

Original Research Article

Surgical Management for Patients with Toxic Megacolon due to Ulcerative Colitis

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Abstract

Objectives: The present study reviewed cases of Toxic megacolon (TM) treated in our department, summarized the timing and technique of surgery, and considered key points for surgical management.

Methods: This single-center retrospective study included the medical records of patients clinically diagnosed with TM who underwent surgery between 1985 and 2020. The diagnostic criteria and screening scores for sepsis, such as the systemic inflammatory response syndrome (SIRS) criteria, quick Sequential Organ Failure Assessment (qSOFA) score, and Modified Early Warning Score (MEWS), were validated. The preoperative clinical features and perioperative findings were also investigated.

Results: There were eight male and six female patients. Nine patients (64.3%) satisfied the criteria for toxemia proposed by Narabayashi, and 10 patients (71.4%) fulfilled the SIRS criteria. A positive qSOFA score was confirmed in 1 patient (7.1%). The MEWS was high in 2 patients (14.3%). Intestinal perforation occurred in 2 patients (14.3%), and 1 of them died from disseminated intravascular coagulation. The mortality rate of TM with perforation was 50%. Eleven patients (78.6%) underwent total colectomy with end ileostomy.

Conclusions: TM does not have well-defined diagnostic criteria, in addition to developing sometimes as borderline or fulminant cases, and must be recognized at an early stage, taking various findings into consideration. The criteria proposed by Narabayashi and the SIRS criteria, which met in a high percentage of our cases, are recommended as indicators for determining the toxicity of TM. It is also important to consider surgery in the early stages of TM, even if clinical findings do not meet all the criteria.

Keywords

surgery, toxic megacolon, ulcerative colitis

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Introduction

Many patients with ulcerative colitis (UC) can avoid surgery, as medical therapy has improved, but in potentially fatal cases complicated with toxic megacolon (TM) and those with perforation, uncontrollable bleeding, cancer, or high-grade dysplasia, surgical intervention is required[1-4].

TM is diagnosed on the basis of findings from a number of examinations, such as vital signs, X-ray studies, blood

tests, and sigmoidoscopy, and there is no modality that alone clinches the diagnosis easily[5]. However, TM must be recognized at an initial stage and treated adequately because it has a risk of worsening rapidly. Early identification and intensive management may help reduce the incidence and mortality of TM in inflammatory bowel disease[6]. In the present study, we reviewed cases of TM treated in our department, summarized the timing and technique of surgery, and considered key points for surgical management of

TM.

Methods

This single-center retrospective study recruited the medical records of patients who were clinically diagnosed with TM (a condition in which colonic ileus is accompanied by sepsis) due to UC and underwent surgery for TM between July 1985 and March 2020 at our hospital. The study protocol was approved by the Ethics Advisory Committee of Fukuoka University Chikushi Hospital (No. C21-01-013) and conformed to the provisions of the Declaration of Helsinki. Consent for the use of data for this research was obtained on an optout basis (<https://www.chikushi.fukuoka-u.ac.jp/rinshou/patient/ushiromuki.html>).

We made a diagnosis of colonic ileus when a patient's abdominal X-ray findings in the supine position demonstrated dilatation, especially in the transverse colon[7]. A clinical diagnosis of "toxemia" was validated on the criteria reported by Jalan[8] and Narabayashi[9]. Jalan et al. reported that a patient was considered to be "toxic," when they showed any 3 of the 4 criteria in group A (pyrexia $>101.5^{\circ}\text{F}$ [38.6°C], tachycardia >120 beats/minute, leukocytosis $>105,000/\text{mm}^3$, and anemia $<60\%$ hemoglobin) together with any 1 of the 4 criteria in group B (dehydration, mental changes, electrolyte disturbance, hypotension). According to the description of Narabayashi, the criteria of the diagnosis for "systemic toxicity" included at least 2 of the following: pyrexia ($>38.6^{\circ}\text{C}$), tachycardia (>100 beats/minute), leukocytosis ($>10,500/\mu\text{L}$), or hypoalbuminemia (<3.0 g/dL).

We also checked which patients met the criteria for Systemic Inflammatory Response Syndrome (SIRS) and measured their quick Sequential Organ Failure Assessment (qSOFA) score and Modified Early Warning Score (MEWS). SIRS is a clinical response of the host to inflammation[10]. The qSOFA is a screening tool that can detect sepsis at an early stage in adult patients[11,12]. The MEWS is a simple bedside tool that can identify patients at risk of deterioration and in need of more active intervention[13]. SIRS is defined in cases with any 2 of the following: a body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, a heart rate >90 beats/minute, respiratory rate >20 breaths/minute, and white blood cell count $>12,000/\text{mm}^3$, $<4,000/\text{mm}^3$, or $>10\%$ immature neutrophils ("bands")[10]. Adult patients were considered more likely to have poor outcomes typical of sepsis if they had at least 2 of the following clinical criteria that together constitute the qSOFA score: a respiratory rate of ≥ 22 breaths/minute, altered consciousness, and a systolic blood pressure of ≤ 100 mmHg[12]. The MEWS was calculated based on a previously published table[13]. Each criterion is described in Table 1.

The clinical findings at the time of the TM diagnosis and perioperative characteristics were also investigated. Total

colectomy with the formation of end ileostomy is conducted as the standard surgical procedure for TM in our department. Numerical data are presented as medians (range) or numbers (percentages).

Results

There were 288 patients who were conducted surgery for UC at our hospital between 1985 and 2020. Fourteen patients clinically diagnosed with TM due to UC and underwent surgery were included in this study. None of patients diagnosed with TM were not treated surgically. Table 2 shows the patients' clinical characteristics and preoperative course. There were eight male and six female patients, and the median (range) age at the onset of TM was 39 (19-75) years old. The median duration from the diagnosis of UC to surgery for TM was 5 (1-239) months. All patients were confirmed to have dilatation of ≥ 6 cm in the transverse colon by plain abdominal X-ray in the supine position (Figure 1). The median time until surgery from the TM diagnosis was 3 (0-57) days. Emergency surgery was performed in 13 of 14 patients (92.9%). Glucocorticoid therapy was administered to all patients, and the median total prednisolone dose was 1,500 (120-30,000) mg. Four patients underwent cytapheresis.

Clinical findings at the TM diagnosis and perioperative characteristics are shown in Table 3, 4, respectively. The records regarding the patients' respiratory rate were often missing. If the respiratory rate was not explicitly described in the medical records, then we assigned no points for the screening scores for sepsis. At the time of the TM diagnosis, only 1 patient (7.1%) had met 3 of the 4 "toxic" criteria in group A that Jalan advocated. In contrast, 9 patients (64.3%) satisfied ≥ 2 of the "systemic toxicity" criteria presented by Narabayashi, and 10 patients (71.4%) met the SIRS criteria. A positive qSOFA score was confirmed in 1 patient (7.1%). The MEWS was high (score ≥ 5 points) in 2 patients (14.3%).

Intestinal perforation occurred in 2 patients (14.3%), with both cases occurring 6 days after the diagnosis of TM. One patient without perforation was able to avoid emergency surgery because the transanal tube successfully decompressed the distended colon. Eleven patients (78.6%) underwent total colectomy with the formation of end ileostomy, and 3 patients underwent total proctocolectomy, ileal pouch anal anastomosis, and diverting ileostomy. The median operative time and blood loss were 147.5 (90-216) minutes and 506 (61-1,900) ml, respectively. Postoperative complications occurred in 9 of 14 patients (64.3%), and 1 patient required unplanned surgical intervention for bleeding. Among all patients investigated, there was 1 death during the postoperative hospital stay, with a 30-day mortality rate of 7.1%. One of two patients with perforation died of disseminated in-

Table 1. The Diagnostic Criteria of Toxemia and Screening Scores for Sepsis.

Jalan criteria							
Any 3 of the 4 criteria in group A together with any 1 of the 4 criteria in group B.							
A)				B)			
Pyrexia (>101.5°F [38.6°C])				Dehydration			
Tachycardia (> 120 beats/minute)				Mental changes			
Leucocytosis (> 10,500/mm ³)				Electrolyte disturbance			
Anemia (< 60% hemoglobin)				Hypotension			
Narabayashi criteria							
At least 2 of the following:							
Pyrexia (> 38.6°C)							
Tachycardia (> 100 beats/minute)							
Leukocytosis (> 10,500/μL)							
Hypoalbuminemia (< 3.0 g/dL)							
SIRS							
At least 2 of the following:							
A body temperature >38°C or <36°C							
A heart rate >90 beats/minute							
Respiratory rate >20 breaths/minute							
White blood cell count >12,000/mm ³ , <4,000/mm ³ , or >10% immature bands							
qSOFA							
At least 2 of the following:							
A respiratory rate of ≥22 breaths/minute							
Altered consciousness							
A systolic blood pressure of ≤ 100 mmHg							
MEWS							
	3	2	1	0	1	2	3
Systolic blood pressure	<70	71-80	81-100	101-199		200≤	
Heart rate		<40	41-50	51-100	101-110	111-129	130≤
Respiratory rate		<9		9-14	15-20	21-29	30≤
Temperature		<35		35-38.4		38.5≤	
AVPU score				Alert	Reacting to Voice	Reacting to Pain	Unresponsive

Abbreviations: MEWS, Modified Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SIRS, Systemic Inflammatory Response Syndrome

Table 2. The Clinical Characteristics and Preoperative Course.

Clinical characteristics	
Sex (male/female)	8 (57.1%) /6 (42.9%)
The median age at the onset of TM	39 (19-75)
The median duration from the diagnosis of UC to surgery for TM, month	5 (1-239)
Preoperative course	
The median diameter of the transvers colon, cm	8.0 (6.0-14.0)
The median time until surgery from the TM diagnosis, day	3 (0-57)
Emergency surgery	13 (92.3%)
The median total PSL dose, mg	1,500 (120-30,000)
Introduction of cytopheresis	4 (28.6%)

Values are presented as medians (range) or numbers (percentages).

Abbreviations: PSL, prednisolone; TM, toxic megacolon; UC, ulcerative colitis

travascular coagulation (DIC) secondary to sepsis. The mortality rate of patients with TM and perforation was 50%.

The median post-operative hospital stay of patients managed successfully was 32 (17-60) days.

Discussion

In this single-center retrospective study, we reviewed cases of TM treated in our department, summarized the timing and technique of surgery, and considered key points for surgical management of TM.

TM is a severe and potentially lethal complication of UC as well as perforation, profuse bleeding, cancer, or high-grade dysplasia[1-4]. The pathophysiology of TM is thought



Figure 1. The abdominal X-ray finding in the supine position demonstrated dilatation in the transverse colon.

to be colonic ileus accompanied by sepsis[14,15], but Michael et al. stated that TM does not have well-defined limits[16].

Gan et al. reported that dilatation of ≥ 6 cm in the transverse colon on plain abdominal X-ray is suggestive of the diagnosis of megacolon[17], while Narabayashi described megacolon as ≥ 5 -6 cm of dilatation of the colon on X-ray[9]. In addition, the upper limit of the normal diameter of the transverse colon has been defined as 5.5 cm[14,18]. Given these facts, the characteristic colon diameter in cases of TM seems uncertain. In the present study, all patients showed dilatation of ≥ 6 cm in the transverse colon on plain abdominal radiography. We therefore also believe that TM is likely when the transverse colon shows dilation of ≥ 6.0 .

Several criteria concerning a toxic state have been proposed, as have those for megacolon, but toxicity is reportedly difficult to define[5]. We validated the criteria of toxicity advocated by Jalan[8] and Narabayashi[9] in our patients and also checked whether or not the patients showed positive screening scores for sepsis or a critical MEWS. Although the criteria of Jalan and Narabayashi and screening scores for sepsis or deterioration were considered as possible indicators to evaluate the “toxicity”, all indicators were not applicable to all the 14 cases of TM surgically treated in this study. The qSOFA showed higher overall prognostic accuracy than the SIRS criteria[19], and the MEWS also had higher specificity for predicting in-hospital mortality[20]. However, the SIRS criteria have high sensitivity for predicting systemic inflammation and are maintained as a screening tool for early care and the prevention of a missed diag-

Table 3. The Clinical Findings at the Time of the TM Diagnosis.

No.	Sex	Age	ϕ [cm]	BT [°C]	HR [bpm ¹]	sBP [mmHg]	RR (PaCO ₂) [bpm ² (mmHg)]	GCS	WBC [μ L]	Hb [g/dL]	Alb [g/dL]	Jalan criteria	Narabayashi criteria	qSOFA	MEWS	SIRS
1	M	25	14	36.8	90	134	No record	15	18,000	5.9	2.1	-	○	0	0	2
2	F	35	11	38.3	96	98	30	15	9,800	10.6	2.5	-		2	4	3
3	F	39	12	37.3	84	114	21	15	9,500	8.5	2.0	-		0	2	1
4	F	32	8.0	37.1	92	104	No record	15	9,900	12.2	3.0	-		0	0	1
5	F	30	6.0	39.0	106	98	18	15	8,800	8.7	2.4	-	○	1	5	2
6	M	19	8.0	36.7	139	120	No record	15	40,100	6.8	1.4	○	○	0	3	2
7	F	40	8.5	38.5	96	82	No record	15	3,200	8.1	2.4	-		1	3	3
8	M	44	11	37.0	92	97	10 (42.8)	15	6,200	8.3	1.7	-		1	1	1
9	M	33	6.5	36.6	95	140	No record	15	12,500	9.5	1.8	-	○	0	0	2
10	F	42	6.3	37.7	95	104	15	15	11,400	5.9	2.2	-	○	0	2	1
11	M	75	8.6	36.9	137	124	18 (30)	15	7,100	9.1	1.5	-	○	0	4	2
12	M	54	7.2	36.8	116	120	24 (34)	15	16,800	9.7	1.8	-	○	1	4	3
13	M	62	7.1	38.3	107	128	21 (34)	15	19,900	12.0	1.6	-	○	0	3	4
14	M	39	6.0	39.8	111	111	16	15	4,500	7.7	1.3	-	○	0	5	2

Abbreviations: Alb, albumin; BT, Body temperature; bpm¹, beats per minute; bpm², breaths per minute; GCS, Glasgow Coma Scale; Hb, hemoglobin; HR, heart rate; MEWS, Modified Early Warning Score; PaCO₂, partial pressure of carbon dioxide; qSOFA, quick Sequential Organ Failure Assessment; RR, respiratory rate; sBP, systolic blood pressure; SIRS, Systemic Inflammatory Response Syndrome; WBC, white blood cell

Symbols: ϕ , diameter of the transvers colon; ○, met the criteria.

Table 4. The Perioperative Characteristics.

No.	Perforation	Operative procedure	Operative time [minute]	Blood loss [mL]	Post-operative Complication	Outcome	Post-operative Hospital stay [day]
1		TC + ileostomy	216	450	SSI	Survival	35
2		TC + ileostomy	90	750	Ileus	Survival	60
3		TC + ileostomy	170	315	SSI	Survival	42
4		TC + ileostomy	170	443	None	Survival	32
5		TC + ileostomy	110	61	None	Survival	23
6	○	TC + ileostomy	150	1,650	DIC	Death	-
7		TPC + IPAA	137	330	None	Survival	18
8		TC + ileostomy	145	527	Bleeding	Survival	31
9		TC + ileostomy	128	370	SSI	Survival	38
10		TPC + IPAA	185	520	SSI	Survival	21
11		TC + ileostomy	150	720	Cholecystitis	Survival	39
12		TPC + IPAA	145	1,000	None	Survival	47
13	○	TC + ileostomy	190	1,900	DIC	Survival	21
14		TC + ileostomy	145	492	None	Survival	17

Abbreviations: DIC, disseminated intravascular coagulation; IPAA, ileal pouch anal anastomosis; SSI, surgical site infection; TC, total colectomy; TPC, total proctocolectomy

nosis[19-21]. It seems preferable that a screening tool with a high sensitivity be used to identify TM in order to avoid losing the opportunity to perform properly indicated surgical intervention. The criteria proposed by Narabayashi and the SIRS criteria may be recommended to be used to determine “toxicity”, because these criteria were met in a high percentage of our cases.

Typical abdominal symptoms may not present in TM patients complicated with UC, due to the masking effect of steroid therapy[6]. Indeed, 3 of 14 patients (21.4%) in the present study did not satisfy any toxic criteria or show expected screening scores for sepsis. If immunosuppressed patients suffer from bacteremia due to bacterial translocation, their hemodynamic and respiratory status will rapidly become compromised. In borderline cases, it may become necessary to perform assessments repeatedly and entirely rely on clinical judgment without fixating on criteria for the diagnosis of TM[5].

Surgical intervention is indicated if initial conservative management, such as correction of fluids, hydroelectrolytic disorders, anemia, broad-spectrum antibiotics, endovenous corticosteroids, and intubation with an intestinal tube, fails to improve clinical findings within 24-72 h after the onset. Protracted medical management may lead to perforation, and it has been reported that the incidence of perforation in TM is 24%[16]. It has been reported that the mortality rate of TM patients is <10% if surgery is performed without perforation, but it increases to 40%-50% in cases of perforation[22-24]. Similar to the literature findings, our patients with both TM and intestinal perforation had a poor prognosis. Surgery should always be considered, and patients should be informed early that surgical intervention is necessary if clinical findings are refractory to medical manage-

ment[25].

Relatively simple surgical procedures are preferred in emergency cases of TM, as the patient’s general condition is unstable[14,16]. There is also a high risk of peritoneal contamination during surgery, as handling of the massively distended bowel is difficult[26], as was noted on the intraoperative view of a patient in the present study (Figure 2). However, diverting stoma formation alone is reportedly an inadequate procedure in such cases[16]. Given the previous findings, total colectomy with terminal ileostomy seems to be the preferred operative procedure in emergency cases[14,16,25].

Several limitations associated with the present study warrant mention. First, this was a single-center retrospective study with a relatively small number of patients compared with other review articles. In addition, there were many missing values regarding the respiratory rate. We must accept that examinations of toxicity, especially the SIRS criteria, qSOFA, and MEWS, can be inaccurate. However, even if the patients with missing data in our study had a manifested respiratory rate that satisfied the qSOFA criteria or a high MEWS, the SIRS criteria would still have been met in most patients in this study.

There are a few reports of TM secondary to inflammatory bowel disease being successfully treated with non-surgical management, but those might have been rare cases in a limited situation[9,27-29]. The mortality rate increases remarkably if intestinal perforation complicates TM. Our results support the idea that surgical intervention should always be considered from the initial stage.

In conclusion, it is important to consider surgery in the early stages of toxic megacolon, even if symptoms and clinical findings do not meet all the criteria.

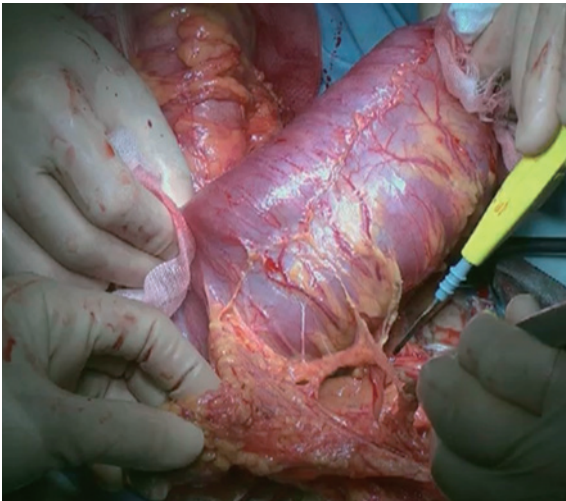


Figure 2.

There is a high risk of peritoneal contamination, as handling of the massively distended bowel is difficult.

Conflicts of Interest

There are no conflicts of interest.

Author Contributions

TW performed the data acquisition, analysis, and interpretation; drafted and revised the manuscript; and accepted responsibility for the conduct of research, final approval, and study supervision. DH contributed to study conception and design, revised the manuscript, and accepted responsibility for the conduct of research, final approval, and study supervision. HK performed data acquisition and interpretation and revised the manuscript. HI, KH, JY, TM, YH and HN interpreted and revised the manuscript. MW interpreted the data and provided critical advice for drafting the manuscript. All authors have read and approved the final manuscript.

Approval by Institutional Review Board (IRB)

This study was approved by the Fukuoka University Chikushi Hospital Ethics Committee (IRB number: C21-01-013).

Availability of Data and Materials

The datasets for the current study are available from the corresponding author upon reasonable request.

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