Electrocardiogram as a Lyme Disease Screening Test

Desiree N. Neville, MD[1], Mark E. Alexander, MD[2], Jonathan E. Bennett, MD[3], Fran Balamuth, MD, PhD[4], Aris Garro, MD, MPH[5], Michael N. Levas, MD[6], Amy D. Thompson, MD[3], Anupam B. Kharbanda, MD, MSc[7], David P. Lewander, BS[8], Arianna H. Dart, BA[8], and Lise E. Nigrovic, MD, MPH[8], for Pedi Lyme Net

Objective To examine the association between electrocardiographic (ECG) evidence of carditis at the time of Lyme disease evaluation and a diagnosis of Lyme disease.

Study design We performed an 8-center prospective cohort study of children undergoing emergency department evaluation for Lyme disease limited to those who had an ECG obtained by their treating clinicians. The study cardiologist reviewed all ECGs flagged as abnormal by the study sites to assess for ECG evidence of carditis. We defined Lyme disease as the presence of an erythema migrans lesion or a positive 2-tier Lyme disease serology. We used logistic regression to measure the association between Lyme disease and atrioventricular (AV) block or any ECG evidence of carditis.

Results Of the 546 children who had an ECG obtained, 214 (39%) had Lyme disease. Overall, 42 children had ECG evidence of carditis, of whom 24 had AV block (20 first-degree). Of the patients with ECG evidence of carditis, only 21 (50%) had any cardiac symptoms. The presence of AV block (OR 4.7, 95% CI 1.8-12.1) and any ECG evidence of carditis (OR 2.3, 95% CI 1.2-4.3) were both associated with diagnosis of Lyme disease.

Conclusions ECG evidence of carditis, especially AV block, was associated with a diagnosis of Lyme disease. ECG evidence of carditis can be used as a diagnostic biomarker for Lyme disease to guide initial management while awaiting Lyme disease test results. *(J Pediatr 2021;238:228-32)*.

Lyme disease is the clinical manifestation of infection with *Borrelia burgdorferi*, which is transmitted by an *Ixodes* species tick. With a rapidly spreading geographic range, current estimates indicate that up to one-half a million new Lyme disease cases are diagnosed each year, of which approximately one-half occur in children.[1-3] There is the potential for substantial underdiagnosis of Lyme carditis, as not all children are symptomatic and many do not have an electrocardiogram (ECG) performed.[1,4-7]

Lyme carditis, first described in 1980,[8] is caused by invasion of cardiac tissue by spirochetes and the subsequent inflammatory response.[9,10] Atrioventricular (AV) block is the most common ECG finding in Lyme carditis,[4,5,7,8] although a wide spectrum of cardiac manifestations have been described, including tachyarrhythmias, myopericarditis, and ventricular dysfunction.[4,6,8,11-16] Lyme carditis typically resolves quickly with appropriate antibiotic treatment.[4,17-20] However, cardiac involvement is important to recognize, as abnormalities may fluctuate rapidly[8,19,21] and can rarely result in sudden death.[22-24] Some patients may need urgent temporary cardiac pacing, intravenous catecholamines, or rarely mechanical support for fulminant myocarditis as part of short-term support.[4,20] Adolescents and adults with Lyme disease are diagnosed more frequently with Lyme carditis and related complications compared with younger children with Lyme disease.[1,10,23]

As Lyme disease diagnostics take several days to return, clinicians must make initial management decisions before results are available. ECGs are performed routinely and interpreted at the time of initial clinical evaluation. We assembled a multicenter cohort of children undergoing emergency department (ED) evaluation for potential Lyme disease to evaluate ECG findings of carditis as a diagnostic marker for Lyme disease in children.

Methods

We performed a prospective cohort study at 8 pediatric EDs, each located in Lyme disease endemic areas and participating in Pedi Lyme Net: Boston Children's Hospital (Boston, Massachusetts), Children's Hospital of Philadelphia (Philadelphia, Pennsylvania), University of Pittsburgh Medical Center Children's Hospital of Pittsburgh (Pittsburgh, Pennsylvania), Children's Hospital

AV	Atrioventricular
COVID-19	Coronavirus disease 2019
ECG	Electrocardiogram
ED	Emergency department

From the [1]Division of Pediatric Emergency Medicine, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA; [2]Arrhythmia Service, Department of Cardiology, Boston Children's Hospital, Boston, MA; [3]Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE; [4]Division of Emergency Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; [5]Department of Emergency Medicine, Rhode Island Hospital, Providence, RI; [6]Division of Emergency Medicine, Medical College of Wisconsin, Milwaukee, WI; [7]Department of Pediatric Emergency Medicine, Children's Minnesota, Minneapolis, MN; and [8]Division of Emergency Medicine, Boston Children's Hospital, Boston, MA

Supported by the Boston Children's Hospital (L.N.) and the Global Lyme Alliance (L.N.). The authors declare no conflicts of interest.

Portions of this study were presented at the Pediatric Academic Societies annual meeting, April 24-May 1, 2019, Baltimore, Maryland.

https://doi.org/10.1016/j.jpeds.2021.07.010

of Wisconsin (Milwaukee, Wisconsin), Children's Minnesota (Minneapolis and St Paul, Minnesota), Nemours/Alfred I. duPont Hospital for Children (Wilmington, Delaware), and Hasbro Children's Hospital (Providence, Rhode Island). The study protocol was approved by the institutional review board at each of the participating centers with permission for data sharing. The Pedi Lyme Net data center was housed at Boston Children's Hospital.

We enrolled children 1-21 years of age undergoing evaluation for symptoms of Lyme disease between June 1, 2015, and October 31, 2020. Enrollment start dates varied by participating center. Study staff approached eligible children and/or their caregivers to obtain informed consent for participation, which included collection of clinical phenotypical data as well as research biological samples. We limited this study to those children who had an ECG obtained by their treating clinician during the index ED encounter.

We collected clinical data from the treating clinicians at the time of enrollment. We defined suspected clinical stage based on clinical symptoms: early (erythema migrans lesion), early-disseminated (fever, cranial neuritis, meningitis, and carditis), or late (arthritis). Study staff reviewed the medical records 1 month after enrollment to determine results of clinical laboratory tests and performed phone follow-up to determine clinical outcome. Based on review of the medical record, we determined whether Lyme disease serology was ordered based primarily on abnormal ECG findings. We abstracted the clinical cardiologist's ECG interpretation. REDCap, hosted by Harvard University, was used for all data capture.[25,26] All abnormal ECGs, as well as any previous ECGs, were deidentified and shared electronically with the Pedi Lyme Net data center.

Every ECG classified as abnormal by the clinical team was reread by the study cardiologist, who was blinded to the clinical history as well as the Lyme disease status. Any of the following ECG findings were considered evidence of potential carditis: AV block (any degree), prolonged QTc[27,28] ($QT/\sqrt{RR} > 460$ milliseconds), ST- or T-wave changes, ventricular enlargement, accelerated junctional rhythm, early repolarization, or right bundle branch block (QRS duration >120 milliseconds).[29] First-degree heart block was defined with PR interval of longer than 200 milliseconds.[30,31] Sinus bradycardia or tachycardia alone were considered nonspecific findings and were not included in our carditis definition. For children with ECG evidence of carditis who had a baseline ECG available, we determined whether the observed findings were present on a previous ECG.

We defined a case of Lyme disease based on the presence of physician-diagnosed erythema migrans lesion or a positive 2-tier Lyme disease serology in a patient with a compatible clinical picture. A positive clinical 2-tier Lyme serology was defined by a positive or equivocal first-tier enzyme immunoassay followed by a positive supplemental immunoblot. For children with symptom duration longer than 30 days, a positive immunoglobulin M immunoblot alone was considered a false positive.[32] For children with an initially negative Lyme disease test, we included any positive Lyme disease serology obtained within 30 days of enrollment as serology may be falsely negative early the in disease process.[33]

First, we compared study patients with and without ECG evidence of carditis using a χ^2 test for categorical variables and a Mann–Whitney U test for continuous variables. We then calculated the accuracy of ECG evidence of carditis for the diagnosis of Lyme disease. Next, we used logistic regression to measure the association between any ECG evidence of carditis overall and AV conduction delay specifically and the diagnosis of Lyme disease. To determine the impact of ECG screening, we calculated the number need to treat with empiric antibiotics defined as the inverse of the absolute risk reduction (ie, rate of Lyme disease minus rate of not having Lyme disease in children with ECG evidence of carditis in this population). We used SPSS, version 27.0.0, for all statistical analyses (IBM SPSS Statistics; IBM Corp).

Results

Over the study period, 2942 patients undergoing evaluation for Lyme disease were enrolled, of whom 546 (18.6%) had an ECG obtained (**Figure**). The proportion of children who had an ECG varied by participating center (range 5.3%-40.1%, $P < .001$). Of those who had an ECG performed, 214 (39.2%) had Lyme disease, of whom 9 (4.2%) had an erythema migrans lesion alone, 200 (93.5%) had positive 2-tiered serology, and 5 (2.3%) had both.

Of the 546 ECGs performed, the clinical ECG report was normal for 399 (73.1%) and abnormal for 147 (26.9%). Based on study cardiologist review, 105 (71.4% of ECGs initially read as abnormal) did not have ECG evidence of carditis: 58 normal, 14 sinus bradycardia, 10 sinus tachycardia, 17 sinus arrhythmia, 4 isolated premature ventricular contractions, and 2 isolated premature atrial contractions.

The remaining 42 (28.6% of ECGs initially read as abnormal) were classified by the study cardiologist as having ECG evidence suggestive of carditis (**Table I**). AV block was the most frequent abnormality, present in 24 ECGs (57.1% of those with abnormal ECGs). The ECGs with AV block had a median PR interval of 255 milliseconds (IQR 220-300 milliseconds). QTc prolongation greater than 460 milliseconds was the second most common finding, observed in 13 ECGs (31.0% of patients with abnormal ECGs). Of those with ECG evidence of carditis, only 3 had a baseline ECG available; none showed previous ECG evidence of carditis.

Children with evidence of carditis were more likely to present for evaluation during peak Lyme disease season (defined as June to October) and to have clinical symptoms of early-disseminated Lyme disease (**Table II**). The majority of children with ECG evidence of carditis had empiric antibiotics started at the time of initial evaluation and most were admitted to the hospital.

For approximately one-half of the children with ECG evidence of carditis, the ECG abnormalities prompted the treating clinician to obtain Lyme disease serology (**Table III**). Although one-half of the children had cardiac symptoms

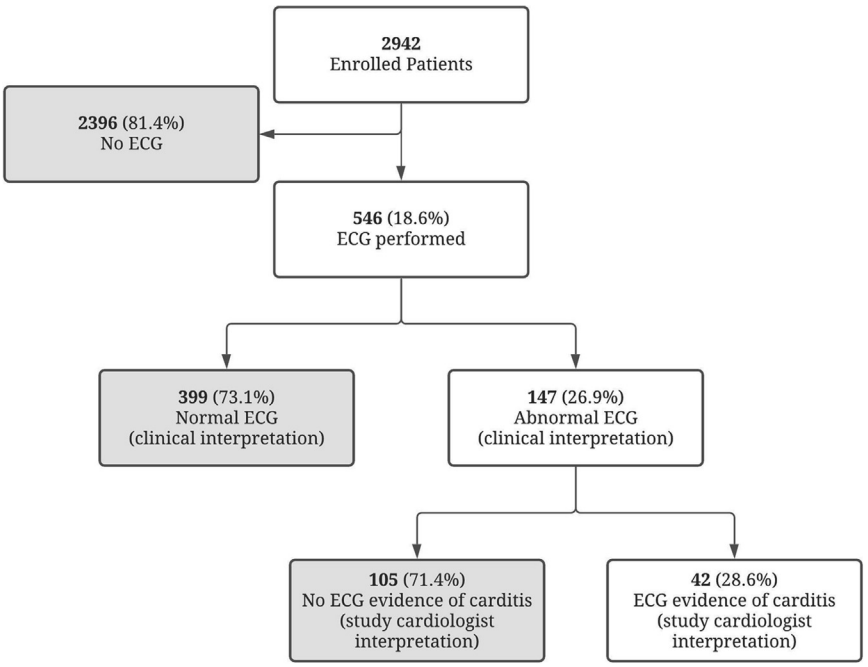

Figure. Study patients.

(eg, syncope, palpitations, dizziness, chest pain, or dyspnea), most had normal vital signs. Most of the patients with Lyme carditis had associated symptoms such as fatigue, facial nerve palsy, arthritis, or meningitis, but carditis was the sole manifestation of Lyme disease in 6 patients. The majority of children with ECG evidence of carditis had at least 1 follow-up ECG identified (n = 32, 76%). All children with Lyme carditis and a follow-up ECG had resolution of the ECG findings.

Of the 42 children with ECG evidence of carditis, 25 (59.5%) had Lyme disease. The sensitivity of ECG evidence of carditis for a diagnosis of Lyme disease was 11.7% (95% CI 8.0%-16.7%) and the specificity was 94.9% (95% CI 92.0%-96.8%; **Table IV**, available at www.jpeds.com). The presence of any ECG evidence of carditis (OR 2.3, 95% CI 1.2-4.3) as well as any AV block (OR 4.7, 95% CI 1.8-12.1) were both associated with a diagnosis of Lyme disease. As the ECG could be interpreted before the availability of Lyme disease serology results, we evaluated the number of study patients with ECG evidence of carditis who would require empiric antibiotics per study patient with Lyme carditis (number need to treat 1.7, 95% CI 1.2-2.2).

Table I. ECG findings consistent with carditis (each ECG could have more than 1 finding)

ECG findings of carditis	Overall (%) N = 42	Lyme disease (%) N = 25	Not Lyme disease (%) N = 17
AV block	24 (57%)	18 (72%)	6 (33%)
First degree	18	14	4
Second degree	4	3	1
Third degree	2	1	1
Other findings	23 (55%)	12 (48%)	11 (65%)
QTc prolongation	13	7	7
ST/T wave changes	6	3	3
Ventricular enlargement	2	1	2
Other*	4	3	1

*Accelerated junctional rhythm (n = 1), early repolarization (n =2), right bundle branch block (n = 1).

Discussion

In this large prospective cohort of children undergoing evaluation of Lyme disease, only one-fifth had an ECG obtained by the treating clinical team. Children with ECG evidence of carditis were older, more likely to present during peak Lyme season, and more likely to be hospitalized. ECG evidence of carditis, especially AV block, was highly associated with Lyme disease. Although Lyme disease serology takes several days to return results, an ECG can be interpreted immediately, providing an opportunity for timely diagnosis and earlier antibiotic initiation when Lyme disease is strongly suspected. Using ECG evidence of carditis as a Lyme disease screening test, approximately three children with Lyme disease would receive empiric antibiotics for every two without Lyme disease.

Similar to previous investigations, we found that children with Lyme disease can have ECG evidence of carditis, frequently without any cardiac symptoms. Depending on the population studied, 2%-10% of children with Lyme disease have ECG evidence of carditis, with greater prevalence in those with clinical manifestations of early-disseminated Lyme disease.[1,4,5,7,8] Given the low sensitivity, a normal

Table II. Comparison between children with and without evidence of carditis on ECG

Characteristics	ECG evidence of carditis N = 42 (%)	No evidence of carditis N = 504 (%)	*P* value
Demographics			
Age, y*	14 (11, 15)	10 (6, 14)	.001
Male	24 (57%)	297 (59%)	.82
Presentation during peak Lyme season	37 (88%)	323 (64%)	.002
Clinical features			
Stage			<.001
Early	3 (7%)	12 (2%)	
Early-disseminated	30 (71%)	283 (57%)	
Late	4 (10%)	193 (38%)	
Nonspecific symptoms	5 (12%)	16 (3%)	
Fever	12 (29%)	170 (34%)	.59
Management			
Admitted	31 (74%)	164 (33%)	<.001
Empiric antibiotics	28 (67%)	275 (55%)	.13
Lyme disease	25 (60%)	189 (38%)	.005

*Median (IQR).

Table III. Clinical characteristics of patients with ECG findings of carditis

Patients with ECG findings of carditis	Overall (%) N = 42	Lyme disease (%) N = 25	Not Lyme disease (%) N = 17*
Patients in whom Lyme evaluation was based on ECG findings	19 (45%)	7 (28%)	12 (71%)
Any cardiac symptoms	21 (50%)	10 (40%)	11 (65%)
Syncope	6	2	4
Palpitations	6	4	2
Dizzy/lightheaded	13	5	8
Chest pain	10	5	5
Dyspnea	8	5	3
Abnormal vital signs	5 (12%)	2 (8%)	3 (18%)
Bradycardic	3	1	2
Tachycardic	1	0	1
Orthostatic	1	1	0
Hypotension	0	0	0
Did ECG evidence of carditis resolve?†	20/32 (63%)	17/17 (100%)	3/15 (20%)

*Six alternate cardiac diagnoses (viral myocarditis [n = 2], congenital heart disease [n = 2], congenital heart block [n = 1], postural orthostatic tachycardia syndrome [POTS; n = 1]), 5 normal variants, and 6 no cause identified.
†For patients with an available follow-up ECG available.

ECG should not be used to exclude Lyme disease. However, the high specificity makes Lyme disease likely in the appropriate clinical scenario.

Most children with Lyme carditis improve rapidly on appropriate antibiotic treatment. However, additional monitoring may be required for some, depending on ECG findings and clinical symptoms. For example, children with significant first-degree block (PR interval ≥300 milliseconds), high-grade AV block (second- or third-degree block), evidence of myocardial dysfunction, or symptoms such as syncope, chest pain, or dyspnea warrant telemetry and cardiology evaluation.[34] Although not all children with carditis had Lyme disease, initiating empiric antibiotics active against *Borrelia* infection while awaiting test results in the appropriate clinical scenario should be strongly considered. However, as the ECG evidence of carditis is not specific to Lyme disease, clinicians should also consider other etiologies of conduction abnormalities. Using an ECG screen for children undergoing initial evaluation for Lyme disease could help ensure that children with Lyme carditis receive prompt diagnosis and treatment.

Our study has several limitations. First, we enrolled a convenience sample of children undergoing evaluation for Lyme disease based on availability of study staff and patient and caregivers willingness to participate, and we cannot determine whether the missed eligible patients differed. Second, as treating clinicians obtained an ECG for a minority of children undergoing Lyme disease evaluation with rates varying across centers, we cannot determine how the association between carditis and Lyme disease would have changed if all children had an ECG performed. A future direction could compare outcomes at centers with high and low ECG use. Third, as ECG findings of Lyme carditis can fluctuate[8,19,21] and we evaluated a single ECG without in-person follow-up, we may have missed some children with carditis. Fourth, as we did not have a baseline ECG for the majority of children, we could not determine whether ECG changes were acute. However, the resolution of all of the ECG changes in the Lyme carditis group suggests that they were, in fact, acute. Fifth, as the study cardiologist did not review ECGs that were read as normal by the clinical cardiologist, we may have missed some subtle abnormalities. Sixth, although only a minority of children with ECG evidence of carditis had a prolonged QTc, we did not collect nonantibiotic medications that could potentially explain this ECG finding. Seventh, Lyme disease serology can be falsely negative in some children with early-disseminated disease, including those with carditis, resulting in the potential misclassification of some children with Lyme disease. However, none of the children with ECG evidence of carditis and negative 2-tier Lyme disease serology seroconverted within 30 days of enrollment. Eighth, we defined carditis using operational definition based on ECG manifestation of conduction system disease. Consistent with the current diagnostic standard for Lyme carditis, we did not include more advanced evaluations of troponin, echocardiography, or biopsy. Finally, the majority of enrollment was done before the coronavirus disease 2019 (COVID-19) pandemic. Both pediatric multisystem inflammatory syndrome and less severe cases of COVID-19 infection may cause conduction system disease, which treating clinicians must consider while COVID-19 is at a pandemic scale.[35,36]

In the appropriate clinical scenario, ECG evidence of carditis should prompt evaluation for Lyme disease as well as initiation of appropriate antibiotics and patient monitoring until definitive diagnostic test results can be obtained. ■

We thank the patients and families who agreed to study participation, as well as the Pedi Lyme research staff who enrolled in this study. We acknowledge John Branda, MD (Massachusetts General Hospital, Boston, Massachusetts), who conducted research Lyme disease testing.

Submitted for publication Mar 31, 2021; last revision received Jul 1, 2021; accepted Jul 6, 2021.

Reprint requests: Desiree N. Neville, MD, Division of Emergency Medicine, Children's Hospital of Pittsburgh, 4401 Penn Ave, Pittsburgh, PA 15237. E-mail: Desiree.Neville@chp.edu

References

1. Schwartz AM, Hinckley AF, Mead PS, Hook SA, Kugeler KJ. Surveillance for Lyme disease—United States, 2008-2015. MMWR Surveill Summ 2017;66:1-12.
2. Hinckley AF, Connally NP, Meek JI, Johnson BJ, Kemperman MM, Feldman KA, et al. Lyme disease testing by large commercial laboratories in the United States. Clin Infect Dis 2014;59:676-81.
3. Kugeler KJ, Schwartz AM, Delorey MJ, Mead PS, Hinckley AF. Estimating the frequency of lyme disease diagnoses, United States, 2010-2018. Emerg Infect Dis 2021;27:616-9.
4. Costello JM, Alexander ME, Greco KM, Perez-Atayde AR, Laussen PC. Lyme carditis in children: presentation, predictive factors, and clinical course. Pediatrics 2009;123:e835-41.
5. Beach CM, Hart SA, Nowalk A, Feingold B, Kurland K, Arora G. Increasing burden of lyme carditis in United States Children's Hospitals. Pediatr Cardiol 2020;41:258-64.
6. Woolf PK, Lorsung EM, Edwards KS, Li KI, Kanengiser SJ, Ruddy RM, et al. Electrocardiographic findings in children with Lyme disease. Pediatr Emerg Care 1991;7:334-6.
7. Welsh EJ, Cohn KA, Nigrovic LE, Thompson AD, Hines EM, Lyons TW, et al. Electrocardiograph abnormalities in children with Lyme meningitis. J Pediatric Infect Dis Soc 2012;1:293-8.
8. Steere AC, Batsford WP, Weinberg M, Alexander J, Berger HJ, Wolfson S, et al. Lyme carditis: cardiac abnormalities of Lyme disease. Ann Intern Med 1980;93:8-16.
9. de Koning J, Hoogkamp-Korstanje JA, van der Linde MR, Crijns HJ. Demonstration of spirochetes in cardiac biopsies of patients with Lyme disease. J Infect Dis 1989;160:150-3.
10. Muehlenbachs A, Bollweg BC, Schulz TJ, Forrester JD, DeLeon Carnes M, Molins C, et al. Cardiac tropism of *Borrelia burgdorferi*: An autopsy study of sudden cardiac death associated with Lyme carditis. Am J Pathol 2016;186:1195-205.
11. Seslar SP, Berul CI, Burklow TR, Cecchin F, Alexander ME. Transient prolonged corrected QT interval in Lyme disease. J Pediatr 2006;148:692-7.
12. Rostoff P, Gajos G, Konduracka E, Gackowski A, Nessler J, Piwowarska W. Lyme carditis: epidemiology, pathophysiology, and clinical features in endemic areas. Int J Cardiol 2010;144:328-33.
13. Cunha BA, Elyasi M, Singh P, Jimada I. Lyme carditis with isolated left bundle branch block and myocarditis successfully treated with oral doxycycline. IDCases 2018;11:48-50.
14. Grella BA, Patel M, Tadepalli S, Bader CW, Kronhaus K. Lyme carditis: a rare presentation of sinus bradycardia without any conduction defects. Cureus 2019;11:e5554.
15. Shabbir MA, Saad Shaukat MH, Arshad MH, Sacco J. Lyme carditis presenting as atrial fibrillation in a healthy young male. BMJ Case Rep 2019;12.
16. Gazendam N, Yeung C, Baranchuk A. Lyme carditis presenting as sick sinus syndrome. J Electrocardiol 2020;59:65-7.
17. Salazar JC, Gerber MA, Goff CW. Long-term outcome of Lyme disease in children given early treatment. J Pediatr 1993;122:591-3.
18. Karadag B, Spieker LE, Schwitter J, Ruschitzka F, Luscher TF, Noll G, et al. Lyme carditis: restitutio ad integrum documented by cardiac magnetic resonance imaging. Cardiol Rev 2004;12:185-7.
19. Fuster LS, Gul EE, Baranchuk A. Electrocardiographic progression of acute Lyme disease. Am J Emerg Med 2017;35:1040.e5-6.
20. Bolourchi M, Silver ES, Liberman L. Advanced heart block in children with Lyme disease. Pediatr Cardiol 2019;40:513-7.
21. van der Linde MR, Crijns HJ, de Koning J, Hoogkamp-Korstanje JA, de Graaf JJ, Piers DA, et al. Range of atrioventricular conduction disturbances in Lyme borreliosis: a report of four cases and review of other published reports. Br Heart J 1990;63:162-8.
22. Forrester JD, Meiman J, Mullins J, Nelson R, Ertel SH, Cartter M, et al. Notes from the field: update on Lyme carditis, groups at high risk, and frequency of associated sudden cardiac death—United States. MMWR Morb Mortal Wkly Rep 2014;63:982-3.
23. Yoon EC, Vail E, Kleinman G, Lento PA, Li S, Wang G, et al. Lyme disease: a case report of a 17-year-old male with fatal Lyme carditis. Cardiovasc Pathol 2015;24:317-21.
24. Marx GE, Leikauskas J, Lindstrom K, Mann E, Reagan-Steiner S, Matkovic E, et al. Fatal Lyme carditis in New England: two case reports. Ann Intern Med 2020;172:222-4.
25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377-81.
26. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019;95:103208.
27. Saarel EV, Granger S, Kaltman JR, Minich LL, Tristani-Firouzi M, Kim JJ, et al. Electrocardiograms in healthy north american children in the digital age. Circ Arrhythm Electrophysiol 2018;11:e005808.
28. Taran LM, Szilagyi N. The duration of the electrical systole, Q-T, in acute rheumatic carditis in children. Am Heart J 1947;33:14-26.
29. Meziab O, Abrams DJ, Alexander ME, Bevilacqua L, Bezzerides V, Mah DY, et al. Utility of incomplete right bundle branch block as an isolated ECG finding in children undergoing initial cardiac evaluation. Congenit Heart Dis 2018;13:419-27.
30. Cheng S, Keyes MJ, Larson MG, McCabe EL, Newton-Cheh C, Levy D, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. JAMA 2009;301:2571-7.
31. Bratincsak A, Kimata C, Limm-Chan BN, Vincent KP, Williams MR, Perry JC. Electrocardiogram standards for children and young adults using Z-scores. Circ Arrhythm Electrophysiol 2020;13:e008253.
32. Lantos PM, Lipsett SC, Nigrovic LE. False positive Lyme disease IgM immunoblots in children. J Pediatr 2016;174:267-9.e1.
33. Branda JA, Body BA, Boyle J, Branson BM, Dattwyler RJ, Fikrig E, et al. Advances in serodiagnostic testing for Lyme disease are at hand. Clin Infect Dis 2018;66:1133-9.
34. Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2006;43:1089-134.
35. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334-46.
36. Dionne A, Mah DY, Son MBF, Lee PY, Henderson L, Baker AL, et al. Atrioventricular block in children with multisystem inflammatory syndrome. Pediatrics 2020;146:e2020009704.

Table IV. Performance of ECG evidence of carditis as a diagnostic biomarker for Lyme disease

Evidence	Lyme disease	Not Lyme disease
ECG evidence of carditis	25	17
No ECG evidence of carditis	189	315
Accuracy		
Sensitivity	25/214 (11.7%; 95% CI 8.0%-16.7%)	
Specificity	315/332 (94.9%; 95% CI 92.0%-96.8%)	
Positive predictive value	25/42 (59.5%; 95% CI 44.5%-73.0%)	
Negative predictive value	315/504 (62.5%; 95% CI 58.2%-66.6%)	