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Practice variability in management of infectious issues in heterotaxy: A survey of pediatric cardiologists

Rohit S. Loomba, MD[1] | Gabrielle Geddes, MD[1] | Amanda J. Shillingford, MD[2] | David A. Hehir, MD, MS[2]

[1]Children's Hospital of Wisconsin/Medical College of Wisconsin, Milwaukee, WI, USA

[2]Nemours/Alfred I. Dupont Hospital for Children, Wilmington, DE, USA

Correspondence
Children's Hospital of Wisconsin/Medical College of Wisconsin, 9000 Wisconsin Avenue, Milwaukee, WI, USA.
Email: loomba.rohit@gmail.com

Abstract

Background: Splenic dysfunction is common in heterotaxy syndrome, and increases the risk of bacteremia and bacteremia related mortality. Despite the risks associated with bacteremia in this setting, best practice guidelines for management of infectious concerns are lacking. We conducted a survey of pediatric cardiologists to characterize practice regarding the diagnosis of splenic dysfunction, approach to antibiotic prophylaxis, and management of possible bacterial infection.

Methods: A 22-item web-based survey was distributed via email to pediatric cardiologists in North America.

Results: We received 230 responses from 63 centers, for a response rate of 22%. The majority (83%) always obtain abdominal ultrasound to define splenic anatomy in the neonate with heterotaxy. Despite a normal ultrasound result, 43% perform additional splenic functional testing. In addition, 21% report prescribing antibiotic prophylaxis regardless of testing results. There was wide variability in timing of stopping of prophylaxis, with 36% responding "never" and 24% "not sure." Those with more years in practice were more likely to obtain functional testing, to indefinitely continue antibiotic prophylaxis once started, and to recommend the 23-valent pneumococcal vaccination.

Conclusion: In a survey of North American cardiologists, significant variability exists in the management of infectious issues in heterotaxy syndrome. The development of practice guidelines for diagnosis of splenic dysfunction, indications for and duration of antibiotic prophylaxis, and management of possible bacterial illness may lead to improved outcomes in this complex patient population.

1 | INTRODUCTION

Heterotaxy occurs in 1 in 10 000 live births[1–4] and can result in anatomic and functional abnormalities in nearly every organ system.[5–12] Heterotaxy represents a rotational abnormality of the thoraco-abdominal organs which occurs during embryologic development. The heterogeneity of associated morphologic abnormalities has led to variation in terminology; most commonly patients are segregated by either atrial (left or right atrial isomerism) or splenic anatomy (asplenia/polysplenia).[3] However, these classification systems fail to accurately predict immune function, and therefore risk of serious bacterial illness. In addition, the presence or absence of splenic tissue does not correlate with splenic function. Therefore relying on anatomic classification may not adequately risk stratify patients in many cases.

Patients with heterotaxy and congenital heart disease may be at particularly high risk of serious complications of bacterial infection. They may undergo multiple surgeries and spend prolonged periods of time hospitalized, incurring the risks inherent to intensive care management. As a consequence, there is an approximately three-fold increase in the incidence of bacteremia with as high as 44% mortality in those with heterotaxy and bacteremia.[13–15] Consensus guidelines for the evaluation and management of these immunologic risks are lacking. The aim of this survey was to determine the variability in: (1) the diagnosis of splenic function in heterotaxy; (2) indications for use of antibiotic prophylaxis; and (3) management of febrile illness and infectious complications in this population. In addition, the survey aimed at determining factors which may influence variability of survey responses including practice type and years of experience.

TABLE 1 Survey items and frequencies of corresponding responses

Survey item	Frequency
What level of postfellowship training are you?	
0 to 5 y	62 (27%)
6 to 15 y	73 (32%)
Over 16 y	95 (41%)
How would you describe your practice?	
Hospital based primarily academic	136 (59%)
Hospital based primarily clinical	80 (35%)
Hospital based private practice	8 (3%)
Nonhospital based private practice	2 (1%)
Other	4 (2%)
To determine splenic anatomy in patients with isomerism, I obtain an abdominal ultrasound:	
Always	182 (83%)
Mostly	0 (0%)
Sometimes	23 (11%)
Never	6 (3%)
Other	6 (3%)
In patients with isomerism who have a normal size spleen in a normal position, I:	
Assume splenic function is normal and perform no additional testing	95 (44%)
Assume splenic function is normal and perform additional functional testing	46 (21%)
Assume splenic function is abnormal and perform no additional functional testing	32 (15%)
Assume splenic function is abnormal and perform additional functional testing	35 (16%)
Other	10 (4%)
In patients with isomerism who have an abnormal spleen identified on ultrasound (abnormal position/inversus, hypoplastic, or multiple), I:	
Assume splenic function is normal and perform no additional functional testing	5 (2%)
Assume splenic function is normal and perform additional functional testing	6 (3%)
Assume splenic function is abnormal and perform no additional functional testing	106 (49%)
Assume splenic function is abnormal and perform additional functional testing	93 (43%)
Other	8 (3%)
If I were to order confirmatory testing of splenic function, I would order the following functional testing (check all that apply):	
Howell-Jolly bodies	156 (72%)
Pitted erythrocyte count	61 (28%)
99m technetium labelled scintigraphy	70 (32%)
Other	25 (12%)
In patients with isomerism and a normal spleen based on ultrasound, I prescribe antibiotic prophylaxis:	
In all patients	42 (21%)
Only in those patients with abnormal testing of splenic function as described previously	108 (53%)
Never	45 (22%)
Other	9 (4%)
In patients with isomerism and an abnormal spleen (absent or normally positioned%) by ultrasound, I prescribe antibiotic prophylaxis:	
In all patients	151 (74%)
Only in those patients with abnormal testing of splenic function as described previously	45 (22%)
Never	0 (0%)
Other	8 (4%)
In patients prescribed antibiotic prophylaxis, I recommend stopping at:	
2 y of age	0 (0%)
5 y of age	29 (14%)
Greater than 5 y of age but less than 18 y of age	25 (12%)
Over 18 y of age	21 (10%)
Never	73 (36%)
Not sure	48 (24%)
Other	8 (4%)
In a febrile isomerism patient I consider the following to be the most concerning risk factor for bacterial infection (select one):	
Age of patient	47 (28%)
Degree of fever	13 (8%)
Anatomic splenic status	10 (6%)
Functional splenic status	88 (52%)
Other	11 (6%)
I routinely assess the vaccination/immunization status of my patients with isomerism at each follow-up visit	
Yes	127 (76%)
No	40 (24%)
I routinely recommend that patients with isomerism receive the supplemental 23-valent pneumococcal vaccination in addition to routine vaccinations if over 2 y of age	
Yes	127 (76%)
No	40 (24%)

2 | METHODS

A 22-item web-based survey was distributed via email to pediatric cardiologists in North America. A total of 1046 attending pediatric cardiologists were invited to take the survey. Attending cardiologists were invited to take the survey via an online forum targeted to pediatric cardiology attendings as well as emails sent to attending pediatric cardiologists listed in the 2014 Congenital Cardiology Today directory. A second email was sent to all those previously contacted as a reminder to complete the survey 2 weeks after the survey was made available. The survey remained open for a total of 4 weeks. No paper copies of the survey were distributed. Responses remained anonymous with no personal identifying information being linked to survey responses. Institutional Review Board review was waved.

The survey consisted of 19 total questions (Appendix A). Three demographic questions were used to describe the characteristics of the responders. Thirteen of the survey questions focused on the cardiologist's clinical practice in evaluating splenic function, use of prophylactic antibiotics, and immunization recommendations. Six questions presented clinical vignettes regarding management of a febrile patient with isomerism.

Frequencies of responses were reported as count and percent. Differences in responses were analyzed using chi-square analysis with characterized by physician experience and practice type statistical analysis was performed using SPSS statistical software version 20.0 (Chicago, IL). A P value of less than 0.05 was considered statistically significant.

TABLE 2 Overview of responses to clinical vignette 1

In a well appearing outpatient with isomerism and presumed splenic dysfunction, who is under 2 y of age and who has a fever >38.5°C but <39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	3 (2.01%)	77 (51.68%)	69 (46.31%)
Have the patient evaluated in clinic	50 (32.47%)	97 (62.99%)	7 (4.55%)
Have the patient evaluated in the ER	28 (17.72%)	124 (78.48%)	6 (3.80%)
Have the patient admitted to an inpatient service	15 (9.74%)	120 (77.92%)	19 (12.34%)
Obtain a blood culture	94 (58.02%)	65 (40.12%)	3 (1.85%)
Obtain a complete blood count	105 (65.63%)	52 (32.50%)	3 (1.88%)
Obtain a C-reactive protein	64 (41.03%)	85 (54.49%)	7 (4.49%)
Obtain a urine culture	56 (35.67%)	98 (62.42%)	3 (1.91%)
Obtain a urinalysis	60 (38.46%)	91 (58.33%)	5 (3.21%)
Obtain a chest x-ray	32 (20.65%)	115 (74.19%)	8 (5.16%)
Administer antibiotics	44 (27.85%)	108 (68.35%)	6 (3.80%)

3 | RESULTS

A total of 1046 pediatric cardiologists were contacted. Two hundred thirty completed the survey, for a response rate of 22%. Responders were affiliated with 63 different institutions. The characteristic of the responders are displayed in Table 1.

3.1 | Approach to diagnosis of splenic dysfunction (Table 2)

When confronted with patients with heterotaxy, 182 (83%) of 230 responded they always obtain an abdominal ultrasound to determine splenic anatomy while 23 (11%) reported they do this sometimes, and 12 (6%) reported never. Regardless of ultrasound result, there is wide variability in approach to confirmatory splenic functional testing and antibiotic prophylaxis as shown in Table 2.

When asked how they would assess splenic function, 156 (72%) reported they would obtain Howell-Jolly bodies, 61 (28%) pitted erythrocyte count, and 70 (32%) 99 m-technetium labelled scintigraphy.

3.2 | Approach to antibiotic prophylaxis and immunization (Table 3)

In regards to prophylactic antibiotics, 108 (53%) reported they would prescribe prophylaxis only in those with abnormal splenic function, 45 (22%) would never prescribe prophylaxis, and 42 (21%) would always prescribe prophylaxis. A free-text field accompanying this question revealed a wide variety of rationale, with the most common that the responder assumed all patients with isomerism to have abnormal splenic function, while the second most common response assumed normal splenic function whenever any splenic tissue is present.

When prophylactic antibiotics are prescribed, 73 (36%) never discontinue antibiotics, 29 (14%) stop at 5 years of age, 25 (12%) between 5 and 18 years of age, and 21 (10%) at 18 years of age or older. Nearly one-fourth, 48 (24%) reported being unsure of when to stop antibiotics once they were started. The most common free-text response regarding discontinuation of prophylaxis was that prophylaxis is never discontinued. The second most common response was that data from the sickle cell population is extrapolated and applied to those with heterotaxy. The third most common response cited guidelines for those with asplenia.

When questioned regarding routine assessment of immunization status follow-up visits for children with heterotaxy, 127 (76%) reported routinely doing so. The same number, 127 (76%) reported routinely recommending that patients with isomerism receive the supplemental 23-valent pneumococcal vaccination in addition to routine vaccinations if over the age of 2 years.

3.3 | Approach to the febrile patient (Table 4)

When asked what factors in febrile patients are associated with greatest risk of bacterial infection, 88 (52%) reported splenic function, 47 (28%) the age of the patient, 13 (8%) reported the degree of fever, and 10 (6%) reported anatomic splenic status. A free-text response yielded additional answers, the most common of which was postoperatively after cardiac surgery, particularly when indwelling catheters are present.

TABLE 3 Overview of responses to clinical vignette 2

In a well appearing outpatient with isomerism and presumed splenic dysfunction, who is between 2 and 5 y of age and who has a fever >38.5°C but <39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	5 (3.40%)	104 (70.75%)	38 (25.85%)
Have the patient evaluated in clinic	36 (23.23%)	112 (72.26%)	7 (4.52%)
Have the patient evaluated in the ER	17 (11.18%)	127 (83.55%)	8 (5.26%)
Have the patient admitted to an inpatient service	9 (6.04%)	115 (77.18%)	25 (16.78%)
Obtain a blood culture	72 (46.15%)	80 (51.28%)	4 (2.56%)
Obtain a complete blood count	78 (50.65%)	72 (46.75%)	4 (2.60%)
Obtain a C-reactive protein	51 (33.77%)	92 (60.93%)	8 (5.30%)
Obtain a urine culture	39 (25.83%)	103 (68.21%)	9 (5.96%)
Obtain a urinalysis	43 (28.48%)	100 (66.23%)	8 (5.30%)
Obtain a chest x-ray	25 (16.45%)	117 (76.97%)	10 (6.58%)
Administer antibiotics	28 (18.18%)	116 (75.32%)	10 (6.49%)

TABLE 4 Overview of responses to clinical vignette 3

In a well appearing outpatient with heterotaxy and presumed splenic dysfunction, who is over 5 y of age and who has a fever >38.5°C but <39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	10 (6.62%)	118 (78.15%)	23 (15.23%)
Have the patient evaluated in clinic	30 (18.99%)	122 (77.22%)	6 (3.80%)
Have the patient evaluated in the ER	11 (7.14%)	129 (83.77%)	14 (9.09%)
Have the patient admitted to an inpatient service	4 (2.61%)	124 (81.05%)	25 (16.34%)
Obtain a blood culture	52 (33.12%)	100 (63.69%)	5 (3.18%)
Obtain a complete blood count	61 (39.35%)	90 (58.06%)	4 (2.58%)
Obtain a C-reactive protein	39 (25.49%)	105 (68.63%)	9 (5.88%)
Obtain a urine culture	29 (18.95%)	112 (73.20%)	12 (7.84%)
Obtain a urinalysis	30 (19.87%)	109 (72.19%)	12 (7.95%)
Obtain a chest x-ray	14 (9.33%)	124 (82.67%)	12 (8.00%)
Administer antibiotics	13 (8.55%)	127 (83.55%)	12 (7.89%)

In the clinical vignettes, there was marked variability in evaluation and management of the febrile child with heterotaxy, testing performed, and administration of antibiotics (Tables 2–8).

3.4 | Impact of responder characteristics: practice type and years of experience (Table 5)

When responses were compared by years of experience, those with increasing experience were more likely to assume splenic function is abnormal and perform functional testing in those with an abnormal spleen on ultrasound ($P = .003$). More experienced cardiologists also tended to discontinue prophylactic antibiotics at a later age or never ($P < .0001$). More experienced cardiologists also tended to be more likely to routinely recommend that patients with isomerism receive the 23-valent pneumococcal vaccination if over 2 years of age.). Responses did not differ by practice type.

4 | DISCUSSION

This survey demonstrated variability in the practice of pediatric cardiologists in approach to diagnosis and management of splenic abnormalities children with heterotaxy. As the risk of bacterial infection in those with isomerism has been documented to be three-fold higher than in those without isomerism and this bacteremia is associated with increased mortality, it is important to establish best-practice guidelines for the evaluation and management of infectious risks in these patients.[13,14]

Abdominal ultrasound is often the initial step in assessing splenic anatomy in heterotaxy. However, splenic anatomy does not correlate well with function, and may not be adequate to risk stratify infectious complications in heterotaxy. Nagel and colleagues have demonstrated that functional asplenia may be present in the setting of a solitary spleen or multiple spleens in those with isomerism.[16] With this mind it becomes concerning that 44% of responders reported that they assume splenic function is normal and perform no additional testing if there is a normal appearing solitary spleen in a child with isomerism. When questioned about prescribing prophylactic antibiotics, 22% said they would never prescribe prophylactic antibiotics in the setting of isomerism with a normal appearing solitary spleen.

The recognition of functional asplenia was much higher when responders were asked about abnormal spleens which included an abnormally located spleen, a hypoplastic spleen or multiple spleens. In this instance only 2% would assume normal function and perform no additional testing despite evidence that functional asplenia may be present in this setting.[16]

While definition of splenic anatomy via ultrasound may add valuable clinical information, this does not accurately predict those at risk for bacteremia and subsequent serious bacterial illness. Therefore, functional splenic testing may be necessary to predict those requiring antibiotic prophylaxis and more aggressive work up of fever. Splenic function may be assessed via Howell-Jolly body testing, pitted erythrocyte count, or 99m technetium labelled scintigraphy. Pitted erythrocyte counts are the most reliable, with a count of above 4% being

TABLE 5 Overview of responses to clinical vignette 4

In a well appearing outpatient with isomerism and presumed splenic dysfunction, who is less than 2 y of age and who has a fever >39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	2 (1.39%)	37 (25.69%)	105 (72.92%)
Have the patient evaluated in clinic	44 (29.73%)	83 (56.08%)	21 (14.19%)
Have the patient evaluated in the ER	48 (31.37%)	99 (64.71%)	6 (3.92%)
Have the patient admitted to an inpatient service	53 (33.97%)	94 (60.26%)	9 (5.77%)
Obtain a blood culture	116 (74.36%)	37 (23.72%)	3 (1.92%)
Obtain a complete blood count	124 (79.49%)	30 (19.23%)	2 (1.28%)
Obtain a C-reactive protein	88 (57.14%)	64 (41.56%)	2 (1.30%)
Obtain a urine culture	89 (57.05%)	66 (42.31%)	1 (0.64%)
Obtain a urinalysis	89 (58.17%)	63 (41.18%)	1 (0.65%)
Obtain a chest x-ray	60 (39.22%)	89 (58.17%)	4 (2.61%)
Administer antibiotics	84 (54.19%)	67 (43.23%)	4 (2.58%)

TABLE 6 Overview of responses to clinical vignette 5

In a well appearing outpatient with heterotaxy and presumed splenic dysfunction, who is between 2 and 5 y of age and who has a fever >39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	3 (2.04%)	69 (46.94%)	75 (51.02%)
Have the patient evaluated in clinic	46 (29.87%)	94 (61.04%)	14 (9.09%)
Have the patient evaluated in the ER	38 (24.20%)	113 (71.97%)	6 (3.82%)
Have the patient admitted to an inpatient service	27 (17.31%)	119 (76.28%)	10 (6.41%)
Obtain a blood culture	108 (67.92%)	49 (30.82%)	2 (1.26%)
Obtain a complete blood count	114 (71.70%)	44 (27.67%)	1 (0.63%)
Obtain a C-reactive protein	76 (49.35%)	74 (48.05%)	4 (2.60%)
Obtain a urine culture	66 (42.04%)	87 (55.41%)	4 (2.55%)
Obtain a urinalysis	71 (45.81%)	81 (52.26%)	3 (1.94%)
Obtain a chest x-ray	46 (29.49%)	106 (67.95%)	4 (2.56%)
Administer antibiotics	65 (41.67%)	84 (53.85%)	7 (4.49%)

consistent with functional asplenia. When the pitted erythrocyte count is between 4 and 8%, Howell-Jolly bodies may actually be absent and thus functional splenic impairment may be missed.[17,18] False negatives may occur with both pitted erythrocyte counts and Howell-Jolly body testing in the first 2 years of life, thus making testing in the first 2 years of life unreliable. Technetium labelled scintigraphy utilizes radiation and is associated with high resource utilization in regards to expense, time, and technician skill. With Howell-Jolly body testing and pitted erythrocyte testing available it is no longer necessary.[19] In this survey, 32% responded that the test they would order to assess splenic function is technetium labelled scintigraphy, while 72% would order Howell-Jolly bodies, and 28% would order pitted erythrocyte counts. A decrease in radiation exposure would result from elimination of use of the technetium labelled scintigraphy without impairing the efficacy of functional assessment. In this survey, we did not assess barriers to obtaining functional testing.

Although no consensus guidelines exist for approach to antibiotic prophylaxis and fever management in heterotaxy patients, such guidelines do exist for similar populations. Data from the sickle cell population, in which a majority of patients will have functional asplenia within the first 5 years of life, demonstrates that prophylaxis is the single most beneficial intervention in increasing lifespan and can safely be discontinued at the age of 5.[20,21] Prolonged prophylaxis may result in infection with resistant organisms and increasing population wide resistance to antibiotics. This survey demonstrated that 36% of responders would never stop prophylactic antibiotics once started while another 24% were unsure of if, and when, to stop. The age of 5 was selected as an appropriate time to stop prophylactic antibiotics by 14% while the remainder would stop at over 5 or 18 years of age. Thus, a large percentage of cardiologists tend to continue prophylactic antibiotics longer than is likely needed. Those who picked 5 years of age as the age at which to discontinue prophylaxis often cited the sickle cell data. While it is unclear if extrapolating sickle cell data to heterotaxy is entirely accurate, this appears reasonable at the time since there is functional asplenia present in both.

Guidelines for the management of patients with functional asplenia recommend prescribing the 23-valent pneumococcal vaccine in this population.[22] In this survey, nearly 25% of responders reported not routinely assessing immunization status and not recommending the 23-valent pneumococcal vaccination. In many cases of complex heterotaxy, the cardiologist serves as medical home in partnership with primary care physicians. Therefore anticipatory guidance regarding appropriate immunizations guided by the cardiologist may be a simple and effective way to improve outcomes.

When confronted with a febrile patient with isomerism, half of responders felt that functional splenic status was the most concerning risk factor for bacteremia. Again, data regarding management of fever in those with asplenia can also be found in the sickle cell population. Baskin and colleagues assessed outpatient management of febrile patients with sickle cell disease. Outpatient management was found to be reasonable for well-appearing patients with temperatures of less than 39.0°C. Laboratory evaluation consisting of at least a blood culture and administration of a long acting antibiotic are recommended over 38.5°C. In this study, only 1 of 482 blood cultures obtained from

TABLE 7 Overview of responses to clinical vignette 6

In a well appearing outpatient with heterotaxy and presumed splenic dysfunction, who is greater 5 y of age and who has a fever >39.5°C, I do the following:	Always	Sometimes	Never
Manage the patient while the patient remains at home	3 (1.99%)	91 (60.26%)	57 (37.75%)
Have the patient evaluated in clinic	45 (28.85%)	100 (64.10%)	11 (7.05%)
Have the patient evaluated in the ER	26 (16.67%)	122 (78.21%)	8 (5.13%)
Have the patient admitted to an inpatient service	15 (9.68%)	125 (80.65%)	15 (9.68%)
Obtain a blood culture	83 (52.87%)	71 (45.22%)	3 (1.91%)
Obtain a complete blood count	95 (60.51%)	60 (38.22%)	2 (1.27%)
Obtain a C-reactive protein	66 (42.86%)	82 (53.25%)	6 (3.90%)
Obtain a urine culture	46 (30.07%)	100 (65.36%)	7 (4.58%)
Obtain a urinalysis	51 (33.33%)	96 (62.75%)	6 (3.92%)
Obtain a chest x-ray	33 (21.85%)	110 (72.85%)	8 (5.30%)
Administer antibiotics	36 (23.38%)	107 (69.48%)	11 (7.14%)

TABLE 8 Survey items and responses that differed by post fellowship experience

	0 to 5 y post fellowship	6 to 15 y post fellowship	Over 16 y post fellowship	*P* value
In patients with isomerism who have an abnormal spleen identified on ultrasound (abnormal position/inversus, hypoplastic, or multiple), I:				.003
Assume splenic function is normal and perform no additional functional testing	0 (0%)	0 (0%)	5 (5.5%)	
Assume splenic function is normal and perform additional functional testing	0 (0%)	0 (0%)	6 (6.6%)	
Assume splenic function is abnormal and perform no additional functional testing	35 (61.4%)	35 (50.0%)	36 (39.6%)	
Assume splenic function is abnormal and perform additional functional testing	22 (38.6%)	30 (42.9%)	41 (45.1%)	
Other	0 (0%)	5 (7.1%)	3 (3.3%)	
In patients prescribed antibiotic prophylaxis, I recommend stopping at:				<.0001
2 y of age	0 (0%)	0 (0%)	0 (0%)	
5 y of age	15 (28.3%)	7 (10.3%)	7 (8.4%)	
Greater than 5 y of age but less than 18 y of age	3 (5.7%)	15 (22.1%)	7 (8.4%)	
Over 18 y of age	4 (7.5%)	6 (8.8%)	11 (13.3%)	
Never	10 (18.9%)	19 (27.9%)	44 (53.0%)	
Not sure	20 (37.7%)	16 (23.5%)	12 (14.5%)	
Other	1 (1.9%)	5 (7.4%)	2 (2.4%)	
I routinely recommend that patients with isomerism receive the supplemental 23-valent pneumococcal vaccination in addition to routine vaccinations if over 2 y of age				.017
Yes	30 (66.7%)	40 (70.2%)	57 (87.7%)	
No	15 (33.3%)	17 (29.8%)	8 (12.3%)	

children with a fever of up to 38.5°C resulted in growth of a pathogen. This child had clinical signs consistent with osteomyelitis as well.[23] Thus, it is reasonable to apply this data and then analyze its efficacy in the isomerism population (Figures 1 and 2).

It is interesting to note that more experienced pediatric cardiologists tended to be more conservative in the evaluation and management of patients with isomerism. This was particularly apparent in the use and prophylactic antibiotics. This may be the result of anecdotal experience with more experienced pediatric cardiologists. It is possible that more experienced cardiologists have had more negative clinical experiences which make them more conservative in their management. Practice type did not influence responses.

The following recommendations have been proposed when evaluating and managing patients with isomerism. All patients should undergo an abdominal ultrasound early in life to determine splenic anatomy. All patients, even those with a solitary spleen or multiple spleens, should be started on prophylactic antibiotics:ampicillin for those not tolerating oral medications and amoxicillin for those tolerating oral medications. The dose of amoxicillin should be 20 mg/kg/day and can be prescribed either twice a day or daily.[15,16]

At 2 years of age, those with a solitary spleen or multiple spleens should have splenic function assessed by means of either pitted red blood cell test or Howell-Jolly body testing. Pitted red blood cell testing is the preferred method of choice as it has less false negative tests and is more sensitive in detecting milder hyposplenism.[17,18] Functional testing by either method is not accurate prior to 2 years of age.[24] Those with a solitary spleen or multiple spleens who demonstrate splenic function at 2 years of age may have antibiotic prophylaxis discontinued. Those who demonstrate no splenic function should have prophylaxis continued.[15]

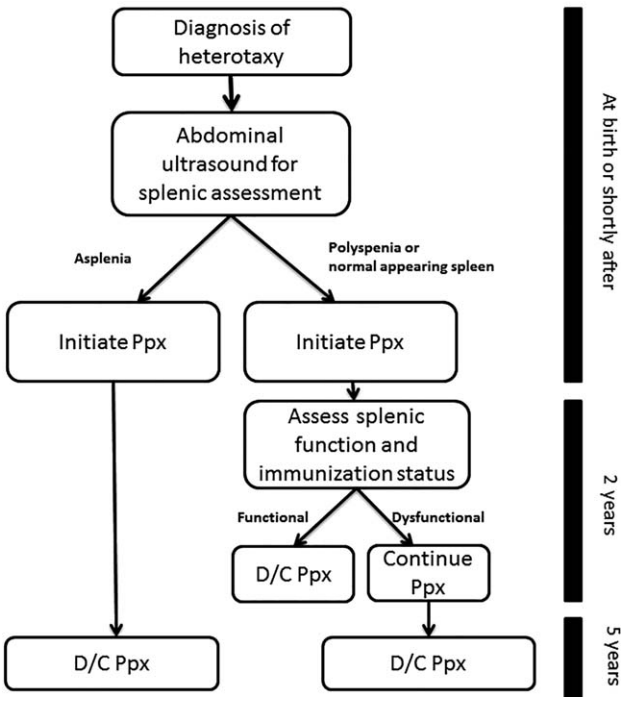

FIGURE 1 Proposed algorithm for evaluation of splenic function and antibiotic prophylaxis in patients with isomerism

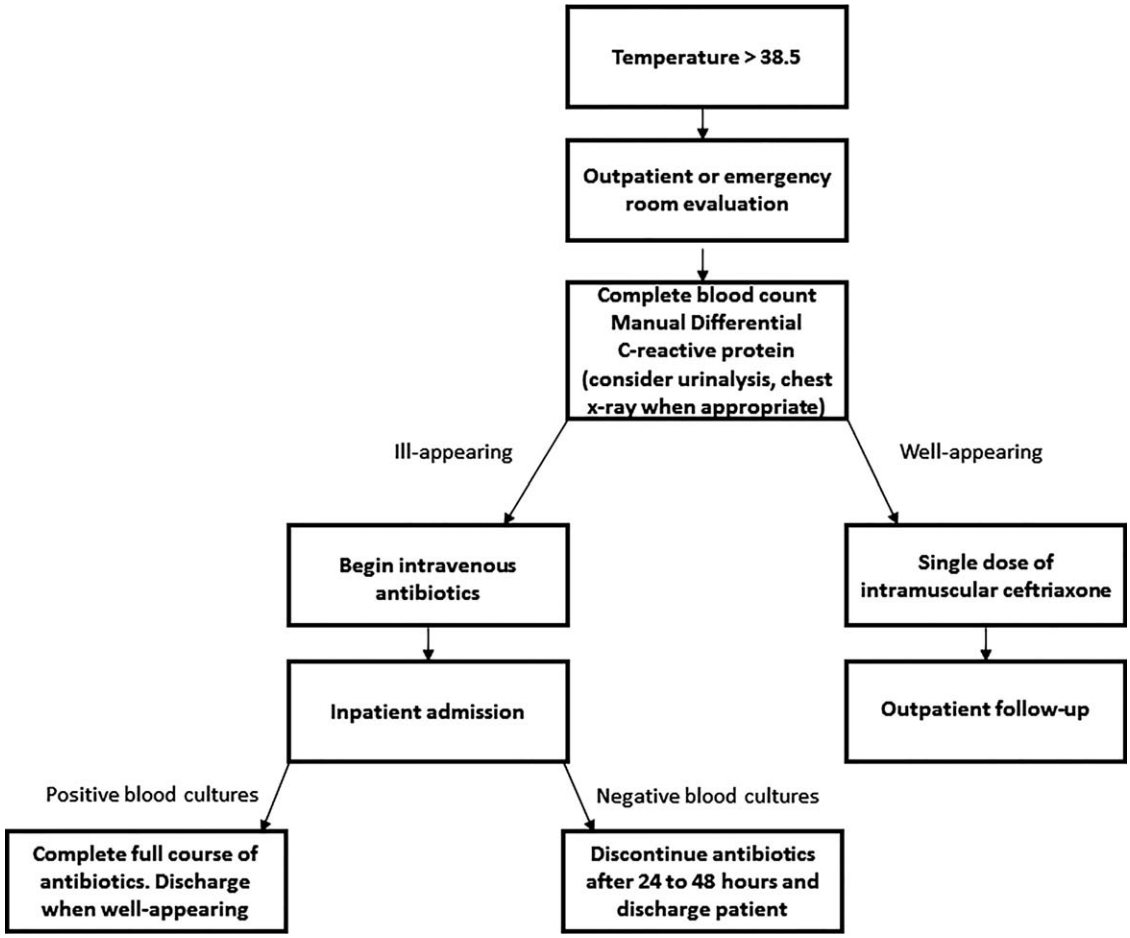

FIGURE 2 Proposed algorithm for evaluation and management of febrile patients with isomerism

For those with absence of a spleen and those who demonstrated functional asplenia and remained on prophylactic antibiotics after 2 years of age, prophylactic antibiotics should be continued until 5 years of age. Data from the sickle cell population as well as isomerism population demonstrates that it should be safe to discontinue prophylaxis at this age.[20,21,25]

Our survey has limitations. The survey was specifically designed for this study and has not undergone previous validation. There is potential for responder bias as the practice of nonresponders is not known. In addition, it cannot be confirmed if the responses of responders actually reflects their actual routine clinical practice. In addition, we used the terminology heterotaxy for the survey as this has been the more popular term used historically. The term isomerism and the subsets of left and right isomerism, however, are likely more appropriate in terms of providing better "syndromic clustering."[3,26] Despite these limitations, however, we feel that the results from the survey underscore the need for consensus guidelines for the evaluation and management of splenic function and infectious complications in heterotaxy.[15]

5 | CONCLUSION

This survey of pediatric cardiologists confirms significant lack of consensus among pediatric cardiologists in the diagnosis of splenic dysfunction, the practice of antibiotic prophylaxis, and the approach to the febrile child with heterotaxy syndrome and congenital heart disease.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Rohit S. Loomba—survey design, dissemination of survey, data collection, data analysis, manuscript preparation, final approval of manuscript

Gabrielle Geddes—survey design, manuscript preparation, final approval of manuscript

Amanda Shillingford—survey design, manuscript preparation, final approval of manuscript

David Hehir—survey design, manuscript preparation, final approval of manuscript

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