

Observational Study

Single institution experience with the Ladd's procedure in patients with heterotaxy and stage I palliated single-ventricle

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Abstract

AIM: To investigate and describe our current institutional management protocol for single-ventricle patients who must undergo a Ladd's procedure.

METHODS: We retrospectively reviewed the charts of all patients from January 2005 to March 2014 who were diagnosed with heterotaxy syndrome and an associated intestinal rotation anomaly who carried a cardiac diagnosis of functional single ventricle and were status post stage I palliation. A total of 8 patients with a history of stage I single-ventricle palliation underwent Ladd's procedure during this time period. We reviewed each patients chart to determine if significant intraoperative or post-operative morbidity or mortality occurred. We also described our protocolized management of these patients in the cardiac intensive care unit, which included pre-operative labs, echocardiography, milrinone infusion, as well as protocolized fluid administration and anticoagulation regimens. We also reviewed the literature to determine the reported morbidity and mortality associated with the Ladd's procedure in this particular cardiac physiology and if other institutions

have reported protocolized care of these patients.

RESULTS: A total of 8 patients were identified to have heterotaxy with an intestinal rotation anomaly and single-ventricle heart disease that was status post single ventricle palliation. Six of these patients were palliated with a Blalock-Taussig shunt, one of whom underwent a Norwood procedure. The two other patients were palliated with a stent, which was placed in the ductus arteriosus. These eight patients all underwent elective Ladd's procedure at the time of gastrostomy tube placement. Per our protocol, all patients remained on aspirin prior to surgery and had no period where they were without anticoagulation. All patients remained on milrinone during and after the procedure and received fluid administration upon arrival to the cardiac intensive care unit to account for losses. All 8 patients experienced no intraoperative or post-operative complications. All patients survived to discharge. One patient presented to the emergency room two months after discharge in cardiac arrest and died due to bowel obstruction and perforation.

CONCLUSION: Protocolized intensive care management may have contributed to favorable outcomes following Ladd's procedure at our institution.

Key words: Congenital heart disease; Heterotaxy; Single-ventricle; Pediatrics; Ladd's procedure; Congenital heart disease

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Core tip: Babies born with congenital heart disease consisting of a functional single-ventricle present a complicated subset of patients to care for. When these patients also have heterotaxy and an intestinal rotational anomaly combined with their heart defect, determining when and how to safely perform a Ladd's procedure is challenging for clinicians involved in their care. Having experienced practitioners involved and using protocolized care may help reduce surgical morbidity and mortality in these patients.

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INTRODUCTION

Heterotaxy syndrome is a relatively rare phenomenon with an incidence of approximately 1 in 10000 live births. It accounts for about 3% of cases of congenital heart disease^[1]. Heterotaxy is synonymous with "visceral

heterotaxy" and "heterotaxy syndrome" and is defined as an abnormality where the internal thoraco-abdominal organs demonstrate abnormal arrangement across the left-right axis of the body. The heterotaxy syndrome is typically associated with complex cardiovascular malformations. These malformations can vary from relatively common defects such as ventricular septal defects to complex anatomy not amenable to complete repair and resultant single ventricle physiology^[2].

Intestinal rotation and fixation abnormalities (IRA) are commonly associated with heterotaxy syndrome. Normal intestinal rotation and fixation occurs between days 32 and 56 in the human fetus^[3]. IRA is a spectrum of disease that depends on the stage of intestinal rotation or fixation that was interrupted. IRA occurs in 40%-90% of children with heterotaxy syndrome^[4,5]. Practice among institutions pertaining to IRA is extremely variable and ranges from observation and conservative management for asymptomatic patients to surgical intervention with a Ladd procedure early in life.

A Ladd procedure may be performed in patients with IRA in an attempt to reduce the risk of bowel ischemia and infarction. During the Ladd procedure, peritoneal bands (Ladd's bands) are divided, and the mesentery of the small bowel is widened. An appendectomy is performed and the bowel is rearranged to a nonrotated state with the small bowel on the right side of the peritoneal cavity and the colon on the left.

The decision of whether or not to perform an elective Ladd procedure in a patient with heterotaxy syndrome becomes more complicated when the patient has complex cardiac anatomy resulting in the need for single ventricle palliation. These patients are at risk for complications such as hypoxia, shunt thrombosis, bowel ischemia and coronary ischemia to name a few. This physiology may increase the risk of morbidity and mortality, particularly in the young infant age group. As such, procedures including major abdominal surgery carry an increased risk of complications and instability.

Our institutional approach to patients with heterotaxy syndrome, IRA and functional single ventricle has been to perform a Ladd procedure if: (1) there are signs of bowel obstruction or ischemia; or (2) there is feeding intolerance and the patient requires a gastrostomy or jejunostomy tube, then a Ladd procedure is performed at the same time.

Substantial morbidity and mortality has been reported in these complex patients^[4-7]. Over a period of several years, we have attempted to protocolize as much as possible our pre-operative and post-operative approach to all stage I single ventricle palliated patients, in hopes of minimizing morbidity and mortality. We report our experience with 8 patients carrying a diagnosis of heterotaxy syndrome, IRA and functional single ventricle status post stage I palliation who underwent Ladd procedure at the time of nissen fundoplication and gastrostomy tube or jejunostomy tube placement. The purpose of this paper is to share our current protocol and experience as well as to

retrospectively determine if complications occurred during or after the Ladd's procedure.

MATERIALS AND METHODS

Following approval by the Arnold Palmer Medical Center institutional review board, we conducted a retrospective chart review. We searched our surgical database for all patients with heterotaxy syndrome and functional single ventricle who underwent a cardiac procedure at Arnold Palmer Hospital for Children between January 2005 and March 2014. For the subset of patients who were diagnosed with an IRA and underwent a Ladd procedure, we collected data including patient sex, age at the time of Ladd procedure, cardiac and segmental anatomy, type of gastrointestinal surgery, intraoperative or post-operative complications from the Ladd procedure and mortality associated with the procedure. We also reviewed each patient's hospital records and clinic notes to ascertain their most up to date feeding status, evidence of post-operative bowel obstruction, or need for further gastrointestinal (GI) procedures.

RESULTS

A total of 8 patients were identified with heterotaxy, IRA and functional single ventricle. All 8 patients had undergone first stage single ventricle palliation. Two patients underwent stenting of the ductus arteriosus. The remaining 6 patients underwent placement of systemic-pulmonary artery shunts. Four of the patients who underwent shunt placement also underwent repair of total anomalous pulmonary venous connection. Each of the 8 patients had an upper GI series with small bowel follow through confirming IRA. Two patients had modified barium swallows showing aspiration. Seven of the 8 patients underwent placement of gastrostomy tube as well as nissen fundoplication at the time of the Ladd procedure. The other patient underwent Roux-en-Y jejunostomy at the time of the Ladd procedure. None of these patients experienced intraoperative complications. One patient had mild postoperative hypotension upon immediate arrival to the cardiovascular intensive care unit, which was responsive to fluid resuscitation. One patient had transient oxygen desaturation upon arrival to the cardiovascular intensive care unit which was found to be mucous plugging and responded immediately to manual bag mask ventilation and suctioning. Neither of these events were considered complications of the procedure as neither of these events recurred and additionally, these can be seen as common, postoperative events in any patient undergoing a procedure.

All eight patients survived to discharge. One patient died as an outpatient. She presented 2 mo after discharge to the emergency department in cardiopulmonary arrest and was found to have bowel perforation and hemodynamic collapse, likely secondary to bowel obstruction. Six patients are currently free from bowel obstruction. One patient had continued feed-

ing intolerance and had suspicion of partial bowel obstruction but was managed conservatively and is currently tolerating full feedings by gastrostomy tube and did not require additional surgery. One patient is feeding entirely per oral, three entirely by gastrostomy tube and the remaining 3 are fed by a combination of oral and gastrostomy tube. Table 1 shows the details for each of the 8 patients with heterotaxy syndrome.

DISCUSSION

Children born with complex cardiac anatomy resulting in a functional single ventricle present a challenging group of patients. Their unstable physiology and typically unbalanced circulation puts all single ventricle patients at risk for morbidity and mortality after stage I palliation. This mortality has improved over the years, however it has still been reported between 10% and 25%^[6,7]. Patients with heterotaxy syndrome and functional single ventricle have been reported to have a mortality rate as high as 41%^[8]. For this reason, procedures and exposures to general anesthesia should be minimized.

Patients with heterotaxy syndrome have an incidence of IRA between 40% and 90%^[4,5,9]. It is understood and agreed upon that patients with heterotaxy and IRA who develop feeding intolerance need immediate evaluation for IRA. However, there is no consensus on whether or not to evaluate asymptomatic patients with heterotaxy for IRA. Additionally, significant institutional variance remains on whether or not to perform an elective Ladd procedure if an IRA is discovered in an asymptomatic patient and if so, the appropriate timing of the procedure. This decision becomes even more complicated when the patient has a functional single ventricle and unbalanced circulation.

In 2013, Pickett *et al*^[10] described their institutional experience of performing elective Ladd procedure in all heterotaxy patients with IRA. They reported a high rate of serious complications (57%) after Ladd procedure in patients with heterotaxy syndrome. They felt that it was likely the limited cardiopulmonary reserve that shunt-dependent and single-ventricle patients have that led to the high rate of complications^[10].

In 2013, Sharma *et al*^[11] reported significant morbidity and mortality in patients undergoing Ladd procedure both prior to and after stage I palliation. Two patients had Ladd procedure prior to stage I palliation. One had recurrent necrotizing enterocolitis and died. Two patients had Ladd procedure after stage I palliation, both of whom developed shunt thrombosis, one of which died. They also reported no mortalities in 5 asymptomatic patients who underwent elective Ladd procedure after second-stage palliation.

Our programmatic approach to heterotaxy syndrome with functional single ventricle is to evaluate for IRA in all patients with heterotaxy. However, we have chosen to intervene surgically only in those patients who develop signs of bowel obstruction or feeding intolerance. All 8 patients described above had feeding

Table 1 Heterotaxy patients

Reason for GI surgery	Studies	Segmental anatomy	Cardiac anatomy	Visceral abnormality	Cardiac procedure	GI surgery	Age at ladd	Intra/postop Complications	Outcome	Current GI status
Poor PO intake, severe GE Reflux	UGI/SBFT	I, D, D	Unbalanced CAVC, PA, LSVC	IRA	PDA stent	Ladd, Roux-en-Y jejunostomy	6 wk	None	Alive	At 5 yr had jejunal perforation resulting in laparotomy and Nissen. Feeds PO and Gtube
Poor PO intake, severe GE Reflux	UGI/SBFT	A, D, D	Unbalanced CAVC, TAPVR, PA, RPA stenosis	IRA	3.5 mm central shunt placement, TAPR repair, RPA plasty	Ladd, Nissen/Gtube	6 wk	None	Alive	No obstruction or GI surgeries. Feeds PO and Gtube
Severe GE Reflux, Vocal cord paralysis with aspiration	UGI/SBFT Mod. Barium Swallow	I, D, S	Dextrocardia, TA, Unbalanced CAVC, Coarctation	IRA	Norwood with 3.5 mm Modified BT shunt	Ladd, Nissen/Gtube	8 wk	None	Alive	No obstruction or GI surgeries. Gtube is removed and now eats entirely PO
Poor PO intake, severe GE Reflux	UGI/SBFT	A, L, D	Unbalanced CAVC, TAPVR, PA	IRA	3.5 Modified BT shunt, TAPVR repair, PA plasty	Ladd, Nissen/Gtube	8 wk	None	Outpatient death from bowel perforation	N/A
Poor PO intake, TE Fistula repair, severe GE Reflux	UGI/SBFT	S, D, D	DORV, right atrial isomerism, BLSVC, CAVC, PS	IRA	PDA stent	Ladd, Nissen/Gtube	5 wk	None	Alive	No obstruction or further GI surgeries. Gtube fed only
Poor PO feeding, GE Reflux,	UGI/SBFT	I, D, D	Dextrocardia, Unbalanced CAVC, TAPVR, PA	IRA	3.5 mm central shunt, TAPVR repair, PA plasty	Ladd, Nissen/GT	6 wk	None	Alive	No obstruction or GI surgeries. Feeds PO and Gtube
Poor PO intake, feeding intolerance, GE Reflux	UGI/SBFT	I, D, D	Unbalanced CAVC, Pulmonary atresia	IRA	3.5 mm Modified BT shunt	Ladd, Nissen/Gtube	6 wk	None	Alive	No obstruction or GI surgeries, All feeds <i>via</i> Gtube
Poor PO feeding, GE reflux, aspiration	UGI/SFT, Modified barium swallow	A, L, L	Unbalanced CAVC, TAPVR, Pulmonary atresia	IRA	4.0 mm Modified BT shunt, TAPVR repair	Ladd, Nissen/Gtube	5 wk	None	Alive	No obstruction or GI surgery. All feeds <i>via</i> Gtube

PA: Pulmonary atresia; BT: Blalock-Taussig; CAVC: Complete atrioventricular canal; TAPVR: Total anomalous pulmonary venous return; GI: Gastrointestinal; GT: Gastrostomy tube; GE: Gastroesophageal; PO: Per oral; TA: Tricuspid atresia; IRA: Intestinal rotation and fixation anomaly; UGI/SBFT: Upper GI with small bowel follow through; DORV: Double outlet right ventricle.

intolerance and were found by upper GI series with small bowel follow through to have IRA. All patients had a Ladd procedure at the time of gastrostomy or jejunostomy tube placement. As a program, we maintain a philosophy of not performing prophylactic Ladd procedures in asymptomatic patients and we would prefer to wait until after the stage two palliation to perform a Ladd's procedure, when the circulation is more balanced. However, all 8 patients had feeding difficulties resulting in the need for an alternate source of enteral feeding. We have maintained the philosophy that if the patient requires GI surgery for an alternate feeding source that we will

perform the Ladd's procedure at that time. To date all patients have required an alternate feeding source and therefore underwent successful Ladd's at that time. To date we have not encountered any patients with heterotaxy syndrome, functional single-ventricle and IRA who developed bowel obstruction requiring urgent Ladd procedure.

At our institution over a period of several years, we have protocolized the pre-operative and post-operative management of patients with functional single-ventricle, status post stage I palliation who are to undergo general anesthesia for any procedure. All patients have preopera-

tive labs performed to evaluate for signs of infection and to monitor hemoglobin, assuring adequate oxygen carrying capacity pre-operatively. All patients get a pre-operative echocardiogram 1-2 d prior to the procedure to evaluate shunt patency and systolic function of the systemic ventricle and all patients regardless of echocardiographic findings, are placed on a milrinone infusion at a dose of 0.5 mg/kg per minute 24 h prior to the procedure and it is continued during the surgery and for 24 h following surgery in an attempt to support the ventricular function during the stress of anesthesia and a major gastrointestinal surgery. Aspirin is not stopped prior to surgery. We have chosen to accept some risk of bleeding in order to have continued antiplatelet affect and avoid any period without some anticoagulation affect in hopes of preserving shunt patency. All patients receive aggressive intraoperative and postoperative fluid resuscitation in addition to maintenance fluids regardless of hemodynamic data to replace assumed fluid losses from gastrointestinal surgery and to prevent intravascular depletion in hopes of minimizing risk of shunt thrombosis. All patients receive a minimum of one 20 mL/kg fluid bolus upon arrival to the cardiac intensive care unit. All patients are placed on postoperative antibiotics for a minimum of 48 h. Anesthesia is performed by experienced cardiac anesthesiologists. The surgery is performed by experienced pediatric surgeons and the patients recover in our dedicated cardiovascular intensive care unit with 24 h in-house attending physician coverage.

While there is still no consensus on the need for evaluation of heterotaxy patients for the presence of IRA and the need for elective Ladd procedure in asymptomatic patients, there will continue to be a need for Ladd procedure in patients with heterotaxy syndrome. As an institution, we do agree with previous reports that suggest waiting until completion of the second stage of palliation to undergo elective Ladd's procedure. However, we feel that if a gastrointestinal surgery, such as gastrostomy tube, is necessary during the stage I palliated phase, that our practice of doing a Ladd's procedure at the same time is acceptable.

It is important to realize that Ladd procedure does not guarantee that a patient will free of partial or complete bowel obstruction later in life as is suspected in our only patient who died following bowel perforation as an outpatient 2 mo after discharge.

While the 8 patients we have presented is a small number, we believe that it does show that a protocolized pre-operative and post-operative management strategy may improve morbidity and possibly survival in this complex patient population. This subset of patients is extremely challenging and each institution must weigh the risk and benefit of the procedure with their own experiences and resources available to care for these patients. While our protocol and results appear satisfactory, we fully recognize that this is a very small group of patients and to say that this strategy is entirely safe and that it would work for every program is not

possible. The combination of heterotaxy syndrome, functional single-ventricle and IRA describes a relatively unique and rare subset of patients. For this reason, further research containing larger cohorts of patients in this field is needed and will likely require data sharing and multi-institution studies.

Our paper does have significant limitations including the fact that it is a retrospective, single institution review and additionally it contains a small cohort of patients.

COMMENTS

Background

Heterotaxy, while rare is often associated with heart defects. When these defects result in single-ventricle physiology and are associated with intestinal rotational anomalies. A Ladd's procedure can carry a high rate of morbidity and mortality in the complex subset of patients and should be undertaken with caution and with the appropriate expertise to care for these patients.

Research frontiers

To our knowledge, no paper has described a protocolized approach to the care of this complicated care of patients undergoing a Ladd's procedure.

Innovations and breakthroughs

The major conclusion from this paper is that with an experienced providers and protocolized approach to the Ladd's procedure in this patient population, morbidity and mortality may be reduced.

Applications

With the current literature reporting high rates of morbidity and mortality when performing the Ladd's procedure in stage I palliated, functional single-ventricle patients, a protocolized approach may improve outcomes.

Terminology

Heterotaxy is defined as an abnormality where the internal thoraco-abdominal organs demonstrate abnormal arrangement across the left-right access of the body.

Peer-review

An interesting article that provides a different perspective in the management of patients with heterotaxy, intestinal rotation anomaly and single-ventricle undergoing the Ladd's procedure.

REFERENCES

- 1 **Hoffman JI**, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002; **39**: 1890-1900 [PMID: 12084585 DOI: 10.1016/S0735-1097(02)01886-7]
- 2 **Jacobs JP**, Anderson RH, Weinberg PM, Walters HL, Tchervenkov CI, Del Duca D, Franklin RC, Aiello VD, Béland MJ, Colan SD, Gaynor JW, Krogmann ON, Kurosawa H, Maruszewski B, Stellin G, Elliott MJ. The nomenclature, definition and classification of cardiac structures in the setting of heterotaxy. *Cardiol Young* 2007; **17** Suppl 2: 1-28 [PMID: 18039396 DOI: 10.1017/S1047951107001138]
- 3 **Langman J**, Sadler T. *Langman's medical embryology*. 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2003
- 4 **Pockett CR**, Dicken BJ, Rebeyka IM, Ross DB, Ryerson LM. Heterotaxy syndrome and intestinal rotation abnormalities: a survey of institutional practice. *J Pediatr Surg* 2013; **48**: 2078-2083 [PMID: 24094961 DOI: 10.1016/j.jpedsurg.2013.03.001]
- 5 **Nakada K**, Kawaguchi F, Wakisaka M, Nakada M, Enami T, Yamate N. Digestive tract disorders associated with asplenia/polysplenia syndrome. *J Pediatr Surg* 1997; **32**: 91-94 [PMID: 9021579 DOI: 10.1016/S0022-3468(97)90103-2]

- 6 **Azaki T**, Merklinger SL, McCrindle BW, Van Arsdell GS, Lee KJ, Benson LN, Coles JG, Williams WG. Evolving strategies and improving outcomes of the modified norwood procedure: a 10-year single-institution experience. *Ann Thorac Surg* 2001; **72**: 1349-1353 [PMID: 11603459 DOI: 10.1016/S0003-4975(01)02795-3]
- 7 **Forbess JM**, Cook N, Roth SJ, Serraf A, Mayer JE, Jonas RA. Ten-year institutional experience with palliative surgery for hypoplastic left heart syndrome. Risk factors related to stage I mortality. *Circulation* 1995; **92**: II262-II266 [PMID: 7586421]
- 8 **Song J**, Kang IS, Huh J, Lee OJ, Kim G, Jun TG, Yang JH. Interstage mortality for functional single ventricle with heterotaxy syndrome: a retrospective study of the clinical experience of a single tertiary center. *J Cardiothorac Surg* 2013; **8**: 93 [PMID: 23591028 DOI: 10.1186/1749-8090-8-93]
- 9 **Ladd WE**. Surgical diseases of the alimentary tract in infants. *N Engl J Med* 1936; **215**: 705-710 [DOI: 10.1056/NEJM193610152151604]
- 10 **Pockett CR**, Dicken B, Rebeyka IM, Ross DB, Ryerson LM. Heterotaxy syndrome: is a prophylactic Ladd procedure necessary in asymptomatic patients? *Pediatr Cardiol* 2013; **34**: 59-63 [PMID: 22644418 DOI: 10.1007/s00246-012-0385-6]
- 11 **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**: 1403-1407; discussion 1407-1048 [PMID: 23434253 DOI: 10.1016/j.athoracsur.2012.11.018]

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