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Use of Echocardiography at Diagnosis and Detection of Acute Cardiac Disease in Youth with Systemic Lupus Erythematosus

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Abstract

Objectives—There are no guidelines on the use of echocardiography to detect cardiac manifestations of child-onset systemic lupus erythematosus (SLE). We quantify the prevalence of acute cardiac disease in youth with SLE, describe echocardiogram utilization at SLE diagnosis, and compare regional echocardiogram use with incident cardiac diagnoses.

Methods—Using the Clinformatics® DataMart (OptumInsight, Eden Prairie, MN) de-identified US administrative database from 2000–2013, we identified youth ages 5–24 years with new-onset SLE (≥ 3 ICD-9 SLE codes 710.0, >30 days apart) and determined the prevalence of diagnostic codes for pericardial disease, myocarditis, endocarditis and valvular insufficiency. Multiple logistic regression was used to identify factors associated with echocardiography during the baseline period, up to one year before or 6 months after SLE diagnosis. We calculated a regional echocardiogram utilization index, which is the ratio of observed use over the mean predicted probability based on all available baseline characteristics. Spearman's rank correlation coefficient was used to evaluate the association between regional echocardiogram utilization indices and percent of imaged youth diagnosed with their first cardiac manifestation following echocardiography.

Results—Among 699 youth with new-onset SLE, 18% had ≥ 1 diagnosis code for acute cardiac disease, of which valvular insufficiency and pericarditis were most common. 25% of all youth underwent echocardiogram during the baseline period. Regional echocardiogram use was

positively correlated with the percent of imaged youth found to have cardiac disease (p 0.71, p 0.05). There was up to a 5-fold difference in adjusted odds of baseline echocardiography between low and high-utilizing regions (OR 0.19, p 0.007).

Conclusion—Nearly one-fifth of youth with new-onset SLE have acute cardiac manifestations, however use of echocardiograms at SLE diagnosis is highly variable. There may be incremental diagnostic value to early use of echocardiography, but prospective studies are needed to determine whether greater use of echocardiograms modifies outcomes.

Key Terms

Pediatric systemic lupus erythematosus; Systemic lupus erythematosus; Cardiovascular diseases; Echocardiography; Diagnostic imaging

Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune condition with multi-organ involvement and a high-risk of cardiac complications, however the acute cardiac manifestations of SLE, including pericarditis, myocarditis, endocarditis and valvular insufficiency, are frequently asymptomatic.^{1,2} Transthoracic echocardiography is useful for assessing structural and functional abnormalities resulting from acute manifestations of SLE.³ It has additional advantages of being non-invasive and free of radiation, which are especially desirable in the care of children and adolescents. In the limited studies of cardiac involvement in child-onset SLE, the vast majority of acute cardiac manifestations occur within 6 months of SLE diagnosis.⁴ Therefore, peri-diagnostic echocardiography has the ability to identify cardiac involvement early in the disease course and may impact treatment choice, duration, and future monitoring. There is no data on current utilization patterns of echocardiography in youth with SLE, nor is there consensus on the appropriate use of echocardiography for the evaluation of cardiac involvement at SLE diagnosis. In addition, just as routine screening echocardiography in asymptomatic adults with SLE remains controversial,^{5–8} it is not known whether screening echocardiography in patients with child-onset disease is warranted. Compared to adult-onset SLE, child-onset disease confers a greater potential for cumulative tissue damage,⁹ and thus efforts directed toward early detection and treatment of major organ involvement are of particular importance. Assessment of current diagnostic imaging practices and exploration of the potential incremental diagnostic benefit of imaging are necessary first steps toward developing appropriate imaging guidelines.

The objectives of this study are to: 1) estimate the prevalence of acute cardiac manifestations of child-onset SLE using a population-based approach, 2) identify factors associated with use of echocardiography during the peri-diagnostic period in youth with SLE, and 3) assess the potential impact of variability in echocardiography use on subsequent rates of cardiac disease detection. We hypothesized that there is high prevalence of acute cardiac manifestations following SLE diagnosis in youth, and geographic areas with greater utilization of echocardiograms will have incrementally higher detection rates of cardiac disease.

Methods

Study Design

Retrospective population-based cohort study.

Data Source and Subjects

Using the Clinformatics® DataMart (OptumInsight, Eden Prairie, MN) de-identified U.S. administrative claims data from 2000 through 2013, we identified youth ages 5–24 years inclusive with an incident diagnosis of SLE. OptumInsight data is derived from a national commercial health insurance and Medicare Advantage (C and D) database that includes approximately 20% of U.S. residents. It contains de-identified patient and encounter-level data, including demographics, medical diagnoses specified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) codes, procedure codes, prescription drug claims, and provider specialty. An exemption for this study was approved by the Institutional Review Board at The Children's Hospital of Philadelphia (IRB #17-013682).

Youth with SLE were defined as individuals having at least 3 hospital or physician visit claims with an ICD-9 diagnosis code for SLE (710.0), each recorded at least 30 days apart. This algorithm has been validated in adults and published in children.^{10,11} As previously described, incident cases were defined as those who also had at least one year of claims data with no SLE codes in any position preceding the first primary or secondary SLE diagnosis code.¹² The date of SLE diagnosis was assigned as the first physician visit with a diagnosis code for SLE or the admission date of the first hospitalization with an SLE code, whichever came first. Individuals with pre-existing ICD-9 codes for congenital heart disease, bacterial endocarditis or rheumatic fever were excluded from the analysis.

Study Measures

Acute cardiac manifestations—Acute cardiac manifestations were defined as a composite outcome of at least one ICD-9 diagnosis code for pericarditis (423.1, 423.9× and 420. ××),^{13,14} myocarditis (422.9×, 429.0), endocarditis (424.91), or valvular insufficiency (424.0–424.3, excluding rheumatic heart disease (394.1) and bacterial endocarditis (421.0–421.9)).¹⁵ As disease manifestations can precede the recognition of SLE by months to years, we included cardiac diagnoses occurring within 12 months preceding the first SLE code until the end of enrollment.

Utilization of non-invasive diagnostic imaging—For assessment of echocardiogram utilization, the outcome was the presence of an ICD-9 procedure code 88.72 or CPT billing code for transthoracic echocardiography within the baseline period,¹⁶ defined as 12 months prior to and up to 6 months after the index date. To determine whether echocardiogram use reflected overall utilization of cardiac diagnostic tests, billing codes for 12-lead electrocardiography (ECG) during the baseline period were included as a secondary outcome.

Acute cardiac manifestations identified following echocardiography—In youth who underwent echocardiography during the baseline period, the primary outcome measure was the percent of youth with their first acute cardiac manifestation occurring on or after the date of initial echocardiography. The main exposures of interest were: 1) regional echocardiogram utilization and 2) the presence of cardiovascular signs and symptoms, defined by the presence of ICD-9 diagnosis codes pertaining to the categories of chest pain, dyspnea, murmur or other abnormal heart sounds, tachycardia and shock.

Covariates of interest included the following—Demographic characteristics (age at diagnosis, calendar year, sex, race/ethnicity, geographic region, household income); hospitalization within 30 days of the first SLE code as a proxy for disease severity; disease characteristics (lupus nephritis, major central nervous system (CNS) involvement as defined by seizure or stroke, any psychiatric disorder, hypertension, venous thromboembolism or antiphospholipid antibody syndrome (APS)); prescription claims for glucocorticoids, immunosuppressants, and anticoagulants. Baseline covariates were assessed 12 months prior to the index date until the date of echocardiogram or 6 months after the index date.

We categorized geographic region using the US Census Bureau groupings into 9 census divisions.¹⁷ Optum Analytics derives household education level from census data, while race and ethnicity are derived from a combination of public records, self-report and proprietary tables. Age was grouped into two categories, 5–17 and 18–24 years, to examine potential differences in utilization between the pediatric population and transition-age young adults. SLE nephritis was identified using a previously validated algorithm.^{10,11} Major CNS disease was defined by at least one ICD-9 code for seizure or cerebrovascular disease,^{18–20} and psychiatric disorders were defined as previously described,²¹ excluding substance abuse codes. Hypertension was identified using a coding algorithm validated in adults.²² ICD-9 codes for antiphospholipid antibody syndrome (289.8x) were combined with validated codes for venous thromboembolism to identify hypercoagulable states.^{23,24} Provider subspecialty was determined using Optum Analytics provider category codes.

Statistical Analysis

Demographic factors and clinical factors were described using standard statistics such as mean and standard deviation or median and interquartile range (IQR) for continuous variables, and count and frequency for categorical variables.

Prevalence of acute cardiac disease—We calculated the proportion of youth with SLE who had diagnosis codes for acute cardiac manifestations and the median time from the first SLE code to the first cardiac diagnosis code.

Factors associated with cardiac diagnostic test utilization—The Cuzick's Wilcoxon rank-sum test of trend was used to assess changes in echocardiogram use by calendar year. To identify factors independently associated with use of echocardiography at baseline, we performed multiple logistic regression with forward selection (p-value for entry 0.2). Covariates a priori determined to be of clinical significance (including age, race, household education level and hypertension) were forced into the model and retained if any

coefficient changed by more than 10%. Goodness of fit was assessed using the Pearson chi-square statistic. In a sensitivity analysis, we excluded youth with any acute cardiac manifestation codes preceding echocardiogram from the multivariable regression analysis of echocardiogram use to eliminate follow-up studies for prevalent cardiac disease. For comparison with other non-invasive cardiac testing, we used the same selection methods to perform a separate multivariable logistic regression analysis with baseline ECG as the dependent variable. To assess potential differences in referral patterns by provider specialty, we performed a subgroup analysis among youth seen by a rheumatologist during the baseline period to compare echocardiogram use in youth seen by pediatric versus adult rheumatologists.

Association between echocardiography use and incident cardiac diagnoses—

We calculated the proportion of youth with SLE within each census division that underwent echocardiography during the baseline period to determine observed regional utilization. Due to the small sample size from the East South Central division, East and West South Central divisions were combined into one South Central region for the analysis. To adjust for patient characteristics, we estimated a separate logistic regression model using all baseline covariates in Table 1 to predict the probability of echocardiogram, and averaged these probabilities across individuals within each census division. For each census division, the ratio of observed echocardiogram use over the mean predicted probability was taken as the utilization probability index. Census divisions with utilization indices greater than 1.0 were thus considered high utilizers, because observed use exceeded expected use given the patient characteristics of the region. We estimated the association between regional utilization probability index and the percent of echocardiograms followed by an incident cardiac diagnosis using Spearman's rank correlation coefficient. Similarly, we estimated the correlation between preceding cardiovascular sign or symptom codes and incident cardiac diagnoses following echocardiography.

We performed two sensitivity analyses for the association between utilization indices and cardiac diagnoses. To investigate the impact of a more stringent SLE case definition, we limited the cohort to youth with a prescription claim for antimalarial medications. Secondly, we excluded valvular insufficiency to assess the validity of a composite outcome including both myopericardial and valvular codes. All data analyses were performed using STATA 14.2 (STATA Corp, College Station TX) statistical software.

Results

We identified a total of 699 youth with new-onset SLE. The average continuous enrollment was 5.6 years, and average follow-up time was 3.6 years from 12 months before SLE diagnosis until the end of enrollment. Demographic and baseline disease characteristics are shown in Table 1. During the baseline period, 17% of the cohort had a diagnosis code for renal disease, 8% had a code for CNS disease, 20% had a psychiatric diagnosis, and 5% had a diagnosis of venous thromboembolism and/or APS. By the time of echocardiogram or 6 months after SLE diagnosis, 539 youth (77%) saw a rheumatologist, 18% saw a nephrologist, and 34% saw a cardiologist. During enrollment, the majority of youth with SLE had prescription claims for antimalarial drugs (82%) and oral glucocorticoids (84%),

5% had claims for cyclophosphamide and 46% had claims for other immunosuppressants (including mycophenolate, methotrexate, azathioprine, tacrolimus and leflunomide).

Prevalence of acute cardiac manifestations

128 youth (18%) had at least one diagnosis code for an acute cardiac manifestation during the observation period. Valvular insufficiency was the most common cardiac diagnosis, followed by pericardial disease (Table 2). There were no significant differences in the prevalence of cardiac diagnoses by age (χ^2 0.45, p-value 0.50). The median time from the first SLE code to the first cardiac diagnosis code was 15 days (IQR 0,338).

Echocardiogram utilization

178 (25%) youth with SLE had a billing code for a transthoracic echocardiogram within the baseline period, including 45% of youth with codes for venous thromboembolism/APS, and 40% of those with renal disease. Median time from the first SLE code to first echocardiogram was 1 day (IQR -18 to 16 days). Approximately 55% of echocardiograms were performed in an ambulatory setting, while the remainder were performed in a hospital setting. The majority (76%) of echocardiograms were billed for by cardiologists, and the remaining were billed primarily by hospitals, internists, and pediatricians. There were no significant temporal trends over time in echocardiogram utilization by calendar year (z-statistic 1.47, p-value 0.14).

Factors associated with echocardiogram utilization

On univariable analysis, hospitalization within 30 days of SLE diagnosis was the most strongly associated with echocardiography use (OR 5.23, 95% CI [3.58, 7.64]). Due to collinearity with renal disease, seizure, stroke, and venous thromboembolism, hospitalization was not included in variable selection for multivariable analysis. The results of the final multivariable analysis are shown in Table 1. Geographic area met criteria for inclusion in the model after adjustment for other subject characteristics (p-value 0.07, likelihood ratio test). Compared to high utilizing areas (E. North Central division), there was up to a 5-fold statistically significant difference in odds of echocardiography in the lowest utilizing areas (adjusted OR 0.28, 95% CI [0.11,0.71] and OR 0.19, 95% CI [0.04,0.89] for the Mid-Atlantic and E. South Central divisions, respectively). Socioeconomic factors did not explain the regional differences in utilization, nor did the re-addition of hospitalization to the multivariable model. Preceding CNS disease and hypercoagulable states were also independently associated with echocardiography (adjusted OR 1.88, 95% CI [1.02,3.47] and OR 2.27, 95% CI [1.11, 4.66], respectively). Exclusion of 11 youth with cardiac manifestation codes preceding echocardiogram from the multivariable regression analysis did not change the variable selection or estimates.

Factors associated with ECG utilization—231 (33%) youth with SLE had an ECG during the baseline period. CNS disease, hypertension, Hispanic ethnicity and higher education level were independently associated with ECG use (Table 3). Unlike echocardiography, geographic region was not associated with ECG use and did not meet criteria for inclusion in the multivariable model (p-value 0.5, likelihood ratio test).

Provider characteristics associated with echocardiogram utilization—In the subgroup analysis of youth seen by a rheumatologist during the baseline period, there was a trend toward higher odds of echocardiography among youth seen by pediatric rheumatology compared to adult rheumatology (adjusted OR 1.78, 95% CI [0.91,3.46], p-value 0.09). Accounting for provider type did not account for the regional variation.

Echocardiography use and incident diagnosis of cardiac disease

Among youth imaged during the baseline period, 80 (45%) received their first diagnosis of an acute cardiac manifestation after a median of 0 days (IQR 0-7) following the first echocardiogram. Of the 37 patients who did not undergo echocardiogram during the baseline period but were later diagnosed with cardiac disease, median time from SLE diagnosis to the first cardiac code was 546 days (IQR 287-1313) and valvular insufficiency comprised the majority of diagnoses (Table 2).

There was a significant positive correlation between the proportion of youth in each region that had an echocardiogram at baseline and the proportion of imaged youth who received an incident cardiac diagnosis following echocardiography (ρ 0.71, p-value 0.05). There was no significant correlation between age or non-white race with incident cardiac diagnosis following echocardiography (ρ 0.09, p-value 0.21) and ρ 0.13, p-value 0.09, respectively). Adjustment for patient characteristics using the regional utilization probability index yielded similar results. There was a strong positive correlation between observed over expected probability of echocardiography and the percentage of imaged youth with incident cardiac diagnoses by region (ρ 0.78, p-value 0.02) (Figure 1). Limiting SLE cases to antimalarial users (ρ 0.95, p-value <0.01) and excluding valvular insufficiency from the outcome (ρ 0.67, p-value 0.07) did not significantly change the results.

Among youth who had echocardiograms, 78% had at least one diagnosis code for a cardiovascular sign or symptom during the baseline period, compared to 38% of youth who did not have an echocardiogram (Table 4). In both groups, the most commonly coded symptom was chest pain, followed by dyspnea. The type of symptom codes did not differ between those with or without echocardiograms (χ^2 9.5, p-value 0.22). Within 30 days preceding the first echocardiogram, 51% of imaged youth had codes for cardiovascular symptoms. There was no correlation between cardiovascular symptoms within 30 days and incident cardiac diagnosis following echocardiography (ρ 0.02, p-value 0.75).

Discussion

In this large population-based study of children and young adults with new-onset SLE, there were several findings regarding acute cardiac disease and early use of echocardiography that may have important clinical implications. First, nearly one-fifth of youth had acute cardiac manifestations of SLE, the majority of which occurred near the time of SLE diagnosis. Second, use of echocardiography at SLE diagnosis was highly variable across regions. Third, we observed an increase in the percent of echocardiograms followed by a new cardiac diagnosis with increasing regional echocardiogram utilization indices. Lastly, preceding codes for cardiovascular symptoms did not correlate with new cardiac diagnoses following echocardiography. Our results point to the need for critical assessment of the incremental

diagnostic benefit of echocardiography in youth newly diagnosed with SLE, and for improved risk stratification to determine which youth warrant imaging at diagnosis.

We observed up to a 5-fold difference across geographic regions in the odds of echocardiography use that was not explained by other patient demographic or disease characteristics. Our results are consistent with previous studies of Medicare beneficiaries, which demonstrate substantial regional variation in the use of echocardiography and other non-invasive diagnostic imaging procedures.²⁵ To explain variation, the authors recommended considering clinical factors, supply of specialists and availability of services.²⁶ As expected, we found positive associations between echocardiography use and markers of disease severity such as renal and CNS involvement, but adjustment for these clinical factors did not explain the geographic variation. Secondly, we assessed potential practice differences between adult and pediatric rheumatologists since many adult rheumatologists care for children in underserved areas of the US. However, adjusting for provider type also failed to explain regional variability. Third, although patterns of echocardiography use may follow overall health service utilization trends,²⁶ the geographic variability we observed for echocardiograms did not follow patterns of ECG use. Our results suggest that there may be factors influencing resource allocation and practice variation specific to echocardiography that need to be explored further.

Heuristic approaches, peer practice norms, and differences between individual physicians' assessments of the value of specific tests may all influence use of non-invasive imaging.²⁷ This may be particularly relevant in pediatric rheumatology, where there are a limited number of providers, and practice norms at single centers may drive service utilization across a large region. Some centers may routinely image all youth at SLE diagnosis, while others selectively image only those suspected of having cardiac involvement. In our study, nearly 40% of youth who did not undergo echocardiography had the same cardiovascular sign and symptom codes as those who did, suggesting there may be differences in physicians' assessment of value of echocardiography in patients presenting with cardiovascular symptoms, or in clinical factors not able to be assessed by claims data. While heuristic approaches to care are not inherently bad, it is important to consider which deviations reflect decreased quality. Several authors have suggested that unexplained regional variability results from inappropriate use of imaging.²⁸ In the context of our study, inappropriate use could refer either to underutilization (failure to detect cardiac involvement), or overutilization (provision of echocardiograms that are not necessary for diagnosis of cardiac disease and lead to increased cost or undue worry). As a result, our study highlights the need to study the potential benefit of diagnostic imaging in this population that already incurs significant health-related expenditures.

To generate preliminary data about the potential value of echocardiograms in youth with SLE, we estimated the relationship between early echocardiogram use and identification of cardiac manifestations of lupus. Interestingly, there was a strong positive correlation between higher adjusted regional echocardiogram use and the proportion of imaged youth diagnosed with their first acute cardiac manifestation following echocardiography. Normally in overuse scenarios, further increases in utilization result in little or no incremental diagnostic benefit. In our study we observed that increases in utilization result in greater

incremental diagnostic benefit. There are several potential explanations for our results. First, the incidence of cardiac disease may simply be higher in regions where utilization is the highest. However, overall severity of SLE is expected to be lower in areas with higher latitude and greater UVB exposure, where echocardiogram use was highest.²⁹ Secondly, providers in regions who request echocardiograms more frequently may be more attuned to identifying or coding cardiac manifestations. Lastly, the low diagnosis rate of cardiac manifestations in low utilizing regions may reflect underuse of echocardiography. While no definitive conclusions can be made about underuse, we can hypothesize that some of the variation in care may result in under-detection of cardiac disease. Underuse is difficult to estimate, because there is no defined therapeutic effect of imaging and the negative effects on outcomes are indirect.²⁷ Prospective studies considering the long-term benefits of early detection and treatment of disease, will be needed to define underuse²⁸—and perhaps more importantly, appropriate use—of echocardiography in youth with SLE.

Risk stratification is an important tool to define appropriate use of cardiovascular imaging.²⁷ Current American Society of Echocardiography (ASE) guidelines only recommend echocardiograms for adults with SLE who have antiphospholipid antibodies or suggestive signs and symptoms,⁵ but there are no guidelines specific to child-onset SLE. In our study, only 45% of youth with antiphospholipid antibody syndrome underwent echocardiography, and the presence of cardiovascular symptom codes was not correlated with cardiac diagnoses after echocardiography. This is consistent with numerous studies in adults with SLE demonstrating a high prevalence of asymptomatic cardiac disease.^{1,2,30} Some authors argue that echocardiography should therefore be performed routinely.^{6–8} In the absence of known risk factors for cardiac involvement, routine echocardiography may be perceived to have a greater impact on child-onset disease due to the higher cumulative risk of organ damage. The trend toward increased use of echocardiography among youth seen by pediatric versus adult rheumatologists may partially reflect such provider preferences, in addition to access to pediatric imaging services and patient factors. Understanding the burden and risk factors for cardiac disease in child-onset SLE will be a necessary step in determining the utility of screening echocardiograms.

There are several limitations to our study. First, rates of echocardiography in this study may not be generalizable to other health systems with different accessibility and reimbursement schema. However, the degree of variation in imaging use within different health systems has been shown to be similar despite differences in absolute utilization rates.³¹ As a result, the geographic variability we observed in our study may be generalizable. A second limitation is that we were not able to assess differences at the level of hospital referral centers. Third, indications for echocardiography cannot be determined using claims data. We examined preceding cardiovascular symptom codes, but future studies with linked medical records or prospective data collection are necessary to corroborate our data. Lastly, there are limitations of using ICD-9 codes to evaluate disease manifestations. We were unable to quantify the severity of cardiac lesions such as valvular insufficiency, which can be trivial or mild in normal subjects. Valvular insufficiency that is coded by physicians is likely to be greater than trivial, however the clinical relevance of these diagnoses will need to be confirmed in future echocardiography studies.

To our knowledge, this is the only population-based study of cardiac manifestations of child-onset SLE, and the first study to evaluate the relationship between early non-invasive cardiovascular imaging use and diagnostic outcomes in youth with SLE. Our data suggest there may be incremental diagnostic value to increasing overall utilization of echocardiography, and the next steps are to determine whether screening echocardiography contributes to this increase in diagnostic value. Studies of unselected youth with SLE with and without cardiovascular signs or symptoms would help determine whether there is under- or over-detection of clinically important cardiac disease. There is a need for improved risk-stratification strategies to reduce practice variation and critical evaluations of how echocardiography affects subsequent care, patient outcomes and cost to determine optimal use.

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Figure 1.

Correlation between the percent of imaged youth diagnosed with their first cardiac manifestation following echocardiography and the regional echocardiogram utilization index (ratio of observed over expected echocardiogram use based on patient baseline characteristics). Value for ρ (p) is given by Spearman's rank correlation coefficient. Marker size reflects sample size of each region.

Table 1

Factors associated with use of echocardiogram at baseline

Baseline characteristics ^a	n	%	Unadjusted			Adjusted		
			OR	95% CI	p-value	OR	95% CI	p-value
Age	402	58	0.69	[0.49,0.96]	0.03	–	–	–
Female	621	89	0.92	[0.54,1.56]	0.75	–	–	–
Race/Ethnicity								
White	392	56	–	–	–	–	–	–
Black	117	17	1.38	[0.86,2.20]	0.18	1.37	[0.83,2.25]	0.21
Hispanic	99	14	1.45	[0.89,2.38]	0.14	1.42	[0.84,2.41]	0.19
Asian	44	6	1.64	[0.83,3.22]	0.16	1.73	[0.84,3.59]	0.14
Income < \$60K	200	29	1.27	[0.86,1.89]	0.23	–	–	–
High school or less	189	27	1.12	[0.76,1.67]	0.57	–	–	–
Census division								
E. North Central	102	15	–	–	–	–	–	–
New England	26	4	0.85	[0.34,2.15]	0.73	0.95	[0.35,2.56]	0.91
Mid-Atlantic	55	8	0.28	[0.11,0.68]	0.01	0.27	[0.11,0.69]	<0.01
W. North Central	76	11	0.73	[0.38,1.40]	0.34	0.83	[0.41,1.68]	0.61
South Atlantic	201	29	0.7	[0.42,1.18]	0.18	0.65	[0.37,1.14]	0.13
E. South Central	19	3	0.23	[0.05,1.03]	0.06	0.19	[0.04,0.91]	0.04
W. South Central	109	16	0.63	[0.35,1.14]	0.13	0.57	[0.30,1.09]	0.09
Mountain	60	9	0.48	[0.23,1.02]	0.06	0.51	[0.23,1.13]	0.10
Pacific	51	7	0.59	[0.27,1.27]	0.18	0.65	[0.28,1.48]	0.30
Renal disease	121	17	1.7	[1.14,2.53]	<0.01	2.23	[1.42,3.52]	<0.01
Hypertension	86	12	2.01	[1.25,3.22]	<0.01	–	–	–
CNS disease	58	8	1.75	[0.99,3.08]	0.05	1.94	[1.05,3.56]	0.03
Seizure	44	6	1.40	[0.72,2.70]	0.32	–	–	–
Stroke	20	3	2.00	[0.80,4.97]	0.14	–	–	–
Psychiatric diagnosis	139	20	1.08	[0.71,1.64]	0.73	–	–	–
VTE/APS ^b	38	5	2.51	[1.29,4.88]	0.01	2.26	[1.12,4.59]	0.02
Hospitalization ^c	165	24	5.23	[3.58,7.64]	<0.01	–	–	–

A multivariable logistic regression model (n=652) was used to identify factors associated with echocardiogram use up to 6 months after SLE diagnosis. 47 observations were dropped due to missing race.

^d Characteristics assessed prior to echocardiogram (n=178) or up to 6 months after SLE diagnosis (n=521)

^e VTE = venous thromboembolism; APS = antiphospholipid antibody syndrome

^c Hospitalization $\pm$ 30 days from diagnosis not included in multivariable selection due to multicollinearity

Table 2

Median time (days) from SLE diagnosis to first acute cardiac diagnosis

Cardiac diagnosis*	All youth (N=699)			Echocardiogram (N=178)			No echocardiogram (N=521)		
	n (%)	Median	IQR	n (%)	Median	IQR	n (%)	Median	IQR
Any cardiac manifestation	128 (18)	15	[0,338]	91 (51)	1	[-6,47]	37 (7)	546	[287,1313]
Pericarditis	60 (9)	6.5	[-1, 442]	45 (25)	0	[-3,23]	15 (3)	812	[458,1019]
Myocarditis	7 (1)	1	[-18, 155]	6 (3)	-1	[-18,20]	1 (0)	838	-
Endocarditis	9 (1)	154	[47, 951]	7 (4)	56	[18,951]	2 (0)	2089	[287,3890]
Valvular insufficiency	84 (12)	22.5	[1, 372]	57 (32)	3	[-31,48]	27 (5)	836	[285,1969]

Median time from 1st SLE code to 1st acute cardiac diagnosis code in days among youth who did or did not undergo echocardiography during baseline period

* Includes n = 11 cardiac diagnoses occurring prior to the first echocardiogram during the baseline period

Table 3
Patient characteristics associated with use of electrocardiography (ECG) at baseline

Baseline characteristics ^a	Unadjusted			Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
Age 18–24 years	1.00	[0.73,1.38]	1.00	–	–	–
Female	0.95	[0.58,1.57]	0.84	–	–	–
Race/Ethnicity						
White	–	–	–	–	–	–
Black	1.43	[0.93,2.22]	0.10	1.42	[0.91,2.22]	0.13
Hispanic	1.82	[1.15,2.87]	0.01	1.85	[1.16,2.94]	0.01
Asian	1.04	[0.52,2.05]	0.92	1.01	[0.51,2.00]	0.98
Income < \$60K	1.07	[0.74,1.54]	0.73	–	–	–
Bachelor degree or more	1.17	[0.8,1.68]	0.41	1.29	[0.88,1.90]	0.19
Census division						
E. North Central	–	–	–	–	–	–
W. North Central	0.63	[0.33,1.19]	0.16			
New England	0.97	[0.40,2.35]	0.94			
Mid-Atlantic	0.82	[0.41,1.62]	0.57			
South Atlantic	0.78	[0.47,1.27]	0.31			
E. South Central	0.29	[0.08,1.06]	0.06			
W. South Central	0.8	[0.45,1.40]	0.43			
Mountain	0.56	[0.28,1.13]	0.11			
Pacific	0.48	[0.22,1.02]	0.06			
Renal disease	1.52	[1.01,2.30]	0.05	–	–	–
Hypertension	1.83	[1.14,2.95]	0.01	1.63	[0.97,2.74]	0.07
CNS disease	1.54	[0.87,2.72]	0.14	1.49	[0.82,2.72]	0.19
Seizure	1.40	[0.74,2.63]	0.30	–	–	–
Stroke	2.44	[0.87,6.82]	0.09	–	–	–
Psychiatric diagnosis	1.18	[0.79,1.76]	0.41	–	–	–
VTE/APS ^b	1.70	[0.85,3.41]	0.14	–	–	–
Hospitalization ^c	5.35	[3.69,7.77]	<0.001	–	–	–

A multivariable logistic regression model (n=652) was used to identify factors associated with ECG use up to 6 months after SLE diagnosis. 47 observations were dropped due to missing race.

^a Characteristics assessed prior to ECG (n=226) or up to 6 months after SLE diagnosis (n=473)

^b VTE = venous thromboembolism; APS = antiphospholipid antibody syndrome

^c Hospitalization $\pm$ 30 days from diagnosis not included in multivariable selection due to multicollinearity

Table 4

Cardiovascular sign and symptom codes during baseline period

	Echocardiogram		No Echocardiogram		p-value
	n	%	n	%	
CV symptom during baseline period	139	78%	197	38%	<0.01
CV symptom category					0.22
Chest pain	62	45%	86	44%	
Tachycardia	11	8%	8	4%	
Palpitations	11	8%	16	8%	
Murmur	14	10%	10	5%	
Dyspnea	40	29%	76	39%	
Shock	1	1%	1	1%	
CV symptom 30 days prior to echocardiogram	90	51	—	—	—

Comparison of frequency and type of cardiovascular sign/symptom codes between youth who did and did not undergo echocardiography during the baseline period using χ^2 tests