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Early Experiences with Ultra-Fast-Track Extubation after Surgery for Congenital Heart Disease at a Single Center

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Background: Early extubation after cardiovascular surgery has some clinical advantages, including reduced hospitalization costs. Herein, we review the results of ultra-fast-track (UFT) extubation, which refers to extubation performed on the operating table just after the operation, or within 1–2 hours after surgery, in patients with congenital cardiac disease. **Methods:** We performed UFT extubation in patients (n=72) with a relatively simple congenital cardiac defect or who underwent a simple operation starting in September 2016. To evaluate the feasibility and effectiveness of our recently introduced UFT extubation strategy, we retrospectively reviewed 195 patients who underwent similar operations for similar diseases from September 2015 to September 2017, including the 1-year periods immediately before and after the introduction of the UFT extubation protocol. Propensity scores were used to assess the effects of UFT extubation on length of stay (LOS) in the intensive care unit (ICU), hospital LOS, and medical costs. **Results:** After propensity-score matching using logistic regression analysis, 47 patients were matched in each group. The mean ICU LOS (16.3±28.6 [UFT] vs. 28.0±16.8 [non-UFT] hours, p=0.018) was significantly shorter in the UFT group. The total medical costs (182.6±3.5 [UFT] vs. 187.1±55.6 [non-UFT] ×100,000 Korean won [KRW], p=0.639) and hospital stay expenses (48.3±13.6 [UFT] vs. 54.8±29.0 [non-UFT] ×100,000 KRW, p=0.164) did not significantly differ between the groups. **Conclusion:** UFT extubation decreased the ICU LOS and mechanical ventilation time, but was not associated with postoperative hospital LOS or medical expenses in patients with simple congenital cardiac disease.

Key words: 1. Congenital heart disease
2. Ultra-fast track
3. Early extubation
4. Medical expenses
5. Intensive care unit length of stay

Introduction

Early extubation after cardiovascular surgery has some clinical advantages, including decreased ventilator-associated morbidity; reduced intrathoracic pressure, which increases systemic and pulmonary venous return and cardiac output; and decreased central venous pressure [1-10]. The costs of hospital-

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ization can be decreased by minimizing intensive care unit (ICU) and hospitalization time [5-7]. Early extubation has been applied in various congenital cardiac surgical procedures, even in pediatric patients, and some authors have reported the results of early extubation, including ultra-fast-track (UFT) extubation (performed on the operating table immediately after the operation or at most 1 or 2 hours after surgery), even in neonates and infants [3,4,11]. Herein, we review the results of our recently introduced early extubation strategy in patients with congenital cardiac disease.

Methods

1) Patients and indications for ultra-fast-track extubation

We started our UFT strategy in September 2016 for patients with congenital cardiac defects who underwent relatively simple procedures, such as atrial septal defect (ASD) or ventricular septal defect (VSD) closure and pulmonary valve replacement after total correction of tetralogy of Fallot. We considered all patients who had ASD or VSD to be candidates for UFT extubation unless they showed severe pulmonary hypertension or left ventricular dysfunction preoperatively. We abandoned the UFT strategy if intraoperative transesophageal echocardiography just after weaning from cardiopulmonary bypass (CPB) showed significantly impaired ventricular function, severe pulmonary hypertension, or other abnormal findings that required sedation in the immediate postoperative period. We tried to apply minimally invasive cardiac surgery in potential candidates for UFT extubation, using a small skin incision with a partial sternotomy. As a result, 72 patients received UFT extubation. However, because of miscommunications between the medical staff in the operating room and the ICU or other non-medical reasons (for example, patients from abroad), 3 patients were extubated or discharged late even if their clinical status was stable enough for the UFT strategy; therefore, a total of 69 patients were included in the UFT group. To investigate the clinical outcomes and financial impacts of our UFT strategy, we reviewed patients who underwent similar cardiac operations in the previous year before the UFT strategy was initiated. From September 2015 to August 2016, 126 such patients were found, and were classified as the non-UFT group.

2) Anesthesia and cardiopulmonary bypass protocol

The anesthesia protocol during congenital cardiac surgery changed since our introduction of UFT extubation in both non-UFT patients and UFT patients. The induction protocol was not changed, and included atropine (0.02 mg/kg), sodium thiopental (5 mg/kg), midazolam (0.1 mg/kg), rocuronium (1.2 mg/kg) and fentanyl (1–2 μg/kg) in both groups. The maintenance drugs were changed from midazolam (0.1–0.2 mg/kg/hr), sufentanil (2.5–5.0 μg/kg/hr), and vecuronium (0.1–0.2 mg/kg/hr) to remifentanil (0.02 μg/kg/min), rocuronium (0.2 mg/kg/hr), and sevoflurane (the concentration of which was adjusted according to a bi-spectral monitoring system [BIS, A-3000; Covidien, Singapore]) in both the UFT and non-UFT groups. When CPB began, additional midazolam (0.1 mg/kg) and rocuronium (0.6 mg/kg) was administered in both groups. When CPB was removed, the maintenance drugs were continued in the non-UFT group, while rocuronium was discontinued and remifentanil was tapered to a half-dose in the UFT group. At the end of surgery, sevoflurane was discontinued, and remifentanil and rocuronium were maintained in the non-UFT group. In the UFT group, remifentanil was discontinued and sugammadex (2 mg/kg) was administered, followed by on-table extubation or ICU transfer. In the UFT group, a nerve stimulator was also applied to check the patient's sedation status at the end of surgery. Some patients were extubated in the ICU rather than the operating room, even if the patient's status would have permitted on-table extubation, as dictated by the operating room schedule.

Two types of cardioplegic solution were used for cardiac arrest: Del Nido cardioplegia (600 mL×body surface area [BSA]) and histidine-tryptophan-ketoglutarate (HTK, Custodiol [Dr. Franz Köhler Chemie GmbH, Germany]; 50 mL×body weight). Hematocrit was maintained above 30% during the operation. During CPB, the rectal temperature was lowered to 32°C–33°C in patients undergoing ASD repair, and to 29°C–30°C in patients undergoing VSD repair. After weaning from CPB, modified ultrafiltration (flow $<$20 mL/min) was conducted.

Table 1. Preoperative characteristics of the patients

Characteristic	Unmatched				Matched			
	UFT (n=69)	Non-UFT (n=126)	p-value	D	UFT (n=47)	Non-UFT (n=47)	p-value	D
Sex (male)	33 (47.8)	64 (50.8)	0.692	0.0655	23 (48.9)	21 (44.7)	0.679	0.0943
Age (mo)	47.8±64.7	21.1±53.3	<0.001	0.5005	35.8±53.6	28.8±36.3	0.459	0.2179
Weight (kg)	18.2±21.9	9.2±6.2	<0.001	0.5005	13.3±9.5	11.5±7.9	0.316	0.2958
Height (cm)	92.9±27.3	73.8±20.4	<0.001	0.5005	87.8±21.7	82.8±21.7	0.264	0.3300
Body surface area	0.637±0.362	0.427±0.207	<0.001	0.5005	0.560±0.251	0.506±0.229	0.278	0.3203
Diagnosis			<0.001				0.027	
VSD	38 (55.1)	22 (17.5)			24 (51.1)	17 (36.2)		
ASD	19 (27.5)	38 (30.2)			13 (27.7)	8 (17.0)		
VSD+ASD	4 (5.8)	36 (23.8)			4 (8.5)	10 (21.3)		
Others	8 (11.6)	30 (23.8)			6 (12.8)	12 (25.5)		
Pulmonary hypertension	1 (1.4)	16 (12.7)	0.008	1.2634	1 (2.1)	3 (6.4)	0.617	0.6302
Extracardiac anomalies	1 (1.4)	5 (4.0)	0.426	0.5696	0	1 (2.1)	>0.999	
Operating time (min)	200.7±92.7	238.4±49.1	<0.001	0.5005	208.7±59.3	213.6±45.8	0.610	0.1499
CPB time (min)	89.5±33.2	109.4±30.8	<0.001	0.5005	94.8±34.6	96.8±29.3	0.763	0.0885
Aortic cross-clamp time (min)	48.4±25.7	62.9±23.2	<0.001	0.5005	55.6±23.6	55.9±22.6	0.961	0.0143
CPB volume (mL)								
Priming volume	540.4±516.9	259.9±244.4	<0.001	0.5005	398.3±310.7	331.1±279.0	0.273	0.3237
Cardioplegia volume	473.6±407.4	310.0±215.4	<0.001	0.5005	432.1±252.3	374.9±274.5	0.295	0.3091
Additional blood	26.2±40.0	36.9±37.8	0.066	0.2769	22.6±25.8	26.8±23.9	0.409	0.2431
Input/output balance	−180.4±183.3	−136.3±105.4	0.010	0.3896	−182.7±140.7	−173.6±142.0	0.757	0.0908

Value are presented as number (%) or mean±standard deviation.
UFT, ultra-fast-track; D, standardized difference; VSD, ventricular septal defect; ASD, atrial septal defect; CPB time, cardiopulmonary bypass time.

3) Analysis and ethics

The preoperative variables were age, sex, body weight, height, BSA, underlying pulmonary hypertension, and congenital extracardiac anomalies. Intraoperative variables included CPB time, aortic cross-clamp (ACC) time, priming volume, infused cardioplegia volume, volume of additionally transfused blood, and intraoperative fluid balance. The Student t-test and Mann-Whitney test were used to compare continuous variables. The chi-square test and Fisher exact test were used to compare categorical variables. The logistic regression model of IBM SPSS (IBM Corp., Armonk, NY, USA), including preoperative and intraoperative variables, was used to estimate the propensity score for UFT. A nearest-neighbor matching algorithm was used for matching. All statistical analyses were conducted using IBM SPSS ver. 23.0 (IBM Corp.).

The primary outcome was the association of UFT extubation with medical expenses. Costs were divided into total medical expenses, costs related to the surgical procedure (for the operation, for anesthesia, and for routine postoperative studies), and hospitalization costs, excluding costs related to the surgical procedure. The secondary outcome was the association of UFT extubation with length of stay (LOS) and clinical outcomes, including mechanical ventilator-related complications. This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB approval no., 1711-005-895).

Results

1) Patients' characteristics

The UFT and non-UFT groups included 69 and 126 patients, respectively. In the non-UFT group, extubation was performed based on the patient's condition without any special extubation protocol. In the UFT group, 38 patients (55.1%) had ASD, 19 (27.5%) had VSD, and 4 had combined ASD and VSD. The others (n=8, 11.6%) had various diseases (ASD or VSD combined with right ventricular outflow-track

obstruction [RVOTO], partial anomalous pulmonary vein return, mitral regurgitation, tricuspid regurgitation, partial atrioventricular septal defect, pulmonary regurgitation, or cardiac mass in the right atrium). In the non-UFT group, 22 patients (17.5%) had ASD, 38 (30.2%) had VSD, and 36 (23.8%) had combined ASD and VSD. The other patients (n=30, 23.8%) had ASD or VSD combined with valvular heart disease or RVOTO (Table 1).

The patients in the UFT group (47.8±64.7 months) were significantly older than those in the non-UFT group (21.1±53.3 months, $p<0.001$). The body weight of the patients in the UFT group (18.2±22.0 kg) was greater than that of the patients in the non-UFT group (9.2±6.2 kg, $p<0.001$). The mean duration of the operation (200.7±92.7 [UFT] versus 238.4±49.1 [non-UFT] minutes, $p<0.001$), CPB time (89.5±33.2 [UFT] versus 109.4±30.8 [non-UFT] minutes, $p<0.001$), and ACC time (48.4±25.7 [UFT] versus 62.9±23.2 [non-UFT] minutes, $p<0.001$) were significantly shorter in the UFT group (Table 1).

2) Clinical results and economic issues after propensity-score matching

Forty-seven patients were matched in each group via propensity-score matching with a logistic regression model. A statistically significant difference in the diagnosis remained despite propensity-score matching, but the other variables showed no significant differences (Table 1). There were no significant differences in postoperative complications, including pneumonia, lung complications other than pneumonia (atelectasis, a large amount of secretions requiring frequent nasotracheal suction, and prolonged mechanical ventilation), re-intubation, re-operation, and postoperative bleeding, between the 2 groups. The incidence of postoperative complications was low in both groups. Arrhythmic events, such as junctional ectopic tachycardia (JET) and temporary atrioventricular conduction block, were the most common complications. Patients who had JET had a significantly longer duration of mechanical ventilator support, ICU stay, and hospitalization (Table 2). The mean duration of mechanical ventilator support (50.2±110.7 [UFT] versus 716.3±697.2 [non-UFT] minutes, $p<0.001$) and ICU LOS (16.3±28.6 [UFT] versus 28.0±16.7 [non-UFT] hours, p=0.01) were significantly longer in the non-UFT group. However, the mean duration of hospital stay after the operation (5.0±2.2 [UFT] versus 5.6±3.1 [non-UFT] days, p=0.303), the mean total hospital expenses (182.6±35.5 [UFT] versus 187.1±55.6 [non-UFT] ×100,000 Korean won [KRW], p=0.639), mean surgery-related costs (132.3±31.5 [UFT] versus 134.3±26.3 [non-UFT] ×100,000 KRW, p=0.737), and costs for the hospital stay (48.3±13.6 [UFT] versus 54.8±29.0 [non-UFT] ×100,000 KRW, p=0.164) did not show significant differences between the groups (Table 3).

Table 2. Postoperative complications

Variable	UFT (n=69)	Non-UFT (n=126)	p-value
Pneumonia	0	0	>0.999
Lung complications[a)]	0	6 (3.9)	0.091
Bleeding	2 (2.9)	0	0.124
Re-intubation	1 (1.4)	1 (0.8)	>0.999
Re-operation	2 (2.9)	1 (0.8)	0.286
Postpericardiotomy syndrome	2 (2.9)	2 (1.6)	0.615
Arrhythmia	5 (7.2)	4 (3.2)	0.284
Heart failure	1 (1.4)	2 (1.6)	>0.999
Seizure	1 (1.4)	1 (0.8)	>0.999
Wound problem	1 (1.4)	1 (0.8)	>0.999
Minor complications	0	5 (4.0)	0.163

Value are presented as number (%)
UFT, ultra-fast-track.
[a)]Any lung complication, including atelectasis, a large amount of secretions requiring frequent nasotracheal suction, or prolonged intubation.

Discussion

The indications for early extubation in pediatric cardiac surgery have gradually expanded [1-4,12-14]. Predictive factors of successful early extubation include older age, greater body weight, shorter CPB time, and the absence of pulmonary hypertension [7,10,11, 15,16]. Thus, some authors have suggested that preoperative pulmonary hypertension should be considered to be a contraindication for early extubation [16-19]. Some authors recommended against early extubation in neonates due to the relatively horizontal alignment of the ribs, weak intercostal muscles, narrow subglottic portion, and post-anesthetic apnea [18,20]. We found that younger age was associated with an increased duration of ventilator use. However, some studies in neonates showed a 20%–50% probability of successful early extubation [3,4,11]. The mean

Table 3. Outcomes associated with UFT

Variable	Unmatched				Matched			
	UFT (n=69)	Non-UFT (n=126)	p-value	D	UFT (n=47)	Non-UFT (n=47)	p-value	D
Extubation time (min)	40.4±92.7	1259.6±1209.7	<0.001	0.5005	50.2±110.7	716.3±697.2	<0.001	1.027
Intensive care unit LOS (hr)	14.7±24.0	45.8±33.6	<0.001	0.5005	16.3±28.6	28.0±16.8	0.018	0.7163
Hospital LOS (day)	4.8±2.0	6.8±3.2	<0.001	0.5005	5.0±2.2	5.6±3.1	0.303	0.304
Medical costs (×100,000 Korean won)								
Total	175.9±33.0	208.8±45.3	<0.001	0.5005	182.6±35.5	187.1±55.6	0.639	0.1378
Surgery	128.8±24.7	149.3±30.0	<0.001	0.5005	132.3±31.5	134.3±26.3	0.737	0.0986
Hospital stay	47.2±13.6	59.5±21.5	<0.001	0.5005	48.3±13.6	54.8±29.0	0.164	0.4127

Value are presented as mean±standard deviation.
UFT, ultra-fast-track; D, standardized difference; LOS, length of stay.

duration of mechanical ventilator support in patients without severe pulmonary hypertension was 22.1 hours, and these patients were mostly extubated within 24 hours, unlike patients with severe pulmonary hypertension. Two patients were extubated 3 hours after surgery despite showing severe pulmonary hypertension in preoperative studies. A multidisciplinary approach is important when deciding to perform UFT extubation, rather than perioperative predictors alone. This will increase its success.

In our study, 27 patients (39.1%) in the UFT group were extubated in the ICU. Of these, 6 patients could not be extubated within 1 hour; however, all of them were extubated within 6 hours (included in the early extubation criteria according to the previous literature). The most common reason for extubation in the ICU rather than the operating room was to free the operating room for another case, except for 3 patients who showed arrhythmia, atrioventricular block, and insufficiently regressed pulmonary hypertensive status after corrective surgery, or unstable vital signs during CPB weaning. The anesthesia protocols for the UFT strategy changed during this study and were modified to make UFT extubation more effective and safer. Our most recent experiences with UFT extubation were successful in terms of timing, which may have been due to the modification of the anesthesia protocol; as such, the success rate will likely be even higher in the future.

The re-intubation rate has been reported to be 1%–11% in the literature, with the rate primarily depending on the underlying congenital cardiac disease [1,3,10,20]. In our study, the re-intubation rate was extremely low in both groups (1.4% in the UFT group, 0.8% in the non-UFT group). This is because we only performed UFT extubation in patients with relatively simple congenital heart disease or who underwent relatively simple cardiac procedures. The main reasons for re-intubation were the need for deep sedation due to postoperative bleeding control and re-operation, rather than respiratory or pulmonary problems. This result is in accordance with those of previous studies of the relationship between simple congenital cardiac anomalies and early extubation.

Some centers have attempted early extubation even in patients with complex congenital cardiac anomalies [7,9,12-14]; however, the success rate of early extubation in such cases was low, and the re-intubation rate was high [10]. We did not aggressively apply our UFT extubation strategy in patients who required complex cardiac procedures or who had a history of repeated cardiac operations. Nevertheless, we plan to expand the indications for UFT extubation to include patients with a history of repeated cardiac operations or who need complicated procedures. Since the patient's own respiration induces adequate negative intrathoracic cavity pressure, which decreases central venous pressure and improves cardiac output, early extubation has many advantages, especially in patients who undergo a bidirectional cavopulmonary connection (BCPC) or the Fontan procedure. Therefore, we plan to apply our UFT strategy to single-ventricle patients who undergo BCPC or the Fontan procedure, in addition to patients who undergo surgery to treat relatively simple congenital cardiac defects. In this study, several intraoperative factors, including CPB time, ACC time,

transfused blood volume, and input/output balance, did not show a significant relationship with successful UFT extubation. However, if we apply the UFT strategy to more complicated cases, these intraoperative factors seem likely to affect the success rate. Simplifying the operative procedure, shortening the operative time, and ensuring a multidisciplinary and safety-oriented approach are necessary to establish the indications for UFT extubation more securely.

After propensity-score matching, only ICU LOS was significantly different between the groups. We showed no clinical advantages of early extubation (in terms of ventilator-associated problems, low-dose inotropic support, hemodynamic benefits, and so on) because the mechanical ventilator support time was short in these patients with simple congenital cardiac disease. Such patients have been described in previous studies [1,3,5,12,13]. Because of the significantly lower cost of hospitalization and medical care in Korea relative to other countries, the total cost of hospitalization was not significantly different between the groups. However, the UFT extubation strategy could significantly shorten the ICU stay. This allows these young patients to be with their parents earlier. We could not evaluate the psychological benefits to the patients and their parents due to the reduction in ICU time by early extubation; however, our unofficial survey of parents showed satisfactory responses.

This study has some limitations. This study was a single-center retrospective study. The diagnoses were slightly different between the UFT and non-UFT groups, and this difference was not satisfactorily controlled after propensity-score matching. The indications for early extubation were limited because our UFT extubation strategy is new. During the study period, a surgeon new to our institution started to apply minimally invasive cardiac surgery more aggressively than before. This may have also affected the results.

In conclusion, UFT extubation decreased the ICU LOS and the duration of mechanical ventilation support. However, UFT extubation was not associated with postoperative hospital LOS or medical expenses in patients with simple congenital cardiac disease. Future work will expand the indications of UFT extubation to include patients who have undergone repeated prior cardiac operations or who have complex heart disease.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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