Effect of early enteral nutrition on the incidence of acute acalculous cholecystitis among trauma patients

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ABSTRACT

Background and Objectives: Acute acalculous cholecystitis (AAC) often occurs in critically ill patients, especially in those that have experienced trauma, surgery, shock, and prolonged fasting. Early enteral nutrition has been shown to significantly reduce morbidity and mortality compared to other nutritional support strategies. The purpose of this study was to evaluate the effect of early enteral nutrition on the incidence of AAC among trauma patients. **Methods and Study Design:** Multi-strategy nutritional protocol was implemented in the intensive care unit (ICU) in 2016 for early enteral nutrition and proper nutritional support. The traumatized critically-ill patients without volitional intake who were admitted to ICU between 2015 and 2017 were included. Basic characteristics, duration of fasting, and the incidence of percutaneous cholecystostomy (PC) due to AAC were analyzed according to the year. **Results:** Enteral nutrition was indicated in 552 trauma patients (28.2%). The mean duration of fasting was shortened from 6.5 days in 2015 to 5.4 days in 2017 (p=0.202). The incidence of PC was significantly decreased from 2015 to 2017 [6/171 (3.5%) vs. 6/204 (2.9%) vs. 0/177 (0%), p=0.023]. The provision of central parenteral nutrition (p=0.001) and fasting over 7 days (p=0.014) proved to be a risk factor of AAC. **Conclusions:** This study showed that the incidence of PC due to AAC was decreased significantly after the implementation of a nutritional protocol among traumatized critically ill patients. Early enteral nutrition may be effective in reducing the AAC among trauma patients who are at high risk of AAC.

Key Words: enteral nutrition, trauma, acute acalculous cholecystitis, effect, critically ill

INTRODUCTION

Acute acalculous cholecystitis (AAC) is defined as an acute inflammatory disease of the gallbladder without gallstones. It is traditionally known to occur in critically ill patients.[1,2] The reported rate of AAC is commonly about 0.2–1.0% of all critically ill patients.[3] The pathophysiology of AAC is known to be multifactorial, likely resulting from bile stasis and gallbladder ischemia.[3,4] The commonly associated risk factors of AAC are trauma, recent surgery, shock, burn, sepsis, total parenteral nutrition, prolonged fasting, transfusion, and opioid therapy.[1,5] The clinical course of AAC tends to be more fulminant compared to acute calculous cholecystitis with a high mortality from 10% up to 90%.[1,3,6-8]

Early enteral nutrition has gained sufficient evidence of superiority over other methods of nutritional support. The beneficial effects of enteral nutrition compared to parenteral nutrition on morbidity and mortality are well documented in numerous randomized clinical trials involving a variety of patient populations in critical illness.[9-11] Early provision of enteral nutrition was associated with a significant reduction in morbidity, mortality, and length of hospital stay compared to delayed enteral nutrition in updated meta-analyses.[12-14] Initiating enteral nutrition within 24–48 hours is commonly recommended by current guidelines from various societies worldwide.[9,15,16]

In the aspect of AAC, early provision of enteral nutrition may reduce or prevent critically ill patients from known risk factors of AAC such as prolonged fasting and provision of total parenteral nutrition. The multi-strategy nutritional protocol was developed and implemented in the trauma intensive care unit (ICU) of Dankook University Hospital based on the current guidelines. The protocol aimed to promote early enteral nutrition and to provide proper nutritional support. The purpose of this study was to evaluate the effect of early enteral nutrition on the incidence of AAC among trauma patients.

MATERIALS AND METHODS

Nutrition protocol

The study was approved by the Institutional Review Board (DKUH 2018-09-015). The nutritional protocol was designed for critically ill patients who were admitted to the ICU (Fig. 1). Patients without volitional intake were assessed for suitability for enteral nutrition. Enteral feeding was initiated with a continuous infusion method at a rate of 20 mL per hour among patients who were hemodynamically stable after resuscitation. The rate of infusion was gradually increased every 8 hours according to the protocol to reach the target calorie within a week after admission. The daily reassessment was done to those who were regarded as inappropriate for enteral nutrition at the initial assessment to start enteral nutrition at the earliest date.

Diagnosis and management of acute cholecystitis

Acute cholecystitis was defined and graded according to the Tokyo guidelines 2018.17-19 Ultrasonography and abdominal CT were used as diagnostic tools. Indications for PC insertion included a failure to respond to initial medical treatment. Since patients were in conditions such as multiple trauma requiring intensive care, shock, or high operative risk, PC was chosen as a treatment modality over emergent cholecystectomy.

In all patients, PC was performed by interventional radiologists under ultrasonographic and fluoroscopic guidance. The catheter was usually indwelled for approximately 3 weeks for achieving maturation of the tract and removed when patients showed resolution of clinical symptoms, fever, leukocytosis, and a patent cystic duct on tubograms. Interval cholecystectomy was performed in those who did not meet these criteria.

Data collection

Since the nutritional protocol was implemented in 2016 in the trauma ICU, patients from January 2015 to December 2017 were included in the present retrospective study. Traumatized, critically-ill patients who were admitted to trauma ICU were reviewed and those fed orally as their first meal were excluded from candidates for enteral nutrition. Among the candidates of enteral nutrition, parameters regarding basic characteristics: trauma-related information, duration of fasting, and incidence of percutaneous cholecystostomy due to AAC were collected. The incidences of percutaneous cholecystostomy catheter insertion before (2015), during (2016), and after (2017) the implementation of nutritional protocol was compared. The risk factor of AAC was also analyzed.

Statistical analysis

Continuous variables were compared by paired t-tests and categorical variables by Chi-square tests. One-way analysis of variance was used to evaluate the difference of outcomes according to the year. Risk factors for AAC were analyzed by multiple logistic regression analysis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. p values < 0.05 were considered statistically significant. All statistical analyses were performed using PASW Statistics 19 (IBM Corp., Somers, NY, USA).

RESULTS

Patient characteristics

A total of 1957 patients were admitted to trauma ICU from 2015 to 2017. Enteral nutrition was indicated in 552 patients (28.2%). The mean age of the candidates of enteral nutrition was 60.2 years and male consisted of 78.3%. Injury severity score over 15 consisted of 77.9% and head injury was observed in 77.5%. Enteral feeding was delivered in 61.6% of the candidates with a mean duration of fasting of 5.8 days (Table 1). The patients who were not able to proceed with enteral nutrition were mortality cases (n=212).

Outcomes

Basic characteristics and trauma-related parameters were not different according to the year among candidates of enteral nutrition (Table 2). Mean duration of fasting was shortened from

6.5 days to 5.4 days, however, there was no statistical significance (p=0.202). There was no difference in the ratio of delivered enteral nutrition (p=0.508), parenteral nutrition (p=0.650), and the time to initiate central parenteral nutrition (p=0.631). Incidence of PC catheter insertion was significantly decreased from 2015 to 2017 [6/171 (3.5%) vs 6/204 (2.9%) vs 0/177 (0%), p=0.023] (Table 3). Regarding overall trauma ICU patients (n=1957), incidence of PC catheter insertion also significantly decreased from 2015 to 2017 [8/589 (1.3%) vs. 6/684 (0.8%) vs 0/684 (0%), p=0.003].

AAC was significantly associated with provision of central parenteral nutrition (58.3% vs. 16.3%, p=0.001) and fasting over 7 days (41.7% vs. 75.4%, p=0.014). In multivariate analysis, provision of central parenteral nutrition was the only risk factor of AAC (OR=5.299, p=0.008) (Table 4).

Patients managed with percutaneous cholecystostomy

Among 12 patients who were managed with percutaneous cholecystostomy, two patients underwent interval cholecystectomy. Six patients removed PC catheter without catheter-related complication or recurrence of AAC. Four patients kept PC catheter until they were transferred to the community hospital or expired. Overall, 5 patients died from various causes other than AAC (Table 5).

DISCUSSION

Among risk factors of AAC, trauma is well known to be associated with AAC according to previous studies[1,5,20,21] and several case series of AAC after trauma have been reported.[5,22-26] The overall incidence of PC catheter insertion in this study (1.0% in 2015 and 0.8% in 2016, respectively) was comparable to the previous reports.[3]

Early diagnosis enables prompt intervention to prevent inflammation of the gallbladder thus providing more chances for early resolution of AAC and favorable outcome. However, traumatized critically ill patients are frequently sedated, intubated, and has an injury of the central nervous system which makes diagnosis challenging. Diagnosis may be often postponed until a patient shows a significant clinical deterioration. There have been several efforts for early diagnosis of AAC after trauma.[5,27] Ultrasonography may provide helpful information,[5] however, routine surveillance has insufficient evidence for its low sensitivity.[27] Severity grading of AAC can also be ambiguous since patients are frequently in shock or organ dysfunction before the development of AAC as in the present study.

Among several treatment options for AAC, urgent/early laparoscopic cholecystectomy is recommended as the first-line treatment in patients with good performance status.[18,19] In critically ill patients, PC is considered as a definitive treatment for AAC without subsequent cholecystectomy, based on the evidence of PC being safe, rapid, and highly efficacious in treating AAC.[2,28-30] According to these guidelines and pieces of evidence, PC was chosen over emergent cholecystectomy in patients of this cohort.

The risk factors of AAC in this study, fasting over 7 days and provision of central parenteral nutrition, were in accordance with previous reports. With huge efforts to implement the nutritional protocol, the duration of fasting was reduced more than one day and the number of patients who needed PC catheter insertion due to AAC was markedly reduced in the current study. This implicates early enteral nutrition might be effective in reducing AAC among trauma patients and protocolized nutritional support which is recommended by the guidelines might be helpful in the prevention or modifying risk factors of AAC.

However, a decrease in the duration of fasting was not statistically significant in the present study. Since all accessible basic parameters of the patients, the ratio of delivered enteral nutrition, parenteral nutrition, and the time to initiate central parenteral nutrition were not different according to year, it can be inferred that decrease in the duration of fasting after the implementation of a nutritional protocol may have influenced the incidence of AAC. Prospective design is needed for more solid evidence on the effect of early enteral nutrition over AAC.

In conclusion, this study showed that the incidence of PC due to AAC was decreased significantly after the implementation of nutritional protocol among traumatized critically ill patients. Early enteral nutrition may be effective in reducing AAC among trauma patients who are at high risk of AAC.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

All the authors had full access to the data and participated in the conceptualization, design, and drafting of this manuscript. The authors report no conflict of interest. The funding body was not involved in study design, data collection, analysis and writing of the study.

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REFERENCES

1. Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. Clin Gastroenterol Hepatol. 2010;8:15-22. doi: 10.1016/j.cgh.2009.08.034
2. Treinen C, Lomelin D, Krause C, Goede M, Oleynikov D. Acute acalculous cholecystitis in the critically ill: risk factors and surgical strategies. Langenbeck's Arch Surg. 2015;400:421-7. doi: 10.1007/s00423-014-1267-6
3. Barie PS, Eachempati SR. Acute acalculous cholecystitis. Gastroenterol Clin North Am. 2010;39:343-57. doi: 10.1016/j.gtc.2010.02.012
4. Orlando R 3rd, Gleason E, Drezner AD. Acute acalculous cholecystitis in the critically ill patient. Am J Surg. 1983;145:472-6.
5. Pelinka LE, Schmidhammer R, Hamid L, Mauritz W, Redl H. Acute acalculous cholecystitis after trauma: a prospective study. J Trauma Inj Infect Crit Care. 2003;55:323-9.
6. Kalliafas S, Ziegler DW, Flancbaum L, Choban PS. Acute acalculous cholecystitis: Incidence, risk factors, diagnosis, and outcome. Am Surg. 1998;64:471-5.
7. Yasuda H, Takada T, Kawarada Y, Nimura Y, Hirata K, Kimura Y et al. Unusual cases of acute cholecystitis and cholangitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg. 2007;14:98-113.
8. Laurila J, Laurila PA, Saarnio J, Koivukangas V, Syrjala H, Ala-Kokko TI. Organ system dysfunction following open cholecystectomy for acute acalculous cholecystitis in critically ill patients. Acta Anaesthesiol Scand. 2006;50:173-9.
9. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient. J Parenter Enter Nutr. 2016;40:159-211. doi: 10.1177/0148607115621863
10. Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. Crit Care Med. 2005;33:213-20.
11. Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Med. 2005;31:12-23.
12. Heyland D, Dhaliwal R, Drover J, Gramlich L, Dodek P. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. J Parenter Enter Nutr. 2003;27:355-73. doi: 10.1177/0148607103027005355
13. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: A systematic review. Crit Care Med. 2001;29:2264-70.
14. Doig GS, Heighes PT, Simpson F, Sweetman EA, Davies AR. Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. Intensive Care Med. 2009;35:2018-27. doi: 10.1007/s00134-009-1664-4
15. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019;38:48-79. doi: 10.1016/j.clnu.2018.08.037
16. Dhaliwal R, Cahill N, Lemieux M, Heyland DK. The Canadian Critical Care Nutrition Guidelines in 2013. Nutr Clin Pract. 2014;29:29-43. doi: 10.1177/0884533613510948

17. Kiriyama S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci. 2018;25:17-30. doi: 10.1002/jhbp.512
18. Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25:55-72. doi: 10.1002/jhbp.516
19. Mayumi T, Okamoto K, Takada T, Strasberg SM, Solomkin JS, Schlossberg D et al. Tokyo Guidelines 2018: management bundles for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25:96-100. doi: 10.1002/jhbp.519
20. Romero Ganuza FJ, La Banda G, Montalvo R, Mazaira J. Acute acalculous cholecystitis in patients with acute traumatic spinal cord injury. Spinal Cord. 1997;35:124-8.
21. Winegarner FG JG. Posttraumatic acalculous cholecystitis: a highly lethal complication. J Trauma Inj Infect Crit Care. 1971;11:567-9.
22. Ahmed N. Acute acalculous cholecystitis complicating major trauma: a report of five cases. South Med J. 2008;101:1146-9.
23. Herlin P, Ericsson M, Holmin T, Jonsson PE. Acute acalculous cholecystitis following trauma. Br J Surg. 1982;69:475-6.
24. Kaplan MD, Darazs B. Acute acalculous cholecystitis in the critically injured patient--the early sonographic diagnosis. Injury. 1994;25:267-8.
25. Cornwell EE, Rodriguez A, Mirvis SE, Shorr RM, Shorr RM. Acute acalculous cholecystitis in critically injured patients. Preoperative diagnostic imaging. Ann Surg. 1989;210:52-5.
26. Raunest J, Imhof M, Rauen U, Ohmann C, Thon KP, Burrig KF. Acute cholecystitis: a complication in severely injured intensive care patients. J Trauma. 1992;32:433-40.
27. Puc MM, Tran HS, Wry PW, Ross SE. Ultrasound is not a useful screening tool for acute acalculous cholecystitis in critically ill trauma patients. Am Surg. 2002;68:65-9.
28. Chang YR, Ahn Y-J, Jang J-Y, Kang MJ, Kwon W, Jung WH, Kim SW. Percutaneous cholecystostomy for acute cholecystitis in patients with high comorbidity and re-evaluation of treatment efficacy. Surgery. 2014;155:615-22. doi: 10.1016/j.surg.2013.12.026.
29. Winbladh A, Gullstrand P, Svanvik J, Sandström P. Systematic review of cholecystostomy as a treatment option in acute cholecystitis. HPB. 2009;11:183-93. doi: 10.1111/j.1477-2574.2009.00052.x.
30. Kuster GGR, Domagk D. Laparoscopic cholecystostomy with delayed cholecystectomy as an alternative to conversion to open procedure. Surg Endosc. 1996;10:426-8.

Table 1. Demographics of the candidates for enteral nutrition

Parameter	n=552
Age (years), mean±SD	60.5±18.8
Sex (male)	432 (78.3%)
Injury Severity Score (ISS), mean±SD	24.0±12.0
ISS ≥15	430 (77.9%)
ISS ≥25	313 (56.7%)
Injured sites	
Head	428 (77.5%)
Chest	227 (41.1%)
Abdomen	163 (29.5%)
Pelvis and extremities	227 (41.1%)
Enteral nutrition delivered	340 (61.6%)
Duration of fasting (days), mean±SD	5.8±4.0
Length of ICU stay (days), mean±SD	14.0±20.1
Length of hospital stay (days), mean±SD	33.1±43.0

SD: standard deviation.

Table 2. Basic characteristics of the candidates for enteral nutrition according to year

Parameter	2015 (n=171)	2016 (n=204)	2017 (n=177)	*p*-value
Age (years), mean±SD	59.5±19.2	61.8±18.7	60.1±18.8	0.541
Sex (male)	135 (78.9%)	155 (76.0%)	142 (80.2%)	0.585
ISS, mean±SD	24.4±13.7	23.6±11.6	24.3±10.8	0.340
ISS ≥25	100 (58.5%)	111 (54.4%)	102 (58.0%)	0.682
GCS score, mean±SD	9.7±4.4	9.5±4.5	9.5±4.9	0.928
Triage-RTS, mean±SD	9.8±2.4	9.6±2.8	9.9±2.5	0.546
TRISS, mean±SD	1.72±1.1	1.81±1.0	1.84 ±1.0	0.607
Initial pH	7.34±0.1	7.34±0.2	7.34±0.1	0.966
Transfused units of pRBC during the initial 24 hours	9.5±15.0	8.8±15.1	7.1±12.9	0.274

GCS: Glasgow Coma Scale; ISS: injury severity score; pRBC: packed red blood cells; RTS: Revised Trauma Score; SD: standard deviation; TRISS: Trauma Score–Injury Severity Score.

Table 3. Outcomes according to year

Parameter	2015 (n=171)	2016 (n=204)	2017 (n=177)	*p*-value
Duration of fasting (days), mean±SD	6.5±6.3	5.6±5.5	5.4±5.4	0.202
Enteral nutrition delivered	103 (60.2%)	132 (64.7%)	105 (59.3%)	0.508
Provision of central PN	54 (9.2%)	53 (7.7%)	56 (8.2%)	0.650
Time to initiate central PN (days), mean±SD	10.8±15.6	10.7±26.5	10.4±16.5	0.631
Percutaneous cholecystostomy due to AAC	6 (3.5%)	6 (2.9%)	0 (0%)	0.023
Length of ICU stay (days), mean±SD	13.5±15.7	14.5±24.6	13.9±18.2	0.753
Length of hospital stay (days), mean±SD (median)	30.1±38.4 (17.0)	40.5±51.0 (22.5)	27.7±35.5 (14.0)	0.001

AAC: acute acalculous cholecystitis; ICU: intensive care unit; SD: standard deviation; PN: parenteral nutrition.

Table 4. Risk factor analysis of acute acalculous cholecystitis

Parameter	PC due to AAC (n=12)	No AAC (n=540)	Univariate	Multivariate	
			p-value	OR (95% CI)	*p*-value
Age (years), mean ± SD	64.2±17.3	60.5±18.8	0.500		
ISS, mean ± SD	28.5±9.0	24.0±12.1	0.197		
Abdominal injury	5 (41.7%)	158 (29.3%)	0.350		
Central PN	7 (58.3%)	88 (16.3%)	0.001	5.299 (1.547-18.148)	0.008
Peripheral PN	10 (83.3%)	350 (64.8%)	0.232		
Fasting > 7 days	6 (50.0%)	132 (24.5%)	0.014	2.708 (0.790-9.285)	0.113

AAC: acute acalculous cholecystitis; CI: confidence interval; ISS: injury severity score; OR: odds ratio; SD: standard deviation; PC: percutaneous cholecystostomy; PN: parenteral nutrition.

Table 5. Details of the patients managed with percutaneous cholecystostomy

Age/sex	ISS	Injured site	Onset of AAC after injury (days)	AAC severity grade*	Final management	Status
78/F	14	C, P, E	12	2	Cholecystectomy	Alive
63/M	26	H, C	17	2	Cholecystectomy	Alive
84/M	26	H	12	3	PC removal → no recurrence	Alive
71/M	35	H	14	2	PC removal → no recurrence	Alive
66/M	29	C, A, P,	20	3	PC removal → no recurrence	Alive
19/F	45	H, Fa, C, E	22	2	PC removal → no recurrence	Alive
74/F	29	H, A, P	108	2	PC removal → no recurrence	Died because of ARDS
51/M	19	C, A, E	34	2	PC removal → no recurrence	Died because of sepsis
57/M	33	H, Fa, A, E	9	2	PC in situ	Alive, transfer
64/M	20	C, A	10	3	PC in situ	Died because of leak
62/M	25	H	8	3	PC in situ	Died because of ARDS
81/M	41	H, Fa, C, A, E	10	2	PC in situ	Died because of fungemia

A: abdomen; AAC: acute acalculous cholecystitis; ARDS: acute respiratory distress syndrome; C: chest; E: extremities; F: female; Fa: face; H: head; ISS: injury severity score; M: male; P: pelvis; PC: percutaneous cholecystostomy.
*Severity was graded according to the Tokyo Guideline 2018 (TG 18).

DKUH Nutrition Protocol

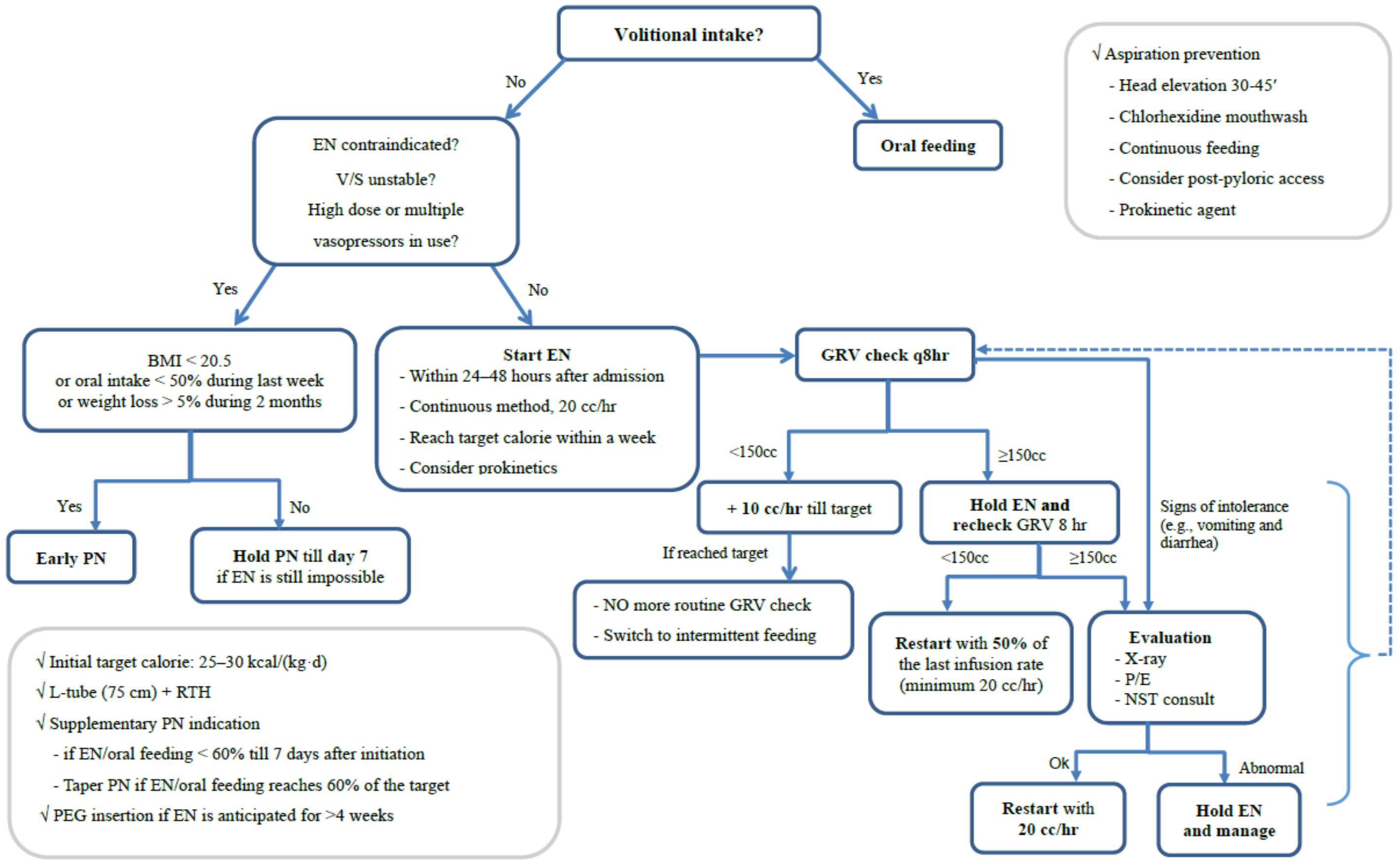

Figure 1. Nutritional protocol of Dankook Univeristy Hospital. BMI: body mass index; EN: enteral nutrition; GRV: gastric residual volume; NST: nutrition support team; P/E: physical examination; PEG: percutaneous endoscopic gastrostomy; PN: parenteral nutrition; RTH: ready to hang.