

Estimated Ventricular Size, Asthma Severity, and Exacerbations

The Severe Asthma Research Program III Cohort

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e-Appendix 1.

Supplemental Methods

Cohort Description and Clinical Definitions

The Severe Asthma Research Program (SARP) is a prospective, multi-center investigation designed to improve the understanding of severe asthma.^{1,2} For this study we utilized data from adult participants with both severe and non-severe asthma from the third phase of SARP (SARP III) as well as from a smaller group of participants characterized as healthy controls.¹ Notably, subjects were excluded from enrollment if they had a history of COPD, were currently smoking, had smoked in the past year, had >10 pack year history (for those ≥ 30 years old) or had >5 pack year history (for those <30 years old).^{1,2}

At the baseline visit, participants provided an extensive questionnaire based history and underwent lung function testing.^{3,4} Participants then returned for annual follow-up visits that included spirometry and an updated history with questions regarding interval asthma exacerbations, which were defined as respiratory events that required at least three days of a systemic steroid burst (a dose > 10mg or double the individual's chronic daily steroid dose). Severe and mild/moderate asthma were defined based on the American Thoracic Society/European Respiratory Society and National Asthma Education and Prevention Program guidelines.^{1,2,5,6}

For the supplemental analyses of the association between corticosteroid dose and cardiac size, participants were subdivided into four groups defined based on self-reported corticosteroid use in the year prior to enrollment, with subgroups defined based on prior work.⁷ These included: those with no corticosteroid use, those with low dose corticosteroid use (inhaled steroids), those with medium dose corticosteroid use (oral or parenteral steroids with an average daily dosage of < 7.5mg of prednisone per day), and those with high dose corticosteroid use (oral or parenteral steroids with an average daily dosage of ≥ 7.5 mg of prednisone per day).⁷ Note that because limited data were available on the use of nasal, topical and rectal steroids in this study, these were not included in the definition. Oral and parenteral steroids given for the treatment of an exacerbation were included in the overall annual total steroid use. However details regarding the dose and duration of steroids given for an exacerbation were not available, therefore it was assumed that for each exacerbation, the equivalent of a total dose of 200mg of prednisone (40mg per day for 5 days) was given.⁸ The distribution of steroid dose by asthma severity category is shown in **e-Tables 4A-B.**

All participants provided informed consent and the study was approved by the institutional review board at each center as detailed in **e-Table 1.**

Non-cardiac Computed Tomography Image Analysis

Volumetric, non-contrast, non-ECG gated CT scans of the chest were performed on a subgroup of individuals enrolled at three clinical centers (the Universities of Pittsburgh and Wisconsin and Washington University in St. Louis) using a previously established protocol.^{9,10} The primary measurements performed in this study, including the PA, aorta and ventricular measures, were obtained using baseline scans acquired at total lung capacity (TLC). Expiratory CT images were obtained in a subset of individuals and were acquired at functional residual capacity (FRC) for consistency with prior SARP studies.¹⁰ The lungs were segmented from the chest wall and other thoracic structures using previously described methods.^{11,12} Percent low attenuation area (LAA%), a measure correlated with emphysema, was defined as the volume of lung on the TLC images with attenuation < -950 Hounsfield units (HU), and percent air trapping (AT%) was defined as the volume of lung with attenuation < -856 HU on images acquired at FRC.¹³

The diameter of the PA and the aorta were measured manually using previously published methods.¹⁴ Briefly, a single reviewer measured the maximal diameters of the main pulmonary artery and the ascending aorta at the level of the PA bifurcation on an axial CT image.¹⁴ Based on a hypothesized intraclass correlation coefficient (ICC) of 0.8 and a null hypothesis value of ICC of 0.5 a sample size of 28 was needed to determine the replicability of these measurements with 80% power and $\alpha=0.05$.¹⁵ Therefore, a second reviewer independently performed the same measurements on a random sample of 28 (12%) of the cases. The correlation between the PA and aorta measurements made by the two reviewers was assessed using Pearson correlation and the ICC. The measurements performed by the two reviewers were highly correlated ($r^2 = 0.85$, ICC=0.91), therefore for consistency the measurements performed by reviewer 1 were utilized in all of the analyses.

To ensure that the results were confounded by the presence of occult emphysema, a single reviewer reviewed all of the axial CT images and visually identified and subclassified emphysema (Centrilobular and/or paraseptal. No panlobular was identified, likely due to the lack of alpha-1-antitrypsin disease in this cohort.) A second reviewer independently reviewed the cases with emphysema as well as a random sample of 10% of the remainder of the cohort. Only 10 individuals had visually defined emphysema (7 with centrilobular, 3 with paraseptal), and there was a high degree of agreement between the two reviewers with regard to the presence of emphysema ($\kappa=0.78$), therefore for consistency the classification performed by reviewer 1 was utilized.

All of the image analysis was performed using the Chest Imaging Platform (<https://chestimagingplatform.org/>) an open source image analysis tool, and the reviewers/operators

performing all of the image processing and analysis were blinded to the clinical characteristics of the participants.^{16,17}

Statistical Analysis

The associations between the pulmonary artery, aortic and cardiac measures and corticosteroid dose were evaluated using multivariable linear regression with the same covariates as the exacerbation analyses, including: age, sex, race body mass index, height normalized CT measured lung volume, percent predicted forced expiratory volume in one second and systolic blood pressure, as well as for asthma severity (mild/moderate vs. severe).

Supplemental References

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e-Table 1: Institutional Review Board Information

Site(s)	Institutional Review Board	Institutional Review Board Number
Brigham and Women's Children's Hospital Boston	Partners Human Research Committee Boston Children's Hospital Institutional Review Board	2012P001528/MGH IRB-P00004759
Emory University	Emory University Institutional Review Board	IRB00058103
Penn State College of Medicine (Data Coordinating Center)	Penn State College of Medicine Institutional Review Board	PRAMS037310EP
Cleveland Clinic	Cleveland Clinic Institutional Review Board	IRB 6185
Rainbow Babies and Children – Case Western	University Hospitals Case Medical Center Institutional Review Board for Human Investigation	09-12-08
University of California – Adult	University of California San Francisco Human Research Protection Program Committee on Human Research	12-09392
University of California – Pediatrics	University of California San Francisco Human Research Protection Program Committee on Human Research	12-09556
University of Pittsburgh – Adult	University of Pittsburgh Institutional Review Board	PRO12070359
University of Pittsburgh – Pediatrics	University of Pittsburgh Institutional Review Board	PRO12070359
University of Virginia	University of Virginia Institutional Review Board for Health Sciences Research	HSR#10742
University of Wisconsin	University of Wisconsin Madison Health Sciences Institutional Review Board	2012-0571
Virginia Commonwealth University	Virginia Commonwealth University Institutional Review Board	HM14883
Wake Forest	Wake Forest University Health Sciences Institutional Review Board	IRB00021507
Washington University	Washington University in St. Louis Institutional Review Board	201206102

e-Tables 2A-B: Multivariable Association between Radiographic Determinants and the Odds of Severe Asthma in the Entire Cohort

e-Table 2A: Pulmonary Artery to Aorta Ratio and Ventricular Volume Ratio

	Odds Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	1.17	0.50	2.79	0.725
Right Ventricular to Left Ventricular Volume Ratio	0.59	0.30	1.13	0.115

Notes:

- 1) Odds ratios expressed as those with high versus those with a low eRV/eLV (greater than the median vs. lower than median) and high versus low PA/A (greater than 1 vs. less than 1).
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume

e-Table 2B: Ventricular Volumes

	Odds Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	2.76	1.36	5.83	0.006
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	3.29	1.63	6.94	0.001
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	3.99	1.91	8.76	<0.001

Notes:

- 1) Odds ratios are expressed as those with lower volume compared to those with higher volume dichotomized at the median
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume

e-Tables 3A-B: Multivariable Association between Radiographic Determinants and the Odds of Severe Asthma in the Subgroup without Visually Defined Emphysema

e-Table 3A: Pulmonary Artery to Aorta Ratio and Ventricular Volume Ratio

	Odds Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	1.01	0.43	2.45	0.976
Right Ventricular to Left Ventricular Volume Ratio	0.57	0.29	1.12	0.104

Notes:

- 1) Odds ratios expressed as those with high versus those with a low eRV/eLV (greater than the median vs. lower than median) and high versus low PA/A (greater than 1 vs. less than 1).
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume

e-Table 3B: Ventricular Volumes

	Odds Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	2.70	1.31	5.81	0.009
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	3.31	1.60	7.16	0.002
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	4.03	1.89	9.09	<0.001

Notes:

- 1) Odds ratios are expressed as those with lower volume compared to those with higher volume dichotomized at the median
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume

e-Table 4A: Distribution of Corticosteroid Use by Asthma Severity in the Entire Cohort

Corticosteroid Group	Asthma Control Category		
	Healthy	Mild/Moderate	Severe
None	10	12	0
Low	0	35	47
Medium	0	19	80
High	0	0	29

e-Table 4B: Distribution of Corticosteroid Use by Asthma Severity in the Subgroup without Visually Defined Emphysema

Corticosteroid Group	Asthma Control Category		
	Healthy	Mild/Moderate	Severe
None	10	12	0
Low	0	33	45
Medium	0	18	79
High	0	0	24

Notes: Corticosteroids dose groups defined as follows: None = no corticosteroid use. Low = non-systemic (e.g., inhaled) corticosteroid use only. Medium = Average oral annual corticosteroid use < 7.5mg of prednisone per day. High = Average oral annual corticosteroid use ≥ 7.5mg of prednisone per day. Additional details available in the **Online Supplemental Methods**.

e-Tables 5A: Multivariable Association between Average Annual Corticosteroid Dose and Pulmonary Artery and Cardiac Measures in the Entire Cohort

Measure	Steroid Dose	Difference	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	None	Reference			
	Low	0.05	-0.03	0.13	0.248
	Medium	0.05	-0.04	0.13	0.251
	High	0.02	-0.06	0.15	0.641
Right Ventricular to Left Ventricular Volume Ratio	None	Reference			
	Low	-0.03	-0.07	0.004	0.089
	Medium	-0.03	-0.07	0.01	0.185
	High	-0.06	-0.10	-0.01	0.019
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	None	Reference			
	Low	-4.6	-16.7	7.4	0.184
	Medium	-4.0	-16.9	8.9	0.447
	High	-10.4	-25.7	5.0	0.543
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	None	Reference			
	Low	-6.4	-14.7	1.8	0.125
	Medium	-5.4	-14.2	3.4	0.231
	High	-12.1	-22.7	-1.6	0.024
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	None	Reference			
	Low	-11.1	-30.7	8.5	0.267
	Medium	-9.4	-30.5	11.7	0.381
	High	-22.5	-47.6	2.5	0.078

e-Tables 5B: Multivariable Association between Average Annual Corticosteroid Dose and Pulmonary Artery and Cardiac Measures in the Subgroup Without Visual Emphysema

Measure	Steroid Dose	Difference	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	None	Reference			
	Low	0.05	-0.03	0.13	0.220
	Medium	0.05	-0.03	0.14	0.228
	High	0.03	-0.08	0.13	0.590
Right Ventricular to Left Ventricular Volume Ratio	None	Reference			
	Low	-0.03	-0.07	0.002	0.071
	Medium	-0.02	-0.06	0.02	0.238
	High	-0.06	-0.10	-0.01	0.021
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	None	Reference			
	Low	-4.2	-16.2	7.8	0.493
	Medium	-5.1	-18.1	7.9	0.441
	High	-10.4	5.0	-25.8	0.184
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	None	Reference			
	Low	-6.3	-14.6	2.0	0.137
	Medium	-5.7	-14.7	3.2	0.209
	High	-12.0	-22.7	-1.4	0.027
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	None	Reference			
	Low	-10.5	-30.2	9.2	0.295
	Medium	-10.8	-32.1	10.5	0.318
	High	-22.4	-47.6	2.8	0.081

e-Table 6: Univariate Associations in those without Visually Defined Emphysema

	PA/A		eRV/eLV		eELVVI		eERVVI		eETVVI	
	r	p	r	p	r	p	r	p	r	p
Duration of Disease	-0.17	0.013	-0.06	0.368	0.08	0.230	0.12	0.085	0.11	0.121
CT Measured Lung Volume	0.03	0.658	0.04	0.528	-0.24	<0.001	-0.28	<0.001	-0.27	<0.001
Percentage of Lung with Density < -950HU (LAA)	-0.07	0.297	0.05	0.435	-0.28	<0.001	-0.33	<0.001	-0.32	<0.001
Air Trapping	-0.17	0.022	0.06	0.406	-0.12	0.104	-0.15	0.056	-0.14	0.065
Percent Predicted FEV1	0.07	0.268	0.03	0.626	-0.06	0.403	-0.09	0.162	-0.08	0.229
Percent Predicted FVC	0.12	0.074	0.10	0.138	-0.08	0.244	-0.15	0.029	-0.12	0.069
Asthma Control Test Score	-0.004	0.957	0.12	0.089	-0.03	0.672	-0.07	0.289	-0.06	0.409
Peripheral Percent Eosinophils	-0.08	0.218	-0.03	0.119	-0.11	0.098	-0.12	0.087	-0.12	0.085
Broncho-reversibility	0.09	0.187	0.11	0.101	0.03	0.621	0.08	0.243	0.05	0.433

Notes:

- 1) CT lung volume normalized by height in meters
- 2) All cardiac volumes normalized (indexed) by body surface area in square meters
- 3) Broncho-reversibility defined as (post-albuterol FEV1-pre-albuterol FEV1)/pre-albuterol FEV1.
- 4) Abbreviations: computed tomography (CT), forced expiratory volume in one second (FEV1), forced expiratory volume (FVC), asthma control test (ACT), pulmonary artery to aorta diameter ratio (PA/A), estimated epicardial left ventricular volume index (eELVVI), estimated epicardial right ventricular volume index (eERVVI), estimated epicardial total ventricular volume index (eETVVI), estimated right ventricular volume to estimated left ventricular volume ratio (eRV/eLV)

e-Tables 7A-B: Multivariable Associations between Asthma Severity, Pulmonary Artery to Aorta Ratio and Right Ventricular Volume to Left Ventricular Volume Ratio in those without Visually Defined Emphysema

e-Table 7A: Healthy Control as Reference

Asthma Severity	Pulmonary Artery/ Aorta Diameter			Estimated Right Ventricular/ Estimated Left Ventricular Volume				
	Difference	95% CI	p	Difference	95% CI	p		
Healthy Control	Reference			Reference				
Mild/Moderate Asthma	-0.031	-0.127	0.065	0.529	-0.024	-0.068	0.019	0.273
Severe Asthma	-0.059	-0.157	0.038	0.233	-0.032	-0.076	0.013	0.161

e-Table 7B: Mild/Moderate Asthma as Reference

Asthma Severity	Pulmonary Artery/ Aorta Diameter			Estimated Right Ventricular/ Estimated Left Ventricular Volume				
	Difference	95% CI	p	Difference	95% CI	p		
Mild/Moderate Asthma	Reference			Reference				
Severe Asthma	-0.029	-0.074	0.017	0.217	-0.007	-0.028	0.013	0.488

Notes:

- 1) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume
- 2) Abbreviations: confidence interval (CI)

e-Tables 8A-B: Multivariable Associations between Asthma Severity and Cardiac Ventricular Volumes in those without Visually Defined Emphysema

Table E8A: Healthy Control as Reference

Asthma Severity	eELVVI				eERVVI				eETVVI			
	Difference	95% CI		p	Difference	95% CI		p	Difference	95% CI		p
Healthy Control	Reference				Reference				Reference			
Mild/Moderate Asthma	-11.6	-25.7	2.4	0.105	-9.8	-19.6	-0.02	0.0496	-21.5	-44.6	1.67	0.069
Severe Asthma	-19.8	-34.1	-5.5	0.007	-15.6	-25.5	-5.6	0.002	-35.4	-58.9	-11.8	0.003

e-Table 8B: Mild/Moderate Asthma as Reference

Asthma Severity	eELVVI				eERVVI				eETVVI			
	Difference	95% CI		p	Difference	95% CI		p	Difference	95% CI		p
Mild/Moderate Asthma	Reference				Reference				Reference			
Severe Asthma	-8.1	-14.8	-1.5	0.017	-5.8	-10.4	-1.1	0.016	-13.9	-24.9	-2.9	0.013

Notes:

- 1) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, percent predicted forced expiratory volume in one second, the percentage of lung occupied by low attenuation area and height normalized computed tomography measured lung volume
- 2) Abbreviations: confidence interval (CI), estimated epicardial left ventricular volume index (eELVVI), estimated epicardial right ventricular volume index (eERVVI), estimated epicardial total ventricular volume index (eETVVI)

e-Tables 9A-B: Multivariable Associations between PA/A and RV/LV Measures and Exacerbations in those without Visually Defined Emphysema

e-Table 9A: Exacerbations in the Year Prior to Enrollment

	Incident Rate Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	0.93	0.53	1.65	0.808
Estimated Right Ventricular to Estimated Left Ventricular Volume Ratio	1.34	0.94	1.91	0.103

e-Table 9B: Exacerbations during Follow up

	Incident Rate Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	1.03	0.58	1.83	0.934
Estimated Right Ventricular to Estimated Left Ventricular Volume Ratio	0.97	0.66	1.42	0.875

Notes:

- 1) Incident rate ratios are expressed as those with high versus those with a low eRV/eLV (greater than the median vs. lower than median) and high versus low PA/A (greater than 1 vs. less than 1).
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, low attenuation area, height normalized CT measured lung volume, percent predicted forced expiratory volume in one second, asthma control test score and asthma severity (mild/moderate vs. severe)
- 3) Prospective analyses also adjusted for exacerbation reported in the year prior to enrollment
- 4) Abbreviations: pulmonary artery to aorta diameter ratio (PA/A), estimated left ventricular volume ratio (eRV/eLV), computed tomography (CT)

e-Tables 10A-B: Multivariable Associations between PA/A and RV/LV Measures and Exacerbations in the Subgroup without Visually Defined Emphysema and with Severe Asthma

e-Table 10A: Exacerbations in the Year Prior to Enrollment

	Incident Rate Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	0.91	0.52	1.59	0.731
Estimated Right Ventricular to Estimated Left Ventricular Volume Ratio	1.36	0.96	1.92	0.081

e-Table 10B: Exacerbations during Follow up

	Incident Rate Ratio	Confidence Interval		p
Pulmonary Artery to Aorta Diameter Ratio	1.76	1.00	3.11	0.049
Estimated Right Ventricular to Estimated Left Ventricular Volume Ratio	0.84	0.58	1.22	0.349

Notes:

- 1) Incident rate ratios are expressed as those with high versus those with a low eRV/eLV (greater than the median vs. lower than median) and high versus low PA/A (greater than 1 vs. less than 1).
- 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, low attenuation area, height normalized CT measured lung volume, percent predicted forced expiratory volume in one second and asthma control test score
- 3) Prospective analyses also adjusted for exacerbation reported in the year prior to enrollment
- 4) Abbreviations: pulmonary artery to aorta diameter ratio (PA/A), estimated left ventricular volume ratio (eRV/eLV), computed tomography (CT)

e-Tables 11A-B: Multivariable Associations between Cardiac Volume Measures and Exacerbations in those without Visually Defined Emphysema

e-Table 11A: Exacerbations in the Year Prior to Enrollment

	Incident Rate Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	1.31	0.88	1.95	0.190
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	1.64	1.08	2.48	0.020
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	1.49	0.98	2.27	0.061

e-Table 11B: Exacerbations during Follow up

	Incident Rate Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	1.54	1.06	2.22	0.022
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	1.51	1.04	2.18	0.050*
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	1.66	1.13	2.45	0.010

- Notes:**
- 1) Incident rate ratios are expressed as those with lower volume compared to those with higher volume dichotomized at the median
 - 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, low attenuation area, height normalized CT lung volume, percent predicted forced expiratory volume in one second, asthma control test score and asthma severity (mild/moderate vs. severe)
 - 3) Prospective analyses also adjusted for exacerbation reported in the year prior to enrollment
 - 4) Abbreviations: computed tomography (CT), estimated epicardial left ventricular volume index (eELVVI), estimated epicardial right ventricular volume index (eERVVI), estimated epicardial total ventricular volume index (eETVVI)
- * Rounded from 0.049951

e-Tables 12A-B: Multivariable Associations between Cardiac Volume Measures and Exacerbations in the Subgroup without Visually Defined Emphysema and with Severe Asthma

e-Table 12A: Exacerbations in the Year Prior to Enrollment

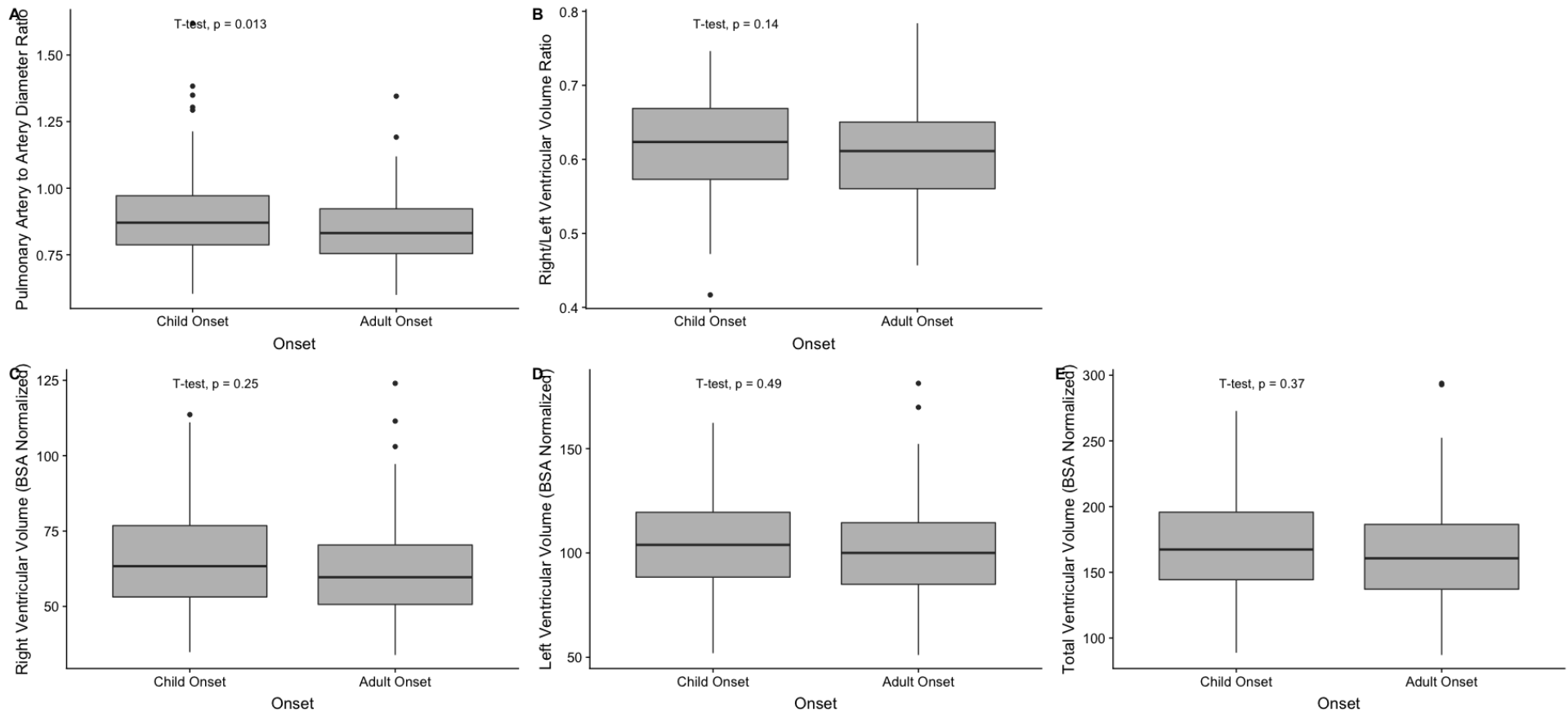
	Incident Rate Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	1.42	0.96	2.10	0.082
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	1.63	1.10	2.43	0.015
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	1.73	1.15	2.60	0.009

e-Table 12B: Exacerbations during Follow up

	Incident Rate Ratio	Confidence Interval		p
Estimated Epicardial Left Ventricular Volume Index (eELVVI)	1.45	1.00	2.10	0.052
Estimated Epicardial Right Ventricular Volume Index (eERVVI)	1.53	1.07	2.20	0.021
Estimated Epicardial Total Ventricular Volume Index (eETVVI)	1.72	1.19	2.49	0.004

- Notes:**
- 1) Incident rate ratios are expressed as those with lower volume compared to those with higher volume dichotomized at the median
 - 2) Multivariable models adjusted for age, sex, race, body mass index, systolic blood pressure, low attenuation area, height normalized CT lung volume, percent predicted forced expiratory volume in one second and asthma control test score
 - 3) Prospective analyses also adjusted for exacerbation reported in the year prior to enrollment
 - 4) Abbreviations: computed tomography (CT), estimated epicardial left ventricular volume index (eELVVI), estimated epicardial right ventricular volume index (eERVVI), estimated epicardial total ventricular volume index (eETVVI)

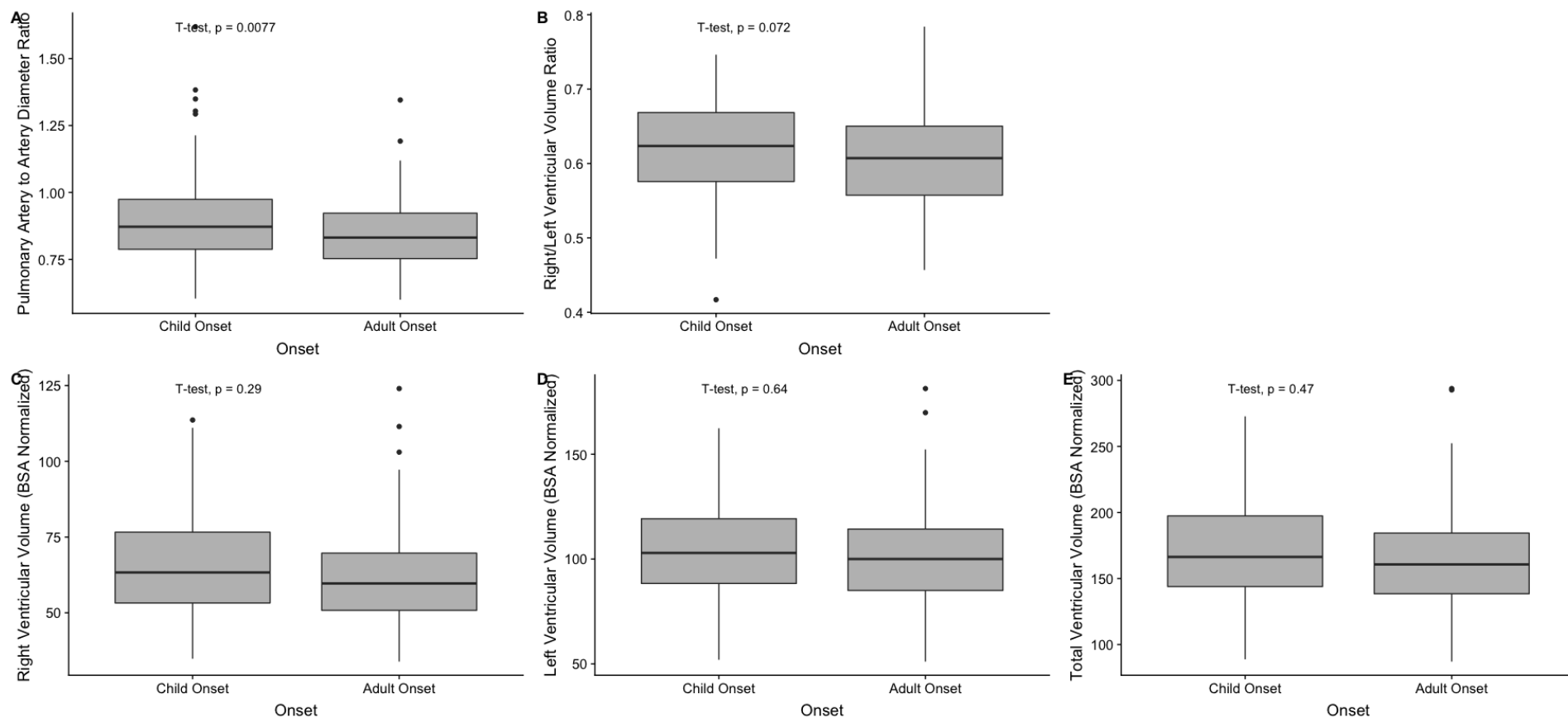
e-Figure 1: Pulmonary artery and cardiac measures by time of asthma diagnosis (childhood versus adult) in the entire cohort



Notes:

- 1) Childhood onset defined as patient reported diagnosis prior to the age of 18
- 2) Comparison between groups performed using t tests

e-Figure 2: Pulmonary artery and cardiac measures by time of asthma diagnosis (childhood versus adult) in those with visual emphysema excluded



Notes:

- 1) Childhood onset defined as patient reported diagnosis prior to the age of 18
- 2) Comparison between groups performed using t tests