

## SUPPLEMENTAL MATERIAL

### **Supplemental Additional Analyses:**

Because several antihypertensive agents (such as angiotensin-converting enzyme inhibitors, ACE inhibitors, and angiotensin receptor blockers, ARB) and statins have been reported to increase adiponectin levels, we performed analyses stratified by these specific medications. No statistically significant difference was present in the adiponectin levels for participants on ACE inhibitors (N = 269) or on statins (N = 212) versus those that were not.

The adiponectin levels in participants on ARB medication ( $4.8 \pm 4.5$   $\mu\text{g/mL}$ ; N = 85) were lower compared with those without ( $5.3 \pm 4.0$   $\mu\text{g/mL}$ ), but the difference was not statistically significant. Among participants without insulin resistance, the association adiponectin – LVMI changed its direction from a non-significant inverse association among those without ARB treatment ( $\beta = -0.25$ ,  $p = 0.47$ ) to a non-significant direct association among those with ARB treatment ( $\beta = 0.03$ ,  $p = 0.99$ ). Among participants with insulin resistance the same association was a non-significant direct association among both those without treatment ( $\beta = 0.52$ ,  $p = 0.43$ ) as well as among those with treatment ( $\beta = 3.80$ ,  $p = 0.40$ ). All the adjustment models used were fully-adjusted models.

**Supplemental Table 1. Relationship between adiponectin raw values and left ventricular mass index according to quartiles of adiponectin examined with linear regression**

Sample of participants	Age- and sex-adjusted ( $\beta$ coefficients)	P-value	Fully-adjusted models* ( $\beta$ coefficients)	P-value
<b>Among all participants (N = 2,649)</b>				
Q1	Reference		Reference	
Q2	- 0.84	0.09	- 0.02	0.97
Q3	- 1.58	0.02	- 0.43	0.40
Q4	- 1.71	0.01	0.02	0.98
Trend	< 0.001		0.77	
<b>Among normotensive (N = 1,206)</b>				

Q1	Reference		Reference	
Q2	- 0.61	0.29	- 0.55	0.32
Q3	- 2.29	< 0.001	- 2.01	0.001
Q4	- 1.85	0.003	- 0.83	0.20
Trend	< 0.001		0.03	
<b>Among hypertensive (N = 1,418)</b>				
Q1	Reference		Reference	
Q2	- 0.71	0.34	0.53	0.53
Q3	- 0.43	0.57	1.06	0.21
Q4	- 0.88	0.25	0.62	0.51
Trend	0.39		0.40	
<b>Among normotensive</b>				

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**without insulin****resistance (N = 998)**

Q1	Reference		Reference	
Q2	- 0.60	0.36	- 0.49	0.44
Q3	- 1.84	0.01	- 1.72	0.01
Q4	- 1.23	0.06	- 0.73	0.30
Trend	0.01		0.09	

**Among normotensive****with insulin resistance (N  
= 208)**

Q1	Reference		Reference	
Q2	0.89	0.51	- 0.40	0.75
Q3	- 1.39	0.36	- 2.71	0.05

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Q4	2.29	0.34	1.94	0.38
Trend	0.65		0.74	
<b>Among hypertensive without insulin resistance (N = 1,087)</b>				
Q1	Reference		Reference	
Q2	- 1.26	0.16	- 0.22	0.85
Q3	- 1.67	0.07	- 0.45	0.69
Q4	- 1.35	0.14	- 0.23	0.85
Trend	0.13		0.79	
<b>Among hypertensive with insulin resistance (N = 331)</b>				
Q1	Reference		Reference	

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Q2	0.65	0.63	0.40	0.74
Q3	3.61	0.01	3.16	0.01
Q4	1.27	0.52	1.23	0.48
Trend	0.19		0.17	

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Q1, Q2, Q3 and Q4 represent the first, second, third and fourth quartile of adiponectin plasma levels;

\*Adjusted for age, sex, BMI, alcohol drinking, HDL-cholesterol, triglycerides, hypertension (among all participants, only), HOMA-IR (not in the models stratified by insulin resistance).

**Supplemental Table 2. Association between adiponectin and left ventricular mass\* stratified by age-groups according to hypertension, diabetes and abdominal obesity**

	Hypertension				Diabetes				Abdominal Obesity			
	Not Present		Present		Not Present		Present		Not Present		Present	
	N = 849	N = 469	N = 1,220	N = 113	N = 598	N = 735						
( ≤ 50 years)	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Crude	- 1.32	< 0.0001	- 0.07	0.90	- 1.26	< 0.0001	2.18	0.06	- 1.30	0.001	- 0.18	0.69
Sex-adjusted <sup>†</sup>	- 1.41	< 0.0001	- 0.59	0.35	- 1.52	< 0.0001	2.37	0.05	- 0.95	0.02	- 0.23	0.63
BMI-adjusted	- 0.70	0.02	0.40	0.46	- 0.50	0.08	1.79	0.11	- 0.73	0.05	0.05	0.91
HOMA-IR-adjusted	- 0.95	0.009	0.18	0.80	---	---	---	---	- 1.05	0.01	- 0.17	0.76
Cholesterol-adj. <sup>§</sup>	- 1.28	0.0001	0.21	0.77	- 1.06	0.005	2.60	0.09	- 0.96	0.03	- 0.26	0.64
Fully-adjusted <sup>#</sup>	- 0.86	0.02	0.19	0.80	- 0.53	0.14	---	---	- 0.30	0.50	- 0.54	0.34

Older Age ( > 50 years)	N = 358		N = 949		N = 1,012		N = 304		N = 449		N = 867	
	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value
Crude	- 0.23	0.70	0.57	0.18	0.04	0.93	1.15	0.16	- 0.66	0.17	1.10	0.02
Sex-adjusted <sup>†</sup>	- 0.62	0.32	0.16	0.72	- 0.41	0.33	0.63	0.45	- 0.53	0.34	0.89	0.08
BMI-adjusted	0.39	0.47	0.63	0.12	0.46	0.22	0.81	0.30	- 0.15	0.75	1.02	0.03
HOMA-IR-adjusted	0.38	0.55	1.37	0.01	---	---	---	---	- 0.29	0.61	2.04	0.001
Cholesterol-adj. <sup>§</sup>	- 0.01	0.99	0.56	0.24	0.36	0.43	0.70	0.47	- 0.08	0.89	0.86	0.11
Fully-adjusted <sup>#</sup>	0.09	0.89	1.20	0.04	0.99	0.03	---	---	0.30	0.66	1.66	0.01

\*Per one standard deviation in the adiponectin log values – beta coefficients presented are for adiponectin;

<sup>†</sup>Model that contain an interaction term between adiponectin and age;

<sup>‡</sup>Not sufficient participants in this category to be reliable;

<sup>§</sup>Adjusted for HDL-cholesterol and triglycerides;



|| Adjusted for age, sex, BMI, alcohol drinking, hypertension status (not in the hypertension categories), HDL-cholesterol, triglycerides and HOMA-IR (not in the diabetes categories);

# Unreliable result due to small cell numbers.

**Supplemental Table 3. Association between adiponectin and left ventricular mass\* by sex according to hypertension, diabetes and abdominal obesity**

	Hypertension				Diabetes				Abdominal Obesity			
	Not Present		Present		Not Present		Present		Not Present		Present	
	N = 470	N = 487	N = 844	N = 126	N = 598	N = 372						
Men	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value
Crude	- 1.22	0.01	- 0.52	0.34	- 0.92	0.02	- 0.55	0.58	- 0.80	0.08	- 0.07	0.92
Age-adjusted <sup>†</sup>	- 1.65	0.36	- 1.47	0.05	- 3.32	0.03	9.98	0.09	- 1.75	0.31	- 1.10	0.71
BMI-adjusted	- 0.45	0.35	0.09	0.86	- 0.06	0.87	- 0.31	0.76	- 0.14	0.75	0.01	0.99
HOMA-IR-adjusted	- 1.11	0.05	0.19	0.78	- 0.24	0.58	---	‡	- 0.63	0.22	0.65	0.44
Cholesterol-adjusted <sup>§</sup>	- 1.10	0.05	- 0.57	0.36	- 0.80	0.08	- 0.72	0.57	- 0.47	0.35	- 1.11	0.13
BMI- and cholesterol-adjusted	- 0.74	0.17	- 0.15	0.80	- 0.32	0.47	- 0.73	0.55	- 0.06	0.90	- 1.13	0.11
Fully-adjusted <sup>  </sup>	1.37	0.02	- 0.10	0.88	- 0.68	0.10	6.04	0.40	- 0.02 <sup>†</sup>	0.99	- 8.16 <sup>†</sup>	0.02

Women	N = 736		N = 931		N = 1,388		N = 291		N = 449		N = 1,230	
	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value	$\beta$	p-value
Crude	- 0.99	0.01	0.30	0.53	- 0.77	0.03	2.30	0.01	- 0.18	0.72	0.86	0.04
Age-adjusted <sup>†</sup>	- 2.11	0.19	0.03	0.99	- 1.15	0.41	- 0.43	0.93	- 0.34	0.86	- 1.09	0.53
BMI-adjusted	0.11	0.75	0.95	0.03	0.41	0.20	2.25	0.01	0.11	0.82	1.17	0.002
HOMA-IR-adjusted	- 0.27	0.52	0.82	0.19	0.58	0.13	--- <sup>‡</sup>	--- <sup>‡</sup>	0.50	0.35	1.02	0.04
Cholesterol-adjusted <sup>§</sup>	- 0.80	0.07	0.50	0.34	- 0.25	0.51	1.92	0.07	0.18	0.74	0.87	0.06
BMI- and cholesterol-adjusted	- 0.01	0.98	1.06	0.49	0.70	0.05	1.66	0.10	0.40	0.43	1.08	0.01
Fully-adjusted <sup>  </sup>	- 0.27	0.50	0.81	0.19	0.72	0.59	- 0.16	0.64	0.13 <sup>†</sup>	0.94	0.70 <sup>†</sup>	0.69

\*Per one standard deviation in the adiponectin log values – beta coefficients presented are for adiponectin;

<sup>†</sup>Model that contain an interaction term between adiponectin and age;

<sup>‡</sup>Not sufficient participants in this category to be reliable;

<sup>§</sup>Adjusted for HDL-cholesterol and triglycerides;

||Adjusted for age, sex, BMI, alcohol drinking, hypertension status (not in the hypertension categories), HDL-cholesterol, triglycerides and HOMA-IR (not in the diabetes categories).

## **Supplemental Figure Legends**

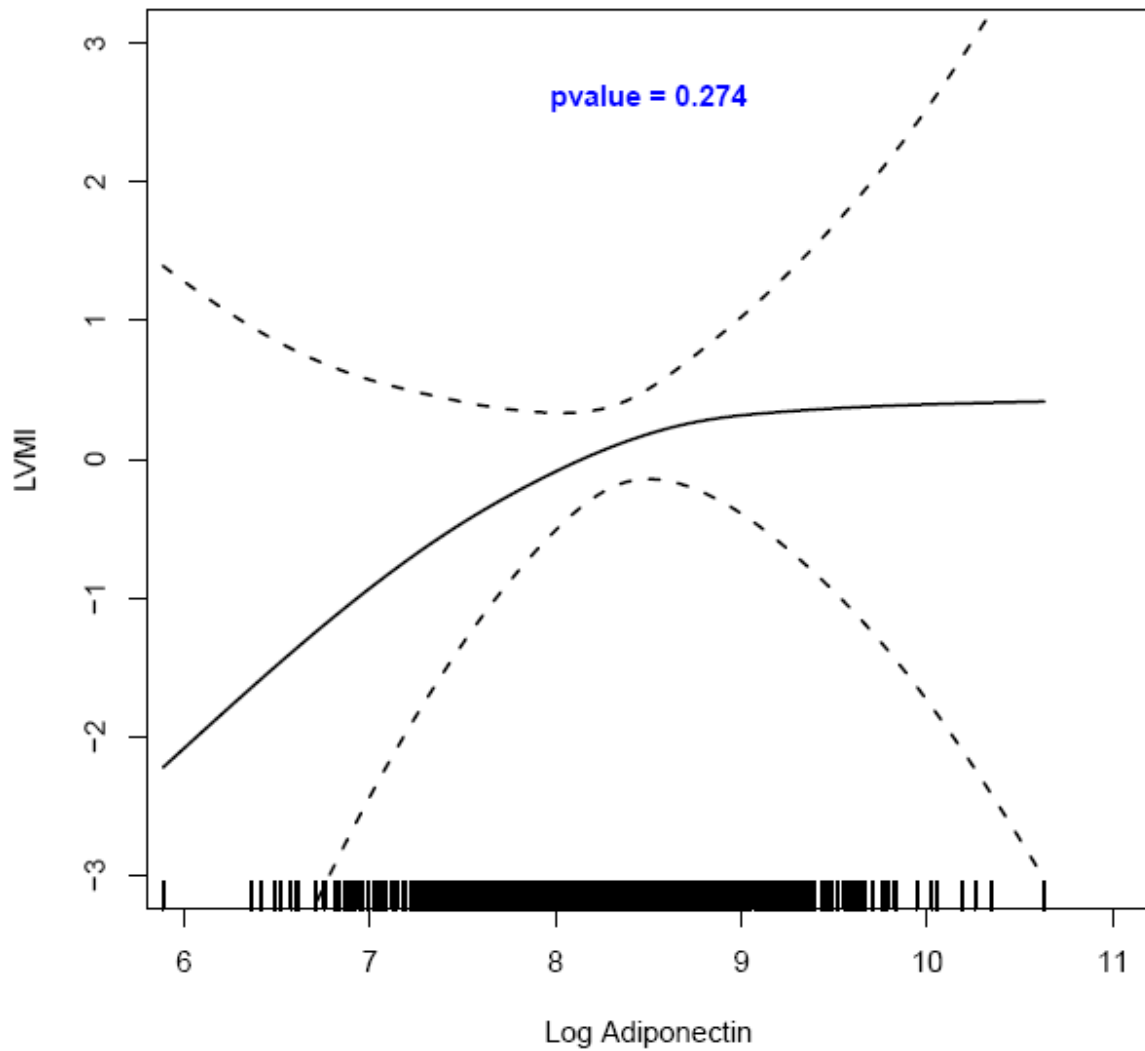
**Supplemental Figure 1.** The relationship between adiponectin and left ventricular mass index by spline regression modeling among participants with hypertension (N = 1,418)

**Supplemental Figure 2.** The relationship between adiponectin and left ventricular mass index by spline regression modeling among participants without hypertension and without insulin resistance (N = 998)

**Supplemental Figure 3.** The relationship between adiponectin and left ventricular mass index by spline regression modeling among participants without hypertension and with insulin resistance (N = 208)

**Supplemental Figure 4.** The relationship between adiponectin and left ventricular mass index by spline regression modeling among participants with hypertension and without insulin resistance (N = 1,087)

Supplemental Figure 1.

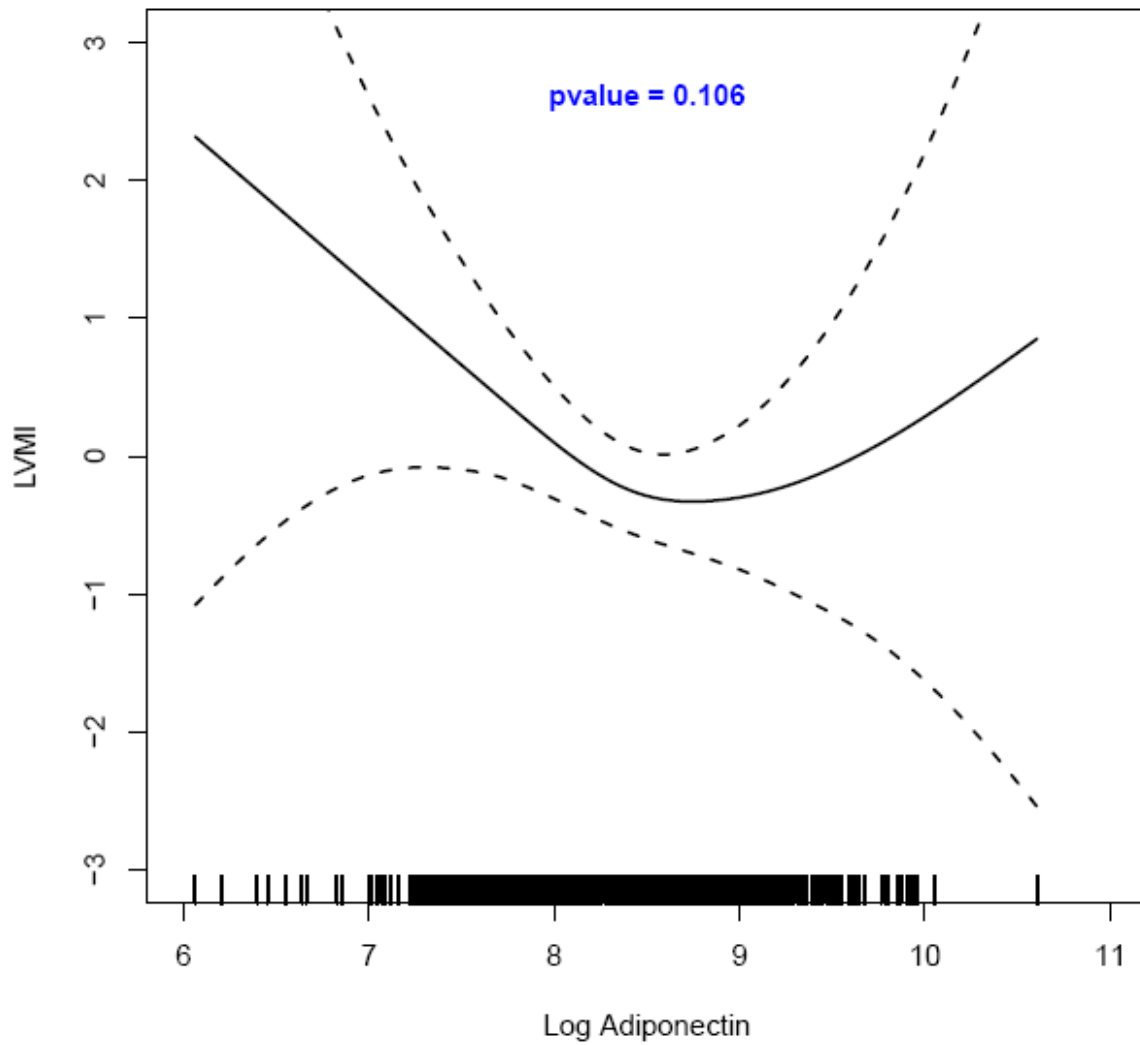


\*Adiponectin was log-transformed from units expressed as  $\mu\text{g/mL}$  (in order to have logarithmic values above the unit);

†Multivariable-adjusted values (residuals) of left ventricular mass index (LVMI);

‡ Adjustment was performed for age, sex, BMI, alcohol drinking, HDL-cholesterol, triglycerides and HOMA-IR (log-transformed).

Supplemental Figure 2.

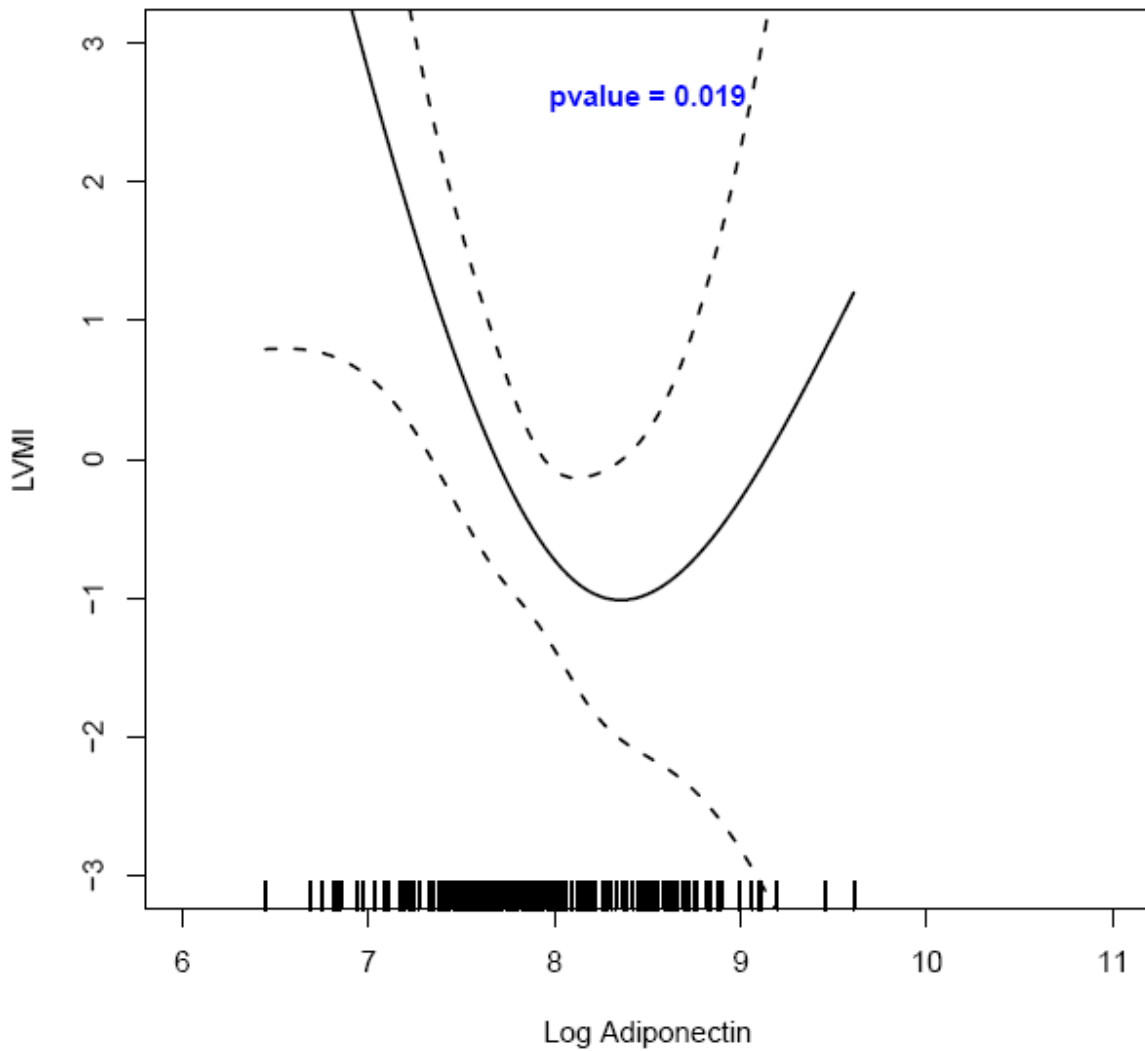


\*Adiponectin was log-transformed from units expressed as  $\mu\text{g/mL}$  (in order to have logarithmic values above the unit);

†Multivariable-adjusted values (residuals) of left ventricular mass index (LVMI);

‡ Adjustment was performed for age, sex, BMI, alcohol drinking, HDL-cholesterol and triglycerides.

**Supplemental Figure 3.**



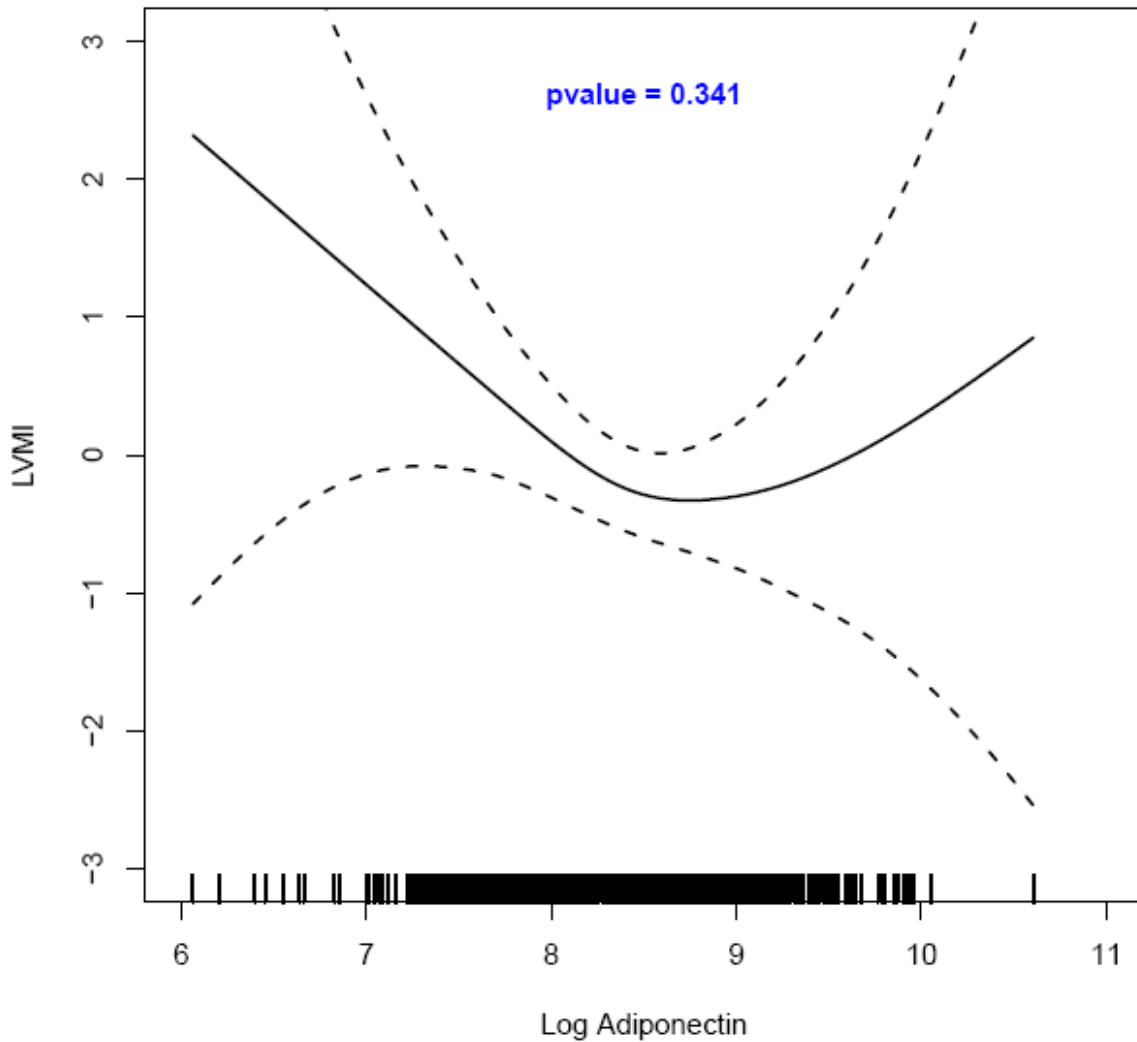
\*Adiponectin was log-transformed from units expressed as  $\mu\text{g/mL}$  (in order to have logarithmic values above the unit);

†Multivariable-adjusted values (residuals) of left ventricular mass index (LVMI);

‡ Adjustment was performed for age, sex, BMI, alcohol drinking, HDL-cholesterol and triglycerides.



Supplemental Figure 4.



\*Adiponectin was log-transformed from units expressed as  $\mu\text{g/mL}$  (in order to have logarithmic values above the unit);

†Multivariable-adjusted values (residuals) of left ventricular mass index (LVMI);

‡ Adjustment was performed for age, sex, BMI, alcohol drinking, HDL-cholesterol and triglycerides.