Is isomerism a risk factor for intestinal volvulus?☆

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A B S T R A C T

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.

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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 non-federal, 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.

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.
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 3.1% had intestinal malrotation and 0.1% resulted in midgut volvulus. Among the 7970 patients admitted 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 significant association between isomerism subtype and functionally univentricular hearts [25]. Our data demonstrate a significant association between isomerism subtype and functionally univentricular hearts [25].

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

close observation is a safe option, as long as no concerns for narrow mesentry 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 to an operative Ladd procedure. 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


