Heterotaxy syndrome and malrotation: Does isomerism influence risk and decision to treat

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Abstract

Purpose: Controversy remains regarding the management of the asymptomatic heterotaxy syndrome (HS) patient with suspected intestinal rotational abnormalities. We evaluated the outcomes for our HS population to identify frequency of malrotation and identify characteristics of children who might benefit from expectant management.

Methods: After IRB approval, a retrospective review of all patients treated for HS at a large tertiary care children’s hospital between January 2008 and June 2012 was performed. For the purpose of this paper, malrotation was defined as an operative note that described the presence of Ladd’s bands and a narrow mesentry.

Results: Thirty-eight patients with HS were identified, including 18 who underwent abdominal exploration. Left atrial isomerisation (LAI) was identified in 13 individuals, and right atrial isomerisation (RAI) was noted in 25. The rate of surgical intervention did not vary between the 2 groups (54%). Malrotation was found in 8 patients: one with LAI and 7 with RAI. This difference in incidence was statistically significant (p = 0.04).

Conclusion: These data suggest that the direction of atrial isomerisation influences the likelihood of true malrotation, where RAI patients are more likely to be malrotated. Given the inherent risk of surgery on this medically fragile patient population, surgeons should consider expectant management for asymptomatic LAI patients.

Our tertiary care children’s hospital is a regional cardiac referral center and frequently cares for infants with HS. Given the lack of consensus among pediatric surgeons for how to manage these medically fragile and complex patients, we reviewed our series of patients with HS in order to determine the best treatment algorithm and reduce variation in care. We evaluated the incidence of malrotation as it relates to cardiac risk factors in order to predict which patients are predisposed to develop the catastrophic diagnosis of mid-gut volvulus.

1. Methods

An IRB approved retrospective analysis was performed on all patients admitted to a tertiary cardiac referral center with the diagnosis of heterotaxy (IRB #12-083). Patients were identified from a database using ICD-9 codes for heterotaxy (746.89). Because of the rapidly evolving improvements in cardiac critical care, the study was limited to patients born between January 1, 2008 and June 30, 2012. Patients who underwent abdominal surgical interventions outside of our hospital network were excluded from analysis.

Medical records were evaluated, noting the patient’s cardiac diagnosis including the direction of atrial isomerism (left atrial isomerism (LAI) or right atrial isomerism (RAI)) and the cardiac...
surgical intervention[s] performed. Clinical and operative notes for patients who underwent abdominal surgery were reviewed for clinical symptoms prior to surgery, rotational anomalies at the time of surgery and the technical procedure[s] performed. Malrotation was defined as the presence of Ladd’s bands and a narrow mesentery at the time of laparotomy or laparoscopy.

The clinical decision to surgically evaluate patients for intestinal rotational anomaly was made based on the surgeon’s preference. The typical practice of our pediatric surgeons has been to offer diagnostic laparoscopy to evaluate all patients with heterotaxy and a suspected rotational anomaly on upper gastrointestinal fluoroscopy (UGI).

Statistical analysis was performed using SPSS software and is presented as mean (±SD) and median (range) where a p value of <0.05 was deemed as statistically significant.

2. Results

During the 4.5 year time period, thirty-eight patients with HS were identified. Average length of follow-up was 28 months (±14.5). There were 22 males. The median age at the time of surgery was 103 days (range 10–400). Eighteen (47%) of these individuals underwent diagnostic laparoscopy or laparotomy based on UGI findings or clinical symptoms worrisome for malrotation. Malrotation was identified in eight (44%) of the patients who underwent diagnostic laparoscopy. One malrotated patient had a true mid-gut volvulus, at the time of operation; however all small bowel was salvaged without the need for resection.

The majority (n = 13, 72%) of the patients treated surgically were asymptomatic at the time of their abdominal operation. Of these asymptomatic patients, 30% (n = 4) had positive findings at the time of exploration. Presence of abdominal symptoms at the time of surgery was predictive of the likelihood of identifying malrotation. Four out of the five patients who were symptomatic at the time of exploration were in fact malrotated. Worrisome signs and symptoms suggestive of malrotation included bilious emesis, abdominal distention and bloody bowel movements.

Patients with true malrotation appeared to be younger at the time of surgery when compared to those who were non-rotated: age 32.5 days (range 10–353) versus 153.5 days (range 20–400) respectively. However, this difference was not statistically significant (p = 0.25). Five patients (13%) died during the study period from complications related to their cardiac disease. None of the individuals who died had undergone abdominal surgery or had abdominal symptoms prior to their death. The median age at the time of death was 60.2 days (range 1–239 days). Average follow-up was 28 months with no difference in follow-up between operative patients and those who were managed expectantly.

The study population was analyzed to determine the influence of the direction of atrial isomerism as determined by echocardiogram (Fig. 1). LAI was identified in 13 and 7 of these underwent abdominal exploration for presumed rotational anomaly (54%). One patient with LAI was found to be malrotated. This 13 day old patient had been noted to have several bloody bowel movements and was being monitored for necrotizing enterocolitis. A screening UGI suggested malrotation with volvulus thus the patient was taken to the operating room urgently. At the time of surgery, the mesentery was found to be malrotated; however, the child did not have any evidence of ischemia or bowel necrosis. Right atrial isomerisation (RAI) was noted in 25 patients, of which 11 underwent abdominal exploration (55%). Seven patients with RAI had malrotation, 50% of malrotated RAI patients were asymptomatic at the time of surgery.

Of the patients who underwent abdominal exploration, patients with left atrial isomerism had significantly lower risk of malrotation compared to those with right atrial isomerism, 1 of 7 (15%) versus 8 of 11 (72%) (p = 0.04). All 5 of the patients who died during the study period had a diagnosis of RAI.

3. Discussion

Despite their complicated cardiac physiology, complex laparoscopic procedures can be performed safely in patients with congenital cardiac disease [8–12]. However, the risks of surgery in this medically fragile patient population should not be minimized.

The proper timing of the surgical procedure and a team approach, with collaboration between cardiac anesthesia and the surgeon, is paramount for safe surgical practice. All team members must have proper consideration of the patient’s physiology and cardiac anatomy. The overall mortality for HS patients ranges 10–50% in some series, although this has improved with advances in perioperative and critical care [13–17].

Patients with LAI and RAI have a range of complex and severe congenital heart disease in addition to extracardiac anomalies. Also described as the “polysplenia syndrome”, left atrial isomerism is a well-recognized spectrum of complex cardiac and noncardiac anomalies. Infants are characterized as having LAI if they are found to have bilateral biliated lungs or bilateral atrial appendage morphology. Additional common findings of the diagnosis include abdominal situs ambiguous and polysplenia. One large historical series found the mortality for infants with LAI to be 19%. Predictors of mortality in this series were infants with single ventricle, congenital AV block and aortic coarctation [15]. RAI has a historically quoted 5-year mortality of 65% [14]. Total anomalous pulmonary venous drainage is quite common in RAI (87% in one large series) and carries poor outcomes. Other predictors of mortality for infants with RAI were major valve anomalies, early cardiovascular surgery and pulmonary venous obstruction [14].

Malrotation, as originally described by Dr. Ladd occurs as a result of improper rotation and/or fixation of the midgut during the second and third months of gestation [18]. The diagnosis of malrotation is traditionally made radiographically with upper gastrointestinal fluoroscopy (UGI) by evaluating the duodenal–jejunal junction in relation to the pylorus and the midline. However, the true clinical significance of the findings of “malrotation” on UGI in an asymptomatic patient with HS is not clear cut. In one recent series, Papillon et al. noted that of 30 asymptomatic HS patients with UGI findings of malrotation, none of the patients had true malrotation or a narrow mesentery at the time of abdominal exploration [19]. It is these patients who are not in fact malrotated who we wish to identify and avoid over-treating.

As pointed out by Biko et al., postoperative complications following Ladd procedure are relatively common in the general population (25%). In their series, small bowel obstructions were the most common event; the vast majority of these patients were treated.
via laparotomy [20]. The risk of postoperative bowel obstructions may be lower with minimally invasive surgery. Thus, the high complication rate of this series may be an overestimate of outcomes in centers where minimally invasive surgery is regularly performed [21–23].

The management strategy for the asymptomatic HS patient has been the subject of academic debate in the literature over the past decade. Yu et al. recently published a retrospective review supporting prophylactic Ladd procedure in all asymptomatic HS patients with suspected malrotation. In their series, outcomes were compared between HS and non-HS patients who underwent Ladd procedures for presumed malrotation. They noted similar rates of complications and hospital stay after Ladd procedure between the two groups. The authors concluded that given the inherent risk of malrotation for this patient population and that the surgery was well tolerated by HS patients, prophylactic Ladd procedures should be performed on an elective basis for asymptomatic HS patients [4]. A similar argument supporting prophylactic Ladd has been published by Tashjian et al. [6]. An alternate opinion has been published out of Toronto [5,7]. In their series, Choi et al. found that over a 9-year follow-up, 14% of HS patients developed GI symptoms requiring exploration. The overwhelming majority (86%) of those who developed symptoms did so in the first eight weeks of life. Based on these results and the recognized complication rate for Ladd procedures, these authors advocated for observation for asymptomatic HS patients [7].

The fundamental discussion stems from balancing the complications and morbidity of unnecessary surgical interventions versus the risk of a patient presenting with a volvulus from an unrecognized malrotation. While this study is underpowered to truly determine the answer to this question, it does offer an algorithm for assessing risk of malrotation for a group of patients who are high risk surgical candidates based on their co-morbidities. Certainly, the underlying answer to this discussion is predicting which patients have a true malrotation, putting them at greater risk of developing midgut volvulus. To date, there has been minimal stratification of patients with HS to identify higher risk individuals.

In this series we have demonstrated a clear difference in the rate of true malrotation between patients with LAI and RAI. The likelihood of a patient with LAL being malrotated is significantly lower than those with RAI. This is especially the case in situations of the asymptomatic LAI patient. Although these individuals may have a radiographically identified minor rotational anomaly, they appear to have a lower risk for developing a clinically significant volvulus, as they are non-rotated, or not truly malrotated. Given this finding, the authors propose a treatment algorithm whereby asymptomatic patients with LAI are managed expectancy rather than prophylactic diagnostic laparoscopy (Fig. 2). Because of the relatively high risk of true malrotation for patients with RAI, the authors support elective surgical evaluation for all patients with RAI once they are stabilized from a cardiac standpoint. Elective abdominal surgery for the purpose of assessing for rotational anomalies should be delayed until stabilized physiologically (i.e. after take-down of a systemic to pulmonary artery shunt).

We recognize that because of the rarity of heterotaxy, this data series is relatively small. A larger, prospective series is needed to determine if these theories hold true. Another key weakness of this retrospective study is the lack of rigor in the description of the general surgical intervention at the time of the diagnostic laparoscopy. If one or 2 minor mesenteric bands that were cauterized, “malrotation” may have been recorded as the diagnosis. With the increased understanding of the implications of this treatment, the prospective assessment of these children may more accurately be described as a “diagnostic laparoscopy and appendectomy” for those that are asymptomatic and “non-rotated”, rather than describing a “laparoscopic Ladd procedure” for malrotation. Thus the data may yet evolve with increased understanding of this situation.

The authors emphasize the importance of a reliable social situation for any patient discharged with a plan of expectant management.
Now, we bring forward as surgeons a different mindset, which is a bit more practical, VACTERL syndrome actually acts as a very good model for understanding heterotaxy. There is a large number of associations, and as you very beautifully pointed out between left and right atrial isomerism has different correlations. As it turns out, I presented at the AAP cardiology section last year a series of 900 patients where I just tried to do the VACTERL thing over again where I looked for correlations, and what you have noticed is similar to what I found, which is there are really two groups, the classic heterotaxies, which turn into isomerisms and often have venoatrial difficulties and then the atypicals, which actually have conotruncal abnormalities like a transposition of the great arteries or double outlet right ventricle, and those are associated with duodenal atresia, so I think we’re in the process of evolving an understanding of heterotaxy more like VACTERL and not left and right isomerism. I would like to encourage work like yours where we try and look at the things in heterotaxy that predict what we should do as opposed to trying to define heterotaxy specifically as a right or left atrial isomerism. Thank you for your work.

Response: Dr. Hill: I don’t think there was a question there, but thank you for your comments.