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Original Article

Predictors of postoperative prolonged mechanical ventilation after left ventricular assist device surgery

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Abstract

Aim: Prolonged mechanical ventilation (PMV) after cardiovascular surgeries is associated with morbidity and mortality. The aim of the study was to determine the risk factors for postoperative PMV (PPMV) after left ventricular assist device (LVAD) surgery.

Material and Methods: We retrospectively analyzed the data of patients who underwent LVAD surgery between 2011 and 2016. Prolonged mechanical ventilation was defined as postoperative tracheal extubation 24 hours after the patient is admitted to the ICU. Patients were divided into two groups whether they were extubated within 24 hours of surgery or extubated after 24 hours following surgery.

Results: During the study period, a total of fifty-seven patients were admitted to ICU. Fifty-seven patients' data were screened. The mean age of the 57 patients enrolled was 44.6 ± 16.1 years. Of them, 82% were male, and 54 (95%) patients had dilated cardiomyopathy diagnosis. A total of 26 (46%) patients required PPMV. The two groups were similar in terms of demographics, duration of surgery, postoperative LVAD flow rates, presence of preoperative MV, infections, and circulatory support devices ($p > 0.05$). Patients who required PPMV underwent more revision surgeries [14 (54%) vs. 2 (7%), $p < 0.001$] and had higher incidences of acute kidney injury (AKI) on the first day after the surgery [13 (50%) vs. 4 (13%), $p = 0.003$] compared with those who did not require PPMV. Furthermore, the patients who required PPMV also required more renal replacement therapies postoperatively [12 (46%) vs. 5 (16%), $p = 0.02$] and had longer intensive care unit stay (30.1±25.2 days vs. 14.0 ±11.4 days, $p = 0.002$) and had higher hospital mortality (58% vs. 35%, $p = 0.043$) and 30-day mortality (38% vs. 16%, $p = 0.042$) than those who did not require PPMV. Logistic regression analysis revealed postoperative AKI as an independent risk factor for PPMV (OR = 0.223, 95% CI 0.067–0.743, $p = 0.015$).

Conclusion: Our results revealed that almost half of the patients who underwent LVAD surgery required PPMV. AKI on the first day following surgery is an independent risk factor for PPMV.

Keywords: LVAD surgery; prolonged mechanical ventilation; ICU

INTRODUCTION

The prevalence of heart failure is increasing in Turkey, similar to many other countries around the world. More than 2 million people live with heart failure in our country.(1) For patients with end-stage heart failure, when all other treatment approaches have failed, the only curative therapy is heart transplantation, although ventricular assist devices (VADs) are also often used in this group because of limited number of donors and certain contraindications for transplantation (such as pulmonary hypertension). These devices are used as a bridge to transplantation, as a bridge to recovery, or as a final treatment. In recent years, increased survival rates has been reported in patients with end-stage heart failure who received VAD support.(2)

Prolonged mechanical ventilation (PMV) has been detected in 3%–22% of the adult patients who underwent cardiac surgery, and reported to be closely associated with morbidity and mortality.(3,4) In addition, the process of weaning a patient off mechanical ventilation has been shown to be prolonged in pediatric patients with VAD. (5) Moreover, literature contains only a limited number of studies that investigated PMV after VAD operation in adults.

This study assessed the incidence of postoperative PMV (PPMV) in VAD-implanted patients in our clinic and

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examined the risk factors in patients who have weaning difficulty.

MATERIAL and METHODS

This study was approved by Baskent University Institutional Review Board (Project no: KA 17/74) and supported by Baskent University Research Fund.

We retrospectively analyzed the records of patients who underwent left ventricular assist device (LVAD) implantation at Baskent University Hospital from January 2011 to December 2016. PMV was defined as postoperative tracheal extubation after 24 h. Patients between 18 and 75 years of age were included in the study. Collected data included demographic characteristics (age, gender, weight, and height), comorbidities, drugs, perioperative laboratory values, hemodynamic parameters, intraoperative features, length of mechanical ventilation, length of ICU/hospital stay, and hospital mortality.

Patients under 18 and over 75 years of age and those with missing data were excluded from this study.

The same opioid-based anesthesia technique was used for all patients. Anesthesia was induced intravenously with midazolam (0.02–0.05 mg/kg), fentanyl (500 µg), and rocuronium bromide (0.6–1 mg/kg). Desflurane at a concentration of 4%–6% and fentanyl 10 µg/kg/h intravenously were used to maintain the anesthesia. In all cases, standard cardiopulmonary bypass protocol and standard perfusion techniques were used. Carbon dioxide insufflation within the surgical field was used to prevent microemboli. LVAD (HeartWare®, Medtronic, MN, USA) implantations were performed through a standard median sternotomy on beating heart, with the use of cardiopulmonary bypass through aortic and right atrial cannulation. The inflow cannula was inserted into the apex of the left ventricle, and the outflow cannula was grafted into the aorta. The driveline was tunneled subcutaneously before systemic heparinization and placed on patient's abdominal wall in the subcostal region. Deairing was performed under transesophageal echocardiography (TEE) guidance. Weaning from CPB was accomplished by gradual increases in VAD pump speed under TEE guidance.

After surgery, all patients were admitted to intensive care unit intubated and mechanically ventilated. The same surgical, anesthesia, and intensivist teams were assigned during the perioperative period for all LVAD surgeries. The patients were extubated when they were awake, responsive, and met the universally accepted criteria (respiratory rate < 35 breaths/min, good tolerance to spontaneous breathing trials, heart rate < 140/min or heart rate variability of >20%, arterial oxygen saturation > 90% or PaO2 > 60 mmHg on FiO2 < 0.4, systolic blood pressure >80 mmHg and <180 mmHg or <20% change from baseline, and no signs of increased work of breathing or distress), including metabolic and hemodynamic stability within 24 h of surgery.

PPMV was defined as the inability to wean from the ventilator for more than 24 hours after surgery and/or a total duration on mechanical ventilation more than 24 hours following admission to intensive care unit.

In our study, AKI was determined on the basis of the KDIGO 2012 criteria. AKI is defined as an increase in serum creatinine by 0.3 mg/dl in 48 h or as an increase of serum creatinine 1.5 times or more than baseline or as urine output less than 0.5 ml/kg/h in the first 6 h (6).

Statistical Analysis

SPPS 25 (IBM Corp., released 2017, IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, USA) statistical package program was used for data analysis. The mean, standard deviation, percentage, and frequency values of variables were used. The variables were considered after accounting for normality and homogeneity of variances (Shapiro–Wilk and Levene's test). For data analysis, the independent two-group t-test (Student's t-test) was used for comparison of two groups, and Mann–Whitney U test was used if prerequisites were not met. Categorical data were analyzed by Fisher's exact and chi-square tests. In cases where the expected frequencies were <20%, the Monte Carlo simulation method was used to include these frequencies in the analysis. For all tests, $p < 0.05$ and $p < 0.01$ were considered as significant.

RESULTS

During the study period, a total of 57 patients (mean age 44.6 ±16.1 years) were admitted to ICU and screened. Of these, only 2 were diagnosed with restrictive cardiomyopathy and 55 with dilated cardiomyopathy before implantation. The demographic characteristics and main diagnosis of the patients included in the study are shown in Table 1.

Table 1. Demographic characteristics and main diagnosis of the study population [mean±SD or n (%)]

	n=57(%)
Age (years)	44.616.1
Female	10 (18)
Diagnosis	
Dilated cardiomyopathy	55 (97)
Restrictive cardiomyopathy	2 (3)
Indications for LVAD	
Destination	28 (49)
Bridge to transplantation	22 (39)
Bridge to recovery	2 (4)
Intraoperative complication	5 (8)

The patients were divided into two groups based on the duration of postoperative mechanical ventilation. A total of 26 (46%) patients required PPMV. The mean duration of mechanical ventilation was 120.1±146.6 h for the patients who required PPMV and 19.4 ± 4.8 h for those who did not. The patients who needed PPMV were similar to those

Table 2. Comparison of two groups in terms of demographics and preoperative features [mean±SD or n (%)]

	PPMV (-) (n=31)	PPMV (+) (n=26)	p
Age (years)	45.1±16.0	43.9±16.5	0.770
Female	3 (10)	7 (27)	0.160
Body weight (kg)	69.1±17.3	72.6±17.9	0.450
Height (cm)	168.0±10.8	167.6±11.6	0.920
Ejection fraction (%)	18.6±3.8	23.2±15.7	0.170
TAPSE (mm)	14.5±3.5	13.8±4.1	0.550
Systolic pulmonary artery pressure (mmHg)	52.3±14.9	56.1±13.1	0.380
Preoperative urine output (mL/day)	2095.0±1243.2	1400.8±1181.9	0.210
Use of bronchodilators	0	1 (4)	0.456
Comorbidities	19 (61)	18 (69)	0.532
Diabetes	9 (29)	7 (27)	0.860
Hypertension	8 (26)	11 (42)	0.261
Chronic renal failure	3 (10)	1 (4)	0.617
COPD	2 (6)	3 (12)	0.651
Coronary artery disease	4 (13)	2 (7)	0.523
ICU stay (day)	18	17	0.598
Mechanical ventilation	3 (10)	3 (12)	0.999
Presence of infections	2 (6)	2 (8)	0.855
Antibiotic use	3 (10)	4 (15)	0.691
History of cardiac arrest	3 (10)	2 (7)	0.999
Use of dobutamin	13 (42)	13 (50)	0.600
Use of dopamin	5 (16)	6 (23)	0.738
Use of milrinone	2 (6)	4 (15)	0.396
Use of adrenaline	3 (10)	1 (4)	0.617
Use of noradrenaline	1 (3)	1 (4)	0.999
Intraaortic baloon pump	1 (3)	0	0.999
Extracorporeal membrane oxygenation	2 (6)	5 (19)	0.228
Delirium	3 (10)	4 (15)	0.441
Acute kidney injury	1 (3)	6 (23)	0.039
Renal replacement therapies	4 (13)	6 (23)	0.486

LVAD: Left ventricular assist device, TAPSE: tricuspid annular plane systolic excursion, COPD: Chronic obstructive pulmonary disease

who did not in terms of demographical and preoperative features ($p > 0.05$) (Table 2). Preoperative laboratory values, preoperative vital signs, and intraoperative parameters were also similar between the two groups ($p > 0.05$) (Tables 3 and 4). Preoperative and postoperative serum albumin levels were lower in patients who required PPMV (3.3 ± 0.6 vs. 3.8 ± 0.4, p = 0.012 and 2.9 ± 0.4 vs. 3.3 ± 0.4, p = 0.002, respectively) (Tables 3 and 5), and they also underwent more revision surgeries after LVAD implantation compared with those who did not [14 (54%) vs. 2 (7%), $p < 0.001$] (Table 6). All revisions were due to bleeding. Two patients underwent revision without PPMV and their durations were less than 24 hours, although their durations were longer than those of the other

Table 3. Comparison of two groups in terms preoperative laboratory values and vital signs [mean±SD or n (%)]

	PPMV (-) (n=31)	PPMV (+) (n=26)	p
Preoperative laboratory values			
Hemoglobin (g/dl)	12.3±2.3	11.8±2.1	0.390
White blood cells (1000/mm^3)	8.8±2.9	9.9±4.1	0.240
Platelets (1000/mm^3)	221.2±96.3	210.9±85.8	0.680
AST (U/L)	23.1±11.4	37.1±19.8	0.020
ALT (U/L)	34.0±44.8	60.6±97.7	0.210
Total bilirubin (g/dl)	1.5±0.9	2.2±1.4	0.200
Direct bilirubin (g/dl)	0.5±0.5	0.7±0.5	0.550
Creatinine (mg/dl)	1.1±0.7	1.1±0.4	0.740
BUN (mg/dl)	25.3±12.2	27.7±15.7	0.510
Albumin (g/dl)	3.8±0.4	3.3±0.6*	0.012
Sodium (mmol/L)	134.5±4.2	134.5±5.3	0.988
Potassium (mmol/L)	4.0±0.5	4.0±0.6	0.936
Calcium (mg/dL)	8.7±1.3	8.6±2.4	0.880
Magnesium (mg/dL)	2.1±0.3	2.1±0.4	0.890
Phosphate (mg/dL)	3.8±0.7	3.9±1.2	0.820
Prothrombin time (sec)	15.2±2.6	17.1±3.9	0.060
INR	1.3±0.3	1.4±0.4	0.230
Systolic blood pressure (mmHg)	108.9±14.8	114.2±14.6	0.190
Diastolic blood pressure (mmHg)	70.1±10.9	71.3±9.8	0.658
Heart rate (bpm)	83.6±12.7	88.7±23.3	0.330
Peripheral oxygen saturation (%)	98.5±2.6	95.0±17.5	0.290

AST: Aspartate aminotransferase. ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, INR: International normalized ratio
*p<0.05: Compared to Group PPMV(-)

Table 4. Comparison of two groups in terms of intraoperative features and duration of postoperative mechanical ventilation [mean±SD or n (%)]

	PPMV (-) (n=31)	PPMV (+) (n=26)	p
Duration of surgery (hours)	5.7±1.5	6.2±2.1	0.380
Duration of CPB (min)	136.5±49.8	166.5±61.7	0.060
FFP (unit)	2.0±1.0	2.1±1.5	0.660
Urine output (ml)	678.0±379.5	700.4±729.0	0.890
Highest lactate level (mmol/L)	4.3±3.1	5.1±3.0	0.330
Lowest systolic blood pressure (mmHg)	77.1±14.1	74.3±13.2	0.450
Highest dose of adrenaline (µg/kg/min)	0.5±1.1	0.4±0.7	0.780
Highest dose of noradrenaline (µg/kg/min)	0.1±0.1	0.2±0.3	0.280
Highest dose of dobutamine (µg/kg/min)	8.8±2.7	9.4±3.0	0.480
Highest dose of dopamine (µg/kg/min)	8.3±3.4	8.5±4.1	0.910
Highest dose of terlipressin (mg)	0±0	1.0±0	0.320
Highest dose of milrinone (µg/kg/min)	0.7±0	1.3±1.8	0.930
Duration of mechanical ventilation (hours)	19.4±4.8	120.1±146.6*	0.001

CPB: Cardiopulmonary bypass, PRBC: Packed red blood cells, FFP: Fresh frozen plasma
*p<0.05: Compared to Group PPMV(-)

Table 5. Comparison of two groups in terms of postoperative features [mean±SD or n (%)]			
	PPMV (-) (n=31)	PPMV (+) (n=26)	p
LVAD flow rate (l/min)	4.3±1.0	3.7±1.4	0.880
Ejection fraction (%)	20.0±4.5	24.7±12.3	0.290
TAPSE (mm)	11.6±2.7	10.6±3.3	0.300
Systolic pulmonary artery pressure(mmHg)	40.0±6.3	49.0±7.4	0.060
Postoperative laboratory values			
Hemoglobin (g/dl)	10.4±1.5	9.6±0.9*	0.010
White blood cells (1000/mm3)	13.8±5.1	14.69±6.84	0.590
Platelets (1000/mm3)	546.6±29.6	124.0±52.1	0.360
AST (U/L)	105.8±121.2	68.9±22.5	0.230
ALT (U/L)	37.9±44.7	52.7±94.9	0.450
Creatinine (mg/dl)	1.3±0.8	1.4±0.6	0.560
BUN (mg/dl)	27.4±11.8	29.4±13.4	0.550
Total bilirubin (g/dl)	1.8±1.5	2.8±2.0	0.070
Direct bilirubin (g/dl)	0.8±0.8	1.8±1.8	0.190
Albumin (g/dl)	3.3±0.4	2.9±0.4*	<0.001
Prothrombin time (sec)	16.3±2.8	19.9±5.9*	0.010
INR	1.4±0.3	1.6±0.5	0.040
Sodium (mmol/L)	137.9±3.3	139.3±4.9	0.210
Potasium (mmol/L)	4.0±0.5	4.2±0.7	0.100
Calcium (mg/dL)	8.9±0.3	8.4±2.3	0.430
Magnesium (mg/dL)	6.6±2.3	2.5±0.6	0.340
Phosphate (mg/dL)	3.5±1.5	4.06±2.0	0.260
Highest lactate level (mmol/L)	5.2±3.8	6.2±3.7	0.320
Highest dose of dobutamine (µg//kg/min)	10.0±8.1	10.3±3.5	0.900
Highest dose of dopamin (µg//kg/min)	7.8±5.6	9.7±4.4	0.260
Highest dose of noradrenaline (µg//kg/min)	0.6±1.6	0.19±0.2	0.440
Highest dose of adrenaline (µg//kg/min)	0.7±1.7	0.3±0.3	0.220
Highest dose of terlipressin (mg)	2.6±2.3	2.3±0.9	0.680
Highest dose of milrinone (µg//kg/min)	0.6±0.2	0.6±0.2	0.880
Fluid balance on POD1 (ml)	1776.6±2231.6	2050.2±1357.7	0.600
Fluid balance on POD2 (ml)	709.9±1191.7	1535.9±2001.5	0.090
Fluid balance on POD3 (ml)	-74.4±1086.5	-212.4±1940.2	0.760

LVAD: Left ventricular assist device, TAPSE: tricuspid annular plane systolic excursion, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, INR: International normalized ratio, POD: Postoperative day
*p<0.05: Compared to Group PPMV(-)

patients in the group (19,1+4.8, 22,0+2.8, respectively). Furthermore, preoperative and postoperative acute kidney dysfunction incidences on the first day after implantation were statistically higher in patients who required PPMV [6 (23%) vs. 1 (3%), p = 0.039, 13 (50%) vs. 4 (13%), p = 0.003, respectively)] (Table 2, 6), and they required more frequent renal replacement therapies postoperatively compared with those who did not require PPMV [12 (46%) vs. 5 (16%), p = 0.020]. In patients who had PPMV, postoperative infection incidences were higher [18 (69%) vs. 9 (29%), p = 0.003], intensive care unit stays were longer (30.1± 25.2 vs. 14.0 ± 11.4, p = 0.010), and hospital mortality (58% vs. 35%, p = 0.043) and 30-day mortality (38% vs. 16%, p = 0.042) were significantly higher than those who did not require PPMV (Table 6).

Logistic regression analysis revealed postoperative acute kidney injury as an independent risk factor for PPMV (OR = 0.061, 95% CI 0.004–0.871, p = 0.039) (Table 7).

Table 6. Comparison of two groups in terms of postoperative follow-up and outcomes [median (IQR) or n (%)]

	PPMV (-) (n=31)	PPMV (+) (n=26)	p
AKI	4 (13)	13 (50)*	0.003
Need for RRT	5 (16)	12 (46)*	0.020
Need for ECMO	3 (10)	7 (27)	0.167
Delirium	5 (16)	7 (27)	0.057
Revision surgeries	2 (6)	13 (50)*	0.001
Infections	9 (29)	18 (69)*	0.003
Cardiac arrest	5 (16)	9 (35)	0.131
Length of ICU stay (days)	14.0±11.4	30.1±25.2*	0.010
Length of hospital stay (days)	31.1±18.9	52.0±39.1*	0.020
30-day mortality	5 (16)	10 (38)*	0.042
Mortality	11 (35)	15 (58)*	0.043

AKI: Acute kidney injury. RRT: Renal replacement therapy. ECMO: Extracorporeal membrane oxygenation. ICU: Intensive care unit
***p<0.05: Compared to Group PPMV(-)**

Table 7. Results of Logistic Regression Analysis to Find Risk Factors Associated With postoperative prolonged mechanical ventilation

	Odds Ratio	95% CI	p
AKI	0.061	0.004-0.871*	0.039

AKI: Acute Kidney Injury, CI, confidence intervals
***p<0.05: Compared to Group PPMV(-)**

DISCUSSION

In this retrospective review of 57 LVAD implanted patients over a period of 5 years, the incidence of PPMV was estimated to be 46%. Postoperatively developed acute kidney injury (AKI) was found to be a risk factor for PPMV development. Preoperative and postoperative albumin levels were also found to be remarkably lower in those who required PPMV, in whom the need for renal replacement therapy and incidences of postoperative infection were found to be considerably higher. PPMV was also found to be associated with prolonged intensive care unit stays, increased 30-day mortality, and an increased hospital mortality rate.

The literature contains several publications that reported a range of 3%–20% of adult patients who required PPMV after cardiac surgery.(3,4) In the study by Papathanasiou et al., in which PMV was defined as the need for MV for >7 days after LVAD implantation, the risk factors for PMV after LVAD implantation were investigated, and a PMV incidence of 43% was identified. The authors attributed the higher PMV incidence after LVAD implantation compared with other open-heart surgical approaches to the increased risk profile, cardiorespiratory function interaction, and increased comorbidities in the patient group (7). In this study, we identified a PPMV incidence of 46%, consistent with the above-mentioned study, but we defined PPMV as the need for MV for >24 h. Similarly, we believe that the higher incidence compared with other open-heart surgeries can be attributed to the high-risk patient group, comorbidities, and affected pulmonary functions of the patients. Although the incidences are similar, the duration in the definition of PPMV differed between the two studies, whereas other studies have defined PPMV as the need for MV for 24 h, 48 h, 72 h, and >4 days postoperatively.(3,4,8-10) It has been noted, especially in recent years, that early extubation speeds up the healing process of patients, is associated with shorter intensive care and hospital stays, and reduces hospital costs (11,12). As a common practice at our clinic, we target extubation as soon as possible if there is no contraindication and if the patient meets the universal weaning criteria. Accordingly, we defined PPMV as the need for MV for >24 h in this study.

It is known that AKI incidence after cardiac surgery is >30%, and it is associated with impaired function in the brain, lungs, and intestines and a considerable increase in in-hospital mortality.(13). In a study that investigated PPMV risk factors after open heart surgery, Siddiqui et al. reported that preoperative renal failure was a risk factor for PPMV development (14). In a separate study Filsoufi et al. investigated early and late outcomes of respiratory failure following cardiac surgery and reported that renal failure was more common in patients with respiratory failure and postoperative renal insufficiency is one of the predictors of hospital mortality in this group of patients (15). Parallel to these studies we found that postoperative development of AKI is a risk factor for PPMV development, which we believe is a result of the impaired pulmonary mechanics associated with fluid overload.

Furthermore, it was also found that preoperative and postoperative levels of albumin were remarkably lower in the patients who had PPMV. Previous studies in the literature have identified hypoalbuminemia as an indicator of PPMV in various patient groups, and some of these studies have attributed this to albumin being an indicator of nutritional status and impaired nutrition being associated with poor survival.(16) In contrast, some other studies have attributed this to impaired albumin synthesis after hypercatabolic process and inflammation (17). All the possible causes result in difficulty in weaning. We also believe that the remarkably significant association between albumin and PPMV established in this study may be attributable to such causes.

Consistent with the publications where respiratory failure after cardiac surgery is associated with sepsis we found that incidences of postoperative infection were statistically higher in PPMV-developed patients than in those without PPMV (15). It is known that the most common infection following cardiac surgery is pneumonia and it is associated with mortality (18,19). Hortal et al. reported that the need for mechanical ventilation for more than 48 hours after major cardiac surgery poses a high risk for the development of ventilator-associated pneumonia (19). Similar to these studies, we conclude that this is associated with an increased incidence of pneumonia owing to prolonged MV. We found that the need for renal replacement therapy (RRT) was remarkably higher in patients who required PPMV than those who did not require PPMV. Furthermore, we concluded that antibiotic therapy exacerbates kidney injury, which leads to a greater need for RRT, on top of the effects of infection on the kidneys.

The literature also contains numerous studies that link post-cardiac surgery PPMV to the length of hospital stay, cost, and mortality (15,20). Rajakaruna et al. reported that PPMV increases mortality approximately 20 times (22.2% vs 1.0%) and hospital costs 7 times (21). In line with the literature, it has been established herein that PPMV is associated with prolonged intensive care unit stay, increased 30-day mortality, and increased hospital mortality.The retrospective nature of our study and as we created our data partially based on the available literature, the insufficient number of reports in the literature that detailed PPMV needs in patients after LVAD surgery can be considered the limitations of this study.

Future prospective studies should, therefore, include higher number of patients.

CONCLUSION

In conclusion, almost half of the patients in our cohort required PPMV. Furthermore, postoperative acute kidney dysfunction in the initial days is an independent risk factor for PPMV. Moreover, PPMV is associated with longer duration of stay in the intensive care unit and hospital mortality.

Competing interests: The authors declare that they have no competing interest.

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