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Is isomerism a risk factor for intestinal volvulus?☆

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ABSTRACT

Introduction: Isomerism, or heterotaxy syndrome, affects many organ systems anatomically and functionally. Intestinal malrotation is common in patients with isomerism. Despite a low reported risk of volvulus, some physicians perform routine screening and prophylactic Ladd procedures on asymptomatic patients with isomerism who are found to have intestinal malrotation. The primary aim of this study was to determine if isomerism is an independent risk factor for volvulus.
Methods: Kid's Inpatient Database data from 1997 to 2012 was utilized for this study. Characteristics of admissions with and without isomerism were compared with a particular focus on intestinal malrotation, volvulus, and Ladd procedure. A logistic regression was conducted to determine independent risk factors for volvulus with respect to isomerism.
Results: 15,962,403 inpatient admissions were included in the analysis, of which 7970 (0.05%) patients had isomerism, and 6 patients (0.1%) developed volvulus. Isomerism was associated with a 52-fold increase in the odds of intestinal malrotation by univariate analysis. Of 251 with isomerism and intestinal malrotation, only 2.4% experienced volvulus. Logistic regression demonstrated that isomerism was not an independent risk factor for volvulus.
Conclusion: Isomerism is associated with an increased risk of intestinal malrotation but is not an independent risk factor for volvulus.
Type of Study: Prognosis study.
Level of Evidence: Level III.

Isomerism, also known as heterotaxy syndrome, affects approximately 1 in 10,000 live births [1–4]. Characterized by mirror-imagery of the organs in the thorax and random arrangement of the abdominal organs, isomerism can impact any organ system [5]. Isomerism can be separated into right and left isomerism subtypes based on morphology of the atrial appendages [6–10]. Importantly, such distinctions between subtypes allows for syndromic clustering and anticipation of associated anomalies or complications [11,12].

The anatomic variations of isomerism have functional implications that are wide-reaching. For example, splenic anomalies (asplenia, polysplenia) in a patient with isomerism may infer abnormal splenic function, cardiac malformations may lead to arrhythmias and hemodynamic perturbations, and pulmonary flow abnormalities can lead to pulmonary vascular disease [13–17]. As a whole, anomalies associated with isomerism may negatively impact postoperative morbidity and overall survival [18,19].

Abnormalities of the gastrointestinal system also manifest in isomerism. Indeed, one of the most common gastrointestinal findings is intestinal malrotation [20]. In fact, in children with isomerism, studies report a prevalence of intestinal malrotation ranging from 40% to 90%. Despite the heightened risk of intestinal malrotation in isomerism, a review of existing studies reported low rates of volvulus in isomerism, though was limited by small sample sizes [21]. Without strong data, individual practice variations persist; as such, providers continue to employ routine screening and prophylactic Ladd procedures if imaging suggests any degree of intestinal malrotation, independent of symptoms or mesenteric width as indicators of risk of volvulus [22].

Therefore, the aim of this study was to identify intestinal malrotation and volvulus in children with and without isomerism to determine whether isomerism is an independent risk factor for volvulus. We hypothesize that isomerism is independently associated with malrotation but not independently associated with volvulus.

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1. Methods

Institutional review board review approval was waived as this study utilized deidentified data from the Kids' Inpatient Database, a large national inpatient database. Consent was not obtained by the authors for this study as the data was derived from a national database. This cross-sectional study is in compliance with the Helsinki declaration.

1.1. Nationwide inpatient sample

The Kids' Inpatient Database, made available by the Healthcare Cost Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ) is a large database designed to capture data from community, non-rehabilitation hospital admissions in the United States. According to the database, community hospitals are defined as all nonfederal, short-term, general, and other specialty hospitals. Freestanding and non-freestanding children's hospitals are both included as are teaching and non-teaching hospitals. Discharges of patients less than 20 years of age are included in the database. Rehabilitation and long-term acute care hospitals are excluded from this database. Patients from all regions of the United States in a total of 44 states with a variety of payer types are captured in this database.

1.2. Patient identification

Data regarding hospital admissions was obtained from all 6 available iterations of the database, spanning from 1997 to 2012. Patients with isomerism were identified using the *International Classification of Diseases, Ninth Revision* (*ICD-9*) code 746.87. Patients with situs inversus were not included in this group as not all situs inversus portends isomerism. Primary and secondary diagnosis fields were used to collect this data. No other patient subsets were excluded from the analysis.

1.3. Data identification and collection

Demographic information including gender, and race were collected for each admission. Admission characteristics such as length of stay, cost of stay, and comorbid conditions were collected. Acute kidney injury was identified using 584.9 and chronic kidney disease using 585.9. Heart failure was identified using 428.0 to 428.9.

Isomerism data of interest included cardiac anatomy as well splenic anatomy. Congenital heart disease was identified using several *ICD-9* codes: double outlet right ventricle (745.11), atrioventricular septal defect (745.60), partial anomalous pulmonary venous connection (747.42), total anomalous pulmonary venous connection (747.41), transposition of the great arteries (745.10), congenitally corrected transposition (745.12), hypoplastic left heart syndrome (746.7), atrial septal defect (745.61), ventricular septal defect (745.5), pulmonary atresia with ventricular septal defect (746.01), tricuspid atresia (746.1), Ebstein anomaly (746.2), truncus arteriosus (745.0), and coronary artery anomaly (746.85). Arrhythmias were identified using codes 427.0 to 427.42 as well as 426.0 to 426.13. Splenic abnormality, either absence of a spleen or presence of multiple spleens, was collected using 759.0. It was not possible to distinguish between those with asplenia or polysplenia due to the *ICD-9* coding strategy.

1.4. Statistical analysis

A cross-sectional study was conducted. Continuous variables were reported using mean and standard deviation while categorical variables are reported using absolute frequency and percentages. Continuous variables were analyzed using a student t-test and categorical variables compared using a Chi-square test (χ^2) or a Fisher's exact test for smaller subsets. Baseline characteristics such as age, gender, race, and comorbid conditions were compared between those with and without isomerism. A univariate cross tabulation analysis was conducted to determine the odds of having intestinal malrotation, volvulus and other events in patients with and without isomerism. Logistic regression analysis was also conducted with volvulus as the dependent variable with the following independent variables: isomerism, age, race, gender, acute kidney injury, chronic kidney disease, all previously described congenital heart malformations, and an aggregate of all previously described arrhythmias. All statistical analysis was done utilizing SPSS Version 20.0 (Chicago, IL).

2. Results

2.1. Admission characteristics for children with and without isomerism

A total of 15,962,403 inpatient admissions were included in this analysis. Of these, 7970 (0.05%) had isomerism. Patients with isomerism were significantly younger and more often of Hispanic or Asian/Pacific Islander race when compared to those without isomerism. Congenital cardiac malformations were found to be more frequent in those with isomerism. Arrhythmias were also more frequently noted in those with isomerism (odds ratio (OR) 22.44, 95% confidence interval (CI): 20.305, 24.806). Pancreatic anomalies (OR 17.39), atresia of the small intestine (OR 7.15), and biliary atresia (OR 12.62) were also more commonly noted in those with isomerism (Table 1). With respect to outcomes, heart failure, acute kidney injury and inpatient mortality were significantly more associated with isomerism.

Intestinal malrotation was documented in 251 out of 7970 children (3.1%) who were noted to have isomerism. Comparatively, 9896 (0.1%) of patients without isomerism (OR 52.39, 95% CI: 46.132, 59.501) were diagnosed with intestinal malrotation. Volvulus was noted in 6 (6/7970, 0.1%) patients with isomerism compared to 3741 (3741/15,954,433, 0.02%) patients without isomerism (OR 3.21, 95% CI: 1.442, 7.157). A Ladd procedure was undertaken in 134 (1.7%) of children with isomerism compared to 16,703 (0.1%) of those without (Table 1).

2.2. Admission characteristics for children with isomerism and intestinal malrotation

On subanalysis of isomerism patients, comparing those with and without intestinal malrotation, several differences were noted (Table 2). Patients with intestinal malrotation were more likely to have cardiac malformations as well as all non-cardiac anomalies.

Volvulus was noted in 6 (2.4%) admissions with isomerism and intestinal malrotation. Of the 134 children with intestinal malrotation who underwent a Ladd procedure, 6 (4.5%) were found to have midgut volvulus on exploration.

2.3. Independent risk factors for volvulus

Using logistic regression analysis with volvulus as the dependent variable, independent risk factors found to be associated with volvulus were acute kidney injury (OR 5.82, 95% CI: 3.005, 11.261) and intestinal malrotation (OR 306.27, 95% CI 230.257, 407.379). Notably, isomerism was not an independent risk factor for volvulus (OR 0.88, 95% CI 0.102, 7.357).

2.4. Characteristics of those with intestinal malrotation and volvulus

When compared to those with intestinal malrotation without volvulus, no statistically significant differences in demographics, cardiac morphology, noncardiac morbidities, or outcomes were appreciated. None of the patients with volvulus experienced inpatient mortality.

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Table 1
Characteristics of admissions with and without isomerism.

Variable	No Isomerism (n = 15,954,433)	Isomerism (n = 7970)	Odds Ratio (95% Confidence Interval)	*p*-value[a]
Demographics				
Age (y), mean (SD)	7.17 ± 7.92	2.77 ± 4.96	--	< 0.001
Race, No. (%)			--	< 0.001
White	6,514,358 (50.6)	3049 (46.0)		
Black	2,273,883 (17.7)	876 (13.2)		
Hispanic	2,931,131 (22.8)	1904 (28.7)		
Asian or Pacific Islander	387,258 (3.0)	309 (4.7)		
Native American	97,342 (0.8)	60 (0.9)		
Other	676,402 (5.3)	435 (6.6)		
Comorbidities, No. (%)				
Cardiac				
Double outlet right ventricle	9694 (0.01)	1062 (13.3)	252.86(236.335 to 270.548)	<0.001
Atrioventricular septal defect	15,834 (0.01)	1026 (12.9)	148.73 (139.038 to 159.096)	<0.001
Partial anomalous pulmonary venous connection	2156 (0.01)	103 (1.3)	79.40 (79.399 to 118,192)	<0.001
Total anomalous pulmonary venous connection	3504 (0.01)	424 (5.3)	255.78 (230.685 to 283.611)	<0.001
Coronary artery anomaly	4059 (0.01)	64 (0.8)	31.81 (24.826 to 40.760)	<0.001
Atrial septal defect	219,386 (1.4)	1485 (18.6)	16.42 (15.521 to 17.379)	<0.001
Tetralogy of Fallot	23,899 (0.1)	182 (2.3)	15.58 (13.441 to 18.054)	<0.001
Ventricular septal defect	120,013 (0.8)	1210 (15.2)	23.62 (22.209 to 25.113)	<0.001
Congenitally corrected transposition	1840 (0.01)	236 (3.0)	264.56 (230.609 to 303.506)	<0.001
Pulmonary atresia	5431 (0.01)	333 (5.8)	128.05 (114.378 to 143.353	<0.001
Tricuspid atresia	6563 (0.01)	211 (2.6)	66.08 (57.513 to 75.926)	<0.001
Ebstein anomaly	3370 (0.01)	32 (0.4)	19.08 (13.462 to 27.045)	<0.001
Hypoplastic left heart syndrome	15,444 (0.1)	260 (3.3)	34.80 (30.726 to 39.421)	<0.001
Truncus arteriosus	3521 (0.01)	32 (0.4)	18.26 (12.886 to 25.883)	<0.001
Non-Cardiac				
Intestinal malrotation	9896 (0.1)	251 (3.1)	52.39 (46.132 to 59.501)	<0.001
Chronic kidney disease	31,216 (0.2)	22 (0.3)	1.41 (0.929 to 2.146)	0.11
Biliary atresia	6055 (0.01)	38 (0.5)	12.62 (9.166 to 17.372)	<0.001
Pancreatic anomaly	1268 (0.01	11 (0.1)	17.39 (9.601 to 31.492)	<0.001
Atresia of the small intestine	10,120 (0.1)	36 (0.4)	7.15 (5.150 to 9.924)	<0.001
Atresia of the large intestine	17,115 (0.1)	144 (1.8)	17.13 (14.521 to 20.218)	<0.001
Outcomes, No. (%)				
Arrhythmia	38,263 (0.2)	408 (5.1)	22.44 (20.305 to 24.806)	<0.001
Heart failure	47,667 (0.3)	582 (7.3)	26.29 (24.149 to 28.616)	<0.001
Acute kidney injury	60,956 (0.4)	129 (1.6)	4.29 (3.604 to 5.106)	<0.001
Ladd procedure	16,703 (0.1)	134 (1.7)	12.96 (10.910 to 15.389)	<0.001
Volvulus	3741 (0.02)	6 (0.1)	3.21 (1.442 to 7.157)	<0.01
Length of hospital stay (d), mean (SD)	4.65 ± 10.03	11.26 ± 22.07	--	<0.001
Inpatient mortality	95,524 (0.6)	429 (5.4)	9.44 (8.566 to 10.410)	<0.001

[a] By *t* test, χ^2 test of independence, or Fisher's exact test, as appropriate.

3. Discussion

This study of children with isomerism serves as the largest analysis investigating the relationships between isomerism, intestinal malrotation and volvulus. Among the 7970 patients admitted with isomerism, 3.1% had intestinal malrotation and 0.1% resulted in midgut volvulus. Moreover, of the 134 patients taken for a Ladd procedure, only 4.5% had volvulus on exploration. These data are consistent with previously reported experiences. Specifically, Landisch and colleagues reported a 1.2% pooled risk of volvulus in patients with isomerism, and similarly demonstrated that 5% of patients taken for a Ladd procedure had operative findings of volvulus [21]. This agreement between studies fortifies the argument that the risk of volvulus among heterotaxy patients is low, and challenges the practice of routine screening and prophylactic Ladd procedure, as this practice may unnecessarily increase cost and morbidity in otherwise asymptomatic patients.

While this study reports a low risk of volvulus among isomerism, higher risk categories of patients may exist which warrant closer monitoring. Malrotation is a spectrum of disorders of intestinal rotation, each which carries a variable risk of volvulus based on mesenteric width. Accordingly, a narrow mesentery, which can twist on its own vascular pedicle, infers greater risk than a broad mesentery, as exists in nonrotation [23]. Hill et al. first described the risk of malrotation, defined in their study as a narrow mesentery on exploration and the presence of Ladd's bands, as a factor of isomerism subtype; namely, patients with left atrial isomerism were at significantly lower risk of malrotation compared to patients with right atrial isomerism [24]. While the current study demonstrates a significant association between isomerism and intestinal malrotation, the low rate of volvulus may suggest that isomerism patients more commonly fit in the spectrum of low risk, broader mesenteric rotational anomalies. Nevertheless, without strong evidence characterizing the correlation between mesenteric width and isomerism subtype, selective screening of higher risk, asymptomatic heterotaxy patients will remain a challenge and practice variation will likely ensue [22].

In addition, Ladd procedures are not without complications. A systematic review of heterotaxy syndrome and intestinal malrotation reported a 30-day mortality of 3% and overall mortality of 21% in children who underwent a Ladd procedure. While mortality was primarily attributable to cardiovascular demise, the authors propose that surgical stress may contribute to mortality risk [21]. Likewise, a study by Sen et al. demonstrated 19% shunt failure in those with isomerism and functionally univentricular hearts [25]. Our data demonstrate a 5.4% inpatient mortality and 7.3% risk of heart failure among isomerism patients. Attempts to mitigate significant perioperative morbidity and mortality often include delaying surgery until after cardiac palliation. While these data do not stratify mortality risk, they do illustrate the medical complexity of patients with isomerism. Moreover, since nearly two-thirds of volvulus occur in the first month of life, the absence of volvulus prior to cardiac palliation may implicitly serve as an indicator that

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Table 2
Characteristics of isomerism admissions with and without intestinal malrotation.

Variable	No Intestinal Malrotation (n = 7719)	Intestinal Malrotation (n = 251)	Odds Ratio (95% Confidence Interval)	*p*-value[a]
Demographics				
Age (y), mean (SD)	2.84 ± 5.00	0.78 ± 0.89	--	< 0.001
Race, No. (%)			--	0.79
White	2958 (46.1)	91 (42.7)		
Black	848 (13.2)	28 (13.1)		
Hispanic	1841 (28.7)	63 (29.6)		
Asian or Pacific Islander	299 (4.7)	10 (4.7)		
Native American	57 (0.9)	3 (1.4)		
Other	417 (6.5)	18 (8.5)		
Comorbidities, No. (%)				
Cardiac				
Double outlet right ventricle	1004 (13.0)	58 (23.1)	2.01 (1.488 to 2.716)	<0.001
Atrioventricular septal defect	937 (12.1)	89 (35.5)	3.98 (3.043 to 5.196)	<0.001
Partial anomalous pulmonary venous connection	95 (1.2)	8 (3.2)	2.64 (1.270 to 5.498)	0.01
Total anomalous pulmonary venous connection	384 (5.0)	40 (15.9)	3.62 (2.544 to 5.155)	<0.001
Coronary artery anomaly	63 (0.8)	1 (0.4)	0.49 (0.067 to 3.519)	0.47
Atrial septal defect	1436 (18.6)	49 (19.5)	1.06 (0.773 to 1.458)	0.71
Tetralogy of Fallot	175 (2.3)	7 (2.8)	1.24 (0.575 to 2.661)	0.59
Ventricular septal defect	1176 (15.2)	34 (13.5)	0.87 (0.604 to 1.258)	0.46
Congenitally corrected transposition	230 (3.0)	6 (2.4)	0.80 (0.351 to 1.811)	0.59
Pulmonary atresia	305 (4.0)	28 (11.2)	3.05 (2.027 to 4.596)	< 0.001
Tricuspid atresia	207 (2.7)	4 (1.6)	0.59 (0.217 to 1.594)	0.29
Ebstein anomaly	32 (0.4)	0 (0)	--	0.31
Hypoplastic left heart syndrome	250 (3.2)	10 (4.0)	1.24 (0.650 to 2.363)	0.51
Truncus arteriosus	32 (0.4)	0 (0)	--	0.31
Non-Cardiac				
Chronic kidney disease	21 (0.3)	1 (0.4)	1.47 (0.196 to 10.944)	0.71
Biliary atresia	32 (0.4)	6 (2.4)	5.88 (2.437 to 14.200)	< 0.001
Pancreatic anomaly	8 (0.1)	3 (1.2)	11.66 (3.075 to 44.215)	< 0.001
Atresia of the small intestine	29 (0.4)	7 (2.8)	7.61 (3.300 to 17.536)	< 0.001
Atresia of the large intestine	142 (1.8)	2 (0.8)	0.43 (0.106 to 1.740)	0.22
Outcomes, No. (%)				
Arrhythmia	391 (5.1)	17 (6.8)	1.36 (0.824 to 2.251)	0.23
Heart failure	556 (7.2)	26 (10.4)	1.49 (0.983 to 2.255)	0.06
Acute kidney injury	117 (1.5)	12 (4.8)	3.26 (1.776 to 5.991)	< 0.001
Volvulus	--	6 (2.4)	--	--
Inpatient mortality	412 (5.3)	17 (6.8)	1.29 (0.780 to 2.129)	0.32

[a] By *t* test, χ^2 test of independence, or Fisher's exact test, as appropriate.

close observation is a safe option, as long as no concerns for narrow mesentery or symptoms are present [26]. As such, the 2.4% rate of volvulus in isomerism may be overshadowed by an even higher prevalence of cardiac and non-cardiac comorbidities and mortality, emphasizing the importance of consideration of close observation as an alternative to an operative Ladd procedure.

This study has limitations. First, we were unable to distinguish isomerism by right and left subtypes or identify symptoms due to limitations of coding in the database. Coding errors may also have occurred, and may have created discrepancies, such as an excess of Ladd procedures in non-isomerism patients, which we are unable to justify. Furthermore, because of the low frequency of volvulus, we were underpowered in our analysis of isomerism patients with and without volvulus, and therefore are unable to detect statistical differences that would help in future discrimination of which patients are at highest risk. In addition, practice variation and changes over the last decade may have influenced the rate of screening and Ladd procedures, and thereby affect the rate of intestinal malrotation. Compared to a 2013 survey wherein 84% of physicians caring for isomerism patients believed in routine screening, a 2015 American Pediatric Surgical Association committee systematic review determined that there is minimal evidence to support screening in asymptomatic patients [22,23]. However, information on screening, prophylactic Ladd procedures and how they vary by center is not available within the Kids' Inpatient. Lastly, it is not possible with the Kids' national database to discriminate unique patients and group admissions by patient; however, the logistic regression analysis should provide an accurate representation of intestinal malrotation as it compares between groups.

4. Conclusion

Isomerism is associated with an increased risk of intestinal malrotation, but is not an independent risk factor for volvulus. With less than 0.1% rate of volvulus in isomerism, these data suggest close observation of asymptomatic patients with isomerism and multiple comorbidities may be a safe alternative to a prophylactic Ladd procedure.

References

[1] Evans WN, Acherman RJ, Restrepo H. Heterotaxy in southern Nevada: prenatal detection and epidemiology. Pediatr Cardiol 2015;36(5):930–4.
[2] Lin AE, Krikov S, Riehle-Colarusso T, et al. Laterality defects in the national birth defects prevention study (1998-2007): birth prevalence and descriptive epidemiology. Am J Med Genet A 2014;164A(10):2581–91.
[3] Lopez KN, Marengo LK, Canfield MA, et al. Racial disparities in heterotaxy syndrome. Birth Defects Res A Clin Mol Teratol 2015;103(11):941–50.
[4] Loomba RS, Hlavacek AM, Spicer DE, et al. Isomerism or heterotaxy: which term leads to better understanding? Cardiol Young 2015:1–7.
[5] Jacobs JP, Anderson RH, Weinberg PM, et al. The nomenclature, definition and classification of cardiac structures in the setting of heterotaxy. Cardiol Young 2007;17 (Suppl. 2):1–28.
[6] Loomba RS, Ahmed MM, Spicer DE, Backer CL, Anderson RH. Manifestations of bodily isomerism. Cardiovasc Pathol 2016;25(3):173–80.
[7] Uemura H, Ho SY, Devine WA, et al. Analysis of visceral heterotaxy according to splenic status, appendage morphology, or both. Am J Cardiol 1995;76(11):846–9.
[8] Uemura H, Ho SY, Devine WA, et al. Atrial appendages and venoatrial connections in hearts from patients with visceral heterotaxy. Ann Thorac Surg 1995;60(3):561–9.
[9] Loomba R, Shah PH, Anderson RH. Fetal Magnetic Resonance Imaging of Malformations Associated with Heterotaxy. Cureus 2015;7(5):e269.
[10] Loomba RS, Shah PH, Anderson RH. Radiologic considerations in heterotaxy: the need for detailed anatomic evaluation. Cureus 2016;8(1):1–12.

Please cite this article as: Landisch RM, et al, Is isomerism a risk factor for intestinal volvulus?, J Pediatr Surg (2018), https://doi.org/10.1016/j.jpedsurg.2018.02.071

[11] Loomba RS, Pelech AN, Shah PH, et al. Determining bronchial morphology for the purposes of segregating so-called heterotaxy. Cardiol Young 2015:1–13.
[12] Van Mierop LH, Eisen S, Schiebler GL. The radiographic appearance of the tracheobronchial tree as an indicator of visceral situs. Am J Cardiol 1970;26(4):432–5.
[13] Smith A, Ho SY, Anderson RH, et al. The diverse cardiac morphology seen in hearts with isomerism of the atrial appendages with reference to the disposition of the specialised conduction system. Cardiol Young 2006;16(5):437–54.
[14] Loomba RS, Aggarwal S, Gupta N, et al. Arrhythmias in adult congenital patients with bodily isomerism. Pediatr Cardiol 2016;37(2):330–7.
[15] Loomba RS, Willes RJ, Kovach JR, Anderson RH. Chronic arrhythmias in the setting of heterotaxy: differences between right and left isomerism. Congenit Heart Dis 2016;11(1):7–18.
[16] Loomba R. Comment on pulmonary hypertension in a patient with congenital heart defects and heterotaxy syndrome. Ochsner J 2015;15(4):401.
[17] Loomba RS, Aggarwal S, Arora RR, Anderson R. Bodily isomerism is an independent risk factor for pulmonary hypertension in adults with congenital heart disease. Ther Adv Respir Dis 2016;10(3):194–9.
[18] Loomba RS. Arterial desaturation due to pulmonary arteriovenous malformations after the Kawashima. Ann Pediatr Cardiol 2015;9(1):1–4.
[19] Loomba RS, Nijhawan K, Anderson R. Impact of era, type of isomerism, and ventricular morphology on survival in heterotaxy: implications for therapeutic management. World J Pediatr Congenit Heart Surg 2016;7(1):54–62.
[20] Sharma MS, Guleserian KJ, Forbess JM. Ladd's procedure in functional single ventricle and heterotaxy syndrome: does timing affect outcome? Ann Thorac Surg 2013;95(4):1403–7 [discussion 7-8].
[21] Landisch R, Abdel-Hafeez AH, Massoumi R, et al. Observation versus prophylactic Ladd for asymptomatic intestinal rotational abnormalities in heterotaxy syndrome: A systematic review. J Pediatr Surg 2015;50(11):1971–4.
[22] Pockett CR, Dicken BJ, Rebeyka IM, et al. Heterotaxy syndrome and intestinal rotation abnormalities: a survey of institutional practice. J Pediatr Surg 2013;48(10):2078–83.
[23] Graziano K, Islam S, Dasgupta R, et al. Asymptomatic malrotation: Diagnosis and surgical management: An American Pediatric Surgical Association outcomes and evidence based practice committee systematic review. J Pediatr Surg 2015;50:1783–90.
[24] Hill SJ, Heiss KF, Mittal R, et al. Heterotaxy syndrome and malrotation: Does isomerism influence risk and decision to treat. J Pediatr Surg 2014 Jun;49(6):934–7.
[25] Sen S, Duchon J, Lampl B, et al. Heterotaxy syndrome infants are at risk for early shunt failure after Ladd procedure. Ann Thorac Surg 2015;99(3):918–25.
[26] Pockett CR, Dicken B, Rebeyka IM, et al. Heterotaxy syndrome: is a prophylactic Ladd procedure necessary in asymptomatic patients? Pediatr Cardiol 2013;34(1):59–63.

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