Potential benefits of laparoscopic repair of duodenal

atresia: Insights from a retrospective comparative study Martin Sidler^{1,2}, Florin Djendov¹, Joseph I Curry¹, Simon Blackburn¹, Stefano Giuliani¹, Simon Eaton², Dhanya Mullassery¹, Kate M Cross¹, Paolo De Coppi^{1,2}

¹Specialist Neonatal and Paediatric Surgery, Great Ormond Street Hospital, Paediatric Surgery, London, United Kingdom.

²Stem Cell and Regenerative Medicine Section, DBC, University College London, Great Ormond Institute of Child Health, London, United Kingdom.

^ Correspondence should be addressed to:

Paolo De Coppi, MD, PhD

Stem Cells and Regenerative Medicine Section,

UCL Great Ormond Street Institute of Child Health

30 Guilford Street, London WC1N 1EH, UK

Tel. +44(0)2079052808,

Fax. +44(0)2074046181

Email: p.decoppi@ucl.ac.uk

Abstract

Aim: Congenital duodenal obstruction (CDO) repair can be performed open or laparoscopically. We aimed to determine the potential benefit of laparoscopic repair regarding tolerance of enteral feeding, postoperative pain, hospital stay and complication rate.

Methods: In a single-centre retrospective cohort study, we compared neonates with isolated CDO operated open versus laparoscopically from 2010 to 2019. No transanastomotic tubes were used and anastomoses were created in a side-to-side fashion in all cases. An early feeding policy is applied for all cases operated at our institution. Statistical comparison was performed using the Mann-Whitney test or Fisher's exact test where appropriate.

Results: The 41 patients analysed were similar regarding body weight, gestational age, and proportion of patients with Trisomy 21. Median follow up was 21 months. Four (20%) out of 20 laparoscopic procedures started laparoscopically were converted to open. Comparing the 21 open to the 16 laparoscopically completed patients, median anaesthetic duration was shorter by 18% in the open vs. laparoscopic completed group (218 minutes vs. 179 minutes, respectively; p=0.025). Median postoperative time to full enteral feeds was shorter by 4 days in the first group (7 vs. 11 days, respectively; p=0.028). In accordance, the median duration of parenteral nutrition was less than half in the laparoscopic completed compared to the open group (5 days vs 11.5 days, respectively; p=0.031).

Postoperative opioids were required for only half the duration in the laparoscopically completed group compared to open (2 days vs. 4 days, respectively; p=0.026). Outcomes such as length-of-stay, the occurrence of strictures or adhesions requiring re-intervention, or line sepsis were similar in both groups.

Conclusion: Patients undergoing laparoscopic CDO repair at our institution benefited from shorter time to full enteral feeds, and reduced need for parenteral nutrition as well as postoperative pain medication.

Introduction

Introduction

The first series of repaired intrinsic congenital duodenal obstruction (CDO) was presented in 19311. Reports of successful minimally invasive surgery (MIS) to repair Duodenal Atresia (DA) were published 70 years later2. Only a few reports have directly compared MIS to the traditional open approach; controversy still exists about the value of minimally invasive CDO repair3-7. On one hand, the latter may be beneficial in terms of earlier feeding, less postoperative pain, earlier discharge and better cosmetic outcome. On the other, MIS for CDO can be technically challenging and lead to longer procedures than open repair. Furthermore, it is unclear whether the rates of anastomotic leakage or stricture are higher after MIS compared to open surgery8. Conversely, bowel adhesions, and associated adhesional obstruction, might plausibly be more common after open repair6,9.

We retrospectively review a single centre experience and test the hypothesis that patients undergoing laparoscopic repair of CDO tolerate gastric feeds earlier, have a correspondingly decreased need for parenteral nutrition, need less postoperative pain medication and have a shorter hospital stay.

Methods

This was a single centre, retrospective review of patients undergoing open or MIS repair of CDO. The study was approved by the institution's audit and governance board (Registration number 2510).

Patients

Patients younger than 2 weeks of age undergoing open or laparoscopic repair of CDO between March 2010 and March 2019 were considered for the study. Exclusion criteria were concomitant anorectal malformation, oesophageal atresia or major cardiac anomalies with only palliative treatment options. Patients either underwent laparoscopic (Lap group) or open (Open group) repair of CDO decided based on anticipated tolerance of a pneumoperitoneum and the operating surgeon's preference. The group of patients having their repair completed laparoscopically is referred to as Lap completed group. For both the open and the laparoscopic approach, the incisions in the proximal and distal duodenum were oriented such as they permitted to do a side-to-side anastomosis, completed with single interrupted stitches of fine monofilament suture material. No transanastomotic tubes (TAT) were placed. Laparoscopic setup comprised an umbilical camera port, 2 working ports and a Nathanson retractor inserted just under the xiphisternum.

Perioperative factors and outcome

Data collected were weight, postnatal age, prematurity, gender, chromosomal anomalies, presence of significant cardiac anomalies (such as large ventricular septal defect, Tetralogy of Fallot or double outlet right ventricle), additional gastrointestinal conditions (such as malrotation) or further small bowel atresias. Since the duration of the operation was only available for a minority of patients, duration of anaesthesia from induction to transfer to neonatal intensive care was used. Given that CDO repair is aimed at enabling the baby to feed normally, postoperative time to full enteral feeds was our primary outcome. Secondary

outcomes were the duration of postoperative ventilation, use of parenteral nutrition (PN), need for opioids (i.e. Morphine sulphate) and postoperative length of stay. We also recorded

any complications, such as anastomotic stricture or bowel adhesions, requiring re-operation and instances of line infection.

Statistical Analysis

Comparison of the preoperative patient characteristics included all patients in the Open and of the Lap groups; in the analysis of the peri- and postoperative data, however, only completely laparoscopic operated patients were included in the Lap group. To assess whether removing the laparoscopic-converted-to-open patients significantly affected the results, we also did a sensitivity analysis by grouping the patients as per their intention-to¬treat. Statistical analysis was performed using IBM SPSS Statistics 25 (SPSS Inc., Chicago, IL, USA). Due to the sample size and since most variables were not normally distributed (as assessed using the Shapiro-Wilk Test) we compared continuous factors and outcome variables using the Mann-Whitney Test and dichotomous factors using the Fisher's exact test. Numerical results are graphically presented using boxplots, whereby the box encompasses the interquartile range from the first quartile to the third quartile, and the bold transverse bar representing the median. The whiskers mark maximum and minimum values. Outliers represented by a circle (o) or an asterisk (*) are more than a 1.5-fold or a 3-fold interquartile range away from quartile 1 or 3, respectively. Probability values of ≤0.05 were considered significant, whereas values >0.05 were considered non-significant (NS).

Results

Results

During the study period, 50 patients of less than 2 weeks postnatal age underwent repair of CDO. Patients with concomitant oesophageal atresia (5 patients) or anorectal malformation requiring a colostomy (3 patients), as well as one patient with tricuspid atresia and large ventricle septum defect who underwent DA repair for palliation only, were excluded from the study.

Patient characteristics

The 21 patients in the Open group and the 20 patients in the Lap group were similar in terms of their weight, age, prematurity, Trisomy 21, presence of intestinal malrotation, cardiac anomalies and gender distribution (Table 1).

Perioperative data and outcome

Intestinal malrotation required a Ladd's procedure in 3 of the 21 patients in the Open group and 2 of the 16 patients in the Lap completed group (NS). Median duration of anaesthesia was shorter by 18% in the Open group compared to the Lap completed group (179 minutes vs. 218 minutes, range 133-274 minutes vs. 155-389 minutes, respectively; p=0.025; Fig. 1); we did not observe a significant change in anaesthetic duration over time. Six of 10 patients with anaesthetic durations of 4 hours or more had cardiac anomalies such as double outlet right ventricle or Tetralogy of Fallot. One patient also had a laparoscopic Ladd's procedure, which added to the duration of surgery. The median postoperative duration of treatment with opioid medication, on the other hand, was half the duration in the Lap completed group compared to the Open group (2 days vs. 4 days, range 1-14 days vs. 0-5 days, respectively; p=0.026; Fig.1). The duration of postoperative ventilation was similar in both groups (median of 1 day in either group; NS).

The median postoperative time to reaching full enteral feeds was shorter by 4 days in the Lap completed group (7 vs 11 days, range 4-24 days vs. 4-18 days, respectively; p=0.028; Fig. 2). In accordance, the median duration of parenteral nutrition was less than half in the

Lap completed group compared to the Open group (5 days vs 11.5 days, range 0-40 days vs. 0-25 days, respectively; p=0.031). The rate of line infections and the rate of anastomotic strictures requiring a further duodenal procedure were similar in the Open compared to the Lap completed group (2 in both groups and 3 [14.3%] patients vs. 2 patients [12.5%], respectively). One patient in the Lap completed group had a localised adhesiolysis prior to a revision of the anastomosis, which did not sufficiently improve passage through the duodenum to resolve symptoms.

There was a tendency to a shorter stay in the Lap completed group, with a median postoperative length of stay of 13.5 days vs. 16.5 days in the Open group (NS). In the Lap completed group, 4 patients stayed longer than the median time because discharge was delayed by the fact, they were awaiting review by another specialty. One patient was awaiting transfer to a local hospital to complete transition from nasogastric tube feedings to oral feeds, whereas the vast majority of our patients were discharged home on oral feeds. Also, in the Lap completed group, one patient required re-intervention due to anastomotic stricture while another patient was kept longer due to poor weight gain. The reasons for prolonged hospital stay were different in the Open group, where 7 out of 10 patients staying longer than median postoperative time to discharge were in fact kept because they had not reached full enteral feedings. Median follow-up was 21 months.

Of the 4 patients converted from Laparoscopy to an open operation, 3 patients had a duodenal web such that the anatomy could not be reliably defined; the other patient had a complete DA, weighed 1.13kg and did not tolerate the pneumoperitoneum.

In an intention-to-treat analysis, we also compared the outcome of the Open group to the Lap group, which included the 4 procedures that were converted to an open operation. Median anaesthesia time was 14% shorter in the Open group compared to the Lap group (179 minutes vs. 208 minutes, respectively; p=0.024). Median duration of postoperative opioid requirements was shorter in the Lap group compared to the Open group although this difference was not significant (2 days vs. 4 days, respectively; p=0.18). Median times to full

enteral feeding and duration of TPN were shorter by 4 days and 5.5 days, respectively (7 days vs. 11 days, respectively; p=0.012; and 6 days vs. 11.5 days, respectively; p=0.28 comparing the Lap group to the Open group,. Median duration of postoperative invasive ventilation and length of postoperative hospital stay similar in the Lap group compared to the open group (0.5 days vs 1 day, respectively; p=0.50; and 11 days vs. 16.5 days, respectively; p=0.54).

Discussion

Treatment of CDO can be performed using an open operation or via laparoscopy.

Controversy still exists about the risks and benefits of either approach; only a few studies have directly compared the open vs. the MIS technique3-7.

In our analysis, the overall anaesthetic time from induction to transfer out of theatres was longer in the laparoscopic patients. Significantly longer surgical procedure times for MIS repair were also found by 3 out of 5 comparative reports3-7. Additionally, cardiac comorbidities may have contributed to the prolonged anaesthetic duration in some laparoscopic cases.

Tolerance of full enteral feedings is undoubtedly the main goal of CDO repair. In our experience, time to full feeding after laparoscopic surgery was clearly shorter than after open surgery; our patients' times to full enteral feeds were similar or even markedly shorter relative to other reports comparing open to MIS CDO repair3,5-7. Correspondingly, the duration of PN was also reduced after laparoscopic repair. While PN is known to increase the risk of cholestasis, thrombosis and the rate of sepsis10,11, we were unable to demonstrate a benefit of MIS regarding the occurrence of line infections in our patient cohort. Interestingly, our experience is similar to other reports when considering MIS, but it is superior to others when considering the open approach in that our patients who had open surgery reached full feeds sooner than in other published series8. This could be related to the early feeding policy we have been following with small intermittent nasogastric feeds starting on or around the 2nd postoperative day. Our policy following this early commencement of enteral feeds is similar to that described by others12. This practice may well contribute to our experience of early tolerance of gastric feeds; the studies describing initial feeds around median day 5.4 to 11 report longer times to reach full feeds after laparoscopic as well as open surgery3-6. Because of our early feeding policy, we have not adopted the use of a transanastomotic tubes (TAT). Placing a TAT is another means by

which enteral (i.e. post-anastomotic) feeds can be advanced more quickly after surgery13,14.

Whilst they might reduce the need for PN, however, TATs have not been proven to reduce time to full pre-anastomotic feeds or to reduce the length of hospital stay15. The reported median times to full post-anastomotic feeds are similar to our findings for full oral and gastric feeds after MIS repair13; placing a TAT tube has not been shown to reduce time to full pre-anastomotic feeds14. Furthermore, the potential benefits of a TAT need to be weighed carefully with its associated risks such as displacement or perforation13,16, which should be set against the potential to reduce the rate of line sepsis13 and of PN-related cholestasis11.

Despite the clearly earlier feeding after laparoscopic repair compared to open surgery in our cohort, the postoperative length of hospital stay was not significantly shorter in the first group. In our laparoscopic patients, the reasons prolonging their hospital stay were predominantly logistic in nature and unrelated to their tolerance of gastric or oral feeds.

There seem to be various reliable techniques to perform a safe duodenal anastomosis. One group found Nitinol U-clips to work well17, while others found running sutures to markedly reduce the risk of an anastomotic leak8; both report formation of a diamond-shaped anastomosis. However, we have been using a side-to-side anastomosis for both, the open and the laparoscopic technique10. The duodenal incisions placed transversely on the proximal segment and longitudinally on the distal one allow us to complete our anastomoses in a side-to-side fashion, with single interrupted stitches of fine monofilament sutures, either absorbable or non-absorbable. This technique has not been modified by the Laparoscopic approach which makes the data presented here comparable. We speculate that one patient in our Lap completed group may have had a small leak leading to localized adhesions and anastomotic stricture, although this patient did not have any other clinical signs of this.

The risk of small bowel adhesions is another important factor when considering the type of approach. Postoperative small bowel adhesions can cause obstruction, chronic pain and even female infertility. Reported rates of small bowel adhesions leading to obstruction after laparotomy for duodenal atresia are around 11% and after laparotomy for intestinal atresia as high as 28%18. While only limited data after neonatal laparoscopic operations are

currently available6, many accept that laparoscopy leads to fewer adhesions than laparotomy9.

This present report as well as other studies comparing open vs. laparoscopic repair of CDO need to be interpreted with caution due to their retrospective methodology. Ideally, the apparent benefits of laparoscopic CDO repair would be confirmed in a randomised controlled trial. However, given the rarity of the condition, it is uncertain whether a randomised controlled trial is feasible. We also analysed our data on an 'intention-to-treat' basis, as in a trial, and the results suggest that overall, it is still seems beneficial to start the operation laparoscopically, although approximately 20% of infants would be expected to require conversion to an open procedure.

Conclusion

Patients with CDO operated laparoscopically appear to benefit from a reduced postoperative need for opioids, earlier full feeds and a reduced need for PN. The duration of MIS repair seems to be longer than open surgery

Acknowledgement

M.S. and P.D.C. are supported by National Institute for Health Research (NIHR-RP-2014-04-046). All research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the NIHR Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the author (s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Figure Legends (see PPT) Figure 1: Figure 2:

Figure 3:

Figure 4:

References

- 1. Ladd, W. E. Congenital Obstruction of the Duodenum in Children. N Engl J Med 206, 277–283 (1932).
- 2. Bax, N. M., Ure, B. M., van der Zee, D. C. & van Tuijl, I. Laparoscopic duodenoduodenostomy for duodenal atresia. Surgical Endoscopy 15, 217–219 (2001).
- 3. Spilde, T. L. et al. Open vs laparoscopic repair of congenital duodenal obstructions: a concurrent series. Journal of Pediatric Surgery 43, 1002–1005 (2008).
- 4. Hill, S., Koontz, C. S., Langness, S. M. & Wulkan, M. L. Laparoscopic Versus Open Repair of Congenital Duodenal Obstruction in Infants. Journal of Laparoendoscopic & Advanced Surgical Techniques 21, 961–963 (2011).
- 5. Jensen, A. R. et al. Laparoscopic Versus Open Treatment of Congenital Duodenal Obstruction: Multicenter Short-Term Outcomes Analysis. Journal of

Laparoendoscopic & Advanced Surgical Techniques 23, 876–880 (2013).

- 6. Cho, M. J., Kim, D. Y., Kim, S. C. & Namgoong, J. M. Transition from Laparotomy to Laparoscopic Repair of Congenital Duodenal Obstruction in Neonates: Our Early Experience. Front Pediatr 5, 217–5 (2017).
- 7. Son, T. N. & Kien, H. H. Laparoscopic versus open surgery in management of congenital duodenal obstruction in neonates: a single-center experience with 112 cases. Journal of Pediatric Surgery 52, 1949–1951 (2017).

- 8. van der Zee, D. C. Laparoscopic Repair of Duodenal Atresia: Revisited. World Journal of Surgery 35, 1781–1784 (2011).
- 9. Schemmer, P., Mehrabi, A., B chler, M. W., Gutt, C. N. & Oniu, T. Fewer adhesions induced by laparoscopic surgery? Surgical Endoscopy 18, 898–906 (2004).
- 10. Bishay, M. et al. The role of parenteral nutrition following surgery for duodenal atresia or stenosis. Pediatr Surg Int 29, 191–195 (2012).
- 11. Jiang, W. et al. Early enteral nutrition for upper digestive tract malformation in neonate. Asia Pac J Clin Nutr 24, 38–43 (2015).
- 12. Ekingen, G., Ceran, C., Guvenc, B. H., Tuzlaci, A. & Kahraman, H. Early enteral feeding in newborn surgical patients. Nutrition 21, 142–146 (2005).
- 13. Hall, N. J. et al. Trans-anastomotic tubes reduce the need for central venous access and parenteral nutrition in infants with congenital duodenal obstruction. Pediatr Surg Int 27, 851–855 (2011).
- 14. Harwood, R. Transanastomotic tubes reduce the cost of nutritional support in neonates with congenital duodenal obstruction. Pediatr Surg Int 35, 457–461 (2019).
- 15. Ruangtrakool, R., Mungnirandr, A., Laohapensang, M. & Sathornkich, C. Surgical treatment for congenital duodenal obstruction. J Med Assoc Thai 84, 842–849 (2001).
- 16. Sun, S. C., Samuels, S., Lee, J. & Marquis, J. R. Duodenal Perforation: A Rare Complication of Neonatal Nasojejunal Tube Feeding. Pediatrics 55, 371–375 (1975).
- 17. Spilde, T. L. et al. Open vs laparoscopic repair of congenital duodenal obstructions: a concurrent series. Journal of Pediatric Surgery 43, 1002–1005 (2008).
- 18. Fredriksson, F., Christofferson, R. H. & Lilja, H. E. Adhesive small bowel obstruction after laparotomy during infancy. Br J Surg 103, 284–289 (2015).

Figure Legends

Figure 1:

Laparoscopic repair was associated with decreased need for opioids yet also with longer procedure times. A) Median duration of postoperative need for opioid pain medication was half in patients after a laparoscopic repair compared to open (2 vs. 4 days, respectively; # p=0.026). B) Median anaesthetic duration was 39 minutes longer in patients operated laparoscopically compared to open (218 vs. 179 minutes, respectively; § p=0.025). Figure 2:

Earlier full enteral feeding and decreased need for parenteral nutrition (PN) after laparoscopic repair. A) Median time to full feeds (i.e. gastric or oral) was 36% shorter in the laparoscopic group compared to open (7 vs. 11 days, respectively; # p=0.028). B) Median duration of PN was less than half after laparoscopic repair compared to open (5 vs. 11.5 days, respectively; § p=0.031).



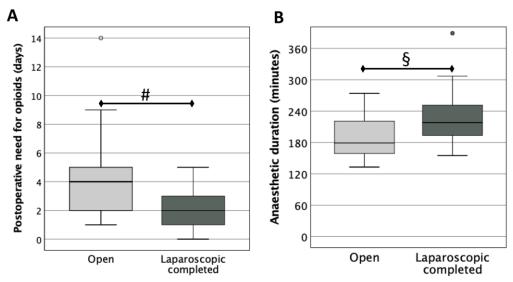


Figure 1: Laparoscopic repair was associated with decreased need for opioids yet also with longer procedure times. A) Median duration of postoperative need for opioid pain medication was half in patients after a laparoscopic repair compared to open (2 vs. 4 days, respectively; # p=0.026). B) Median anaesthetic duration was 39 minutes longer in patients operated laparoscopically compared to open (218 vs. 179 minutes, respectively; § p=0.025).



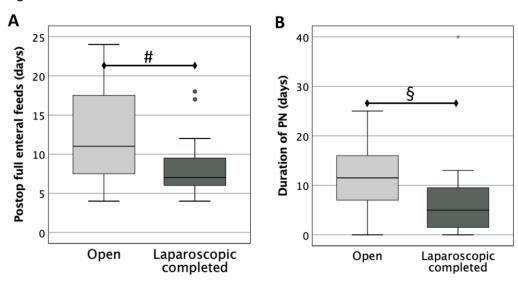


Figure 2: Earlier full enteral feeding and decreased need for parenteral nutrition (PN) after laparoscopic repair. A) Median time to full feeds (i.e. gastric or oral) was 36% shorter in the laparoscopic group compared to open (7 vs. 11 days, respectively; # p=0.028). B) Median duration of PN was less than half after laparoscopic repair compared to open (5 vs. 11.5 days, respectively; § p=0.031).

Table 1: Preoperative patient characteristics

	Primary open repair n=21	Laparoscopic repair n=20	p Value
Weight at operation (kg)*	2.64 [1.1 – 4.0]	2.67 [1.1 – 3.6]	0.76
Age (days)*	2 [0 – 8]	2 [0 – 14]	0.81
Prematurity [§]	8 (38%)	7 (35%)	>0.99
Trisomy 21	6 (29%)	5 (25%)	>0.99
Cardiac Anomaly	5 (24%)	6 (30%)	0.73
Male:Female Ratio	11:10	8:12	0.54
Intestinal malrotation	3 (14.3%)	2 (10%)	>0.99

^{*} Data reported as median and range

[§] Born before 37 weeks gestation

Table 2: Perioperative data and outcome

	Primary open repair n=21	Laparoscopic completed repair n=16	p Value
Concomitant Ladd's Procedure	3 (14.3%)	2 (12.5%)	>0.99
Postoperative invasive ventilation (days) *	1 (0.5 – 5)	1 (0.5 – 2)	0.63
Line Infection	3 (14.3%)	2 (12.5%)	>0.99
Postoperative length of stay (days) *	16.5 (5 – 27)	13.5 (5 – 58)	0.94
Anastomotic Stricture requiring Procedure	2 (9.5%)	2 (12.5)	>0.99