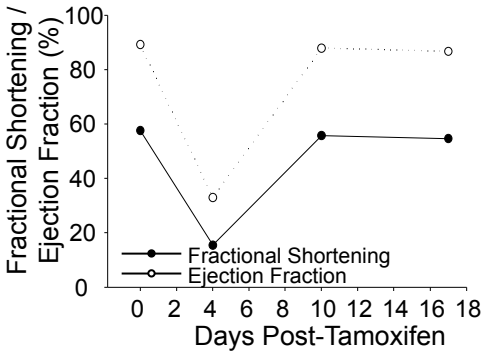

### Posterior Wall; Diastole



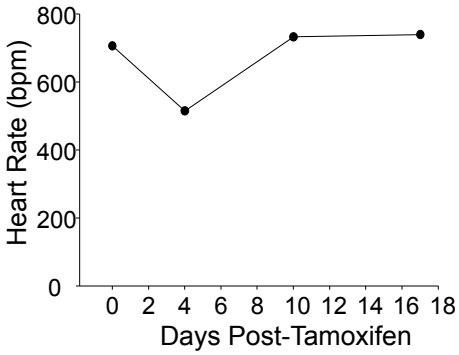

### LVID; Diastole




### Systolic Function (%)

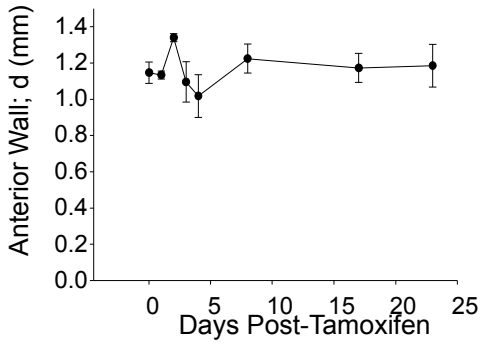



### Heart Rate

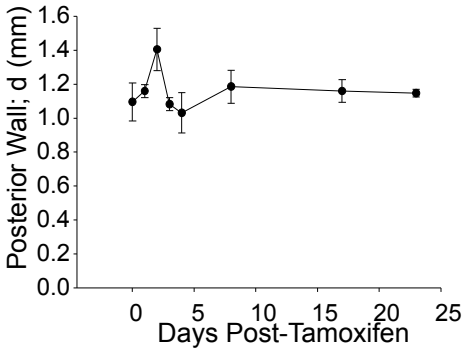



## Mouse 45 M

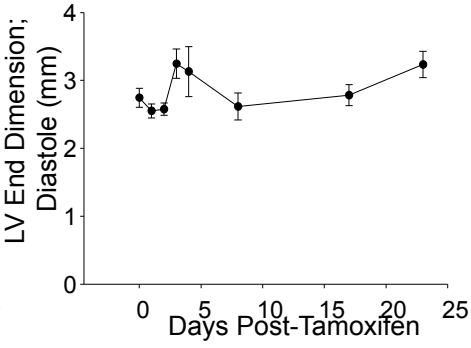
### Anterior Wall; Diastole



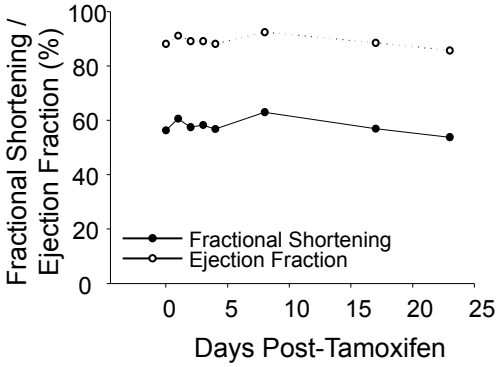

### Posterior Wall; Diastole



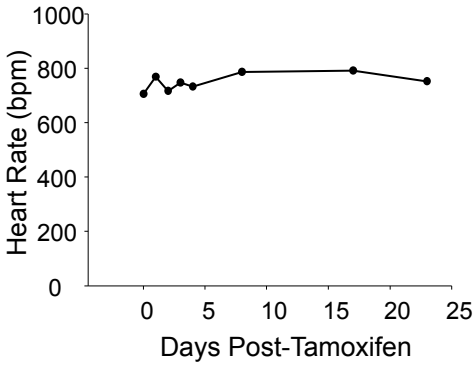

### LVID; Diastole




### Systolic Function (%)



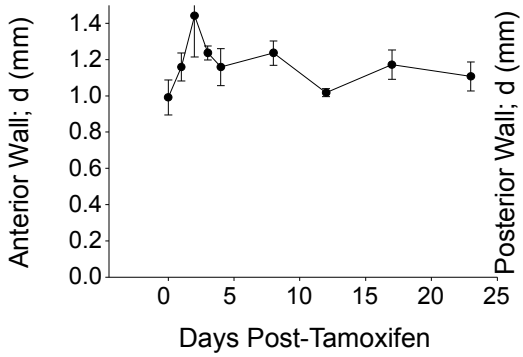

### Heart Rate



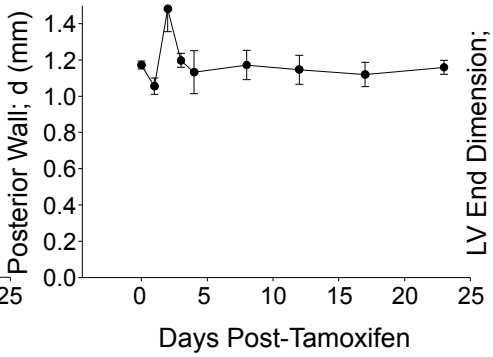
## Mouse 48 M

# Grp 1 Brm-- /flx/flx No Tg Chow Diet

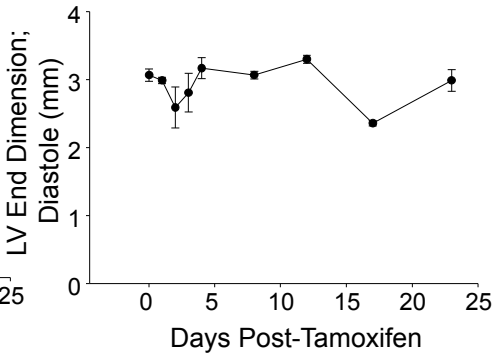
### Anterior Wall; Diastole



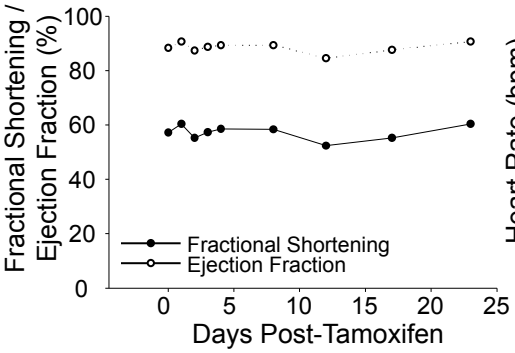

### Posterior Wall; Diastole



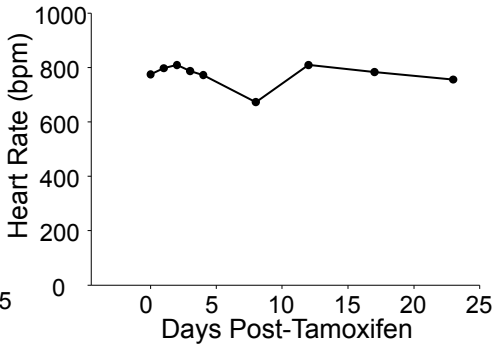

### LVID; Diastole




### Systolic Function (%)

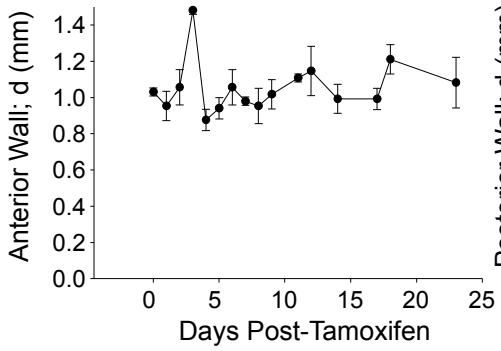



### Heart Rate

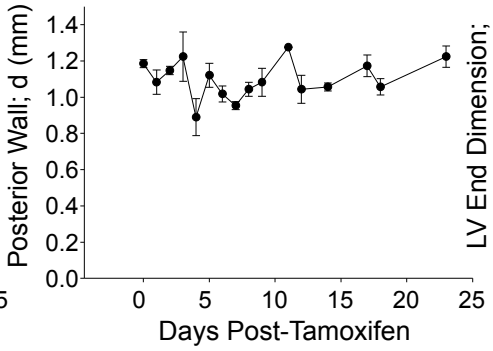



## Mouse 49 F

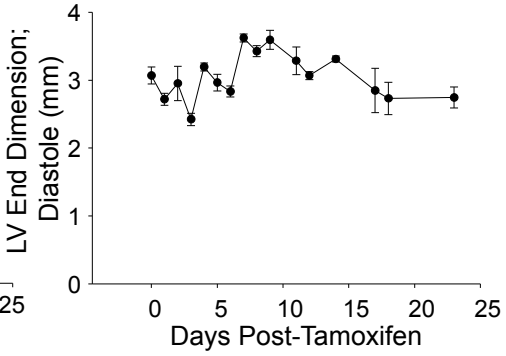
### Anterior Wall; Diastole



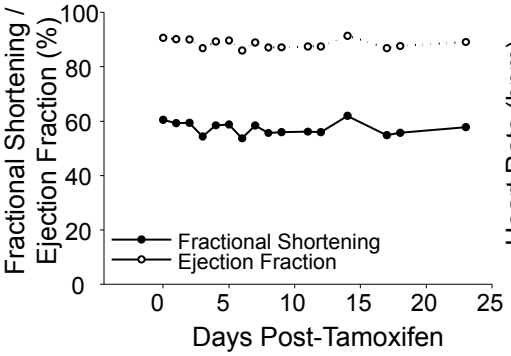

### Posterior Wall; Diastole



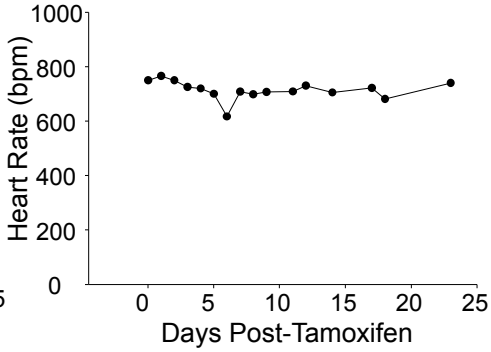

### LVID; Diastole




### Systolic Function (%)



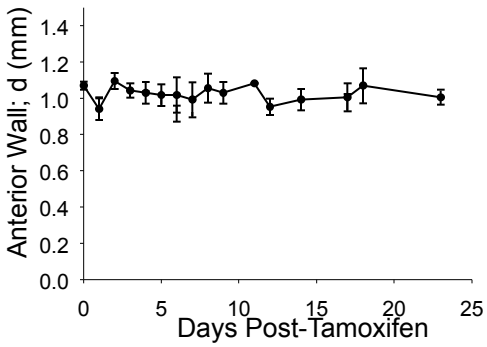

### Heart Rate



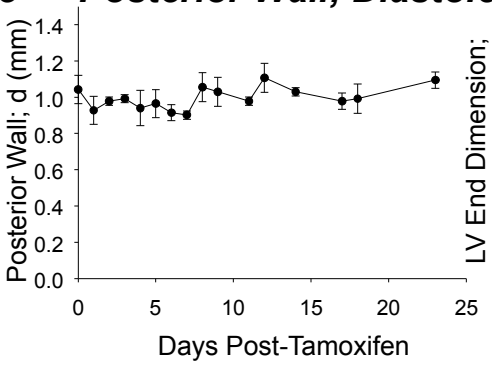
# Mouse 50 F

# Grp 1 Brm-- /flx/flx No Tg Chow Diet

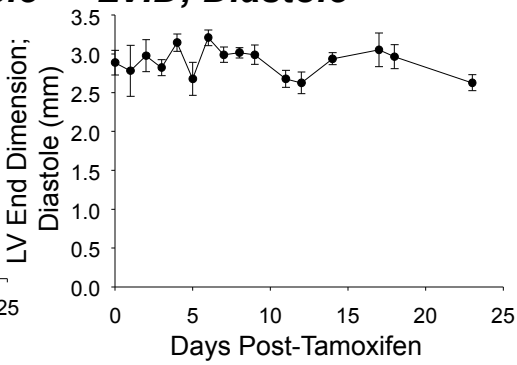
## Anterior Wall; Diastole



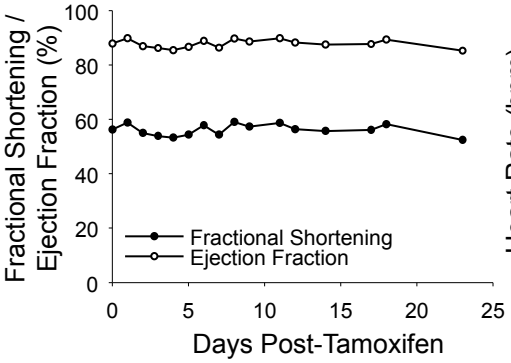

## Posterior Wall; Diastole



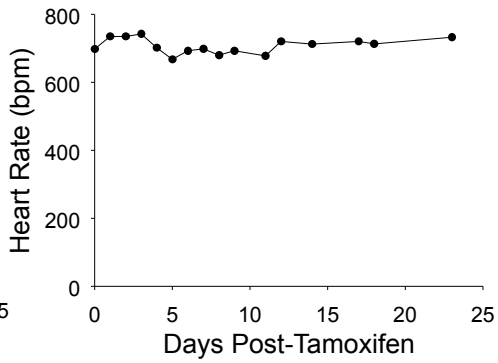

## LVID; Diastole




## Systolic Function (%)



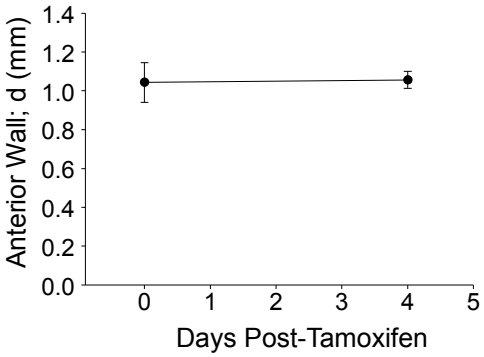

## Heart Rate



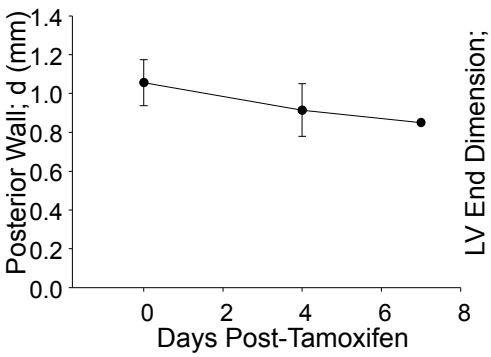
## Mouse 20 M

## Grp 2 Brm-/- flx/flx No Tg +TAM

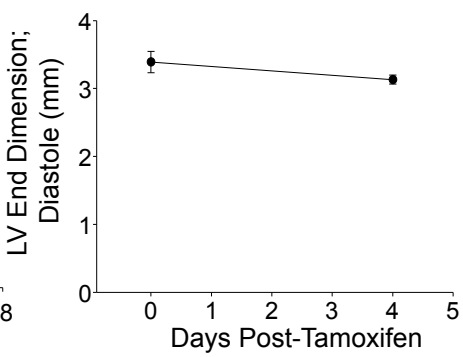
### Anterior Wall; Diastole



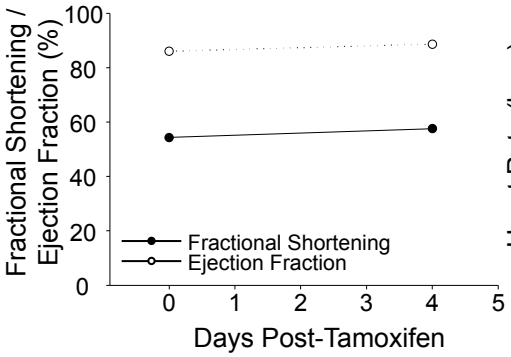

### Posterior Wall; Diastole



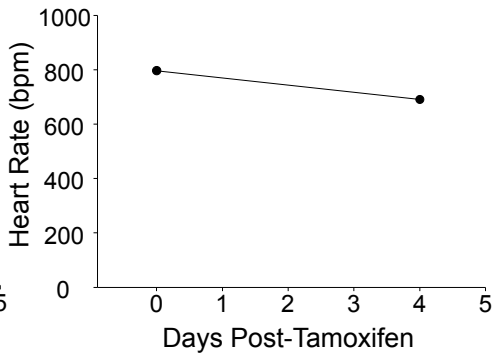

### LVID; Diastole




### Systolic Function (%)

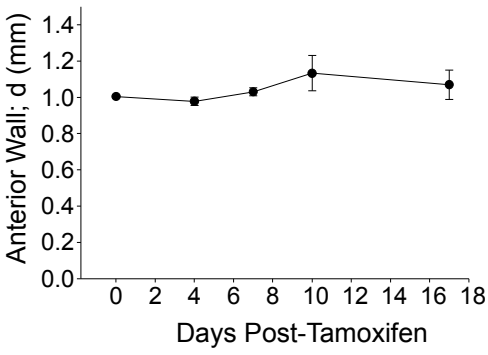



### Heart Rate

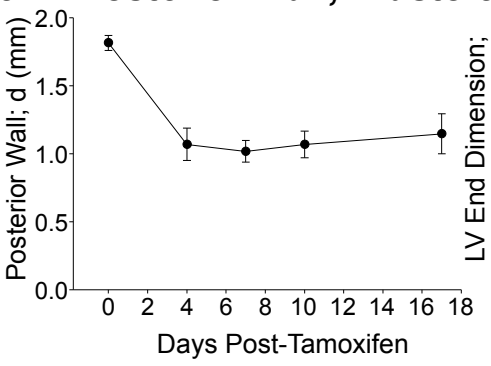



## Mouse 21 M

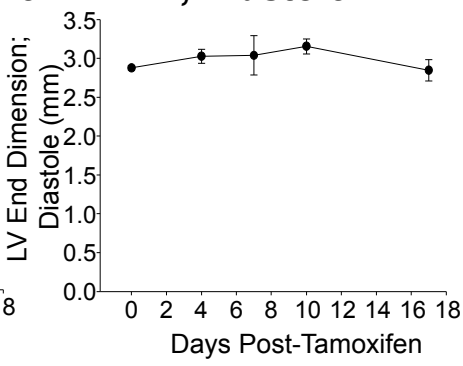
### Anterior Wall; Diastole



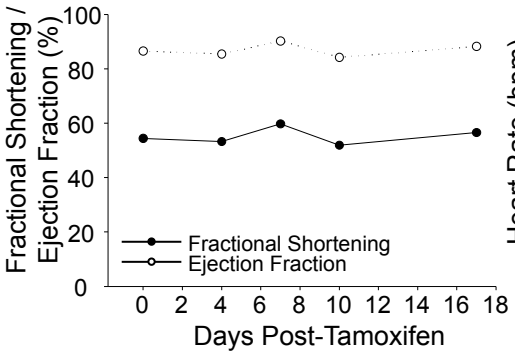

### Posterior Wall; Diastole



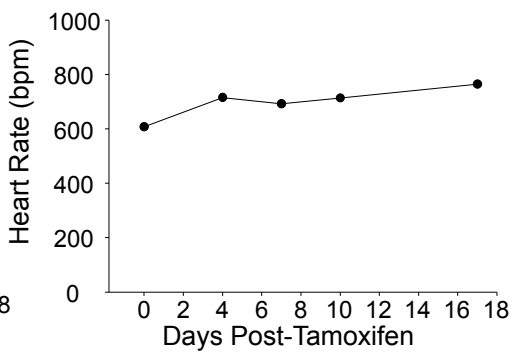

### LVID; Diastole




### Systolic Function (%)

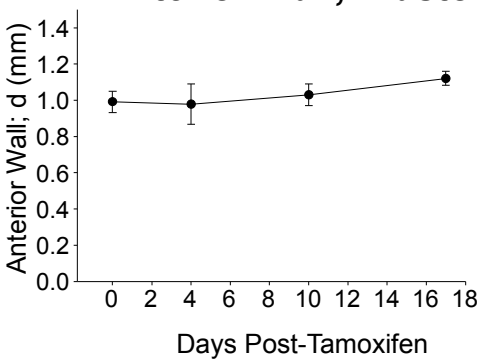



### Heart Rate

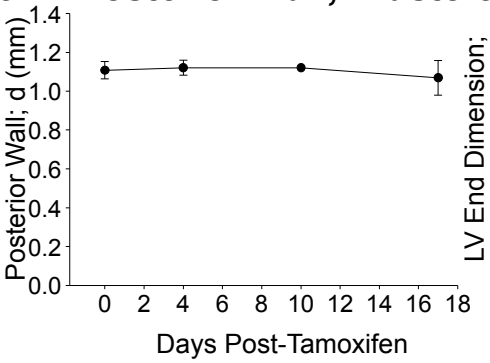


## *Mouse 26 M* *Grp 2 Brm-/- flx/flx No Tg +TAM*

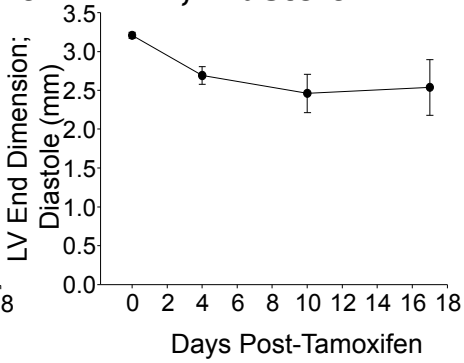
### *Anterior Wall; Diastole*



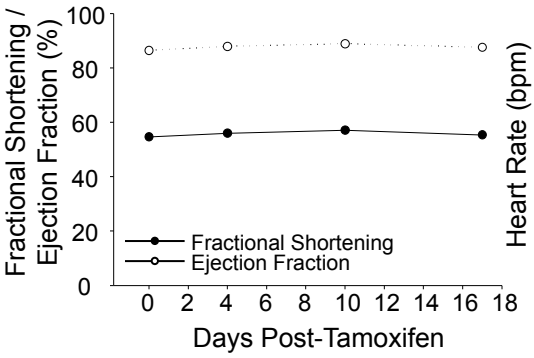

### *Posterior Wall; Diastole*



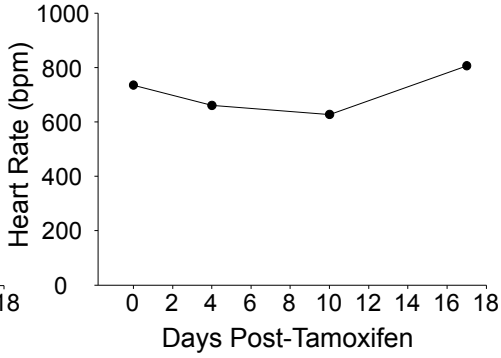

### *LVID; Diastole*




### *Systolic Function (%)*



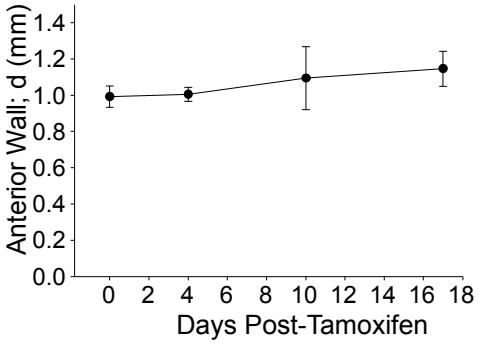

### *Heart Rate*



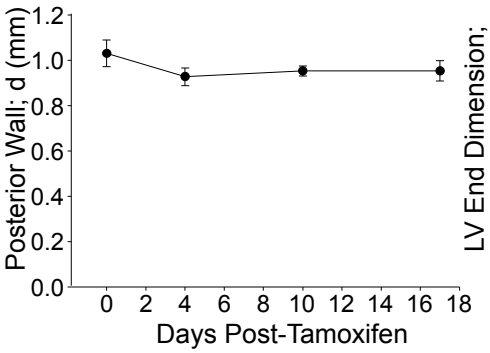
## Mouse 28 F

## Grp 2 Brm-/- flx/flx No Tg +TAM

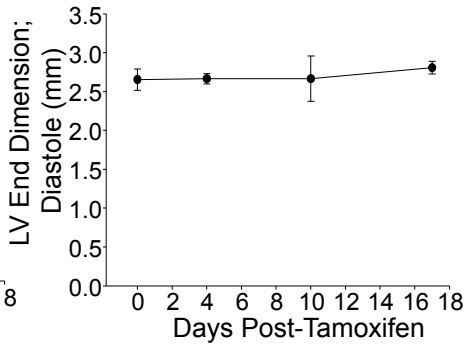
### Anterior Wall; Diastole



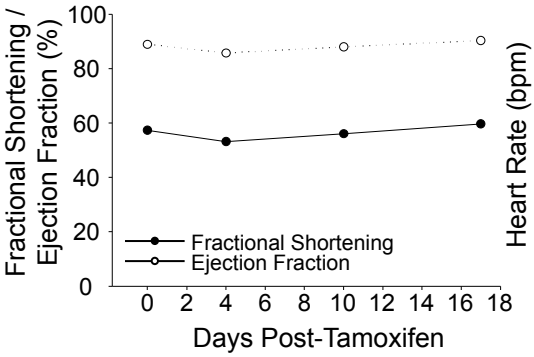

### Posterior Wall; Diastole



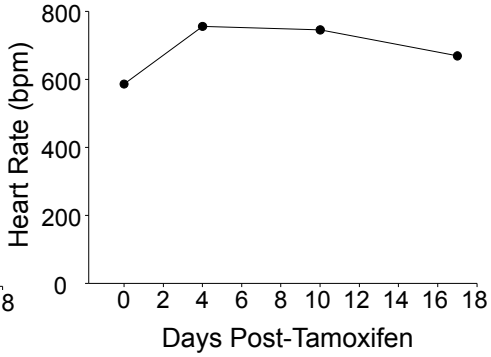

### LVID; Diastole




### Systolic Function (%)

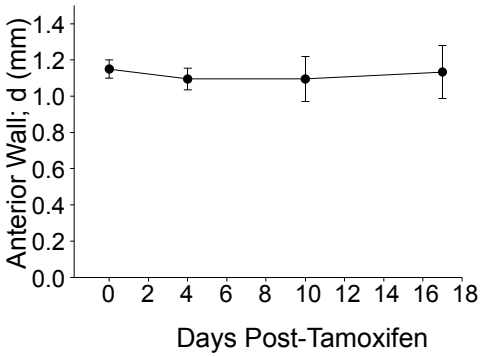



### Heart Rate

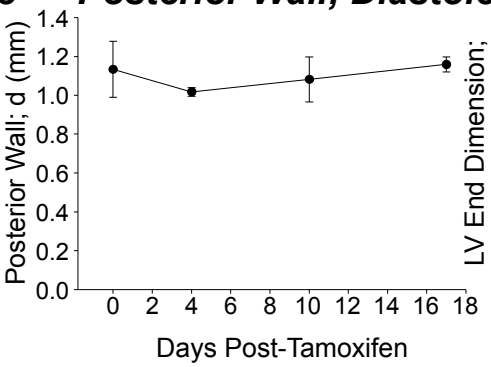



## Mouse 32 M

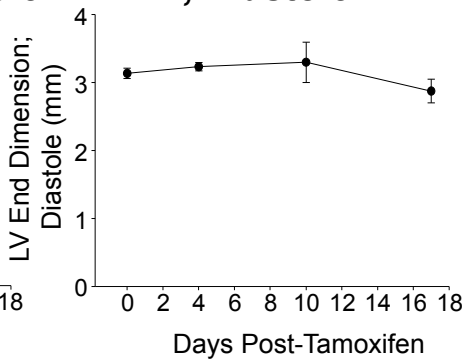
### Anterior Wall; Diastole



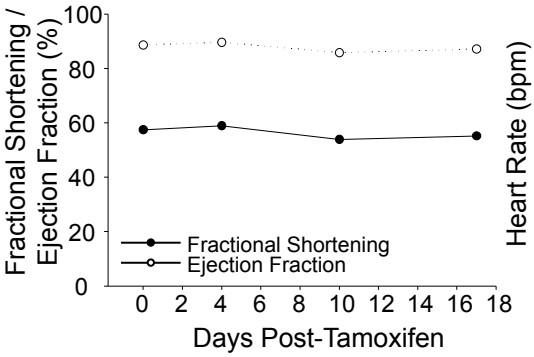

### Posterior Wall; Diastole



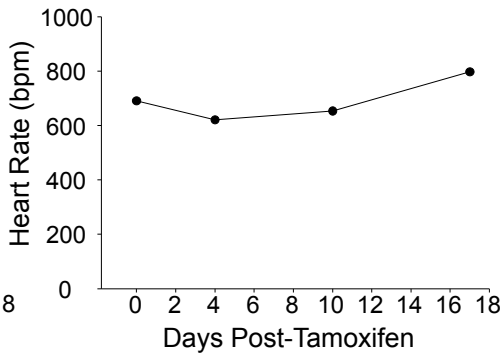

### LVID; Diastole




### Systolic Function (%)



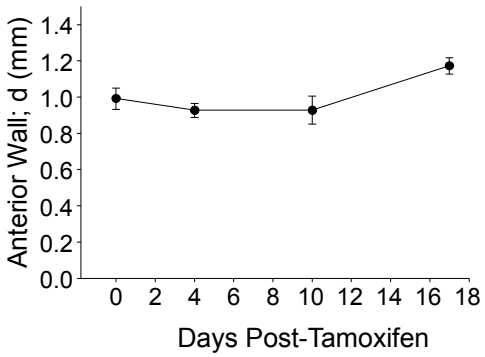

### Heart Rate



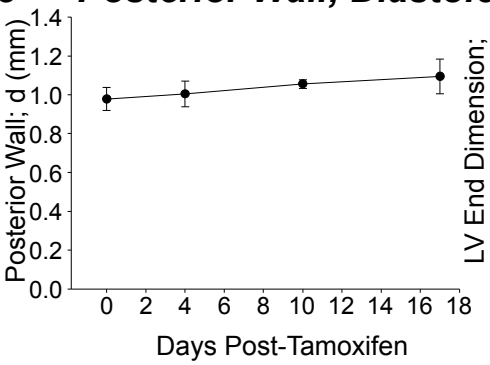
# Mouse 34 M

# Grp 2 Brm-/- flx/flx No Tg +TAM

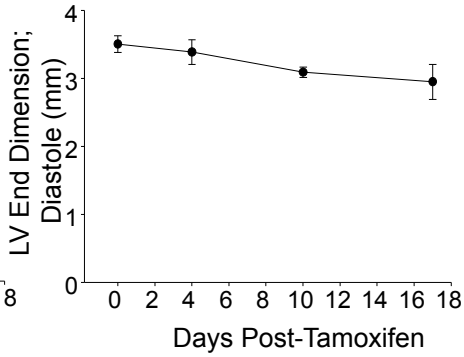
### Anterior Wall; Diastole



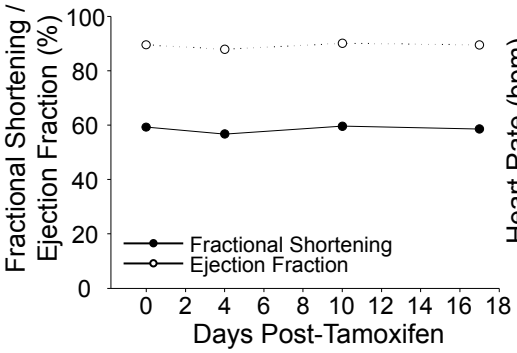

### Posterior Wall; Diastole



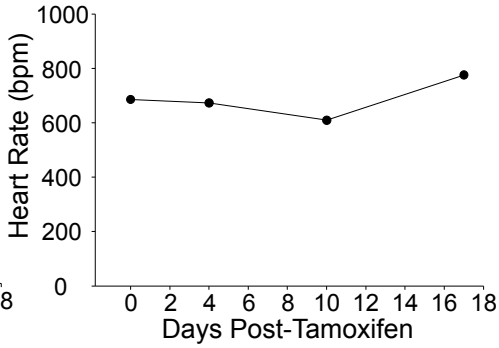

### LVID; Diastole




### Systolic Function (%)

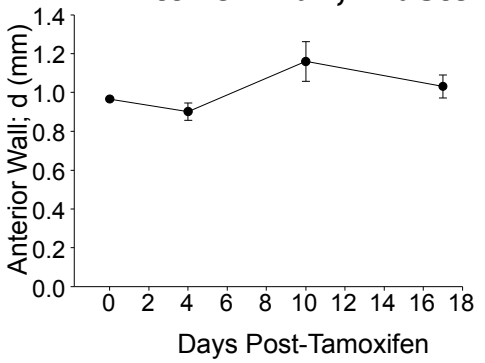



### Heart Rate

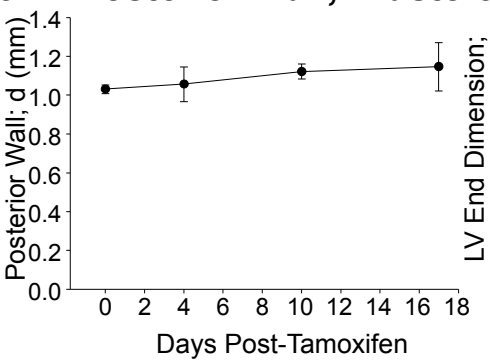



# Mouse 35 M

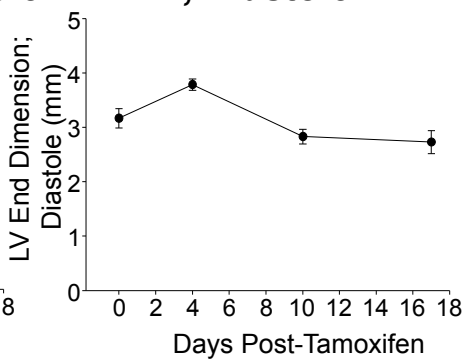
### Anterior Wall; Diastole



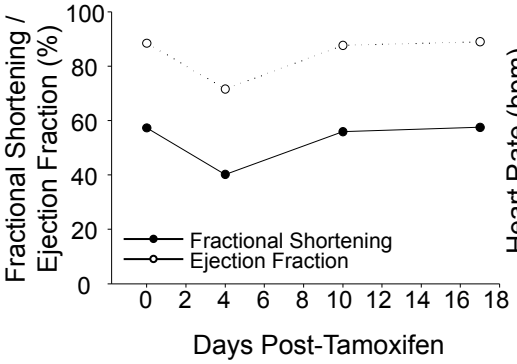

### Posterior Wall; Diastole



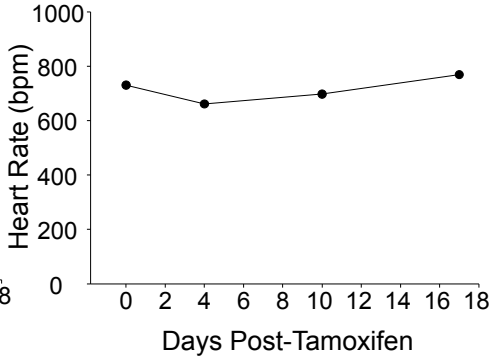

### LVID; Diastole




### Systolic Function (%)



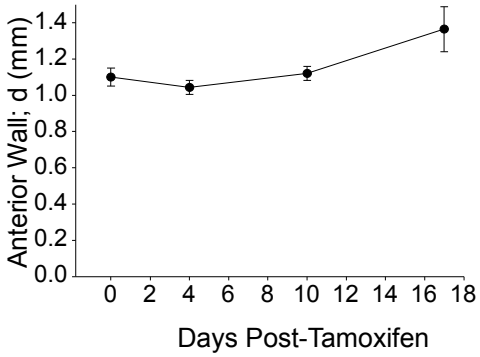

### Heart Rate



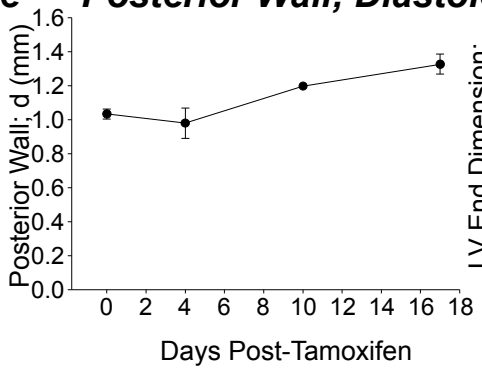
## Mouse 36 M

## Grp 2 Brm-/- flx/flx No Tg +TAM

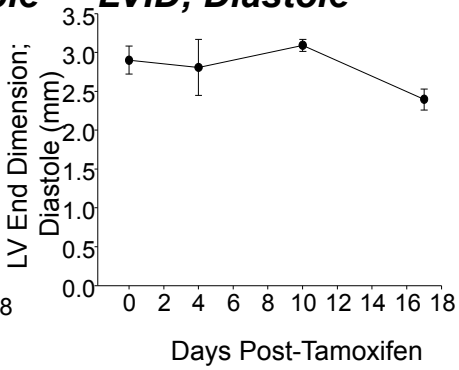
### Anterior Wall; Diastole



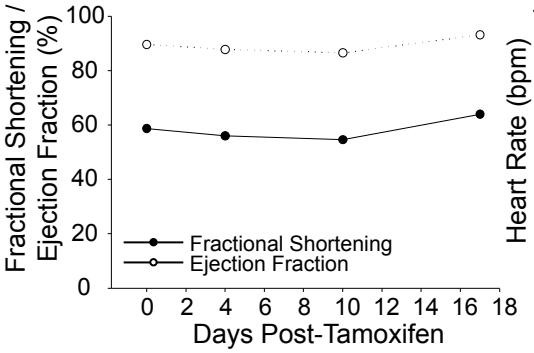

### Posterior Wall; Diastole



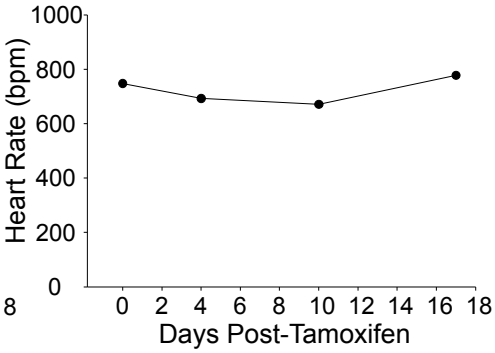

### LVID; Diastole




### Systolic Function (%)

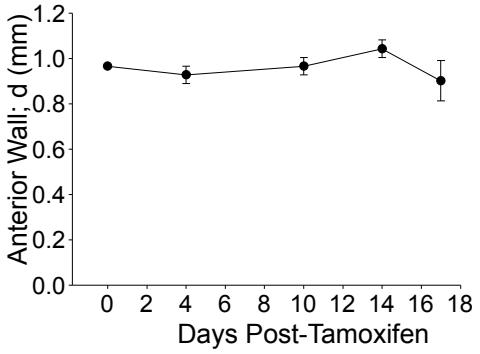



### Heart Rate

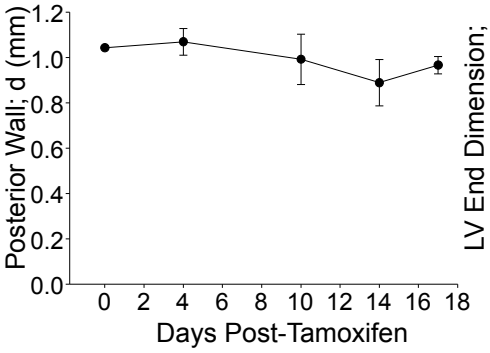



## Mouse 40 F

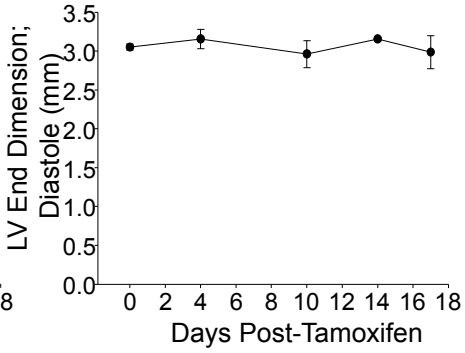
### Anterior Wall; Diastole



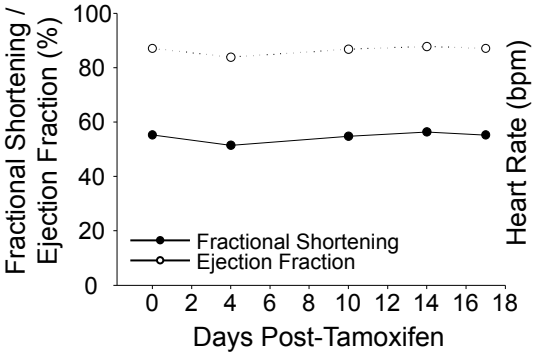

### Posterior Wall; Diastole



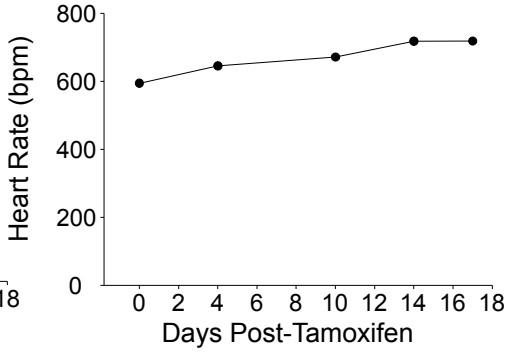

### LVID; Diastole




### Systolic Function (%)



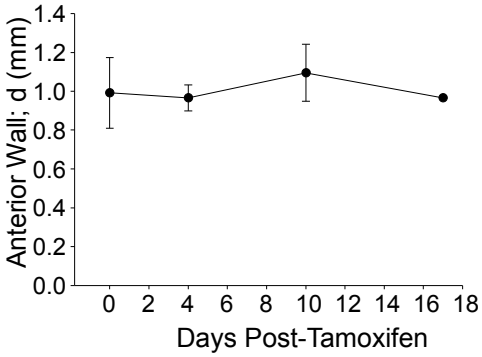

### Heart Rate



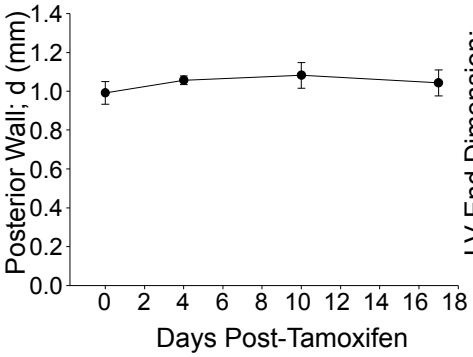
## Mouse 29 F

## Grp 3 Brm-/- flx/flx Brg1 Tg+ Chow

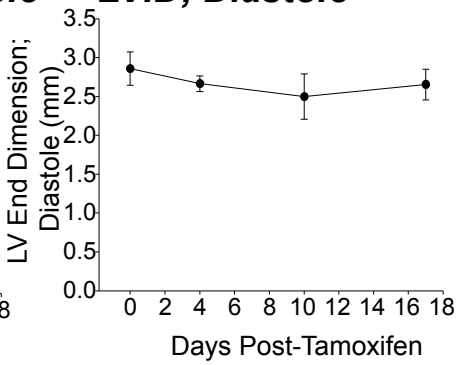
### Anterior Wall; Diastole



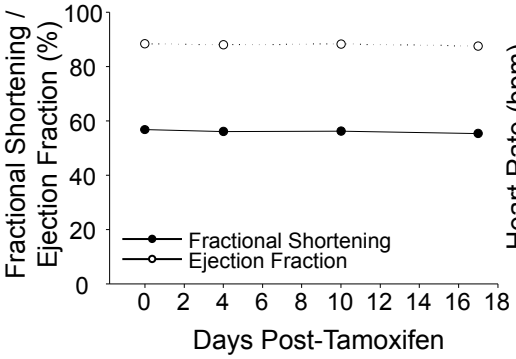

### Posterior Wall; Diastole



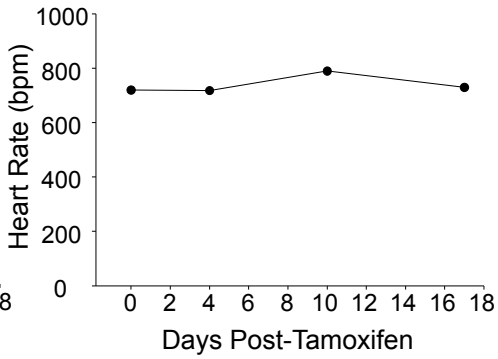

### LVID; Diastole




### Systolic Function (%)

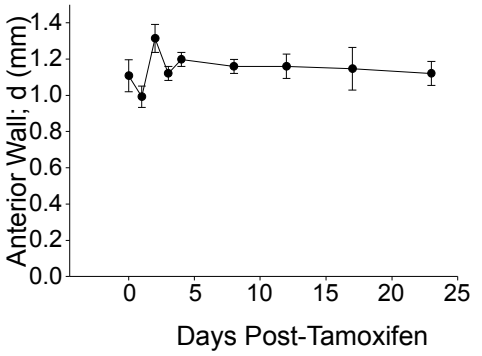



### Heart Rate

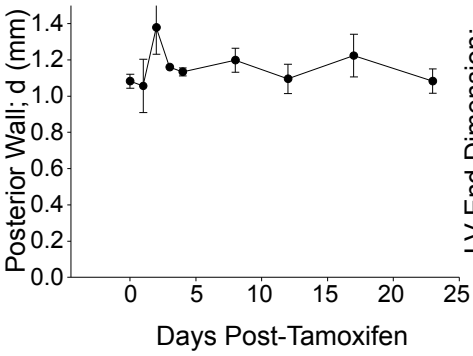



## Mouse 47 M

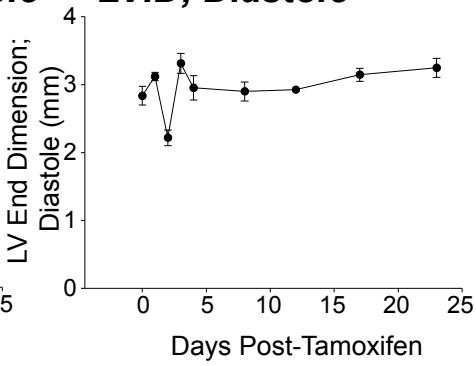
### Anterior Wall; Diastole



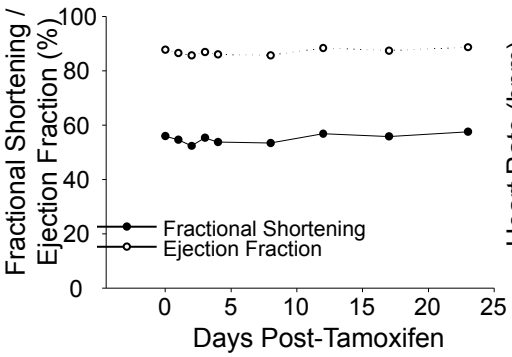

### Posterior Wall; Diastole



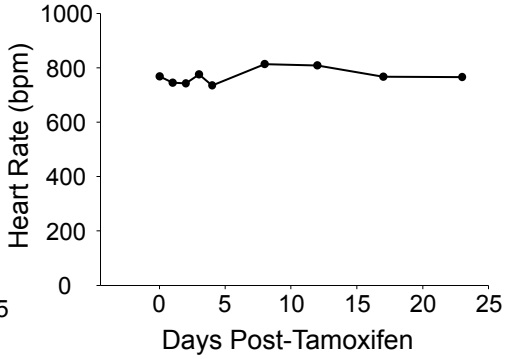

### LVID; Diastole




### Systolic Function (%)



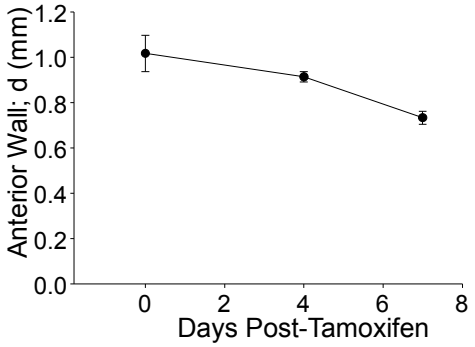

### Heart Rate



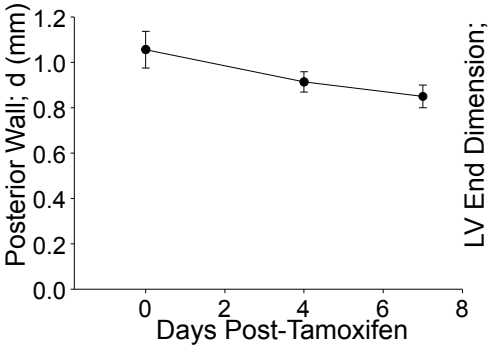
# Mouse 18 M

# Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

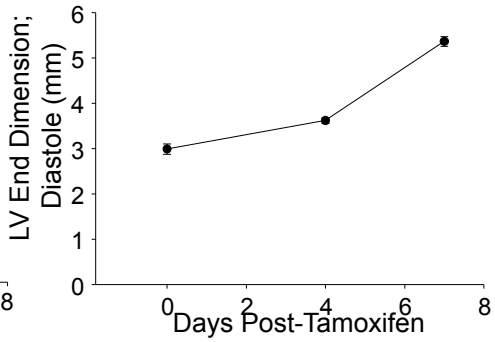
### Anterior Wall; Diastole



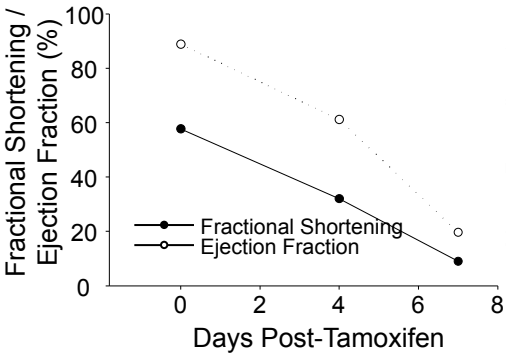

### Posterior Wall; Diastole



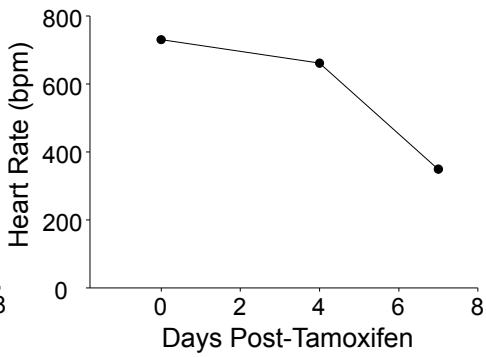

### LVID; Diastole




### Systolic Function (%)

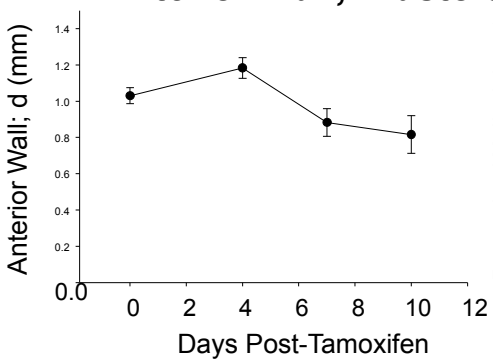



### Heart Rate

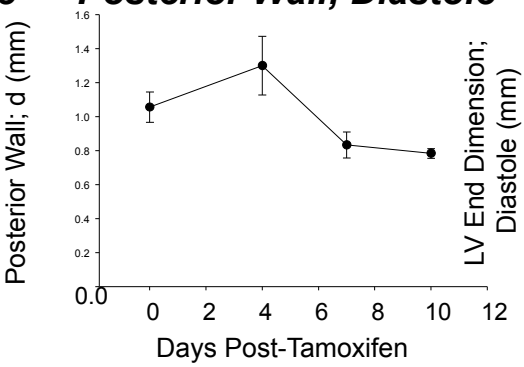



# Mouse 19 M

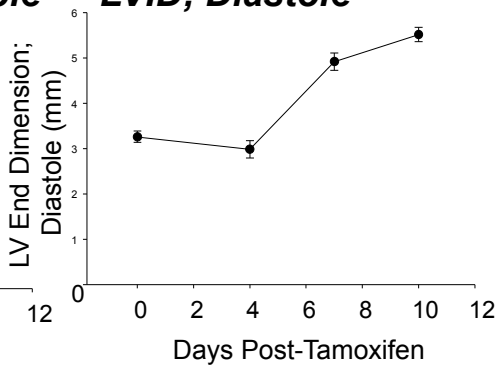
### Anterior Wall; Diastole



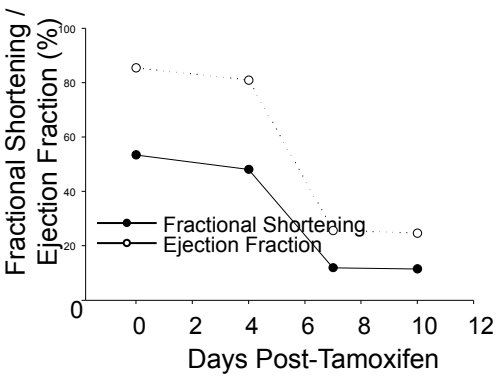

### Posterior Wall; Diastole



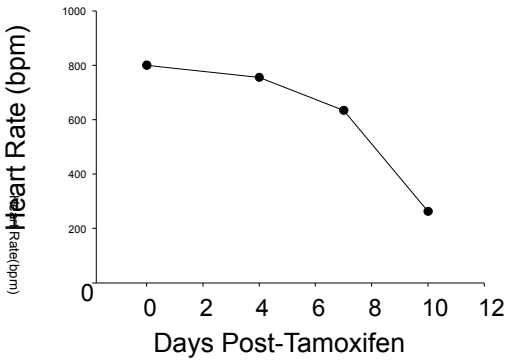

### LVID; Diastole




### Systolic Function (%)



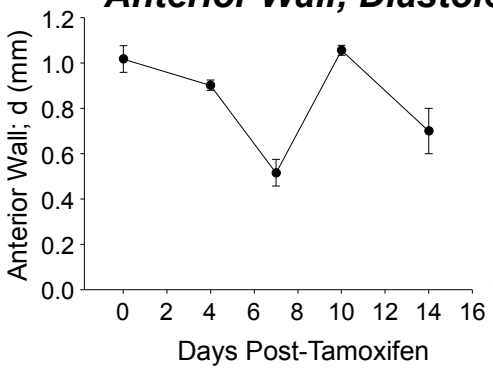

### Heart Rate



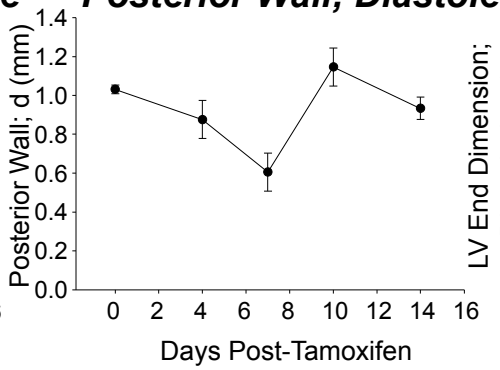
# Mouse 23 F

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

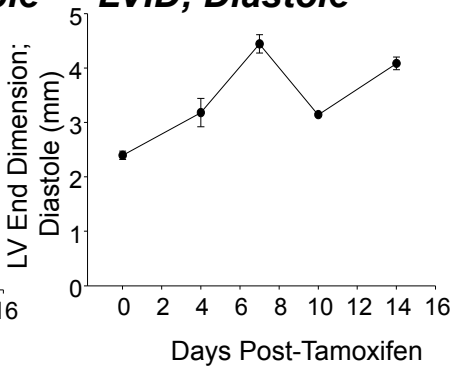
### Anterior Wall; Diastole



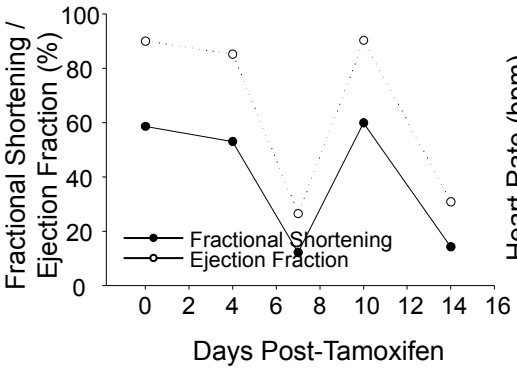

### Posterior Wall; Diastole



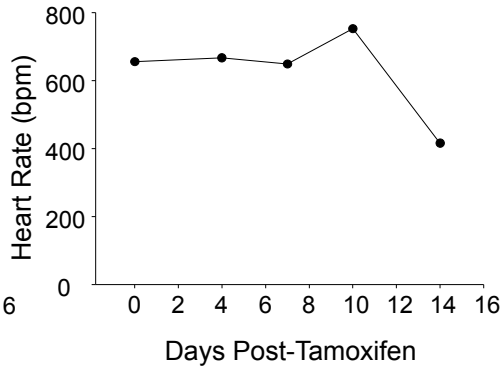

### LVID; Diastole




### Systolic Function (%)

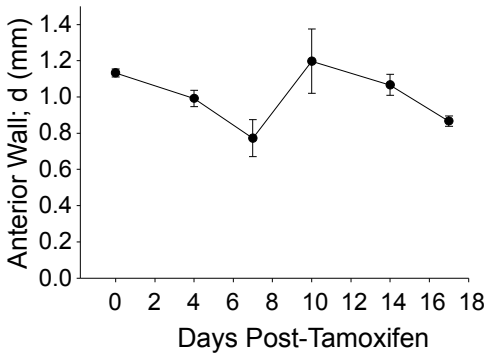



### Heart Rate

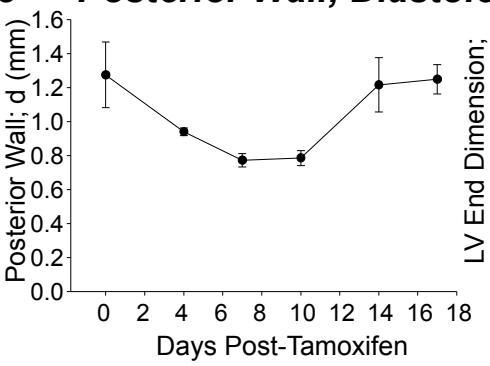



# Mouse 24 F

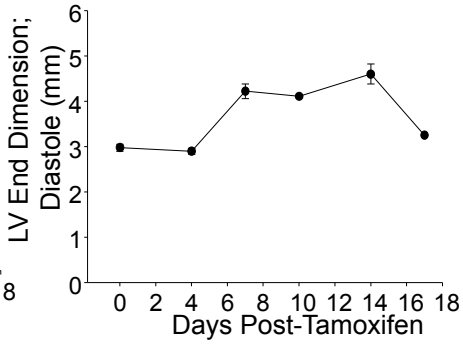
### Anterior Wall; Diastole



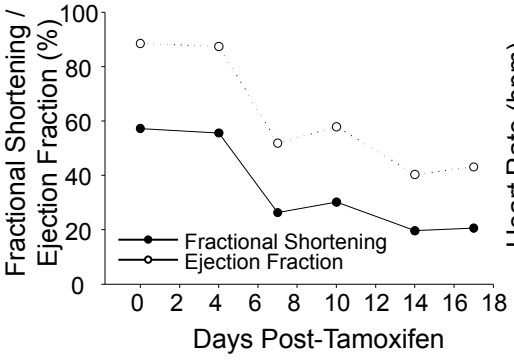

### Posterior Wall; Diastole



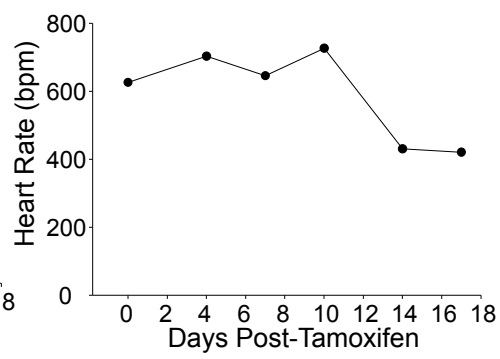

### LVID; Diastole




### Systolic Function (%)



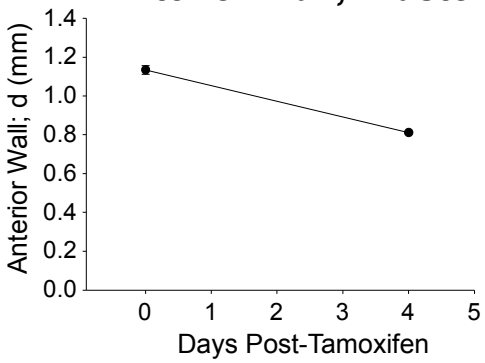

### Heart Rate



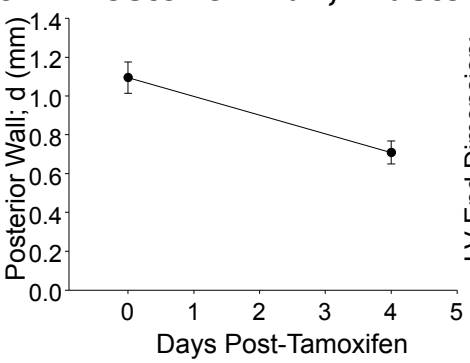
# Mouse 33 M

# Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

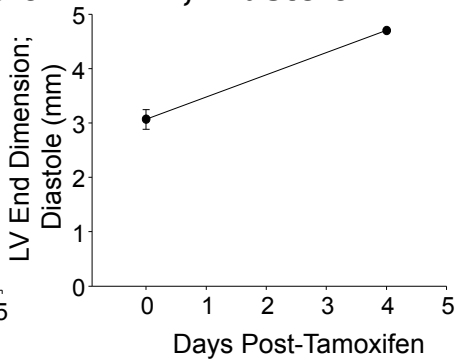
### Anterior Wall; Diastole



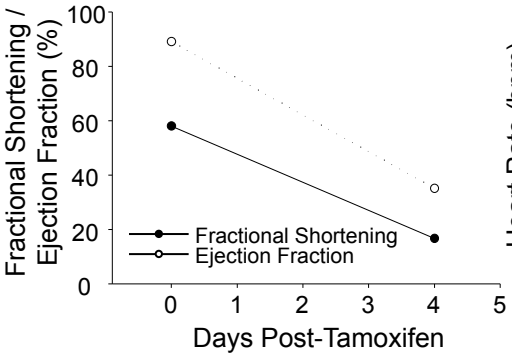

### Posterior Wall; Diastole



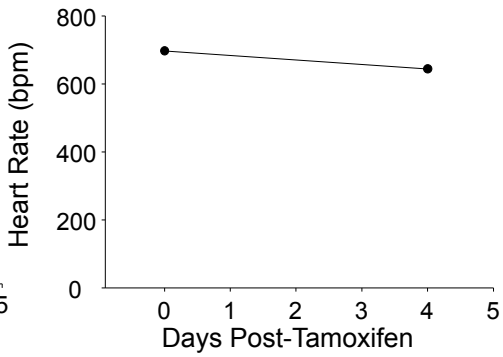

### LVID; Diastole




### Systolic Function (%)

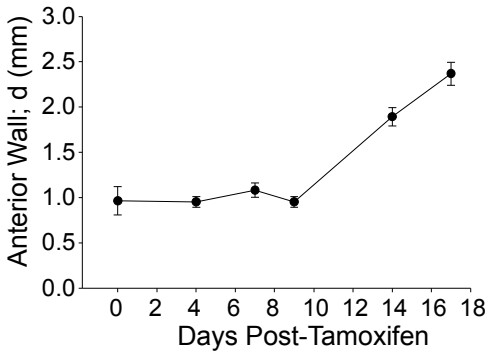



### Heart Rate

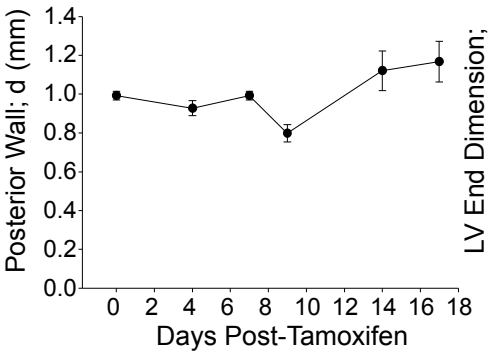



# Mouse 37 F

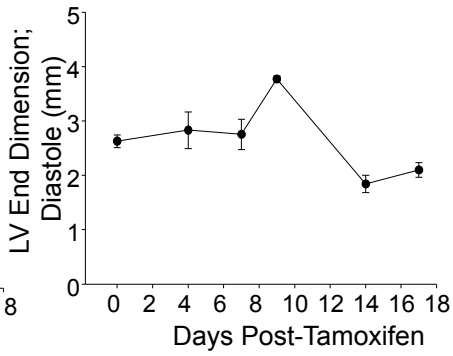
### Anterior Wall; Diastole



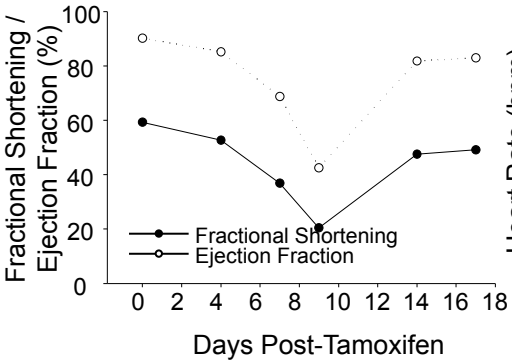

### Posterior Wall; Diastole



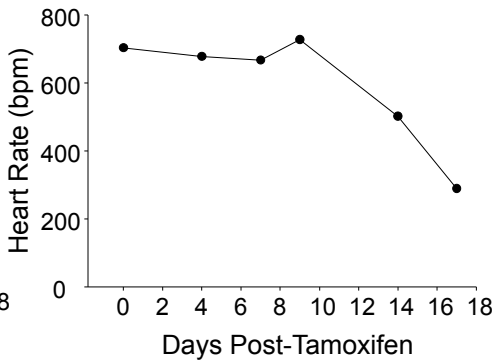

### LVID; Diastole




### Systolic Function (%)



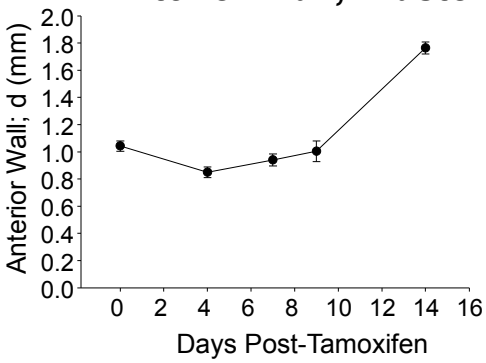

### Heart Rate



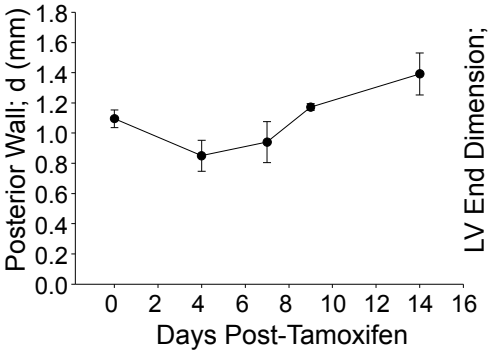
## Mouse 38 F

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

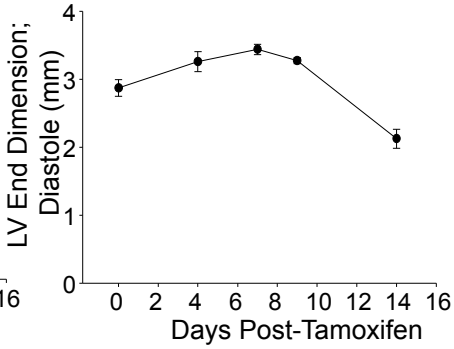
### Anterior Wall; Diastole



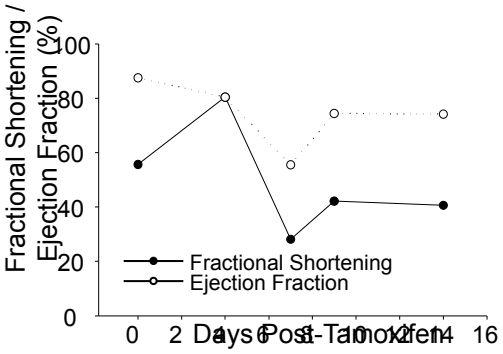

### Posterior Wall; Diastole



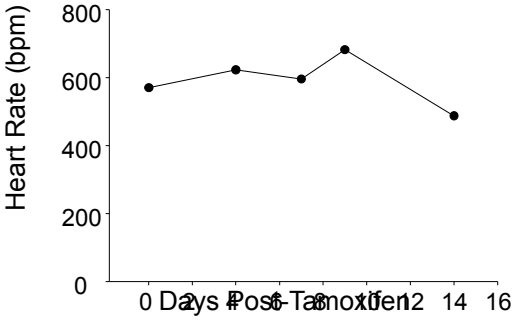

### LVID; Diastole




### Systolic Function (%)

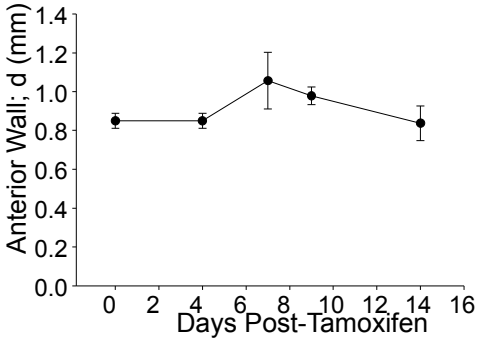



### Heart Rate

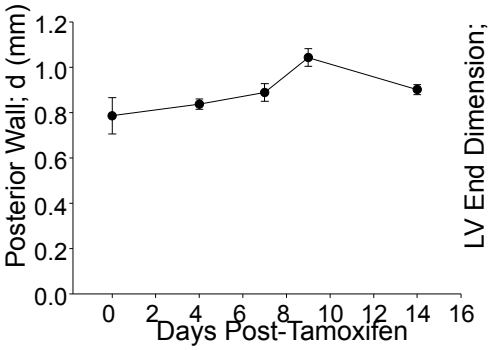



## Mouse 39 F

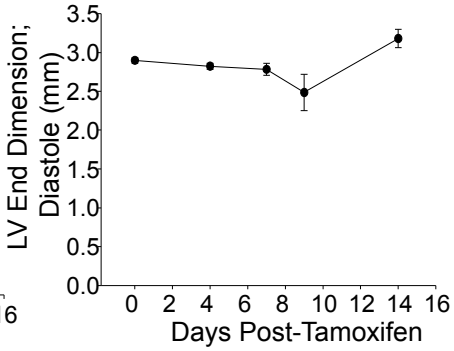
### Anterior Wall; Diastole



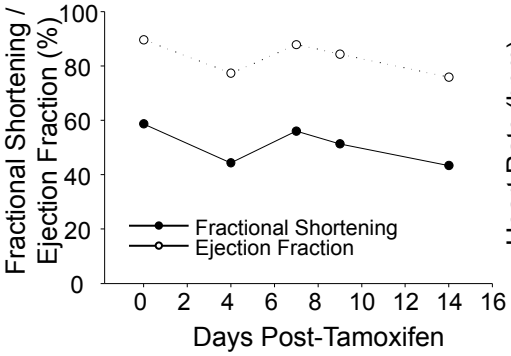

### Posterior Wall; Diastole



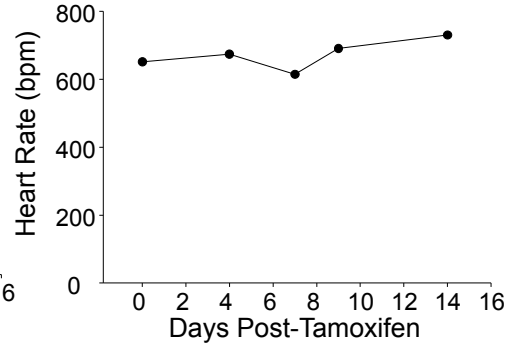

### LVID; Diastole




### Systolic Function (%)



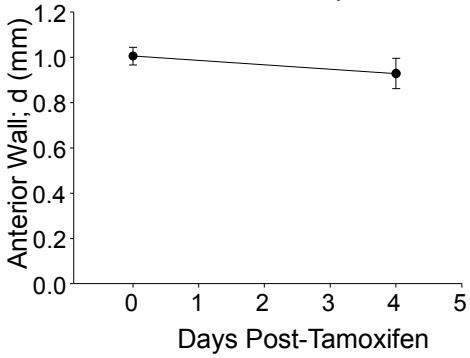

### Heart Rate



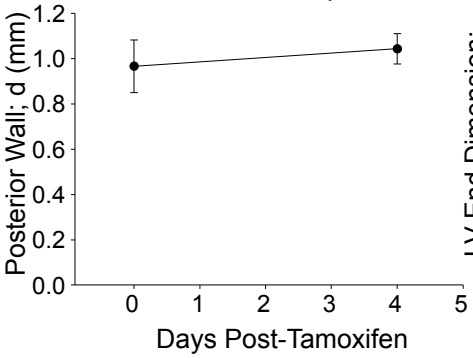
## Mouse 41 F

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

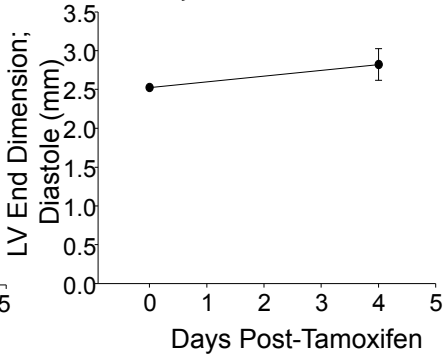
### Anterior Wall; Diastole



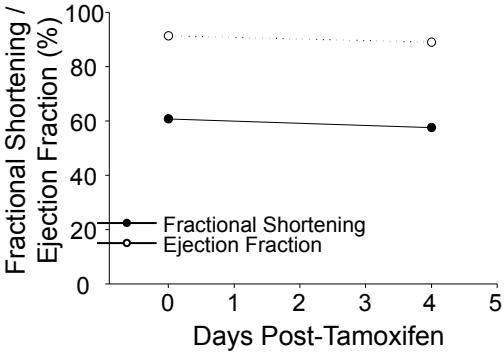

### Posterior Wall; Diastole



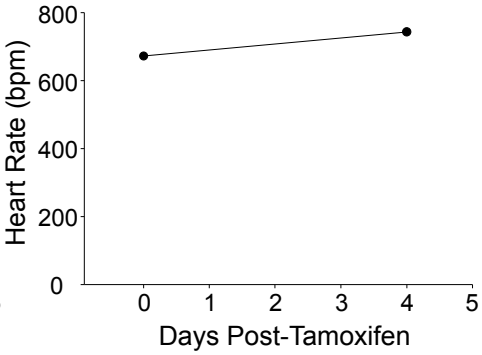

### LVID; Diastole




### Systolic Function (%)

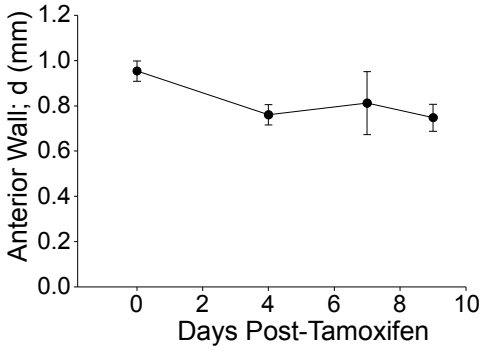



### Heart Rate

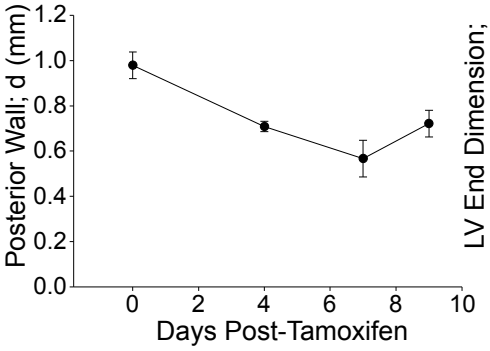



## Mouse 43 F

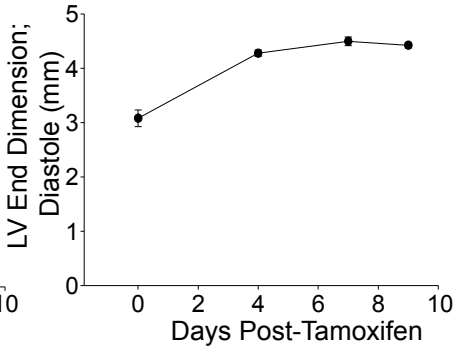
### Anterior Wall; Diastole



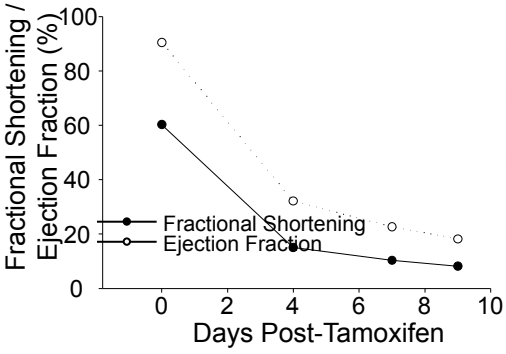

### Posterior Wall; Diastole



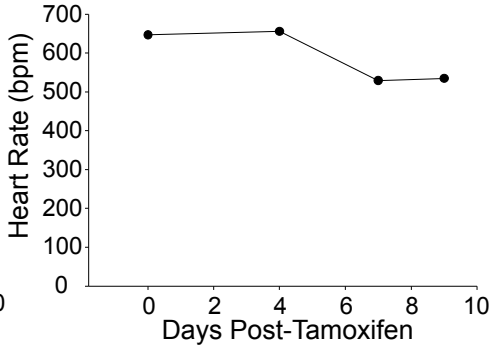

### LVID; Diastole




### Systolic Function (%)



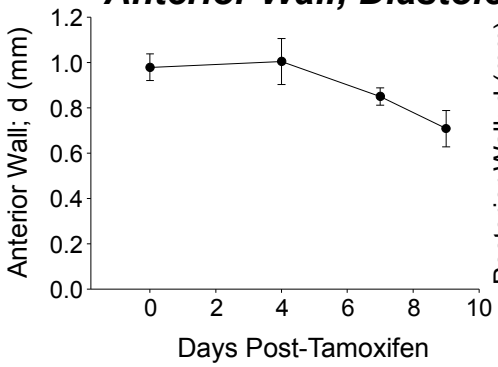

### Heart Rate



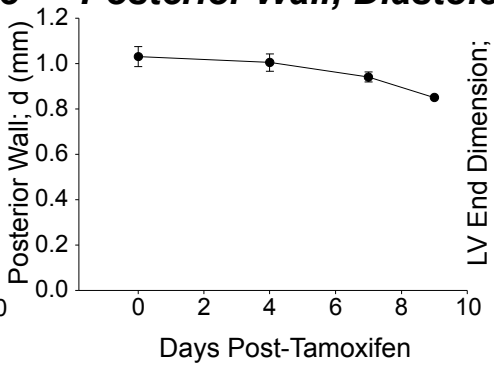
# Mouse 44 F

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

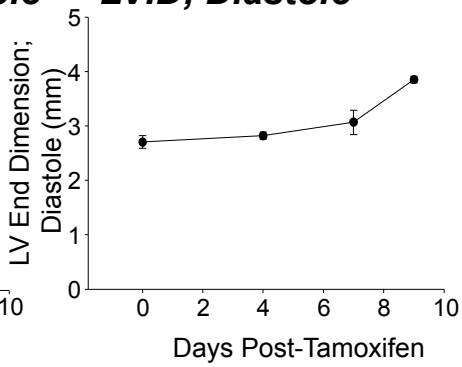
### Anterior Wall; Diastole



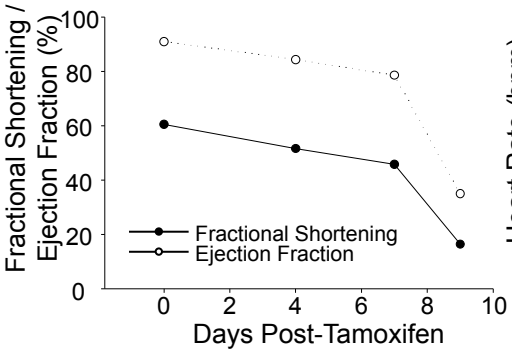

### Posterior Wall; Diastole



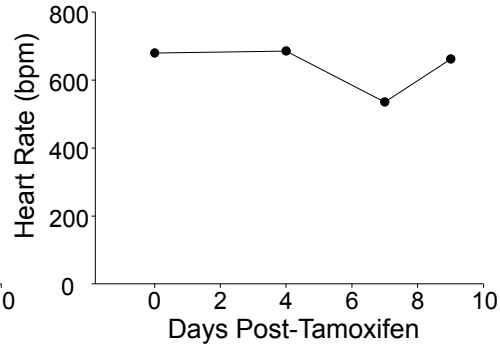

### LVID; Diastole




### Systolic Function (%)

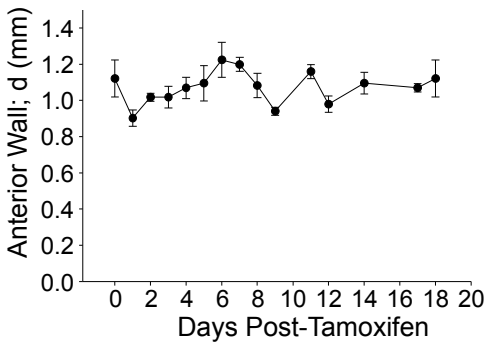



### Heart Rate

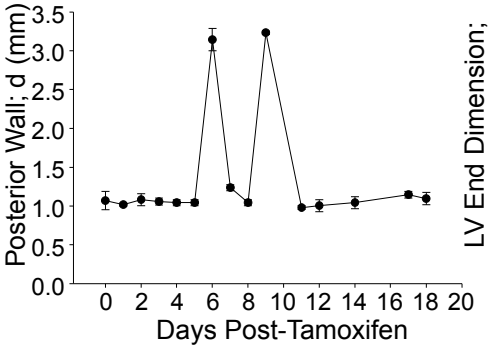



# Mouse 55 F

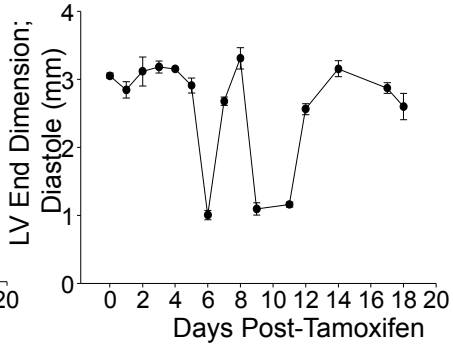
### Anterior Wall; Diastole



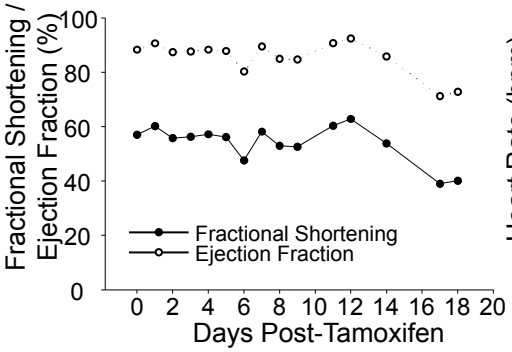

### Posterior Wall; Diastole



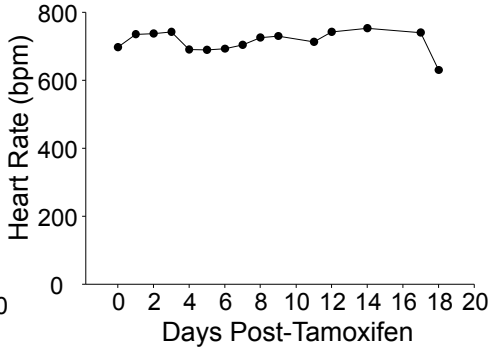

### LVID; Diastole




### Systolic Function (%)



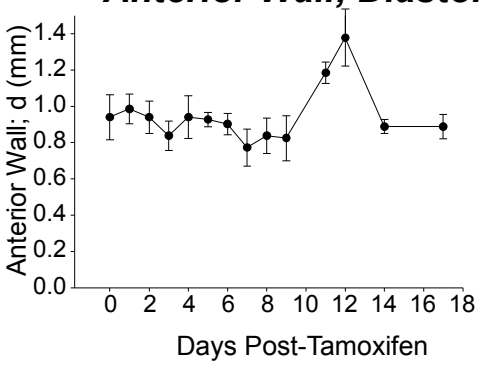

### Heart Rate



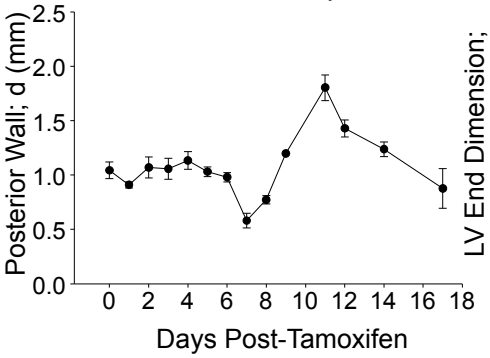
## Mouse 56 F

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

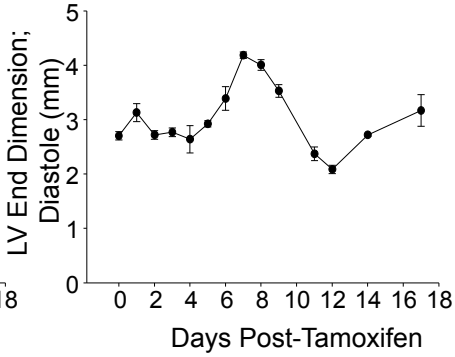
### Anterior Wall; Diastole



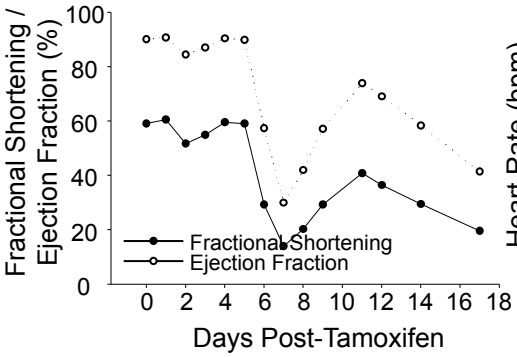

### Posterior Wall; Diastole



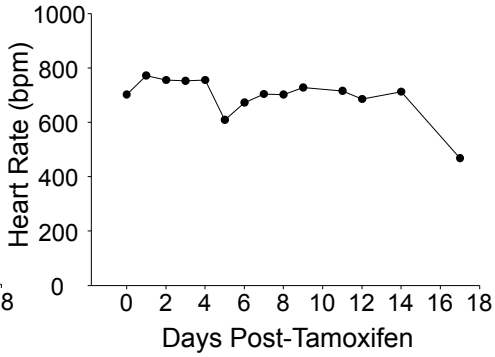

### LVID; Diastole




### Systolic Function (%)

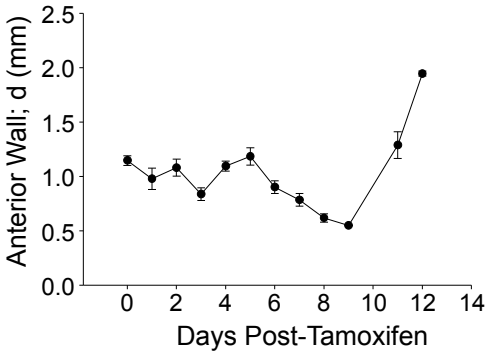



### Heart Rate

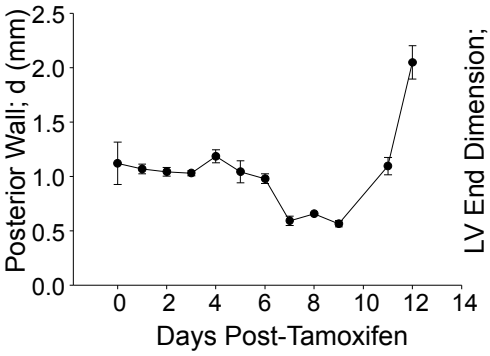



## Mouse 57 F

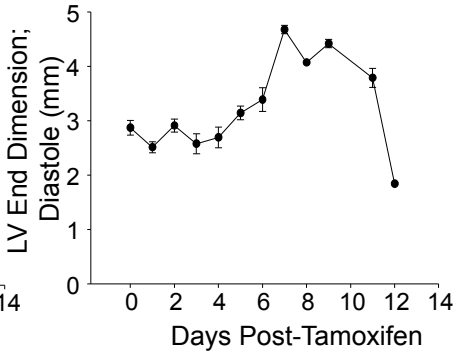
### Anterior Wall; Diastole



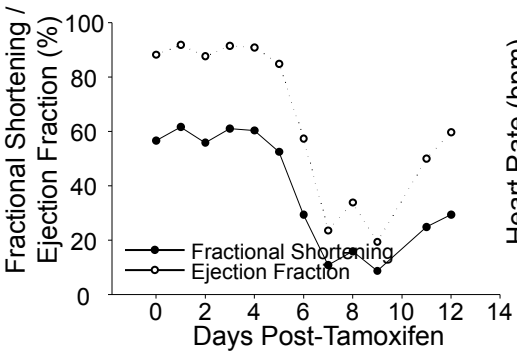

### Posterior Wall; Diastole



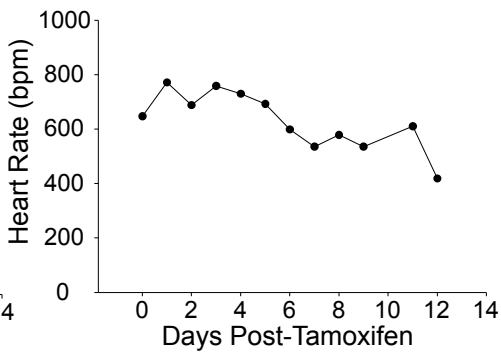

### LVID; Diastole




### Systolic Function (%)



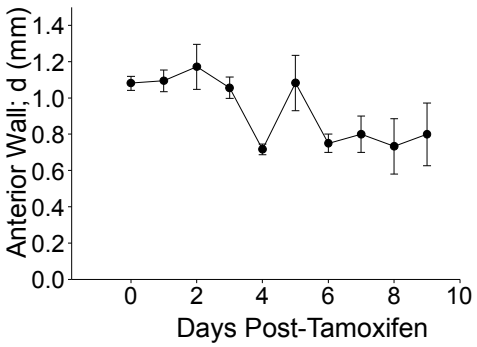

### Heart Rate



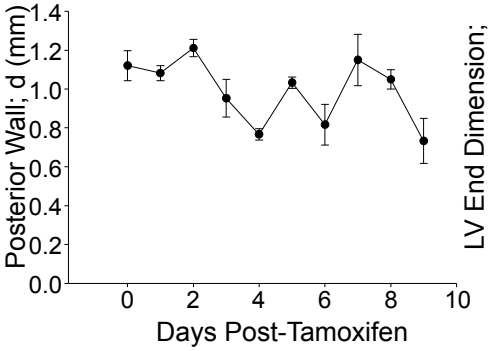
## Mouse 58 M

## Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

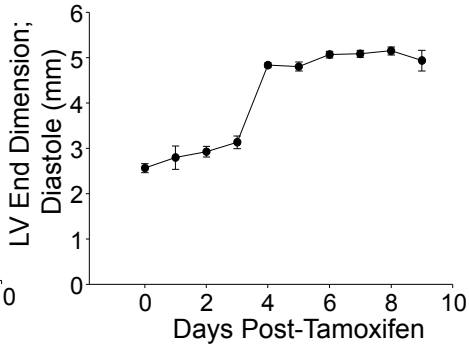
### Anterior Wall; Diastole



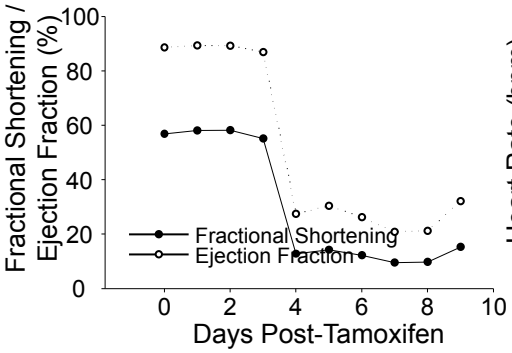

### Posterior Wall; Diastole



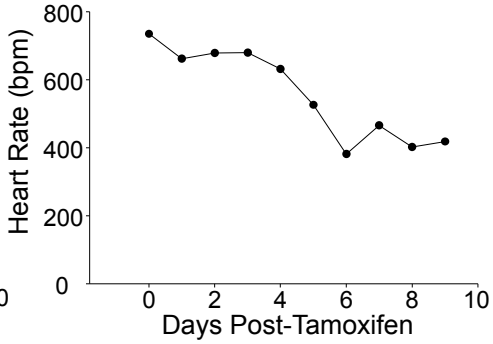

### LVID; Diastole




### Systolic Function (%)

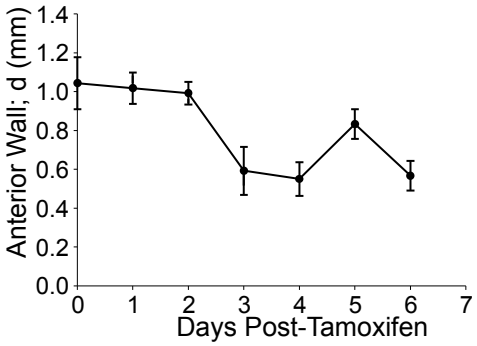



### Heart Rate

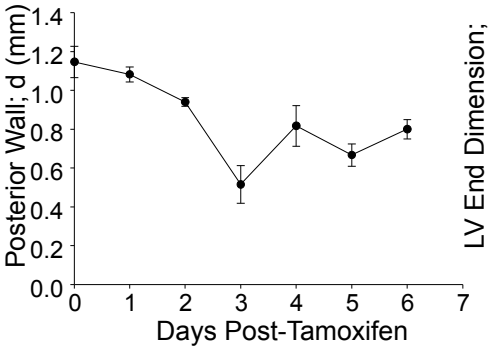



## Mouse 59 M

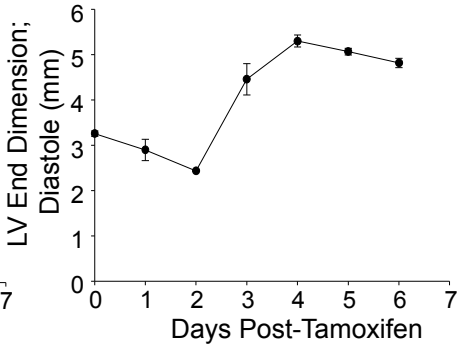
### Anterior Wall; Diastole



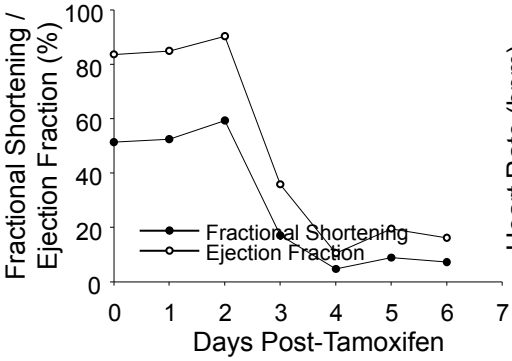

### Posterior Wall; Diastole



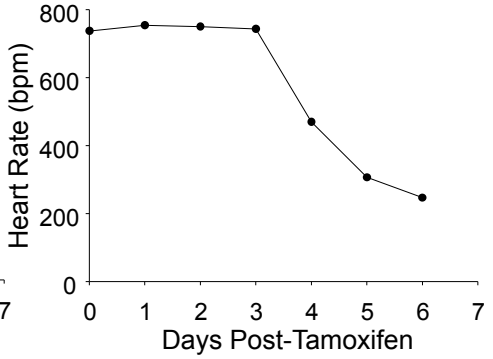

### LVID; Diastole




### Systolic Function (%)



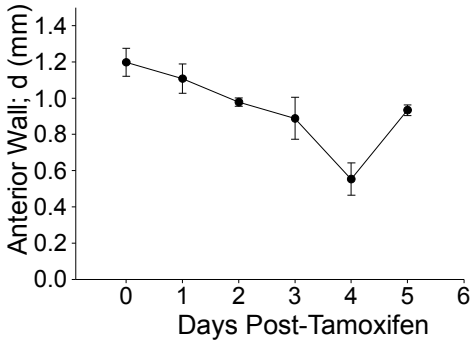

### Heart Rate



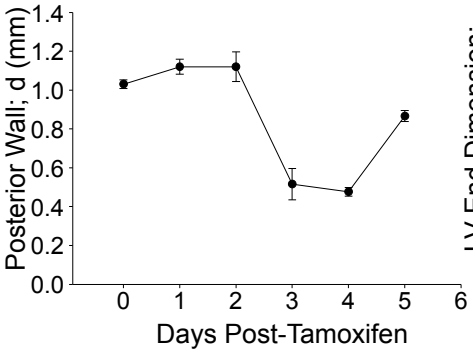
# Mouse 60 M

# Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

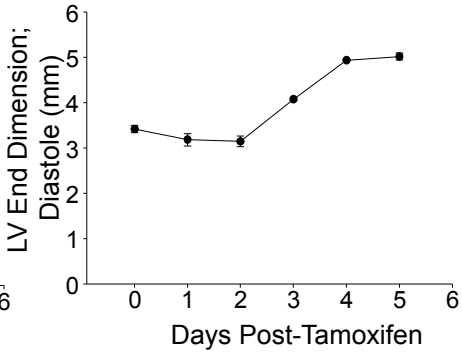
### Anterior Wall; Diastole



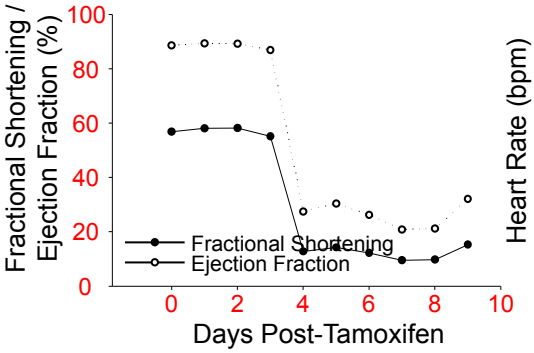

### Posterior Wall; Diastole



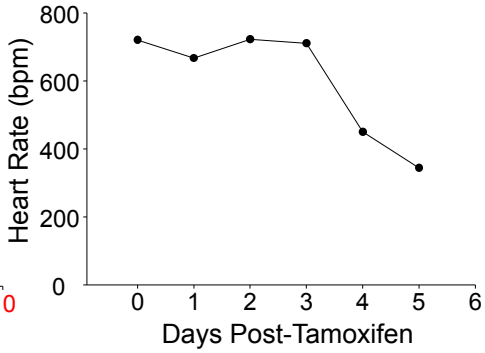

### LVID; Diastole




### Systolic Function (%)

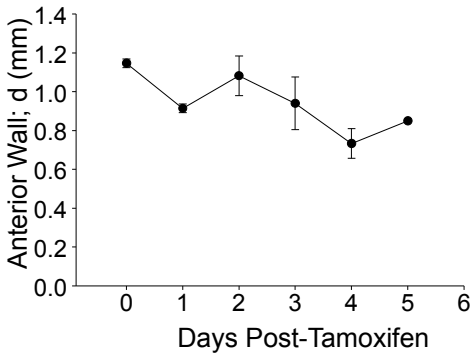



### Heart Rate

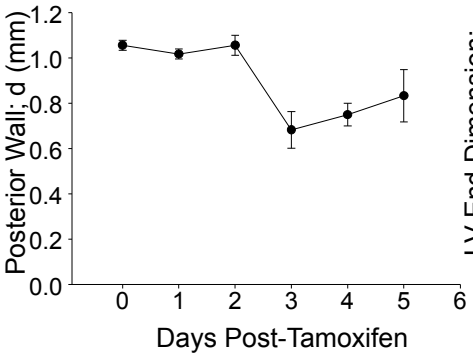



# Mouse 65 M

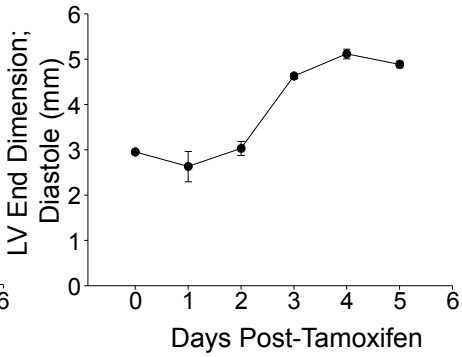
### Anterior Wall; Diastole



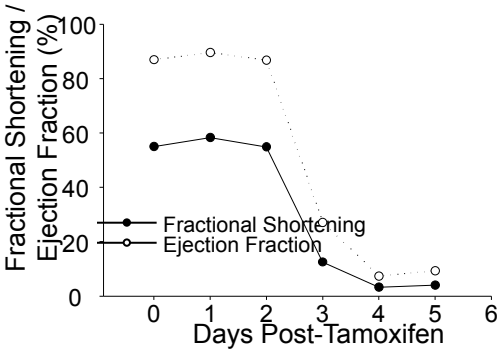

### Posterior Wall; Diastole



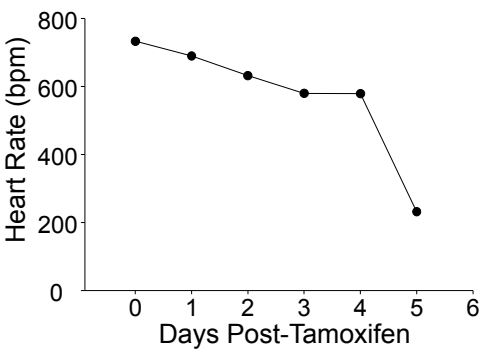

### LVID; Diastole




### Systolic Function (%)



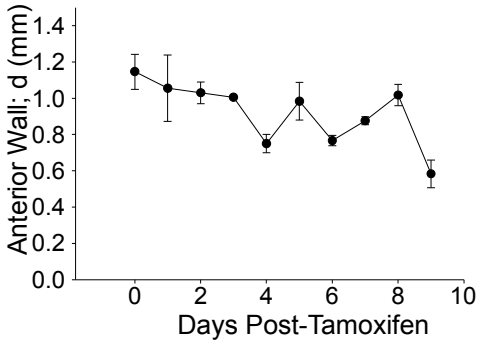

### Heart Rate



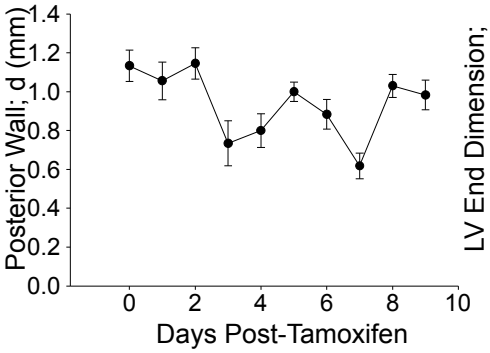
# Mouse 66 M

# Grp 4 Brm-/- flx/flx Brg1 Tg+ +TAM

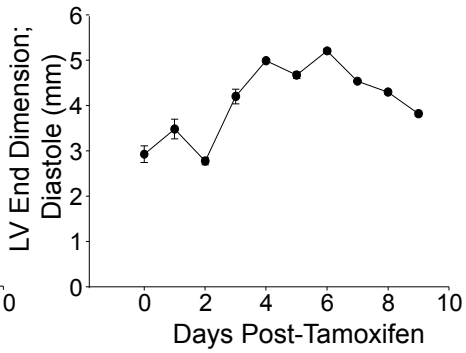
### Anterior Wall; Diastole



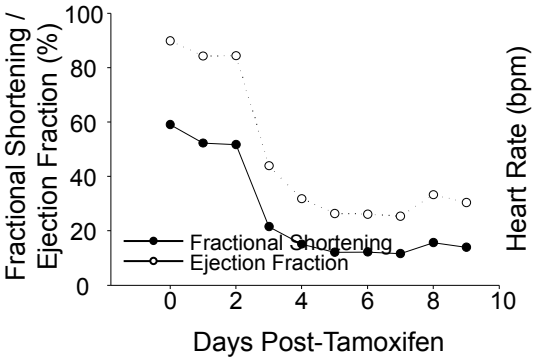

### Posterior Wall; Diastole



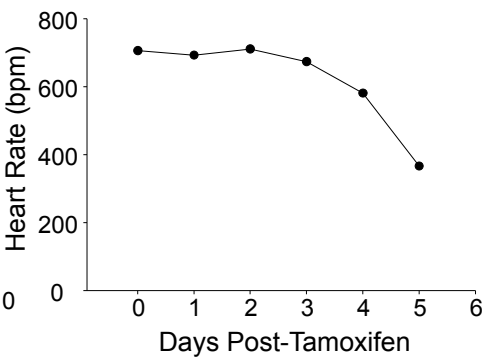

### LVID; Diastole




### Systolic Function (%)

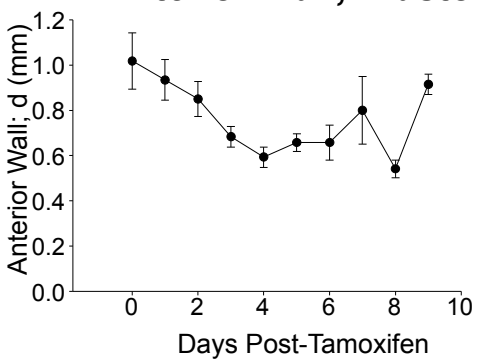



### Heart Rate

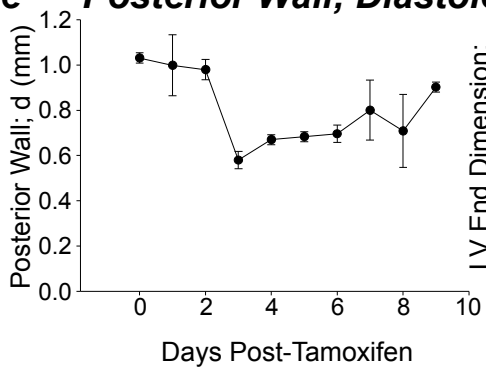



# Mouse 70 F

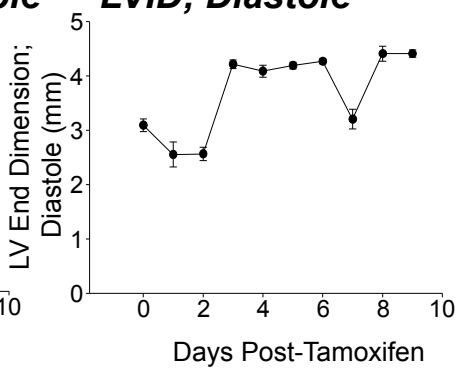
### Anterior Wall; Diastole



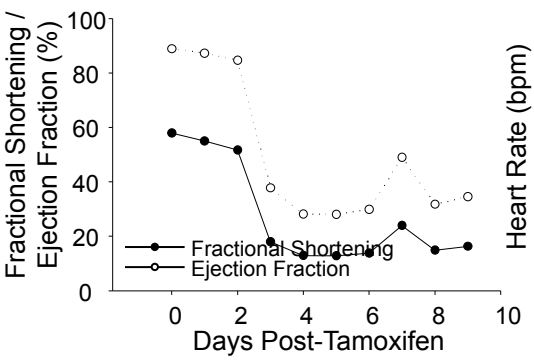

### Posterior Wall; Diastole



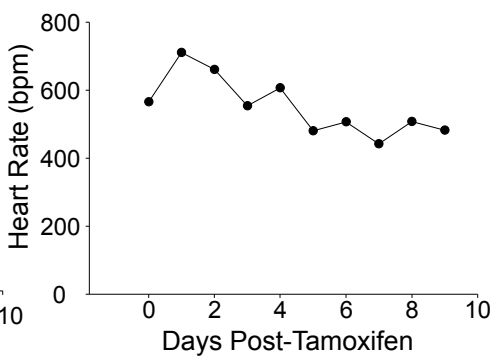

### LVID; Diastole




### Systolic Function (%)



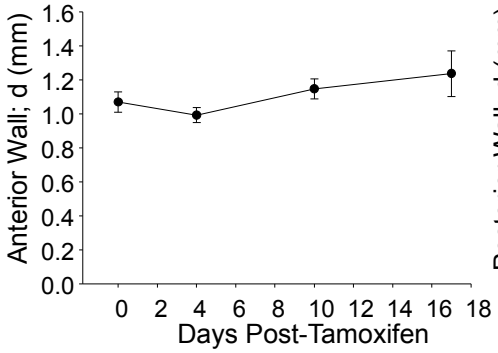

### Heart Rate



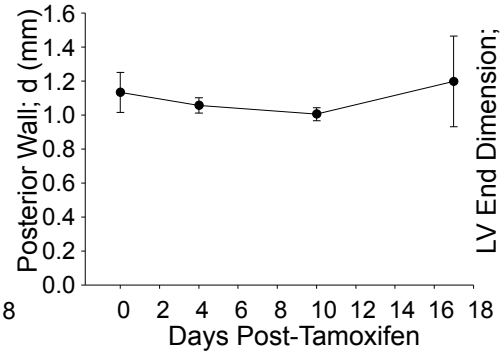
# Mouse 25 F

# Grp 5 Brm-/- flx/+ Brg1 Tg+ Chow

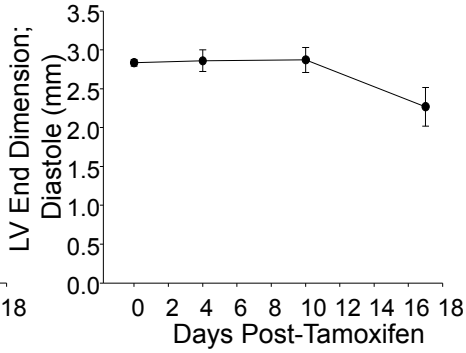
### Anterior Wall; Diastole



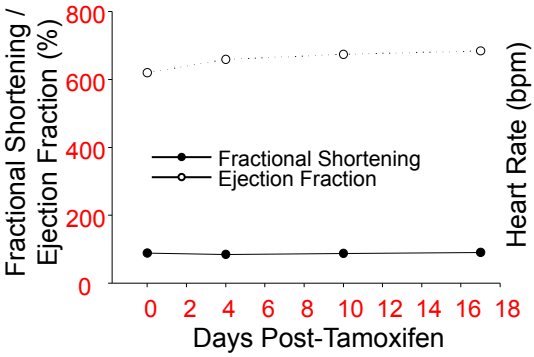

### Posterior Wall; Diastole



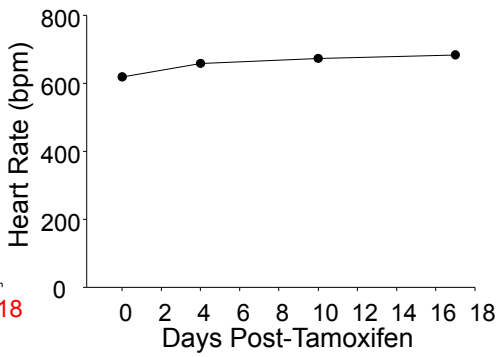

### LVID; Diastole




### Systolic Function (%)

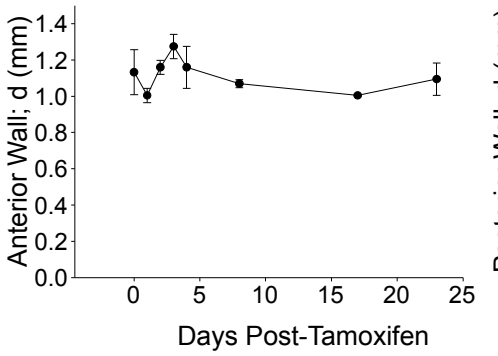



### Heart Rate

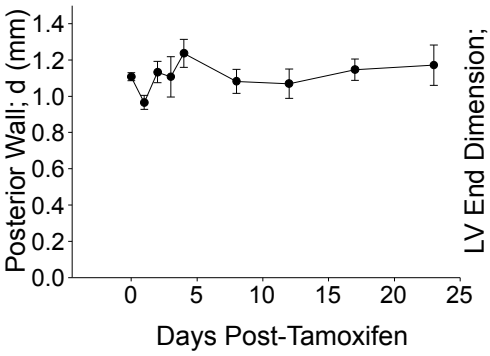



# Mouse 46 M

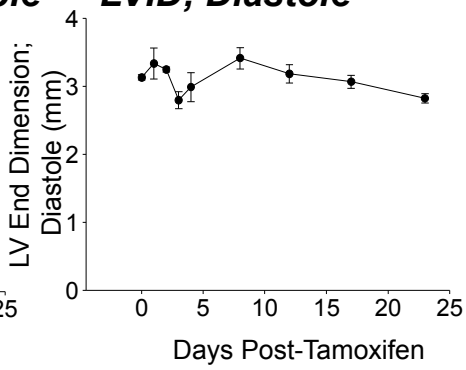
### Anterior Wall; Diastole



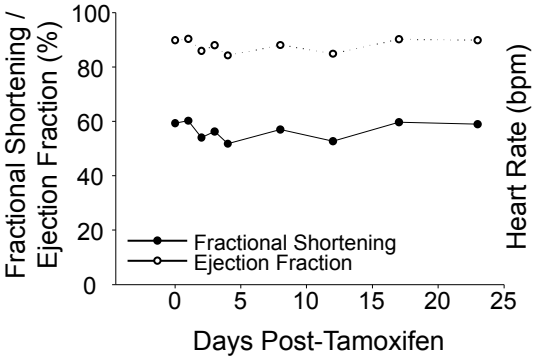

### Posterior Wall; Diastole



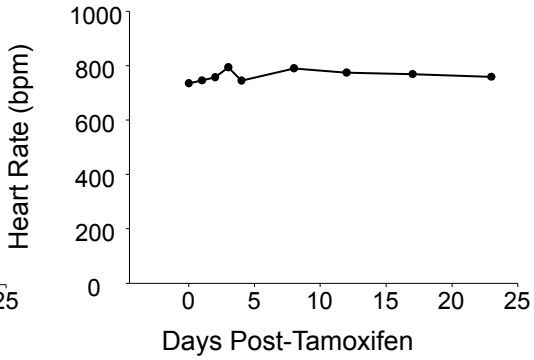

### LVID; Diastole




### Systolic Function (%)



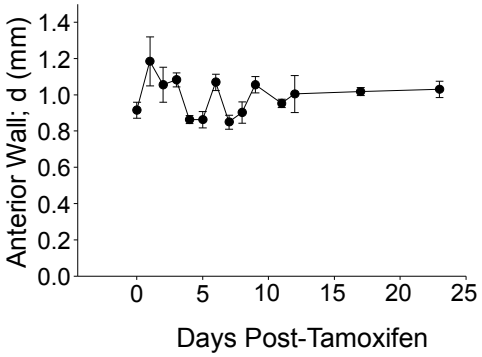

### Heart Rate



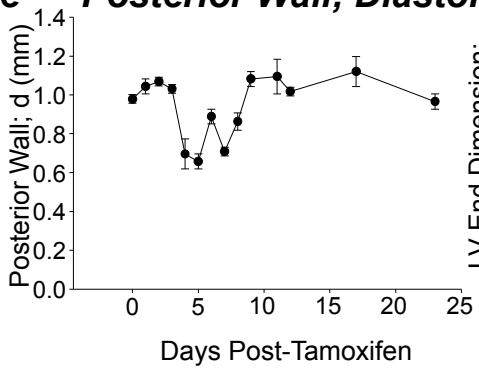
# Mouse 71 F

# Grp 6 Brm-/- flx/+ Brg1 Tg+ Tam

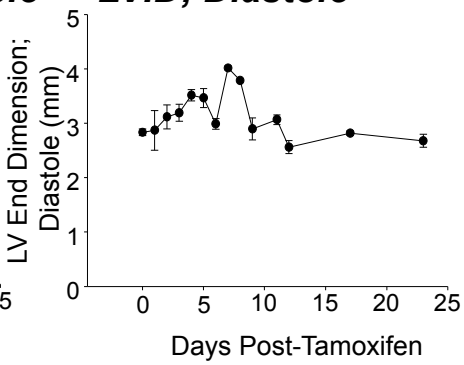
### Anterior Wall; Diastole



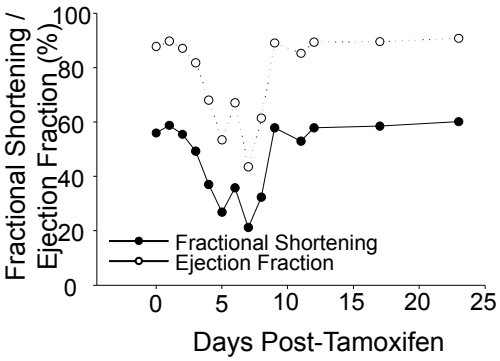

### Posterior Wall; Diastole



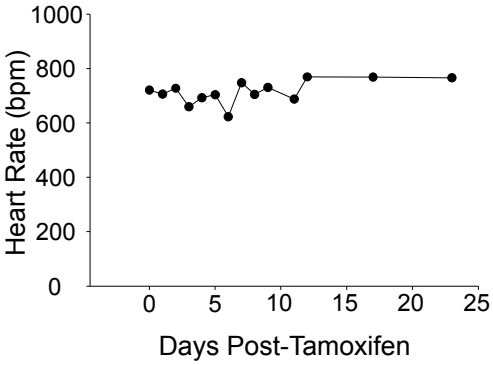

### LVID; Diastole




### Systolic Function (%)

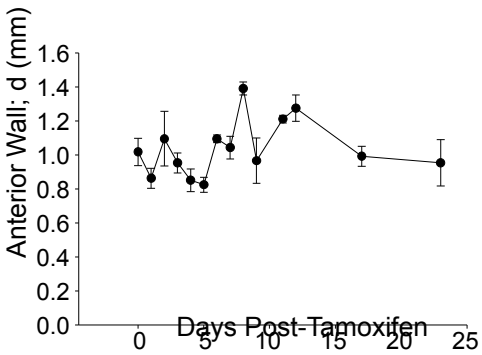



### Heart Rate

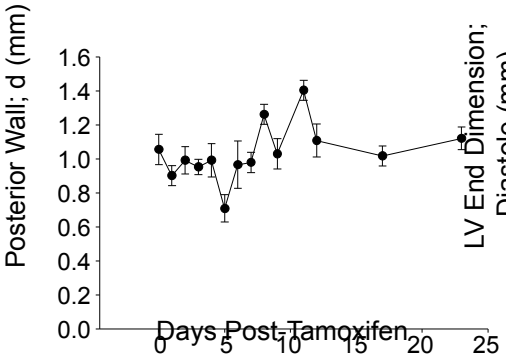



# Mouse 72 F

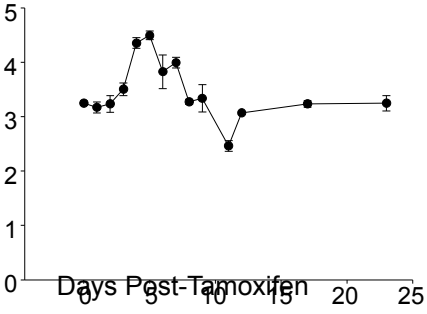
### Anterior Wall; Diastole



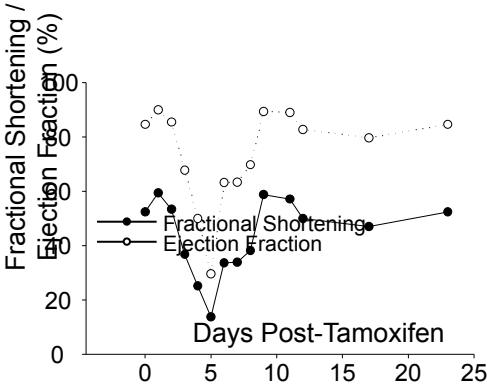

### Posterior Wall; Diastole



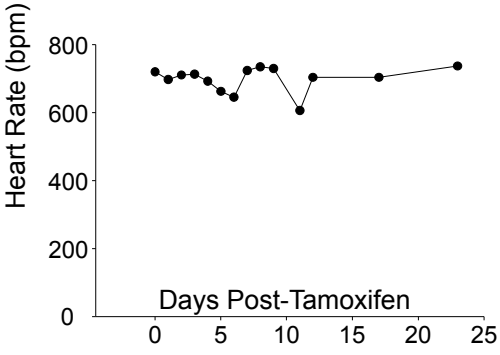

### LVID; Diastole




### Systolic Function (%)



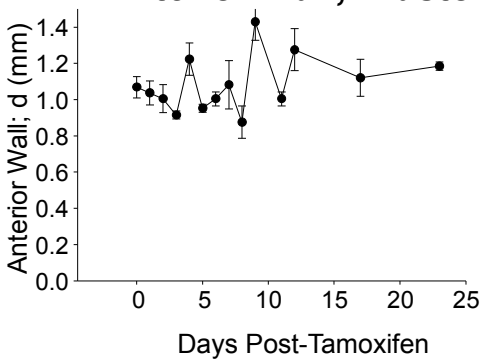

### Heart Rate



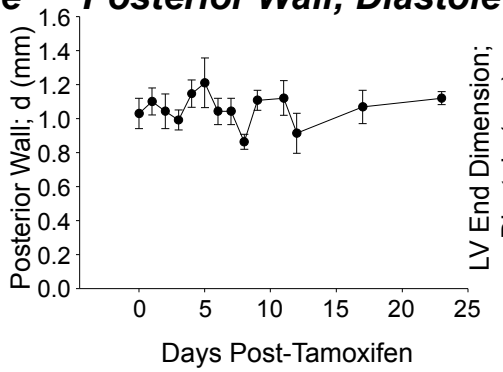
## Mouse 73 F

## Grp 6 Brm-/- flx/+ Brg1 Tg+ Tam

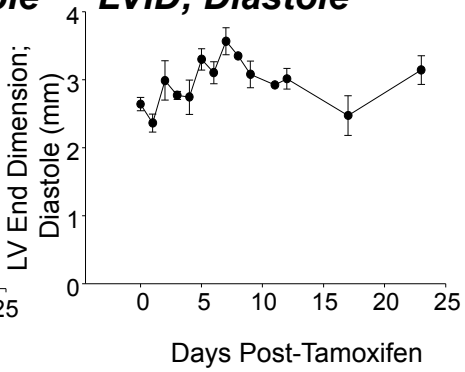
### Anterior Wall; Diastole



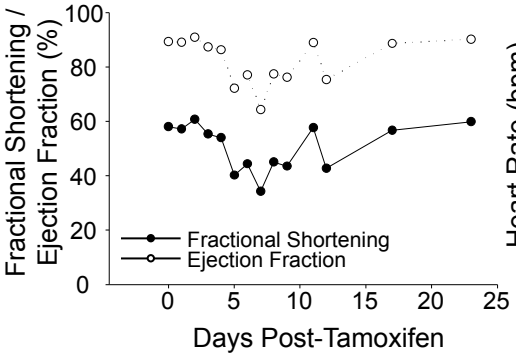

### Posterior Wall; Diastole



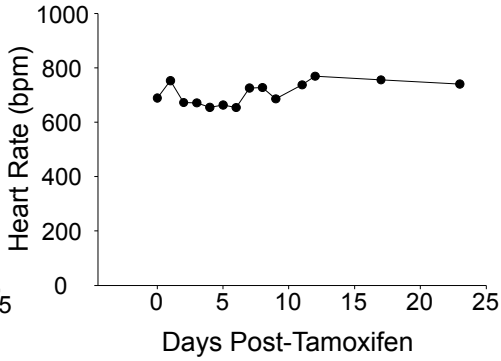

### LVID; Diastole




### Systolic Function (%)

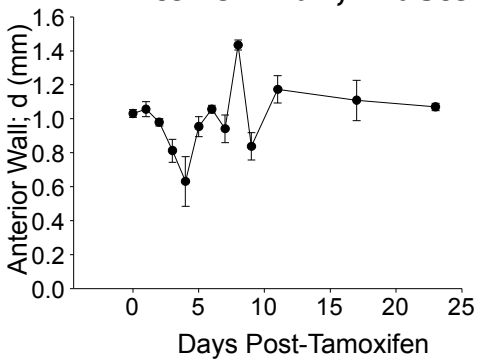



### Heart Rate

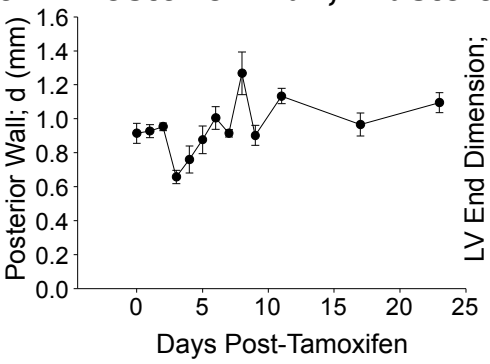



## Mouse 75 F

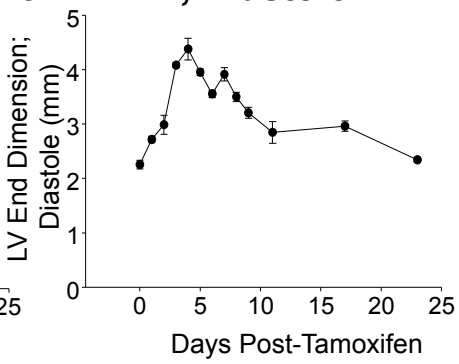
### Anterior Wall; Diastole



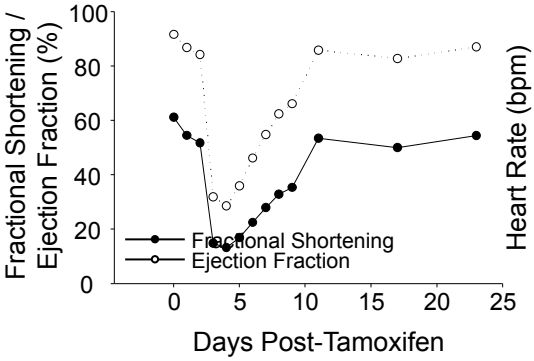

### Posterior Wall; Diastole



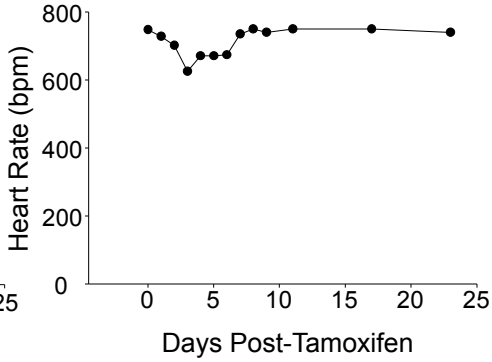

### LVID; Diastole




### Systolic Function (%)



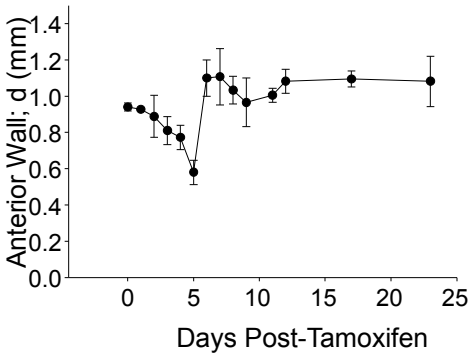

### Heart Rate



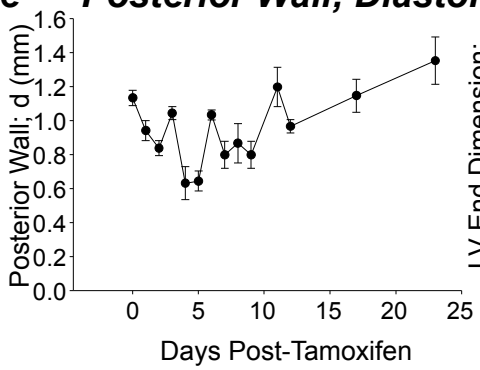
# Mouse 80 M

# Grp 6 Brm-/- flx/+ Brg1 Tg+ Tam

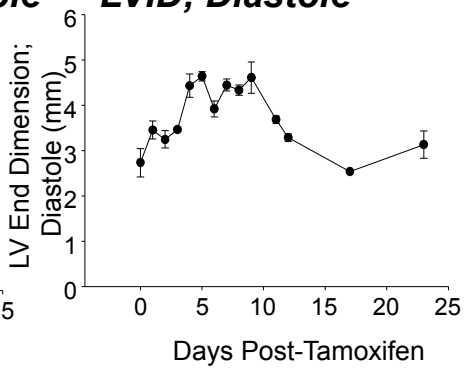
### Anterior Wall; Diastole



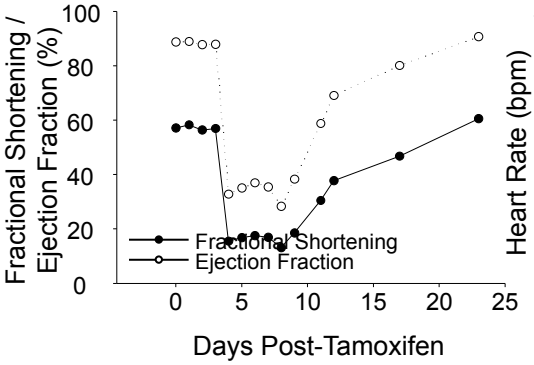

### Posterior Wall; Diastole



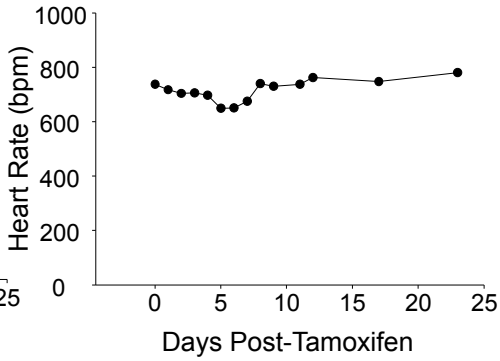

### LVID; Diastole




### Systolic Function (%)

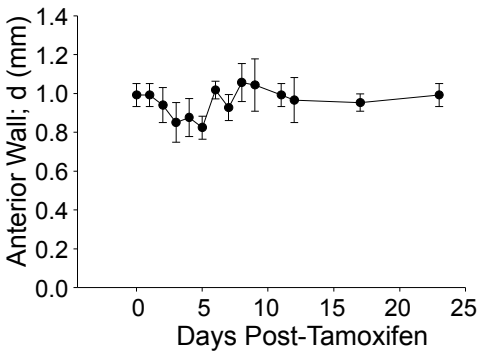



### Heart Rate

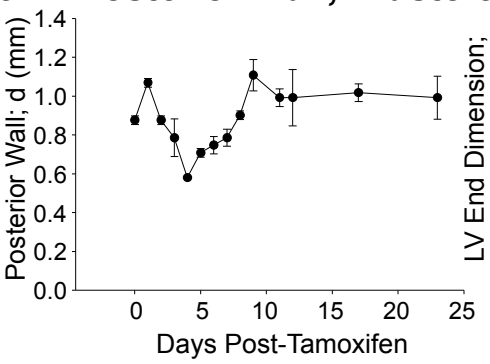



# Mouse 83 F

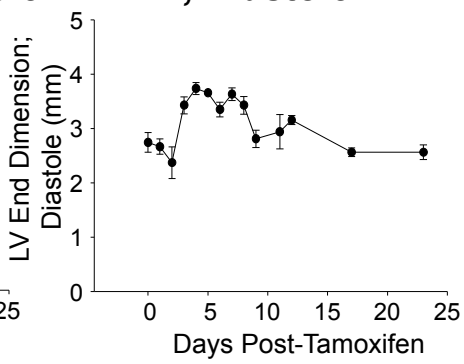
### Anterior Wall; Diastole



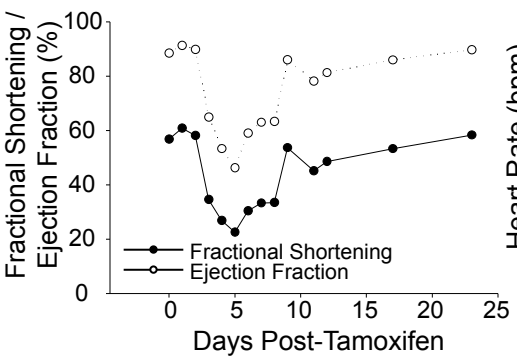

### Posterior Wall; Diastole



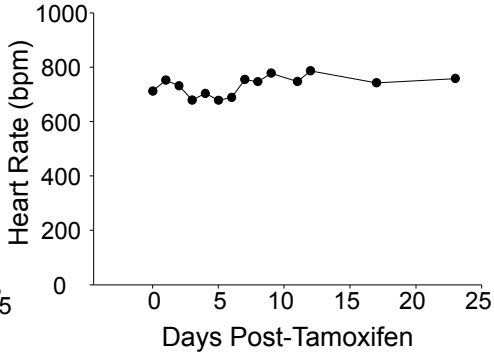

### LVID; Diastole




### Systolic Function (%)



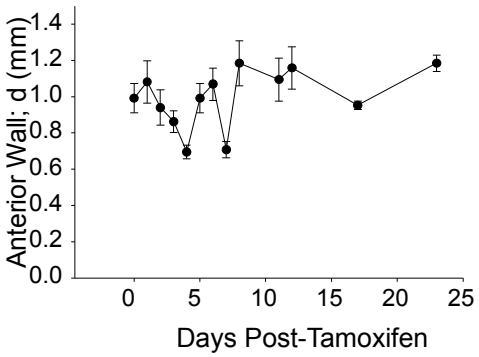

### Heart Rate



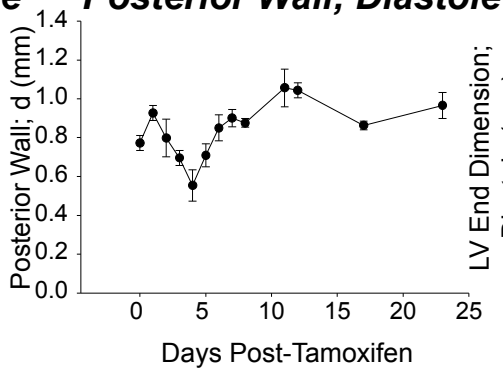
## Mouse 85 F

## Grp 6 Brm-/- flx/+ Brg1 Tg+ Tam

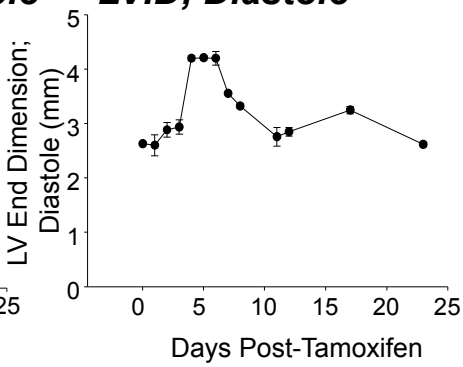
### Anterior Wall; Diastole



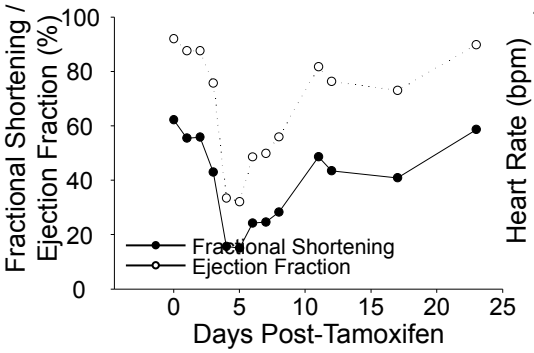

### Posterior Wall; Diastole



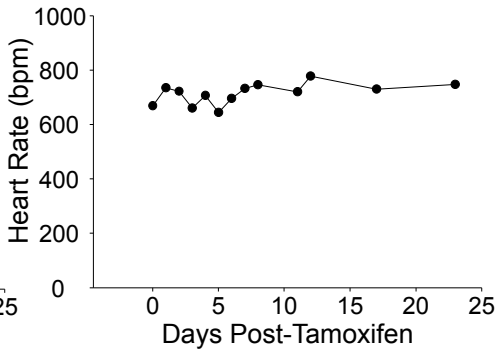

### LVID; Diastole




### Systolic Function (%)




### Heart Rate



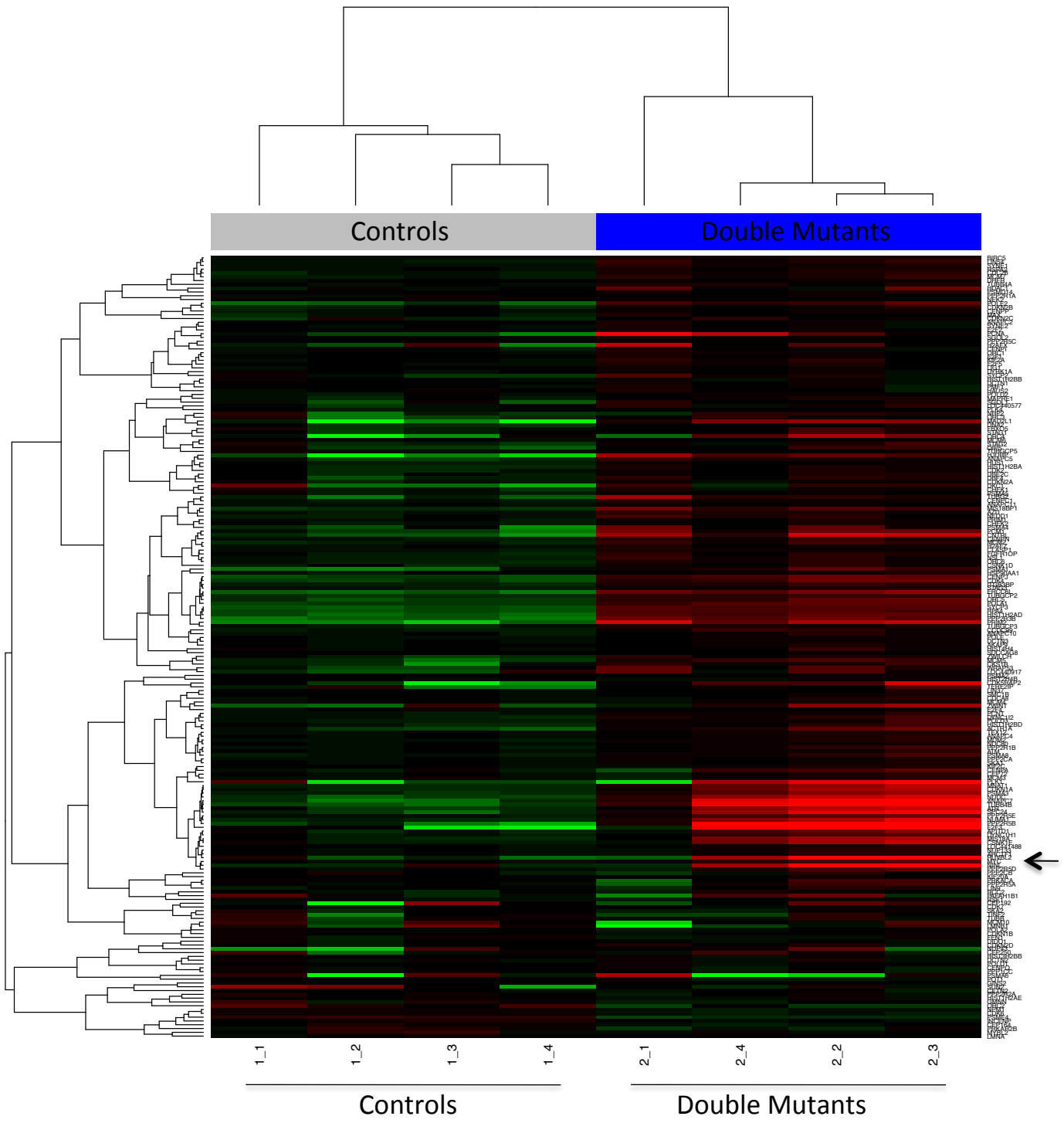



**Figure S3. Heat map showing relative expression levels of genes in cell-cycle reactome pathway.** Unsupervised hierarchal clustering with controls (4 biological replicates) shown on left, and *Brg1/Brm* double mutants (4 biological replicates) shown on right. Genes upregulated in double mutants are shown in red, while genes downregulated in the double mutants are shown in green. Gene names are indicated at far right, and an arrow highlights *c-Myc.*

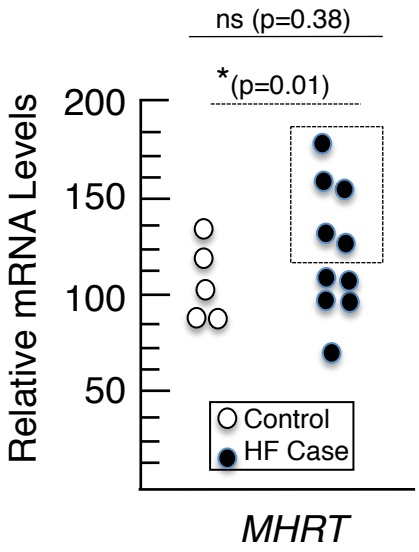



**Figure S4. RT-qPCR analysis of human *MHRT* mRNA levels normalized to *GAPDH* mRNA levels.** Scatter plots shows relative values of 5 controls (open symbols) and 10 heart failure cases (filled symbols). The top p value compares all 10 cases to controls while the lower p value (underlined by dashed lines) compares a subset of cases enclosed by dashed box. *, significant difference (*$p<0.05$); ns, not significant.