

## Safety and feasibility of primary radical surgery for meconium peritonitis considering patients' general condition and perioperative findings

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### ABSTRACT

We reviewed the outcomes of meconium peritonitis and evaluated the safety and feasibility of primary radical surgery for meconium peritonitis. A total of 21 cases of meconium peritonitis between 2006 and 2020 were retrospectively reviewed. The patients were classified into two groups based on the type of surgery: group I (primary radical surgery, n = 16) and group II (multistage surgery; drainage only or ileostomy, followed by elective surgery, n = 5). Patient backgrounds and surgical outcomes were compared between the two groups. The term of prenatal diagnosis, preoperative white blood cell count, and preoperative catecholamine use were not significantly different between the two groups. Group I included more mature neonates than group II (gestational age at birth, 35w1d vs 30w1d, p = 0.02; birth weight, 2.5 kg vs 1.1 kg, p < 0.01). Preoperative C-reactive protein was significantly lower in group I (0.37 mg/dL vs 2.8 mg/dL, p < 0.05). Operation time, blood loss, time to enteral feeding, and complication rates were not significantly different between the two groups. The surgical outcomes of primary radical surgery were comparable to those of multistage surgery, although the patients' backgrounds were different. Our strategy of selecting one-stage or multiple-stage surgery for treatment of meconium peritonitis, depending on the patient's general condition and degree of intestinal ischemia, was reasonable.

Keywords: meconium peritonitis, primary radical surgery, multistage surgery

Abbreviations:

MP: meconium peritonitis

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## INTRODUCTION

Meconium peritonitis (MP) results from perforation of the intestine in the fetal period, causing chemical peritonitis. Treatment approaches for MP are either multistage surgery, that involves drainage or ileostomy followed by radical surgery, or primary radical surgery. The surgical approach that provides better outcomes is still controversial. In our hospital, we perform early surgical interventions for MP as far as possible to improve patients' outcomes.<sup>1</sup> We select primary radical surgery for MP on principle, except for cases of extremely low birth weight infants, poor general condition, and severe adhesions that prevents confirmation of the perforation site. In this study, we retrospectively reviewed recent cases of MP at our institution and also evaluated the safety and feasibility of primary radical surgery for MP by comparing its surgical outcomes to those of multistage surgery for MP at our institution.

## MATERIALS AND METHODS

A total of 21 patients with MP were treated at our institution between January 2006 and December 2020. Our institution's policy was to perform primary radical surgery for MP; however, if patients met certain selection criteria such as very low birth weight, poor general condition, or unusual intraoperative findings such as massive intestinal necrosis or ischemic color change of intestine, multistage surgery was selected. Multistage surgery included drainage only or ileostomy followed by elective radical surgery. Drainage was performed in cases with shock and extreme difficulty in open operation due to adhesions, followed by ileostomy or elective radical surgery within seven days. In patients who underwent ileostomy, stoma closure was performed at around 2 months of age. The patients were classified into two groups based on the type of surgery: group I (primary radical surgery) and group II (multistage surgery: drainage only or ileostomy followed by elective radical surgery). Patients' backgrounds and surgical outcomes were compared between the two groups. The data collected included term of prenatal diagnosis, gestational age, weight at birth, age and weight at surgery, sex, preoperative white blood cell count, preoperative C-reactive protein, preoperative catecholamine use, diagnosis including the type of MP,<sup>2</sup> image findings, procedure, operation time, blood loss, time to enteral feeding, and postoperative complications. Complications were classified using the Clavien-Dindo classification,<sup>3</sup> and those with grade 3a or worse were evaluated. Short-term surgical outcomes were defined as outcomes within postoperative day 90. Long-term surgical outcomes were defined as outcomes after postoperative day 90.

The purpose of this study was to review the short- and long-term surgical outcomes of primary radical surgery for MP at our institution. We also evaluated the safety and feasibility of primary radical surgery for MP by comparing those of multistage surgery. If the first surgery was drainage only, the surgical outcomes of elective surgery were used as comparative data.

### *Operation technique*

In group I, resection of the perforated small bowel with anastomosis was performed. Intestinal anastomosis was performed either as a single-layer end-to-end anastomosis in an interrupted fashion using 5-0 or 6-0 monofilament, or as functional end-to-end anastomosis using ENDOPATH® ETS-FLEX 35 mm, Powered ECHELON FLEX® 7 (Ethicon; Johnson & Johnson Medical, N.V., Belgium), and JustRight™ 5 mm Stapler (AMCO Inc., Tokyo, Japan).

In group II, drainage was performed with a penrose drain. Ileostomy was performed by bringing out the perforation site. Elective radical surgery was performed by ileostomy closure

or small bowel resection with single-layer end-to-end anastomosis.

### *Statistical analysis*

Continuous variables were expressed as median (interquartile range). The Mann-Whitney U-test was used to compare continuous variables. Fisher's exact probability test was used to analyze the differences between discrete variables. Statistical significance was set at  $p < 0.05$ . All statistical analyses were performed using R software 3.5.0 (The R Foundation for Statistical Computing, Vienna, Austria).<sup>4</sup>

### *Ethics approval*

This study was approved by the Institutional Review Board of Nagoya University Graduate School of Medicine (No. 2020-0607) and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards.

## RESULTS

Group I included 16 patients (76%) and group II included 5 patients (24%). In group II, three patients were treated with only drainage as primary surgery due to their poor general condition or presence of severe adhesions, and two were treated with ileostomy because of massive intestinal necrosis and necrotic color change of the intestine. In the former, one patient out of three was cured with only drainage, and the other two underwent ileostomy or radical surgery within 7 days of birth (Table 1).

**Table 1** Reasons of multistage surgery

	Gestational age	Birth weight	1 <sup>st</sup> surgery	2 <sup>nd</sup> surgery	Reason of multistage surgery
1	28w5d	1140 g	Drainage	None	Severe adhesion
2	Unknown	1140 g	Drainage	Intestine resection with anastomosis	Severe adhesion
3	25w3d	411 g	Drainage	Ileostomy	Poor general condition
4	35w1d	2451 g	Ileostomy	Stoma closure	Massive intestine necrosis
5	31w5d	1772 g	Ileostomy	Stoma closure	Necrotic color change

### *Patients' backgrounds (Table 2)*

Group I included more mature neonates than group II in terms of gestational age and weight at birth. Weight at surgery was significantly higher in group I, whereas preoperative C-reactive protein levels were significantly lower. Group I included cystic type MP in 14 (88%), fibroadhesive in 0 (0%), and generalized in 2 (13%) patients. Group II included cystic type MP in 3 (60%), fibroadhesive in 0 (0%), and generalized in 2 (40%) patients. Types of anastomoses in Group I included 12 cases of hand-sewn and 4 cases of functional end-to-end anastomosis.

**Table 2** Patients' details

	Group I (n = 16)	Group II (n = 5)	p value
Number of prenatal diagnosis, n (%)	14 (88%)	4 (80%)	> 0.99
A term of prenatal diagnosis	32w (29w–33w)	27w3d (22w3d–32w)	0.4
Gestational age at birth, day <sup>a</sup>	35w5d (34w1d–36w6d)	30w2d (28w1d–32w4d)	0.02 *
Weight at birth, kg <sup>a</sup>	2.4 (2.3–2.7)	1.1 (1.1–1.8)	< 0.01 *
Age at surgery, day <sup>a</sup>	0 (0–0)	0 (0–0)	0.3
Weight at surgery, kg <sup>a</sup>	2.5 (2.2–2.7)	1.1 (1.1–1.8)	< 0.01 *
Male, n (%)	11 (69%)	1 (20%)	0.1
Pre-operative WBC, $\times 10^3/\mu\text{L}$ <sup>a</sup>	15.6 (11.0–17.9)	16.8 (12.3–20.5)	0.7
Pre-operative CRP, mg/dL	0.37 (0.04–0.70)	1.6 (1.2–2.8)	0.02 *
Pre-operative catecholamine use	4 (25%)	2 (40%)	0.6
Type of meconium peritonitis			
Cystic/Fibroadhesive/Generalized	14/0/2	3/0/2	
Cause of meconium peritonitis			
Intestinal volvulus	13 (81%)	3 (60%)	0.5
Complex obstruction	2 (13%)	1 (20%)	> 0.99
Intussusception	1 (6%)	0 (0%)	> 0.99
Unknown	0 (0%)	1 (20%)	0.2
Radiographic evidence of calcification, n (%)	7 (44%)	1 (20%)	0.6

<sup>a</sup> Median (interquartile range)

WBC: white blood cell

CRP: C-reactive protein

\* Significant difference

### *Surgical outcomes (Table 3)*

The short-term surgical outcomes of group I were not significantly different from those of group II in terms of time to initial enteral feeding, time to full enteral feeding, operation time, blood loss, hospitalization days, and complications. Regarding specific complications such as leakage, stricture, obstruction, and sepsis, the data did not significantly differ between the two groups. Overall mortality was 5% (1 of 21 cases), which was due to sepsis and neonatal asphyxia in group II. The source of infection for sepsis was unknown.

The long-term surgical outcomes were also not significantly different between the two groups. 20 patients (95%) survived without any significant complications.

**Table 3** Short and long term surgical outcomes

	Group I (n = 16)	Group II (n = 5)	p value
Time to initial enteral feeding, day <sup>a</sup>	6 (4–7)	7 (6–9)	0.4
Time to full enteral feeding, day <sup>a</sup>	20 (14–32)	38 (30–45)	0.2
Operation time, min <sup>a</sup>	110 (93–125)	111 (99–123)	> 0.99
Blood loss, mL <sup>a, b</sup>	39 (25–55)	84 (54–175)	0.3
Hospitalization days, day <sup>a, b</sup>	57 (35–103)	84 (51–138)	0.5
Short-term complications, n (%)	3 (19%)	1 (20%)	> 0.99
Leakage	1 (6%)	0 (0%)	> 0.99
Stricture	1 (6%)	0 (0%)	> 0.99
Obstruction	1 (6%)	0 (0%)	> 0.99
Sepsis	0 (0%)	1 (20%)	0.2
Long-term complications, n (%)			
Obstruction	2 (13%)	0 (0%)	> 0.99
Abdominal incisional hernia	0 (0%)	1 (20%)	0.2
Postoperative mortality	0 (0%)	1 (20%)	0.2

<sup>a</sup> Median (interquartile range)

<sup>b</sup> The case of drainage only was excluded.

## DISCUSSION

In this study, 95% cases (20/21) of MP demonstrated good long-term outcomes without significant complications. Primary radical surgery for MP had equivalent surgical outcomes compared to multistage surgery, although patients' backgrounds, such as maturity and preoperative C-reactive protein level, were significantly different between the two groups.

Some studies have reported that primary anastomosis had similar surgical outcomes compared to stoma opening in low birth weight infants with focal intestinal perforation<sup>5</sup> and infants weighing less than 1000 g with necrotizing enterocolitis.<sup>6</sup> Meanwhile, MP includes other aspects of focal intestinal perforation and necrotizing enterocolitis, such as severe adhesions and chemical peritonitis, because meconium mediates inflammation.<sup>7</sup> This specificity affects the choice of surgical method. We prefer primary anastomosis, except in extremely low birth weight infants and those with poor general conditions; however, if severe adhesions prevent observation of the perforation site, we need to perform multistage surgery. MP includes three types, ie fibroadhesive, cystic, and generalized<sup>2</sup>; however, we consider primary anastomosis as the first choice of treatment in any type of MP, if possible, because we believe that the type itself does not affect the surgical outcomes significantly. Some studies reported that primary anastomosis can be performed safely in patients with MP in appropriate cases.<sup>8,9</sup> Our study findings were consistent with those of previous studies regarding the surgical outcomes of primary anastomosis.

In contrast, multistage surgery has also been performed safely. It is preferable for patients with low birth weight and poor general conditions. A study supporting multistage surgery for MP suggests that drainage or ileostomy at first surgery improves the general condition of the neonates and also alleviates peritoneal adhesions over time; therefore, it facilitates elective radical surgery.<sup>10</sup> In fact, we also performed five cases of multistage surgery (three of drainage and two

of ileostomy) because we considered that these patients' intestinal condition was not good for anastomosis.

It is true that multistage surgery is considered a safety measure. Certain data also suggests that primary anastomosis in preterm neonates with isolated intestinal perforation has a higher risk for development of life-threatening complications than ileostomy.<sup>11</sup> However, ileostomy has disadvantages including prolonged hospitalization, ileostomy management, and transparent nutrition in drainage cases. Furthermore, the appropriate timing of elective radical surgery, especially in drainage cases, has not been determined yet. Our institution's policy for drainage cases is to perform elective surgery within 7 days of drainage because prolonged retention of drainage tube increases risk of infection, and peritoneal adhesions do not necessarily alleviate empirically over time. Prolonged total parental nutrition in drainage cases also causes total parental nutrition-related liver injury. Therefore, primary radical surgery is our first choice for treatment of MP. In case of drainage only, the second operation, ie ileostomy or anastomosis, should be performed soon after the first operation.

16 of the 21 patients (76%) with MP in this study were able to undergo primary radical surgery without mortality. Moreover, the surgical outcomes of primary radical surgery were equivalent to those of multistage surgery in terms of enteral feeding, complications, and hospitalization days. Our study showed that primary radical surgery for MP was safe and feasible in appropriate cases. Our exclusion criteria for primary radical surgery, ie cases of very low birth weight, poor general condition, and intraoperative findings such as massive intestine necrosis and ischemic color change of intestine, was considered as one of the options to select appropriate cases for primary anastomosis. Further studies are needed to obtain better outcomes of MP. The development of an evaluation standard may be useful to determine the choice of surgical method, ie, primary radical surgery or multistage surgery. In multistage surgery, the appropriate timing of elective radical surgery should also be verified.

## LIMITATIONS

Our study has several limitations. First, it was a single-center retrospective study with a limited number of cases. Less statistical power can lead to the appearance of a lack of significant differences between the two groups. Second, selection bias was present in this study. Patients undergoing multistage surgery were more immature, resulting in a tendency toward a high complication rate.

## CONCLUSION

The long-term and short-term outcomes of MP were comparable in this study. Our strategy of selecting one-stage multiple-stage surgery for treatment of meconium peritonitis, depending on the patient's general condition and degree of intestinal ischemia, was reasonable. Primary radical surgery can be the first choice for the treatment of MP, considering patients' general condition and perioperative findings.

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None.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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