

Effect of Defecation Delay in Patients After Tricuspid Valve Replacement: A Retrospective Study

Chen Qian,^{1,2} Li Ning,^{1,3} Qin Ming,^{1,2} Xu Xiangyang,¹ Zhong Keng,¹ Lu Fanglin,¹
Li Bailing,¹ Han Lin,¹ Xu Zhiyun¹

¹Department of Cardiovascular Surgery of Changhai Hospital Affiliated to Naval Military Medical University, Shanghai, China;

²College of Basic Medical Sciences, PLA Naval Medical University, Shanghai, China;

³Department of Cardiothoracic Surgery of PLA Naval Medical Center, Shanghai, China

ABSTRACT

Background: Defecation delay is a common symptom in patients after tricuspid valve replacement (TVR). Previous studies have demonstrated that defecation delay was associated with worse clinical outcomes of critically ill patients. Our study aimed to investigate the incidence and risk factors of defecation delay in patients after TVR and its adverse clinical outcomes.

Methods: A retrospective study was conducted in 206 patients undergoing TVR under cardiopulmonary bypass from May 2005 to July 2021. According to the first postoperative defecation time after surgery, patients were divided into the delayed group (>3 days) and control group (\leq 3 days). Baseline characteristics and preoperative, intraoperative, and postoperative data were collected to investigate the clinical outcomes of defecation delay.

Results: Among the 206 patients, 51.9% (107/206) cases were classified into the defecation delay group. Univariate analysis showed that age ($P = 0.043$), preoperative platelets (PLT) ($P < 0.001$), cardiopulmonary bypass (CPB) time ($P = 0.013$), minimum rectal temperature ($P = 0.042$), and the use of prokinetic drugs ($P = 0.015$) were significantly different in the two groups. In addition, the perioperative adverse events in the defecation delay group were significantly higher than that of the control group. Logistic regression analysis indicated that the mortality of patients was associated with postoperative renal dysfunction ($P = 0.047$) and postoperative respiratory failure ($P = 0.004$) but was not associated with defecation delay ($P > 0.05$).

Conclusion: Patients with defecation delay after TVR were more likely to appear adverse events, however, defecation delay was not associated with mortality after TVR.

INTRODUCTION

Tricuspid regurgitation (TR) is a common cardiovascular disease with structural anomaly of tricuspid valve or tricuspid annulus, usually due to primary dysfunction or secondary dysfunction, such as pulmonary hypertension, atrial fibrillation, or left heart valve disease [Antunes 2017]. Recent data reported that the morbidity of TR is as high as 0.55% in the community, with a higher incidence in the elderly population [Topilsky 2019]. Surgery under cardiopulmonary bypass is considered for severe TR or progressive TR with either signs/symptoms of right-sided heart failure or tricuspid annular dilation, or the presence of vegetation [Correction 2021]. Clinical epidemiological data suggested that the mortality rate of patients after tricuspid valve replacement (TVR) is as high as about 10% during hospitalization, and the follow-up period is accompanied by high mortality and readmission rate [Dreyfus 2020; Zack 2017]. Patients with severe TR often are accompanied with severe right ventricular dysfunction, which could increase systemic venous pressure [Pahwa 2021], leading to gastrointestinal congestion, increased intestinal wall thickness and liver enzymes, and ultimately result in gastrointestinal-related clinical symptoms and cardiac cachexia [Valentova 2016; Raja 2004]. Prolonged postoperative mechanical ventilation, intensive care unit (ICU) stays, and hospital stays are more likely to occur in patients with early gastrointestinal dysfunction after cardiac surgery [Seilitz 2021].

Gastrointestinal peristalsis weakness is a common postoperative symptom, and its pathological mechanism is mainly associated with surgical and drug factors [Diebakate-Scordamaglia 2022]. Delayed gastric emptying and intestinal transit are the main causes of defecation delay, which may result in multiple health problems and low quality of life [Belsey 2010]. A large number of patients undergoing thoracic surgery were reported to be with defecation delay, and this symptom may persist even after hospital discharge [Rasmussen 2010]. Defecation delay may also prolong the length of mechanical ventilation, ICU stays, and increase the probability of acquired bacterial infection [Launey 2021; Gacouin 2010]. Of note, delayed defecation for more than 3 days is one common symptom of early postoperative mechanical ileus [Vather 2013], which manifests as an abnormal pattern of gastrointestinal motility [Stewart 2007]. However, it is difficult to recognize exact gastrointestinal complications as patients may be given

Received November 9, 2022; accepted December 6, 2022.

Correspondence: Xu Zhiyun and Han Lin, Department of Cardiovascular Surgery of Changhai Hospital Affiliated to Naval Military Medical University, Shanghai, 200433, China (e-mails: xuzhiyunsh@163.com, dr_hanlin@163.com).

analgesics or vasopressors, thereby the vital signs and symptoms of gastrointestinal conditions were concealed.

Defecation delay in the perioperative period is not yet clearly defined and hasn't received sufficient attention, and there is no relevant literature report on gastrointestinal symptoms and treatment after cardiovascular surgery. Therefore, it's one worthy of in-depth study on whether defecation delay is a potential mechanism resulting in adverse events of TVR in the perioperative period, as patients with severe TR are more likely to develop symptoms of gastrointestinal dysfunction due to right heart dysfunction. In our study, we retrospectively analyzed clinical data of TR patients undergoing TVR to identify adverse outcomes and risk factors of defecation delay after TVR.

METHODS

Subject enrollment: A retrospective analysis of 206 patients undergoing TVR under cardiopulmonary bypass (CPB) from May 2005 to July 2021 was conducted in Cardiovascular Surgery, Changhai Hospital, China. This study was approved by the Ethics Committee of Shanghai Hospital affiliated to Naval Medical University. Inclusion criteria: (I) Patients clinically diagnosed as TR and who met the criteria for surgery; and (II) Patients received TVR under CPB.

Data collection: The baseline characteristics, preoperative examination and test, defecation situation, and treatment were obtained from the patients' medical records. Postoperative respiratory failure was defined as the length of mechanical ventilation exceeding 72 hours or reintubation, according to a previous study on patients who received cardiothoracic surgery [Ivanov 2016]. Patients with the first postoperative defecation time exceeding 3 days (3 days not included) were classified into the delayed group, while other patients were classified into the control group, according to a similar study on thoracic surgery [Li 2021].

Statistics: All data were statistically analyzed by IBM SPSS Statistics 21. For univariate analysis, a normality test first was conducted. An independent sample t-test was performed and data were reported as mean ± standard deviation, if the data obeyed normal distribution or a rank sum test was performed and data were reported as median [first quartile, third quartile]. Categorical variables were analyzed with the chi-square test and reported as quantity (percentage). To analyze risk factors for death, a bivariate logistics regression analysis was performed based on the results of univariate analysis and professional knowledge. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics, preoperative data of TR patients: A total of 107 patients whose postoperative defecation time exceeded 3 days were classified into the delayed group. The other 99 patients with postoperative defecation time less than or equal to 3 days were classified into the control group. (Figure 1) The mean age of the delayed group was

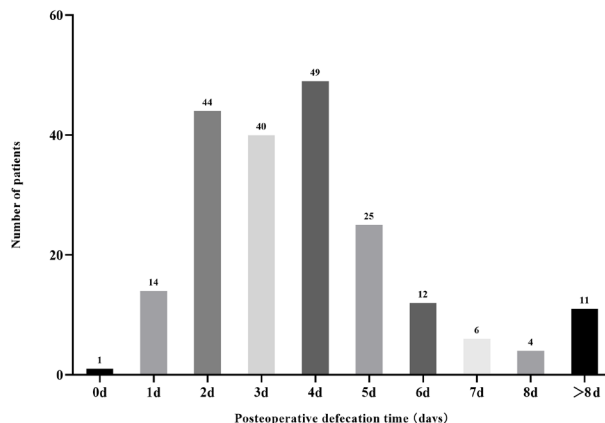


Figure 1. First postoperative defecation time in patients after tricuspid valve replacement.

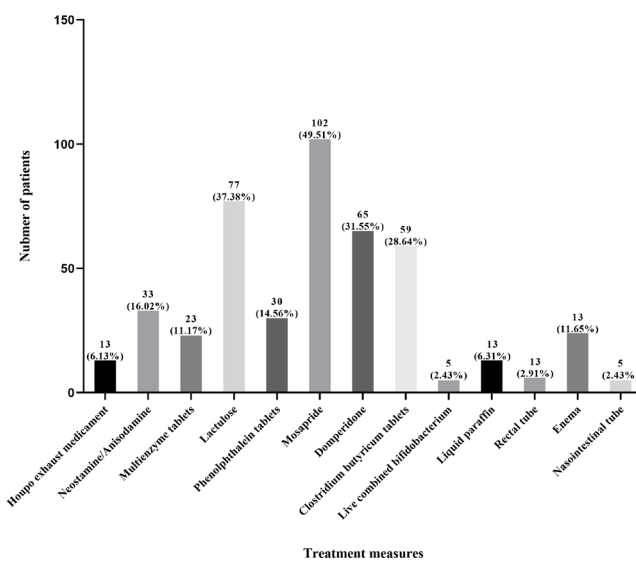


Figure 2. Prokinetic drugs and other digestive system treatments of tricuspid valve replacement patients.

significantly higher than that of the control group. There was no significant difference in gender, body mass index (BMI), New York Heart Association (NYHA) classification, underlying disease, and previous abdominal or cardiac surgery history. (Table 1) The platelets in the delayed group were significantly less than in the control group ($P < 0.001$). Preoperative symptoms, fecal hardness value, and echocardiography results were not statistically significant between the two groups ($P > 0.05$). (Table 2) (Table 3)

Intraoperative data of TR patients: There was no significant difference in types of artificial valves, minimum pharyngeal temperature, and surgical method between the delayed group and control group ($P > 0.05$). Notably, the CPB time in the delayed group was significantly higher than that of the control group (79.2 vs. 65.6 min, $P = 0.013$). Additionally, the minimum rectal temperature in the delayed group was significantly lower than that of the control group (34.2 vs. 34.5°C,

Table 1. Basic characteristics of patients

Characteristic	Overall (N = 206)	Delayed (N = 107)	Control (N = 99)	P-value
Age, years	56.2	57.8 (50.0, 66.0)	54.4 (46.0, 65.0)	0.043
Gender, n (%)	-	-	-	0.745
Male	85	43 (40.2)	42 (42.4)	
Female	121	64 (59.8)	57 (57.6)	
BMI (kg/m ²), n (%)	22.2	22.1 (19.8, 23.9)	22.3 (20.2, 23.7)	0.844
Low (BMI<18)	13	7 (6.5)	6 (6.1)	
Normal (18≤BMI<24)	313	76 (71.0)	72 (72.7)	
Overweight (24≤BMI<28)	35	22 (20.6)	17 (17.2)	
Obese (BMI≥28)	6	2 (1.9)	4 (4.0)	
Hypertension, n (%)	25	14 (13.1)	11 (11.1)	0.665
Diabetes, n (%)	15	8 (7.5)	7 (7.1)	0.911
Preoperative renal dysfunction, n (%)	5	4 (3.7)	1 (1.0)	0.413
Previous abdominal surgery, n (%)	11	6 (5.6)	5 (5.1)	0.859
Liver cirrhosis, n (%)	7	6 (5.6)	1 (1.0)	0.069
Liver congestion, n (%)	81	47 (43.9)	34 (34.3)	0.160
AF, n (%)	127	66 (61.7)	61 (61.6)	0.992
NYHA classifications, n (%)	-	-	-	0.388
I-II	52	23 (21.5)	29 (29.3)	
III	130	72 (67.3)	58 (58.6)	
IV	24	12 (11.2)	12 (12.1)	
Previous cardiac surgery, n (%)				
Left heart valve surgery	128	69 (64.5)	59 (59.6)	0.471
Right heart valve surgery	47	28 (26.2)	19 (19.2)	0.233
Re-TVR	152	81 (75.7)	71 (71.7)	0.516

BMI, body mass index; AF, atrial fibrillation; NYHA, New York Heart Association; Re-TVR, re-tricuspid valve replacement

$P = 0.042$). For concomitant surgeries, there was a statistical difference in the rate of TVR combined with mitral valve surgery between the two groups, while there was no statistical difference in other operations ($P > 0.05$). (Table 4)

Digestive system treatments of TR patients after surgery: Prokinetic drugs and other digestive system treatments were used after surgery. Lactulose, mosapride, domperidone, and clostridium butyricum were the most commonly used medicines. (Figure 2) We further examined the difference of prokinetic drug application and defecation delay within 3 days after surgery between these two groups to identify whether prophylactic use of prokinetic drugs would avoid the occurrence of defecation delay. As shown in Table 5, 64 (59.8%) cases in the delayed group were treated with prokinetic drugs at the initial 3 days after tricuspid valve surgery, which was significantly lower than that of the control group (75.8%) ($P = 0.015$). (Table 5)

Clinical outcomes and perioperative adverse events of TR patients: As shown in Table 6, non-survivors all were

from the delayed group, accounting for 16.8% of the delayed group. (Table 6) Furthermore, the length of ICU stays ($P < 0.001$) and hospital stays ($P < 0.001$), postoperative respiratory failure ($P < 0.001$), length of nasogastric tube decompression time ($P < 0.001$), and pleural drainage volume after surgery at the first 24h ($P = 0.039$) were significantly higher in the delayed group than in the control group. In addition, the incidence of complications, such as pulmonary infection ($P = 0.002$), renal dysfunction needing hemodialysis ($P < 0.001$), delirium/seizures ($P = 0.027$), and cardiac dysfunction ($P = 0.009$) were significantly higher in the delayed group than in the control group. TR patients with postoperative delayed defecation were more likely to occur adverse events when compared with patients in the control group. However, there was no significant difference in postoperative nausea/emesis/anorexia ($P = 0.761$), cerebral infarction/cerebral hemorrhage ($P = 0.761$), gastrointestinal bleeding (0.151), hemiplegia ($P = 0.151$), and redo thoracotomy on account of bleeding ($P = 0.397$) between these two groups. (Table 6)

Table 2. Preoperative symptoms and test results

Characteristic	Delayed (N = 107)	Control (N = 99)	P-value
Abdominal distension, n (%)	28 (26.2)	18 (18.2)	0.169
Anorexia, n (%)	18 (16.8)	16 (16.2)	0.898
Ascites, n (%)	10 (9.3)	10 (10.1)	0.855
Stool consistency, n (%)	-	-	0.438
Normal	103 (96.3)	93 (93.9)	
Mushy	4 (3.7)	6 (6.1)	
HB, g/L	123.3 (105.0, 139.0)	124.7 (105.0, 144.0)	0.381
HCT, %	38.0 (33.0, 41.7)	37.8 (33.8, 42.8)	0.55
WBC, $\times 10^9/L$	5.2 (3.4, 5.8)	5.4 (3.8, 6.2)	0.349
PLT, $\times 10^9/L$	124.0 (83.0, 146.0)	157.4 (109.0, 203.0)	<0.001
Creatinine, $\mu\text{mol/L}$	76.6 (59.0, 88.0)	72.3 (60.0, 87.0)	0.913
TBIL, $\mu\text{mol/L}$	23.4 (13.9, 28.6)	22.6 (14.0, 28.6)	0.333
ALT, $\mu\text{mol/L}$	31.5 (13.0, 23.0)	20.3 (14.0, 24.0)	0.813
AST, $\mu\text{mol/L}$	52.1 (22.0, 32.0)	26.7 (21.0, 29.0)	0.510
Albumin, g/L	40.1 (38.0, 43.0)	40.1 (38.0, 43.0)	0.561

HB, hemoglobin; HCT, hematocrit; WBC, white blood cell; PLT, platelets; TBIL, total bilirubin; ALT, alanine transaminase; AST, aspartate aminotransferase

Table 3. Preoperative echocardiography

Characteristic	Delayed (N = 107)	Control (N = 99)	P-value
LVEF (%)	62.3 \pm 7.3	62.3 \pm 8.2	0.993
Tricuspid regurgitation (mL)	66.1 (31.0, 92.0)	58.2 (33.0, 63.0)	0.209
LA volume (mL)	169.9 (84.0, 215.0)	157.5 (60.0, 198.0)	0.360
LV volume (mL)	102.2 (73.0, 115.0)	90.9 (70.0, 103.0)	0.104
RA volume (mL)	216.0 (122.0, 281.0)	216.0 (126.0, 251.0)	0.884
RV volume (mL)	117.2 (65.0, 131.0)	104.1 (71.0, 129.0)	0.677
Pulmonary trunk diameter (cm)	2.7 (2.4, 3.2)	2.6 (2.4, 3.2)	0.583

LVEF, left ventricular ejection fraction; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

Multivariate analysis of death: Patients after TVR were re-classified into the survival group (N = 188) and non-survival group (N = 18). The result of univariate analysis indicated that preoperative platelets, creatinine, total bilirubin (TBIL), NYHA classifications, postoperative renal dysfunction, pulmonary infection, gastrointestinal bleeding, delirium/seizures, cardiac dysfunction, postoperative respiratory failure, and postoperative defecation time were associated with death of patients after TVR. (Supplementary Table 1) (Supplementary Table 2) (Supplementary Table 3) The results of logistic regression analysis indicated that postoperative renal dysfunction and respiratory failure were independent risk factors for perioperative death of TR patients after TV, while defecation delay exceeding 3 days was not associated with mortality. (Table 7)

DISCUSSION

Defecation delay occurred in 51.9% (107/206) of the TR patients after TVR in our study, which was similar to the results (55%) of a study aimed at lung tumor surgery [Li 2021]. The occurrence of postoperative delayed defecation may be related to age, preoperative platelets, interoperative CPB time, minimum rectal temperature, and the use of prokinetic drugs. The proportion of patients who experience renal dysfunction, lung infection, cardiac dysfunction, postoperative respiratory failure, and delirium/seizures in the delayed group was extremely higher than that in the control group. In addition, the length of ICU stays and hospital stays were significantly prolonged in patients of the delayed group.

Table 4. Intraoperative data

Characteristic	Delayed (N = 107)	Control (N = 99)	P-value
Artificial valve, n (%)	-	-	0.299
Mechanical valve	41 (38.3)	45 (45.5)	
Bioprosthetic valve	66 (61.7)	54 (54.5)	
CPB time, min	79.2 (51.8, 97.5)	65.6 (46.0, 75.0)	0.013
Minimum pharyngeal temperature (°C)	33.5 (32.6, 34.1)	33.7 (33.0, 34.5)	0.166
Minimum rectal temperature (°C)	34.2 ±1.0	34.5 ±0.8	0.042
Surgical approach, n (%)	-	-	0.458
Open heart surgery	52 (48.6)	43 (43.4)	
Small incision thoracotomy cardiac surgery	55 (51.4)	56 (56.6)	
Combined surgery, n (%)			
MVP/MVR	15 (14.0)	1 (1.0)	<0.001
AVR	1 (0.9)	1 (1.0)	1
CABG	2 (1.9)	0 (0)	0.512
VSD	0 (0)	1 (1.0)	0.969
ASD	5 (4.7)	6 (6.1)	0.658
Pacemaker implantation	2 (1.9)	0 (0)	0.512

CPB, cardiopulmonary bypass; MVP, mitral valvuloplasty; MVR, mitral valve replacement; CABG, coronary artery bypass graft; VSD, ventricular septal defect; ASD, atrial septal defect

Table 5. Postoperative digestive treatment of patients

Characteristic	Delayed (N = 107)	Control (N = 99)	P-value
Prokinetic drugs within 3 days after surgery, n (%)	-	-	0.015
Yes	64 (59.8)	75 (75.8)	
No	43 (40.2)	24 (24.2)	
Types of prokinetic drugs within 3 days after surgery, n (%)	-	-	0.013
0	43 (40.2)	24 (24.2)	
1	18 (16.8)	15 (15.2)	
2	36 (33.6)	34 (34.3)	
3	9 (8.4)	23 (23.2)	
4	1 (0.9)	3 (3.0)	

However, defecation delay may not be associated with the mortality of TVR patients, in contrast, renal dysfunction and respiratory failure were independent risk factors for death.

Recent studies manifested that defecation delay was related to weaning difficulty, prolonged ICU and hospital stays, a high probability of acquired infection, multiple organ disorders, acute pulmonary embolism, and death for patients requiring long-term mechanical ventilation [Gacouin 2010; Kollef 1991]. We, for the first time, identified that TVR patients in the delayed group were more likely to experience adverse events. Patients with severe TR often

are accompanied with severe right heart failure, which may lead to long-term increased splanchnic venous pressure, and result in long-term ischemia of enterocytes and disruption of normal intestinal barrier function [Polsinelli 2019]. Whether gastrointestinal dysfunction resulting from right heart failure is the cause of defecation delay in patients with TR remains to be further investigated, but existing studies suggest that patients with severe TR may have impaired gastrointestinal function. The results of our study suggested that TVR and other cardiac surgeries required continued attention to gastrointestinal symptoms in the future.

Table 6. Clinical outcomes and perioperative adverse events

Characteristic	Delayed (N = 107)	Control (N = 99)	P-value
Mortality, n (%)	18 (16.8)	0 (0)	<0.001
Length of ICU stay, h	194.2 (48.0, 159.0)	62.2 (23.0, 64.0)	<0.001
Length of hospital stay, d	18.2 (10.0, 18.0)	13.5 (9.0, 14.0)	0.002
Length of nasogastric tube decompression, h	154.2 (18.0, 130.0)	31.8 (7.0, 21.0)	<0.001
Nausea/emesis/anorexia, n (%)	19 (17.8)	16 (16.2)	0.761
Pulmonary infection, n (%)	17 (15.9)	3 (3.0)	0.002
Renal dysfunction, n (%)	18 (16.8)	0 (0)	<0.001
Redo thoracotomy, n (%)	7 (6.5)	3 (3.0)	0.397
Postoperative respiratory failure, n (%)	24 (22.4)	2 (2.0)	<0.001
Cerebral infarction/cerebral hemorrhage, n (%)	2 (1.9)	0 (0)	0.512
Gastrointestinal bleeding, n (%)	6 (5.6)	1 (1.0)	0.151
Delirium/seizures, n (%)	7 (6.5)	0 (0)	0.027
Cardiac dysfunction, n (%)	9 (8.4)	0 (0)	0.009
Hemiplegia, n (%)	1 (0.9)	0 (0)	1
Pleural drainage volume of the day of surgery, mL	477.2 (190.0, 670.0)	394.7 (150.0, 450.0)	0.039

ICU, intensive care unit

Table 7. Logistic regression of death

Characteristic	Odds ratio	95% confidence interval	P-value
Preoperative PLT, $\times 10^9/L$	0.991	0.964-1.019	0.543
TBIL, $\mu\text{mol/L}$	0.984	0.893-1.085	0.748
NYHA classification, n (%)			
I-II	1.000		
III	4.133	0.009-1872.288	0.649
IV	1.301	0.003-623.149	0.933
Postoperative renal dysfunction			
No	1.000		
Yes	1041.049	8.638-125461.367	0.004
Pulmonary infection			
No	1.000		
Yes	19.715	0.227-1708.673	0.190
Postoperative respiratory failure			
No	1.000		
Yes	47.649	1.059-2144.879	0.047
Postoperative defecation time, d	0.802	0.369-1.745	0.578

PLT, platelets; TBIL, total bilirubin; NYHA, New York Heart Association

Similar to other postoperative functional gastrointestinal diseases, defecation delay is related to various factors, including the patient's diet, toilet habits, environment, culture, race, and genetics [Barberio 2021]. Anxiety, depression, and sleep disorders may be aggravated during hospitalization, which may result in postoperative defecation delay through brain-gut axis regulation [Zhu 2012]. Furthermore, the decrease of the amount and variety of food intake during perioperative period and low level of physical activity may lead to defecation delay [Vargas-García 2013]. Patients undergoing cardiac surgery need to be treated with diuretics and reduce water intake. The reduction of body water may increase the reabsorption of water in feces and thus increase stool hardness and reduce frequency of defecation [Boilesen 2021]. The decline of gastrointestinal motility in patients with cardiothoracic surgery also leads to the long retention time of feces in the intestinal tract, and the excessive absorption of water in the feces, which will lead to stool hardening and defecation difficulty [Włodarczyk 2021; Zoumprouli 2017]. In addition, not only for patients undergoing TVR, but also for patients undergoing other operations, immobilization, anesthesia, pain, electrolyte imbalance and other factors could result in reduced intestinal motility and defecation delay [Li 2021; Hellstrom 2021]. It is worth exploring the mechanism that causes postoperative defecation delay in future research.

Intestinal mucosal blood flow supplies sufficient oxygen and nutrients to mucosal cells for maintaining normal digestive function under normal physiological conditions [Kawano 2000], while intestinal mucosa ischemia and reperfusion injury may occur after CPB, which may lead to increased intestinal permeability and impaired barrier function [Braun 2004; Wang 2011], further to alter the gastrointestinal peristaltic function of patients [Ballabeni 2002]. Our study also confirmed that the occurrence of postoperative defecation delay was closely related to the duration of CPB. Inhibition of intestinal peristalsis may lead to bacterial overgrowth in the intestines [Adike 2018]. With the disruption of the intestinal barrier, bacterial translocation could lead to the initiation of systemic inflammatory response syndrome, multiple organ dysfunction syndromes, or even death [Puleo 2011]. Defecation delay also may result in increased intra-abdominal pressure, which can further lead to dysfunction of the abdominal organ [Al Ali 2021; Kongkatong 2022].

Postoperative gastrointestinal dysfunction increased hospital stays, cost of care, and postoperative morbidity, and therefore there is currently more focus on positive strategies for prevention rather than treatment [Venara 2016]. The proportion of defecation delay symptoms in patients using prokinetic drugs at the first 3 days after TVR was significantly lower than in those who hadn't taken prokinetic drugs at the first 3 days after surgery. This evidence suggested that prophylactic use of prokinetic drugs may reduce the occurrence of defecation delay, while needs to be further verified in the future.

Previous studies have shown that prokinetic drugs are effective in reducing feeding intolerance in critically ill patients after surgery, but the incidence of the length of ICU stays and other adverse events outcomes remained unclear [Lewis 2016; Peng 2021]. Reasonable preoperative lifestyle and

dietary measures, postoperative thoracic epidural analgesia, water and electrolyte balance, alvimopan, and gum chewing can play roles as effective preventive measures [Diebakate-Scordamaglia 2022; Bragg 2015]. One recent study suggested that prophylactic use of laxatives also reduces gastrointestinal dysfunction in patients requiring long-term mechanical ventilation [de Azevedo 2015]. It's of great significance to relieve the symptoms through the intervention, such as osmotic or mucilaginous laxatives, prokinetic drugs, and keeping water-electrolyte balance for patients who already developed defecation delay [Chor 2020]. Lubricant laxatives and enemas may be options for patients with end-stage constipation, and for those with refractory defecation delay, stimulant laxatives or surgery may be required [Mounsey 2015].

The occurrence of defecation delay may provide valuable prognostic information for ICU patients. Our study indicated that the mortality and adverse event rate were higher in the delayed group, and other ICU clinical studies reported the same conclusion [Gacouin 2010]. However, the results of logistic regression analysis indicated that only renal dysfunction and respiratory failure were independent risk factors for death in hospital, which is consistent with similar studies. A retrospective observational study involving 1933 patients reported that defecation delay was not associated with in-hospital mortality [Yoshida 2022]. The multivariate analysis of another prospective observational study involving 396 patients also showed that defecation delay was associated with prolonged mechanical ventilation and ICU stays, but not mortality [Launey 2021]. In conclusion, patients with defecation delay after TVR were more likely to appear adverse events, such as mortality, prolonged ICU and hospital stays, and postoperative respiratory failure. However, defecation delay was not associated with the mortality of patients who underwent TVR.

ACKNOWLEDGEMENT

Funding: This study was funded by National Natural Science Foundation of China (Grant NO. 81870287, 82070402 and 82100383) and Military Medical Research Special Project (Grant NO. 2019YSL003).

REFERENCES

- Adike A, DiBaise JK. 2018. Small Intestinal Bacterial Overgrowth: Nutritional Implications, Diagnosis, and Management. *Gastroenterol Clin North Am.* 47(1):193-208.
- Al Ali A, Singh R, Filler G, et al. 2021. Abdominal compartment syndrome secondary to chronic constipation in MECP2 duplication syndrome. *BMJ Case Rep.* 14(6).
- Antunes MJ, Rodríguez-Palomares J, Prendergast B, et al. 2017. Management of tricuspid valve regurgitation: Position statement of the European Society of Cardiology Working Groups of Cardiovascular Surgery and Valvular Heart Disease. *Eur J Cardiothorac Surg.* 52(6):1022-1030.
- Ballabeni V, Barocelli E, Bertoni S, et al. 2002. Alterations of intestinal motor responsiveness in a model of mild mesenteric ischemia/reperfusion in rats. *Life Sci.* 71(17):2025-35.

Supplementary Table 1. Preoperative data

Characteristic	Non-survival (N = 18)	Survival (N = 188)	P-value
Age, years	60.6 (49.8, 70.3)	55.8 (49.0, 64.8)	0.112
Gender, n (%)	-	-	0.774
Male	8 (44.4)	77 (41)	
Female	10 (55.6)	111 (59)	
BMI (kg/m ²)	22.2 (20.2, 23.7)	22.2 (19.7, 23.9)	0.943
Hypertension	1 (5.6)	24 (12.8)	0.605
Diabetes, n (%)	2 (11.1)	13 (6.9)	0.857
Preoperative renal insufficiency, n (%)	2 (11.1)	3 (1.6)	0.088
Previous abdominal surgery, n (%)	1 (5.6)	10 (5.9)	1
Liver cirrhosis, n (%)	2 (11.1)	5 (2.7)	0.226
Liver congestion, n (%)	8 (44.4)	73 (38.8)	0.641
AF, n (%)	14 (77.8)	113 (60.1)	0.141
NYHA classifications, n (%)	-	-	0.004
I-II	1 (5.6)	51 (27.1)	
III	11 (61.1)	119 (63.3)	
IV	6 (33.3)	18 (9.6)	
Previous cardiac surgery, n (%)			
Left heart valve surgery	11 (61.1)	117 (62.2)	0.925
Right heart valve surgery	3 (16.7)	44 (23.4)	0.721
Re-TVR	11 (61.1)	141 (75)	0.318
Abdominal distension, n (%)	5 (27.8)	41 (21.8)	0.776
Anorexia, n (%)	5 (27.8)	29 (16.5)	0.381
Ascites, n (%)	2 (11.1)	18 (9.6)	1
Stool consistency, n (%)	-	-	0.668
Normal	18 (100)	178 (94.7)	
Mushy	0 (0)	10 (5.3)	
HB, g/L	114.7 ±25.4	124.9 ±25.3	0.105
HCT, %	37.9 (28.8, 40.5)	37.9 (33.8, 42.1)	0.087
WBC, ×10 ⁹ /L	6.2 (3.3, 6.5)	5.2 (3.6, 6.1)	0.792
PLT, ×10 ⁹ /L	111.7 (69.0, 169.0)	142.7 (101.0, 182.0)	0.011
Creatinine, μmol/L	102.6 (62.5, 119.0)	71.9 (59.0, 86.0)	0.014
TBIL, μmol/L	29.5 (18.8, 37.2)	22.5 (13.8, 25.3)	0.021
ALT, μmol/L	87.8 (10.0, 27.3)	20.6 (13.0, 22.3)	0.356
AST, μmol/L	165.0 (21.8, 37.5)	28.0 (21.0, 29.5)	0.287
Albumin, g/L	39.6 (35.8, 42.5)	40.1 (34.7, 43.0)	0.533
LVEF (%)	60.6 (52.0, 68.3)	62.6 (57.0, 69.0)	0.363
Tricuspid regurgitation (mL)	60.1 (30.5, 82.3)	62.4 (20.4, 77.0)	0.920
LA volume (mL)	161.1 (68.8, 228.8)	164.9 (80.0, 200.0)	0.502
LV volume (mL)	102.2 (68.8, 127.5)	93.3 (72.0, 107.0)	0.756
RA volume (mL)	205.5 (132.5, 303.0)	217.0 (124.5, 258.0)	0.649
RV volume (mL)	93.1 (68.5, 126.5)	112.6 (68.0, 131.8)	0.702

Pulmonary trunk diameter (cm)	2.8 (2.5, 3.0)	2.6 (2.4, 2.8)	0.087
-------------------------------	----------------	----------------	-------

BMI, body mass index; AF, atrial fibrillation; NYHA, New York Heart association; Re-TV, re-tricuspid valve replacement; HB, hemoglobin; HCT, hematocrit; WBC, white blood cell; PLT, platelets; TBIL, total bilirubin; ALT, alanine transaminase; AST, aspartate aminotransferase; LVEF, left ventricular ejection fraction; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

Supplementary Table 2. Intraoperative data

Characteristic	Non-survival (N = 18)	Survival (N = 188)	P-value
Artificial valve, n (%)	-	-	0.114
Mechanical valve	3 (16.7)	83 (44.1)	
Bioprosthetic valve	15 (83.3)	105 (55.9)	
CPB time, min	73.9 (50.0, 88.0)	72.5 (49.0, 84.0)	0.654
Minimum pharyngeal temperature (°C)	34.6 (32.8, 34.3)	33.6 (32.9, 34.3)	0.450
Minimum rectal temperature (°C)	34.1 ±1.0	34.3 ±0.9	0.300
Surgical approach, n (%)	-	-	0.762
Open heart surgery	9 (50)	87 (46.3)	
Small incision thoracotomy cardiac surgery	9 (50)	101 (53.7)	

CPB, cardiopulmonary bypass; MVP, mitral valvuloplasty; MVR, mitral valve replacement; CABG, coronary artery bypass graft; VSD, ventricular septal defect; ASD, atrial septal defect.

Supplementary Table 3. Postoperative data

Characteristic	Non-survival (N = 18)	Survival (N = 188)	P-value
Redo thoracotomy, n (%)	1 (5.6)	9 (4.8)	0.966
Postoperative respiratory failure, n (%)	16 (88.9)	10 (5.3)	<0.001
Cerebral infarction/cerebral hemorrhage, n (%)	1 (5.6)	1 (0.5)	0.413
Renal dysfunction, n (%)	16 (88.9)	2 (1.1)	<0.001
Pulmonary infection, n (%)	12 (66.7)	8 (4.3)	<0.001
Gastrointestinal bleeding, n (%)	5 (27.8)	2 (1.1)	<0.001
Delirium/seizures, n (%)	4 (22.2)	3 (1.6)	<0.001
Cardiac dysfunction, n (%)	6 (33.3)	3 (1.3)	<0.001
Hemiplegia, n (%)	0 (0)	1 (0.5)	1
Pleural drainage volume of the day of surgery (mL)	420.6 (182.5, 610)	439.2 (150, 580)	0.873
Prokinetic drugs within 3 days after surgery	-	-	1
Yes, n (%)	9 (50)	130 (69.1)	
No, n (%)	9 (50)	58 (30.9)	
Postoperative defecation time, d	8.3 (5, 11)	3.6 (2, 4)	<0.001
Defecation delay	-	-	<0.001
Yes, n (%)	18 (100)	89 (47.3)	
No, n (%)	0 (0)	99 (52.7)	

- Barberio B, Judge C, Savarino EV, et al. 2021. Global prevalence of functional constipation according to the Rome criteria: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol.* 6(8):638-648.
- Belsey J, Greenfield S, Candy D, et al. 2010. Systematic review: impact of constipation on quality of life in adults and children. *Aliment Pharmacol Ther.* 31(9):938-49.
- Boilesen SN, Dias FC, Tahan S, et al. 2021. Fluid intake and urinary osmolality in pediatric patients with functional constipation. *Eur J Nutr.* 60(8):4647-4655.
- Bragg D, El-Sharkawy AM, Psaltis E, et al. 2015. Postoperative ileus: Recent developments in pathophysiology and management. *Clin Nutr.* 34(3):367-76.
- Braun JP, Schroeder T, Buehner S, et al. 2004. Splanchnic oxygen transport, hepatic function and gastrointestinal barrier after normothermic cardiopulmonary bypass. *Acta Anaesthesiol Scand.* 48(6):697-703.
- Chor CYT, Mahmood S, Khan IH, et al. 2020. Gastrointestinal complications following cardiac surgery. *Asian Cardiovasc Thorac Ann.* 28(9):621-632.
- Correction to: 2020 ACC/AHA Guideline on the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2021. 143(10):e784.
- de Azevedo RP, Freitas FG, Ferreira EM, et al. 2015. Daily laxative therapy reduces organ dysfunction in mechanically ventilated patients: a phase II randomized controlled trial. *Crit Care.* 19(1):329.
- Diebakate-Scordamaglia L, Voican CS, Perlemuter G. 2022. Iatrogenic constipation in gastrointestinal surgery. *J Visc Surg.* 159(1s):S51-s57.
- Dreyfus J, Flagiello M, Bazire B, et al. 2020. Isolated tricuspid valve surgery: impact of aetiology and clinical presentation on outcomes. *Eur Heart J.* 41(45):4304-4317.
- Gacouin A, Camus C, Gros A, et al. 2010. Constipation in long-term ventilated patients: associated factors and impact on intensive care unit outcomes. *Crit Care Med.* 38(10):1933-8.
- Hellstrom EA, Ziegler AL, Blikslager AT. 2021. Postoperative Ileus: Comparative Pathophysiology and Future Therapies. *Front Vet Sci.* 8:714800.
- Ivanov A, Yossef J, Tailon J, et al. 2016. Do pulmonary function tests improve risk stratification before cardiothoracic surgery? *J Thorac Cardiovasc Surg.* 151(4):1183-9.e3.
- Kawano S, Tsuji S. 2000. Role of mucosal blood flow: a conceptual review in gastric mucosal injury and protection. *J Gastroenterol Hepatol.* 15 Suppl:D1-6.
- Kollef MH, Schachter DT. 1991. Acute pulmonary embolism triggered by the act of defecation. *Chest.* 99(2):373-6.
- Kongkatong MM, Patel MM, Thom C, et al. 2022. Fatal Abdominal Compartment Syndrome Due to Constipation: A Case Report. *Clin Pract Cases Emerg Med.* 6(1):8-12.
- Launey Y, Painvin B, Roquilly A, et al. 2021. Factors associated with time to defecate and outcomes in critically ill patients: a prospective, multicentre, observational study. *Anaesthesia.* 76(2):218-224.
- Lewis K, Alqahtani Z, McIntyre L, et al. 2016. The efficacy and safety of prokinetic agents in critically ill patients receiving enteral nutrition: a systematic review and meta-analysis of randomized trials. *Crit Care.* 20(1):259.
- Li J, Yang T, Cen L, et al. 2021. Defecation delay in patients after lung tumor surgery: a prospective nested case-control study. *Ann Transl Med.* 9(12):980.
- Mounsey A, Raleigh M, Wilson A. 2015. Management of Constipation in Older Adults. *Am Fam Physician.* 92(6):500-4.
- Pahwa S, Saran N, Pochettino A, et al. 2021. Outcomes of tricuspid valve surgery in patients with functional tricuspid regurgitation. *Eur J Cardiothorac Surg.* 59(3):577-585.
- Peng R, Li H, Yang L, et al. 2021. The efficacy and safety of prokinetics in critically ill adults receiving gastric feeding tubes: A systematic review and meta-analysis. *PLoS One.* 16(1):e0245317.
- Polsinelli VB, Marteau L, Shah SJ. 2019. The role of splanchnic congestion and the intestinal microenvironment in the pathogenesis of advanced heart failure. *Curr Opin Support Palliat Care.* 13(1):24-30.
- Puleo F, Arvanitakis M, Van Gossom A, et al. 2011. Gut failure in the ICU. *Semin Respir Crit Care Med.* 32(5):626-38.
- Raja K, Kochhar R, Sethy PK, et al. 2004. An endoscopic study of upper-GI mucosal changes in patients with congestive heart failure. *Gastrointest Endosc.* 60(6):887-93.
- Rasmussen LS, Pedersen PU. 2010. Constipation and defecation pattern the first 30 days after thoracic surgery. *Scand J Caring Sci.* 24(2):244-50.
- Seilitz J, Edström M, Sköldberg M, et al. 2021. Early Onset of Postoperative Gastrointestinal Dysfunction Is Associated With Unfavorable Outcome in Cardiac Surgery: A Prospective Observational Study. *J Intensive Care Med.* 36(11):1264-1271.
- Stewart D, Waxman K. 2007. Management of postoperative ileus. *Am J Ther.* 14(6):561-6.
- Topilsky Y, Maltais S, Medina Inojosa J, et al. 2019. Burden of Tricuspid Regurgitation in Patients Diagnosed in the Community Setting. *JACC Cardiovasc Imaging.* 12(3):433-442.
- Valentova M, von Haehling S, Bauditz J, et al. 2016. Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. *Eur Heart J.* 37(21):1684-91.
- Vargas-García EJ, Vargas-Salado E. 2013. Food intake, nutritional status and physical activity between elderly with and without chronic constipation. A comparative study. *Cir Cir.* 81(3):214-20.
- Vather R, Trivedi S, Bissett I. 2013. Defining postoperative ileus: results of a systematic review and global survey. *J Gastrointest Surg.* 17(5):962-72.
- Venara A, Neunlist M, Slim K, et al. 2016. Postoperative ileus: Pathophysiology, incidence, and prevention. *J Visc Surg.* 153(6):439-446.
- Wang YB, Liu J, Yang ZX. 2011. Effects of intestinal mucosal blood flow and motility on intestinal mucosa. *World J Gastroenterol.* 17(5):657-61.
- Włodarczyk J, Waśniewska A, Fichna J, et al. 2021. Current Overview on Clinical Management of Chronic Constipation. *J Clin Med.* 10(8).
- Yoshida T, Uchino S, Sasabuchi Y. 2022. Epidemiology of constipation in critically ill patients and its impact on in-hospital mortality: a retrospective observational study. *J Anesth.* 36(3):349-358.
- Zack CJ, Fender EA, Chandrashekar P, et al. 2017. National Trends and Outcomes in Isolated Tricuspid Valve Surgery. *J Am Coll Cardiol.* 70(24):2953-2960.
- Zhu LM, Fang XC, Liu S, et al. 2012. Multi-centered stratified clinical studies for psychological and sleeping status in patients with chronic constipation in China. *Zhonghua Yi Xue Za Zhi.* 92(32):2243-6.
- Zoumprouli A, Chatzimichali A, Papadimitriou S, et al. 2017. Gastrointestinal motility following thoracic surgery: the effect of thoracic epidural analgesia. A randomised controlled trial. *BMC Anesthesiol.* 17(1):139.