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ORIGINAL ARTICLE

Clinical features and practice patterns of gastroschisis: a retrospective analysis using a Japanese national inpatient database

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Abstract

Purpose The number of infants with gastroschisis is increasing worldwide, but advances in neonatal intensive care and parenteral nutrition have reduced gastroschisis mortality. Recent clinical data on gastroschisis are often from Western nations. This study aimed to examine clinical features and practice patterns of gastroschisis in Japan.

Methods We examined treatment options, outcomes, and discharge status among inpatients with simple gastroschisis (SG) and complex gastroschisis (CG), 2010–2016, using a national inpatient database in Japan.

Results The 247 eligible patients (222 with SG) had average birth weight of 2102 g and average gestational age of 34 weeks; 30% had other congenital anomalies. Digestive anomalies were most common, followed by circulatory anomalies. In-hospital mortality was 8.1%. The median age at start of full enteral feeding was 30 days. The median length of stay was 46 days. There were no significant differences in outcomes except for length of stay, starting full enteral feeding and total hospitalization costs between the SG and CG groups. About 80% of patients were discharged to home without home medical care. The readmission rate was 28%.

Conclusion This study's findings on the clinical characteristics and outcomes of gastroschisis are useful for the clinical management of gastroschisis.

Keywords Pediatric surgery · Neonatal · Gastroschisis · Complex gastroschisis · Abdominal wall defect

Introduction

Gastroschisis is a full-thickness defect of the abdominal wall, usually located to the right side of the normal umbilical cord. It is a rare birth defect, presenting in one to five of 10,000 live births [1–3]. However, the number of infants with gastroschisis are increasing steadily worldwide [4, 5].

Numerous studies about the clinical future or practice patterns of gastroschisis have been conducted [6–11]. These studies suggest that there is no standardized practice for gastroschisis. There may be variability across institutions and countries in the management of patients with gastroschisis in terms of closure techniques, timing of closure, and postoperative feeding protocols. Previous studies have demonstrated racial disparities in survival among infants with abdominal wall defects [12–14]. However, large cohort studies have only been carried out in Europe, North America, and Australia. There has been a dearth of data on the clinical features and practice patterns for gastroschisis in Asia.

The present study therefore aimed to examine patient characteristics, practice patterns, and outcomes of gastroschisis, using a national inpatient database in Japan.

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Patients and methods

Data source

This descriptive study used the Diagnosis Procedure Combination (DPC) database. The details of the database have been described elsewhere [15]. Briefly, the database is a national inpatient database that includes administrative claims and discharge data collected from more than 1000 acute care hospitals in Japan. All 82 university hospitals in Japan are obliged to participate in the database, and participation by community hospitals is voluntary. The database includes data on approximately seven million inpatients every year, representing approximately 50% of all inpatients in Japan. About 90% of Japanese hospitals with neonatal intensive care units are included in the Diagnosis Procedure Combination database [16].

The database includes unique identifiers for hospitals; patient's age, body weight at admission or at birth, body height, gestational age, and sex; emergency or elective admission; diagnoses, comorbidities at admission, and complications after admission recorded as textual data in the Japanese language and using International Classification of Diseases, Tenth Revision (ICD-10) codes [17]; length of stay; surgical and nonsurgical procedures recorded using the original Japanese coding system; date of each procedure; date of use during the hospitalization for each drug, blood product, and device; and discharge status.

Study population

We identified babies (≤2 days old) who were admitted with gastroschisis (ICD code: Q793) from July 2010 to March 2016. We excluded the following patients: (1) those who were diagnosed with both gastroschisis and omphalocele; (2) those who were transferred to a different hospital within 2 days; and (3) those with missing data on drugs or surgery.

We divided the eligible patients into two groups: those with simple gastroschisis (SG) and those with complex gastroschisis (CG). We defined SG as gastroschisis with intact bowel. Following previous studies [6, 18], we defined CG as gastroschisis with at least one of the following intestinal pathologies: intestinal atresia/stenosis (ICD-10 codes: Q410-2, Q419, Q421, Q428-9), perforation (K631, P780), intestinal necrosis (K550), or volvulus (K562).

Measurements of variables

We investigated patients' backgrounds, including sex, gestational age (in weeks), body weight (at birth or at admission), and associated malformations. Gestational age was categorized as <28 weeks (extremely preterm), 28–31 weeks (very preterm), 32–36 weeks (moderate to late preterm), or ≥37 weeks (term). Body weight was categorized as <1000 g (extremely low birth weight), 1000–1499 g (very low birth weight), 1500–2499 g (low birth weight), or ≥2500 g (normal weight).

We identified the following associated malformations: congenital malformations of the nervous system (Q00–07); eye, ear, face, or neck (Q10–18); circulatory system (Q20–28); respiratory system (Q30–34); cleft lip or cleft palate (Q35–37); digestive system without gastroschisis (Q38–45); genital organs (Q50–56); urinary system (Q60–64); musculoskeletal system (Q65–79); other congenital malformations (Q80–89); trisomy 21 (Q90); trisomy 18 (Q91.0-3); trisomy 13 (Q91.4-7); and other chromosome abnormalities (Q92–99).

We investigated practice patterns for treating gastroschisis in terms of using catecholamines (dopamine, noradrenaline, adrenaline, and dobutamine), immunoglobulin, albumin, antithrombin, and blood transfusion (red blood cells, fresh frozen plasma, and platelets), anti-disseminated intravascular coagulation drugs, anti-apnea drugs (anhydrous caffeine, theophylline, and aminophylline) and surfactants. Supportive measures assessed included the insertion of a central venous catheter, mechanical ventilation (with nitric oxide or with extracorporeal membrane oxygenation), continuous blood purification (i.e., intermittent or continuous renal replacement therapy, exchange transfusion, or plasma exchange), and phototherapy for icterus neonatorum. We also examined in-hospital deaths, postoperative length of stay (LOS), length of intensive care unit stay, age (in days) at start of enteral feeding, age (in days) at start of full enteral feeding, and total hospitalization costs. We also examined requirements for home medical care after discharge, including tracheostomy, tube feeding (i.e., gastrostomy or transnasal tube), home respirator, home oxygen therapy, and home parenteral nutrition. We also investigated 1-year rates of readmission because of intestinal obstruction and the proportion with postoperative intestinal obstruction or ileus (ICD-10 codes: K561-2, K564-7, K660, K913) as a reason for 1-year readmission.

Statistical analyses

We used Fisher's exact tests and Chi-square tests to compare proportions for categorical variables (such as sex), and *t* tests and Mann–Whitney *U* tests to compare averages or medians for continuous variables (such as age). We used a significance level of $p < 0.05$ for all statistical tests, and all reported *p* values were two-sided. All statistical analyses were conducted using Stata/MP 14.0 (Stata Corp., College Station, TX, USA).

Results

A total of 277 babies (≤ 2 days old) were diagnosed with gastroschisis during the study period. We excluded patients who were diagnosed with both gastroschisis and omphalocele ($n = 3$), those who were transferred to another hospital within 2 days ($n = 11$), and those with missing data on drugs or surgery ($n = 16$). We thus identified a total of 247 eligible patients, including 222 SG patients (89.9%) and 25 CG patients (10.1%).

Table 1 shows the patient characteristics. Overall, there were slightly more male patients than female patients. The averages (standard deviations) of gestational age and birth weight were 34.0 (7.9) weeks and 2102 (523) g, respectively. Prematurity (< 37 weeks of gestation) was documented in 148 patients (60%). Overall, 78% of the patients had low birth weight (< 2500 g). There was no significant difference in birth weight between the SG and CG groups. Associated anomalies were detected in 73 patients (30%). Forty-three (17%) patients had digestive system anomalies, and 14 (5.7%) had circulatory system anomalies. The circulatory anomalies were all cardiac anomalies, including nine patients with patent ductus arteriosus and four with other cardiac anomalies. Four patients (1.6%) had a chromosomal anomaly.

Table 2 shows the treatment options for gastroschisis. We excluded four patients who died within 2 days of admission. There were no significant differences in the number of operations or age at first operation between the SG and CG

Table 1 Characteristics of patients with gastroschisis

	Simple gastroschisis ($n = 222$)		Complex gastroschisis ($n = 25$)		Total ($n = 247$)	
Sex, *n* (%)						
Male	120	54.1	13	52.0	133	53.8
Gestational age (in weeks), average (standard deviation)	34.1 (7.6)		32.8 (10.0)		34.0 (7.9)	
Extremely preterm (< 28)	13	5.9	2	8.0	15	6.1
Very preterm (28–31)	4	1.8	0	0.0	4	1.6
Moderate to late preterm (32–36)	116	52.3	13	52.0	129	52.2
Term (≥ 37)	75	33.8	10	40.0	85	34.4
Missing	14	6.3	0	0.0	14	5.7
Birth weight (g), average (standard deviation)	2086 (527.6)		2237 (469.2)		2102 (523.1)	
Extremely low birth weight infant (< 1000 g)	3	1.4	0	0.0	3	1.2
Very low birth weight infant (1000–1499 g)	19	8.6	1	4.0	20	8.1
Low birth weight infant (1500–2499 g)	152	68.5	18	72.0	170	68.8
Normal weight infant (≥ 2500)	46	20.7	6	24.0	52	21.1
Missing	2	0.9	0	0.0	2	0.8
Anomaly, *n* (%)						
Any anomaly	50	22.5	23	92.0	73	29.6
Any anomaly without intestinal atresia	50	22.5	3	12.0	53	21.5
Nerve system	1	0.5	0	0.0	1	0.4
Eye, ear, face, or neck	1	0.5	0	0.0	1	0.4
Circulatory system	13	5.9	1	4.0	14	5.7
Respiratory system	6	2.7	0	0.0	6	2.4
Cleft lip or cleft palate	0	0.0	0	0.0	0	0.0
Digestive system	20	9.0	23	92.0	43	17.4
Genital organs	9	4.1	0	0.0	9	3.6
Urinary system	1	0.5	0	0.0	1	0.4
Musculoskeletal system	4	1.8	2	8.0	6	2.4
Other	2	0.9	0	0.0	2	0.8
Chromosomal anomaly, *n* (%)	4	1.8	0	0.0	4	1.6
Trisomy 21	1	0.5	0	0.0	1	0.4
Trisomy 13	0	0.0	0	0.0	0	0.0
Trisomy 18	3	1.4	0	0.0	3	1.2
Other chromosomal anomalies	0	0.0	0	0.0	0	0.0

Table 2 Treatments of gastroschisis

	Simple gastroschisis ($n=218$)		Complex gastroschisis ($n=25$)		Total* ($N=243$)		p value
	n	%	n	%	n	%	
Number of operations							0.18
1 time	111	50.9	8	32.0	119	49.0	
≥ 2 times	106	48.6	17	68.0	124	50.6	
Missing data	1	0.5	0	0.0	1	0.4	
Age (in days) at first operation							1.00
Early (on birthday)	175	80.3	20	80.0	195	80.3	
Delay (after birthday)	52	23.9	5	20.0	47	19.3	
Missing data	1	0.5	0	0.0	1	0.4	
Mechanical ventilation	196	89.9	22	88.0	218	89.7	0.73
Requiring ECMO	1	0.5	0	0.0	1	0.4	1.00
Requiring nitric oxide	7	3.2	1	4.0	8	3.3	0.59
Catecholamine use	107	49.1	15	60.0	122	50.2	0.40
Dopamine	91	41.7	12	48.0	10	42.4	0.67
Noradrenaline	2	0.9	1	4.0	3	1.23	0.28
Adrenaline	31	14.2	3	12.0	34	14.0	1.00
Dobutamine	46	21.1	8	32.0	54	22.2	0.21
Blood transfusion	156	71.6	22	88.0	178	73.3	0.10
Red blood cells	62	28.4	15	60.0	77	32.0	0.003
Fresh frozen plasma	41	18.8	10	40.0	51	21.0	0.02
Platelets	15	6.9	4	16.0	19	7.8	0.12
Albumin	148	67.9	20	80.0	168	69.1	0.26
Immunoglobulin	62	28.4	13	52.0	75	30.9	0.02
Insertion of central venous catheter	185	84.9	25	100	210	86.4	0.03
Continuous blood purification	4	1.8	1	4.0	5	2.1	0.42
Use of anti-DIC drugs	14	6.4	4	16.0	18	7.4	0.10
Use of anti-apnea drugs	9	4.1	0	0.0	9	3.7	0.60
Use of surfactants	25	11.5	4	16.0	29	11.9	0.50
Phototherapy for icterus neonatorum	37	17.0	4	16.0	41	16.9	1.00

* Four patients were excluded because of death within 2 days of admission

ECMO extracorporeal membrane oxygenation, *DIC* disseminated intravascular coagulation

groups. About a half of the patients underwent abdominoplasty or abdominal surgery more than twice. There were no significant differences in the use of mechanical ventilation, catecholamines, blood transfusion, continuous blood purification, anti-disseminated intravascular coagulation drugs, anti-apnea drugs, surfactants, or phototherapy for icterus neonatorum between the SG and CG groups. The percentages with insertion of central venous catheter and with the administration of red blood cells, fresh frozen plasma, or immunoglobulin were significantly higher in the CG group than in the SG group.

Table 3 shows the outcomes of gastroschisis. We excluded four patients who died within 2 days of admission. The average length of stay differed between the SG and CG groups (45 vs. 91 days; $p<0.001$). Regarding enteral feeding, we excluded 20 patients because of missing data. Age (in days) at start of full enteral feeding differed significantly between the two groups (29 vs. 73 days; $p<0.001$). The total hospitalization cost of the SG group was 1.7 times higher than that of the CG group.

Table 4 shows patient discharge and readmission status. There was no significant difference in in-hospital mortality between the SG and CG groups. About 80% of all patients discharged to home did not require home medical care. Patients with home parenteral nutrition were observed only in the CG group ($n=4$). There were five patients with home oxygen therapy and nine with tube feeding at the time of discharge. No patient had a history of tracheostomy or home mechanical ventilation. Sixty patients (28%) were readmitted within 1 year of discharge, and 11 (5.1%) were readmitted because of intestinal obstruction.

Table 3 Outcomes of gastroschisis

	Simple gastroschisis ($n=218$)	Complex gastroschisis ($n=25$)	Total[a] ($n=243$)	p value
Length of stay (in days), median (IQR)	45 (35–70)	91 (71–185)	46 (37–78)	< 0.001
Length of ICU stay, n (%)				0.89
< 2 weeks	37 (17.0)	5 (20.0)	42 (17.3)	
2–4 weeks	83 (38.1)	10 (40.0)	93 (38.3)	
≥ 4 weeks	98 (45.0)	10 (40.0)	108 (44.4)	
Age at start of enteral feeding (in days), median (IQR)	9 (1–17)	13 (2–22)	9 (1–17)	0.35
Age at start of full enteral feeding (in days), median (IQR)[b]	29 (20–47)	73 (44–119)	30 (21–52)	< 0.001
Age at start of full enteral feeding ≥ 28 days, n (%)[b]	101 (51.0)	17 (89.5)	118 (54.4)	0.001
Length of mechanical ventilation (in days), median (IQR)	7 (4–13)	9 (4–12)	7 (4–13)	0.64
Total hospitalization costs (in United States dollars), median (IQR)	42,393 (34,090–56,368)	71,688 (49,152–117,490)	44,382 (34,814–61,306)	< 0.001

IQR interquartile range, *ICU* intensive care unit

[a]Four patients were excluded because of death within 2 days of admission

[b]Six patients were excluded because of discharge to home with parenteral nutrition

Table 4 Discharge and readmission status

	Simple gastroschisis ($n=222$)		Complex gastroschisis ($n=25$)		Total ($n=247$)		p value
	n	%	n	%	n	%	
Discharge status							0.05
Discharge to home without home medical care[a]	182	82.0	16	64.0	198	80.2	
Discharge to home with home medical care[a]	12	5.4	4	16.0	16	6.5	
Discharge to other facilities	12	5.4	1	4.0	13	5.3	
In-hospital death	16	7.2	4	16.0	20	8.1	
Readmission within 1 year of discharge[b]	48	24.7	12	60.0	60	28.0	0.003
Because of intestinal obstruction or ileus	9	4.6	2	10.0	11	5.1	0.27

[a]Home medical care includes tube feeding, home oxygen therapy, and home parenteral nutrition

[b]Three patients were excluded because of death or being discharged other than to home

Discussion

We examined 247 patients with gastroschisis using a national inpatient database in Japan. Overall, in-hospital mortality was 8.1%, and we found no significant differences in mortality between the SG and CG groups. Our study provides an overview of patient characteristics, practice patterns, and discharge status for patients with gastroschisis.

Most previous nationwide studies on gastroschisis were carried out in Western nations. There was a Japanese national questionnaire survey conducted from 1975 to 1997 [19], but it lacked detailed information about patient demographic characteristics and practice patterns.

Previous studies in Western countries found percentages of low birth weight births ranging from 52 to 59%, [9, 10, 20, 21], whereas this percentage was 78% in our study in Japan. This may be because the number of infants with low birth weight has been increasing since 1970 in Japan [22, 23]. The percentages of premature births ranged widely, from 46 to 65%, in previous studies [6, 8–10, 20]; this percentage was found to be 60% in the present study. Associated anomalies were reported to range from 7.9 to 36% in previous studies [8, 10, 20, 24, 25]; in this study, we found anomalies in 29% of the patients. Associated chromosomal abnormalities have previously been reported to be found in 0% to < 1% of cases [8, 10, 20, 24], whereas we found these abnormalities in 1.6% of the patients. In the present study, about 90% of the patients had SG. This

figure was similar to those reported in previous studies [6, 9, 18, 26].

LOS in this study was similar to the findings of previous studies [10, 20, 21, 27]. In line with previous studies, the present study showed that the CG group was associated with a higher risk of prolonged hospital stays, compared with the SG group [28, 29].

Intestinal function is considered the most important outcome for patients with gastroschisis. In previous studies, "intestinal failure" was defined as a status requiring parenteral nutrition for ≥ 28 days [6], and the reported percentages of intestinal failure were 41% in the SG group and 81% in the CG group. Similarly, our results showed the percentages of patients who started full enteral feeding ≥ 28 days after birth to be 51% in the SG group and 90% in the CG group.

One previous study reported that mortality was 2.2% among infants weighing ≥ 1500 g at ≥ 29 weeks of gestation [8]; this was found to be 4.7% in the present study. Another study reported that mortality was 2.3% in infants at ≥ 33 weeks gestation [7], whereas this was found to be 6.7% in the present study. Neonatal mortality was reported as 2% in another previous study [9], whereas neonatal mortality was 3.6% in our study. Thus, mortality appeared to be higher in the present Japanese study than in previous Western studies. However, neonatal mortality can be affected by the proportions of in utero deaths and spontaneous abortions. A difference may exist between Japan and other countries in the proportion of selective abortions following the prenatal diagnosis of anomalies, because late termination is allowed in Europe, for example, but not in Japan [30], and there may be differences in people's ways of thinking about fetal palliative care [31–33].

In 2001, a previous study reported that those with CG had higher mortality, longer LOS, and delayed start of enteral feeding, compared with those with SG [18]. Our study showed somewhat similar results, but we did not find a significant difference in mortality between the SG and CG groups. This may be explained by the low overall mortality in our study, which is possibly because of recent advances in neonatal intensive care.

Several limitations of this study should be acknowledged. First, because of data availability, we did not have information on outpatients. Second, we were unable to assess detailed surgical methods (e.g., primary or secondary closure, fascial or flap closure, silo or sutureless techniques). Third, we were unable to confirm the direct cause of death (e.g., gastroschisis, cardiac anomaly, chromosomal anomaly, complication). Finally, our data lacked information about the prenatal diagnosis of congenital anomalies, which may have influenced the choice of aggressive care, as has been suggested in previous studies [34, 35].

Conclusions

This large retrospective observational study using a national database in Japan suggested that there are no major differences in patient characteristics and outcomes between Japan and Western nations. Our findings provide useful information for clinicians and families of patients with gastroschisis.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Study approval was obtained from the Institutional Review Board at the University of Tokyo.

Informed consent The requirement for informed consent was waived for this study because of the anonymous nature of the data.

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