The long term survival of successfully weaned prolonged mechanical ventilation patients

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Research

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Abstract

Background Over six years, five hundred and seventy-four patients were admitted to the respiratory care center. Three hundred and ninety-one patients were successfully weaned from the ventilator. How is the long term outcome of these successfully weaned prolonged mechanical ventilation patients? Very few articles were discussing the long term outcome of successfully weaned prolonged mechanical ventilation patients. We will explore this issue in-depth in this article.

Methods We analyzed retrospective data from successfully weaned prolonged mechanical ventilation patients to investigate the clinical variables, discharged status, long term survival, the cause of death, end-of-life decisions.

Results We can further gather long term follow-up data on 243 patients. The factors between patients who died in the ward and those who survived ≥1 year revealed the poorer survival of patients who died in the ward was due to a higher percentage of end-stage renal disease comorbidity, a higher percentage of malignant comorbidity, higher percentage of ≥ four comorbidities and a higher percentage of signed do-not-resuscitate / do-not-intubate orders. The factors between patients who survived <1 year and those who survived ≥1 year revealed the poorer survival of patients who survived <1 year was due to older age, a higher percentage of signed do-not-resuscitate / do-not-intubate orders. That 81 patients (33.3%) who signed a do-not-resuscitate / do-not-intubate orders, indicates that, at most, 66.7% of survivors were willing to receive mechanical ventilation again.

Conclusion The end-of-life decision (signed do-not-resuscitate / do-not-intubate orders) is one of the major influence factors of long term survival of successfully weaned prolonged mechanical ventilation patients. In all, 81 patients (33.3%) in our study signed do-not-resuscitate / do-not-intubate orders, meaning that, at most, 66.7% of survivors were willing to receive mechanical ventilation again.

Introduction

The "Trial Plan for National Public Health Insurance Ventilator Dependent Patients Comprehensive Care System" began in Taiwan in July 2000 [1]. After several revisions, this program covers mechanical ventilator care in the following settings: intensive care unit (acute stage, ≤ 21 days), Respiratory Care Center (RCC) (a subacute stage for weaning training, ≤ 42 days), respiratory care ward (RCW) (a chronic phase or long-term care), and home care service (a stable period during which the patient is cared for by family caregivers or by nursing home nurses). We retrospectively studied 574 RCC patients and reported in 2019 the comprehensive clinical experience of prolonged mechanical ventilation (PMV) patients [2]. From these, we were able to further gather long term follow-up data on 243 successfully weaned PMV patients up to 31 December 2018. The goal of this study was to determine the factors associated with survival in these patients.

Methods

We retrospective studied the medical records of patients admitted to the RCC of Dalin Tzu Chi Hospital for six years, from January 2012 to December 2017. Patients were included who received PMV ≥ 21 days, and patients were eligible for RCC admission if they met the Taiwan National Health Insurance requirements: (a) hemodynamic stability; (b) no vasoactive drug infusion needed; (c) stable oxygen condition (O2 saturation ⩾ 90% or PaO2 ⩾ 60 mmHg) with the requirement fraction of inspired oxygen less than 40% and positive end-expiratory pressure less than10 cm H2O; (d) no critical acute hepatic or renal failure; (e) no massive upper gastrointestinal bleeding; (f) no requirement for surgical intervention within the ensuing 2 weeks

or no large open surgical wound; (g) no uncontrolled severe infectious diseases; (h) no life-threatening arrhythmia. We collected data on all patients successfully weaned from the ventilator, including age, gender, comorbidities, cause of respiratory failure, cause of death, long term survival, and end-of-life decisions. We also studied the factors affecting the long term survival of these patients.

Definition of outcomes

A PMV patient was defined as one using a mechanical ventilator for at least six hours daily for ≥ 21 consecutive days [3]. Successful weaning was defined as the patient being independent from the invasive ventilator for five consecutive days and nights. These patients were transferred to the ward for further care. Three groups of successfully weaned PMV patients were studied in this article. Group1: patients died in the ward (ward mortality patients) before they discharged from the hospital. Group 2: patient was discharged from the hospital and they survived less than 1 year. Group3: patient was discharged from the hospital and they survived more than 1 year, including surviving patients.

The causes of acute respiratory failure requiring PMV

We classified patients who required PMV into 11 categories according to the cause of acute respiratory failure leading to the need for PMV. The categories were: (1) pneumonia, (2) intracranial hemorrhage (ICH), (3) sepsis, (4) postoperative condition, (5) chronic obstructive pulmonary disease (COPD), (6) cardiac disease (including decompensated heart failure, coronary atherosclerotic disease, and acute myocardial infarction), (7) underlying malignancy, (8) cervical spine diseases, (9) post cardiopulmonary-cerebral resuscitation (CPCR) hypoxic encephalopathy, (10) cerebral infarction, and (11) miscellaneous causes.

Comorbidities

The number of comorbidities was assessed. These included: cardiovascular disease (such as essential hypertension, decompensated heart failure, coronary atherosclerotic disease, acute myocardial infarction), chronic lung disease (such as COPD, asthma, bronchiectasis, interstitial lung disease), chronic kidney disease (CKD) (not requiring dialysis), end-stage renal disease (ESRD) (requiring dialysis before admission), neurologic disease (such as bed-ridden stroke survivors, or those with dementia or parkinsonism), chronic liver disease (such as chronic hepatitis, liver cirrhosis), metabolic disease (such as

diabetes mellitus or other endocrine disorders requiring treatment), malignant diseases, and miscellaneous diseases.

End-of-life decisions:

For every patient who successfully liberated from the ventilator in the RCC, we would discuss with patient's family before endotracheal tube extubation for patient about whether patient receives endotracheal tube intubation and uses an invasive ventilator again. If patient's family do not want patient to receives endotracheal tube intubation again. Patient's family will sign do-not-resuscitate (DNR) and do-not-intubate (DNI) order for patient.

Ethics approval and consent to participate:

Our study is not a prospective clinical trial and is a retrospective medical records data collection and analysis. The possibility and severity of injury or discomfort are not higher than in daily life, routine physical examination, or psychological test. The legal biological database cannot identify a specific individual. It cannot identify the particular individual's data, files, documents, information, or samples for research. The study is the lowest risk, and the possible risk to the research subject does not exceed the non-participating researchers, and exemption from prior consent does not affect the rights of the researcher. Research risk does not exceed minimal risk. Exempt informed consent does not affect the subject right and well-being. Research cannot be performed without exempting informed consent. The project approved by the Buddhist Dalin Tzu Chi general hospital research ethics committee (Approved IRB No.: B10802009).

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median, whereas categorical variables were expressed as frequencies and percentages. The differences in baseline characteristics, causes of respiratory failure, and comorbidities were evaluated using the Student's t-test for continuous variables and Pearson chi-square tests for categorical variables. Univariate analysis was used to analyze the association of each variable among three patient groups (ward mortality patients, < 1-year survival patients, and ≥ 1-year survival patients). Multivariate stepwise logistic regression models were used to assess the impact of each variable on three patient groups. All statistical analyses were conducted using the statistical package SPSS for Windows (Version 17.0, SPSS, Inc., Chicago, IL), and a P value < 0.05 was considered to show statistical significance.

Results:

Over six years, 574 patients were admitted to the RCC. Of these, 428 patients (74.6%) were older than 65 years, 357 (62.2%) were men, and 217 (37.8%) were women. Three hundred and ninety-one patients (68.1%) were successfully weaned from the ventilator, including 242 males and 149 females. We can further gather long term follow-up data on 243 patients (62.1%) that were successfully weaned PMV patients. Of the 243 PMV patients who were successfully weaned, 86 died in the ward before being

discharged, 78 survived < 1 year, and 79 survived ≥ 1 year, as of December 31, 2018. The 1-year survival rate of successfully weaned PMV patients was 32.5%. Table 1 shows the clinical variables of all three groups of successfully weaned PMV patients. The mean age was significantly different between patients who died in the ward and those who survived < 1 year (73.95 vs. 78.04 years, P = 0.020). The mean age was also significantly different between patients who died in the ward and those who survived ≥ 1 year (73.95 vs. 66.80 years, P = 0.001). The mean age was significantly different between patients who survived < 1 year and ≥ 1 year (78.04 vs. 66.80 years, P < 0.001). Table 2 shows the causes of death in patients who died in the ward and those who survived < 1 year. Pneumonia was the most frequent cause of death in patients who died in the ward and patients who survived < 1 year (44 patients and 39 patients, respectively). The next most common cause of death was respiratory failure in patients who died in the ward (15 patients) and outside hospital cardiac arrest (OHCA) in patients who survived < 1 year (13 patients).

Table 1

Comparison of clinical variables among successfully weaned prolonged mechanical ventilation patients.

	< 1-year survival (N = 78)	≥ 1-year survival (N = 79)	Died in ward (N = 86)
Age groups (years), No (%)	0	4	3
< 45, No (%)	2	12	6
45–54, No (%)	5	17	7
55–64, No (%)	19	18	20
65–74, No (%)	29	21	36
75–84, No (%)	23	7	14
≥ 85, No (%)	39	27	30
Causes of respiratory failure leading to	9	22	20
need for PMV	6	5	10
pneumonia	4	3	2
ICH	6	2	6
sepsis	2	0	3
COPD	5	7	3
Cardiac disease	1	2	0
malignant patients	0	2	2
Post-operation	0	3	3
Cervical spine diseases	6	6	7
Post-CPCR	57	44	58
Cerebral infarction	19	17	13
miscellaneous causes	12	4	16
Comorbidity	6	3	12
cardiovascular disease, No (%)	29	23	27
chronic lung disease, No (%)	30	25	40
chronic kidney disease, No (%)	9	6	16
end-stage renal disease, No (%)	4	16	4
neurologic disease, No (%)	15	18	24
metabolic disease, No (%)	28	24	28
malignant diseases, No (%)	21	19	14
No comorbidity	10	2	16
one comorbidity			
two comorbidities			
three comorbidities			
4 + comorbidities			

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Table 2
The causes of death in patients who died in the ward and patients who survived < 1 year, between successfully weaned prolonged mechanical ventilation patients.

Cause of death	Died in the ward (%)	Died within a year (%)
Pneumonia	44 (51.2%)	36 (46.2%)
sepsis	8	9 (11.5%)
Cardiogenic shock	2	3
Respiratory failure	15 (17.4%)	0
Malignant diseases	8	5
Renal failure	3	3
COPD	4	8
Miscellaneous causes	2	14#
Total	86 (100%)	78 (100%)
# includes 13 (16.7%) who died of cardiac arrest outside the hospital		

We explored the end-of-life decisions, including do-not-resuscitate and do-not-intubate orders, for all 243 patients or the patient's surrogates (Table 3). By far, a higher percentage of those who survived ≥ 1 year did not sign DNR/DNI orders (55.7%) compared to those who died in the ward (11.6%) or who died within one year (15.4%).

Table 3
The end-of-life decisions of successfully weaned prolonged mechanical ventilation patients according to survival.

	Died in the ward (N = 86)	Survival < 1 year (N = 78)	Survival ≥ 1 year (n = 79)	Total patients (N = 243)
Signed DNR	76 (88.4%)	66 (84.6%)	35 (44.3%)	177 (72.8%)
Signed DNR/ DNI	60 (69.8%)	19 (24.4%)	2 (2.5%)	81 (33.3%)

Univariate analysis and multivariate analysis of the differences in clinical variables and end-of-life decisions between patients who died in the ward and those who survived ≥ 1-year patients are shown in Table 4. The statistically significant variables, in multivariate analysis, were signing DNR/ DNI, having ESRD, having malignant comorbidity and 4 + comorbidities.

Table 4

The difference in clinical variables and end-of-life decisions between patients who died in the ward and those who survived ≥ 1 year

	odds ratios	95% confidence	P
Univariate analysis	0.415	0.221–0.777	0.006
Age ≥ 75 years	0.233	0.074–0.732	0.013
CKD comorbidity	0.243	0.066–0.898	0.034
ESRD comorbidity	0.360	0.133–0.972	0.044
Malignancy comorbidity	5.266	1.659–16.341	0.005
No comorbidity	0.114	0.025–0.512	0.005
4 + comorbidities	0.110	0.003–0.049	< 0.001
Sign DNR/ DNI	0.009	0.002–0.043	< 0.001
Multivariate analysis	0.125	0.024–0.658	0.014
Sign DNR/ DNI	0.219	0.049-0;983	0.047
ESRD comorbidity	0.139	0.022–0.880	0.036
Malignant comorbidity			
4 + comorbidities			

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Univariate and multivariate analysis of the difference in clinical variables and end-of-life decisions between patients who survived < 1 year and ≥ 1 year is shown in Table 5. The statistically significant variables, in multivariate analysis, were signing DNR/ DNI and age ≥ 75 years.

Table 5

The difference in clinical variables and end-of-life decisions between patients who survived < 1 year and those who survived ≥ 1 year.

	odds ratios	95% confidence	P
Univariate analysis	0.275	0.142–0.531	< 0.001
Age ≥ 75 years	0.239	0.090–0.954	0.041
CKD	4.698	1.494–14.799	0.008
No comorbidity	0.177	0.037–0.835	0.029
4 + comorbidities	0.081	0.018–0.360	0.001
Sign DNR/ DNI	0.293	0.131–0.655	0.003
Multivariate analysis	0.093	0.018–0.468	0.004
Age ≥ 75 years			
Sign DNR/ DNI			

Multivariate analysis of the clinical variables of patients and end-of-life decisions who died in the ward and those who survived < 1 year showed only signing DNR/ DNI orders was significantly different between the two groups (P < 0.001, OR = 0.112, 95% confidence interval: 0.052–0.240).

Disussion:

Many articles have discussed the factors affecting the successful weaning rate of PMV patients [2, 4–11]. The successfully weaned rate ranges from 32.3–68.1%. In Damuth reports, only 50% were successfully liberated from mechanical ventilation [12]. The many predictors of successful weaning

include cause of leading patient to need for PMV, blood urea nitrogen levels, APACHE II score, albumin level, and the number of comorbidities. Many articles also discuss the factors related to 1-year survival in PMV patients. The 1-year survival rate of PMV patients also ranges widely, from about 24.3–61% [2, 5, 13–20]. The many factors related to 1-year survival include successful weaning from the ventilator, age, comorbidity, APACHE II score, thrombocytopenia, and the need for vasopressors. The literature demonstrates that being weaned from mechanical ventilation is a key factor in the long term outcomes of PMV patients. Although several studies of the PMV successful weaning rate and 1-year survival rate have been published, they vary in their definition of PMV and in their definition of the discharge status of successfully weaned PMV patients. Besides, PMV patients are admitted to weaning centers in western countries, and those successfully weaned PMV patients are immediately discharged; thus, none of these patients die in the ward. Our RCC is a weaning unit in an acute care hospital. Many PMV patients were successfully liberated from the ventilator in the RCC, then transferred to the ward, only to die before being discharged. To our knowledge, no studies have yet included successfully weaned PMV patients who died in the ward, nor did we find any article in the international literature that addressed long term survival in successfully weaned PMV patients. Therefore, in the discussion, we can analyze only our research results, and cannot compare these with results from other institutions.

Factors affecting survival in successfully weaned PMV patients who died in the ward

The outcome of patients who died in the ward was the worst in the three groups of successfully weaned PMV patients. The most common cause of death in patients who died in the ward was pneumonia (44 patients), followed by respiratory failure. When patients suffer from pneumonia or impending respiratory failure, they may need ventilator support again. Because the patients or their surrogates signed DNR/ DNI orders, these patients received no additional critical care or ventilator support, and they expired before they were discharged from the hospital.

The multivariate analysis of clinical variables and end-of-life decisions between patients who died in the ward and those who survived < 1 year showed that only signing DNR/ DNI orders was significantly different between the two groups. Signing DNR/ DNI orders is the key factor in the worse survival of patients who died in the ward compared to those who survived < 1 year.

The multivariate analysis of clinical variables between patients who died in the ward and those who survived ≥ 1 year revealed the poorer survival of patients who died in the ward was due to a higher percentage of ESRD comorbidity (13.9%) and a higher percentage of malignant comorbidity (18.6%) and higher percentage of ⩾ Four comorbidities (18.6%). As above, another factor in poorer survival was the higher percentage of signed DNR/ DNI orders in patients who died in the ward than in those who survived ≥ 1 year.

Factors affecting survival in successfully weaned PMV patients who survival < 1 year

The most common cause of death in patients who survived less than one year was pneumonia (39 patients), followed by OHCA at home. We could not trace the cause of OHCA but considered that sudden respiratory failure might have been a common cause.

The multivariate analysis of clinical variables of poor survival in survived less than one-year patients that were associated with two factors. One was age; patients who survived < 1 year were older than those who survived longer. Of those who survived < 1 year, 66.7% were older than 75 years, compared to only 35.4% of those who survived ≥ 1 year. Another factor is end-of-life decision (signed DNR/ DNI orders) was significantly different between successfully weaned PMV patients who survived < 1 year and those who survived ≥ 1 year.

End-of-life decisions in successfully weaned PMV patients

In our study, 177 patients (72.8%) signed the DNR order, including 81 patients (33.3%) who signed DRN and DNI orders. This result means that, at most, 66.7% of the survivors were willing to receive mechanical ventilation again. In Jubran's series, 84.7% of survivors indicated a willingness to undergo mechanical ventilation again [21]. Our patients were less willing to receive second mechanical ventilation than were Jubran's patients.

Do we need to improve the survival outcome of successfully weaned PMV patients who died in the ward?

Patients in our series displayed an excellent successful weaning rate (68.1%) but an abysmal 1-year survival rate (24.3%), and we inferred this abysmal 1-year survival rate resulted from our high ward mortality. Only 305 successfully weaned PMV patients were discharged. Fully 86 (22.0%) patients died before they were discharged from the hospital. Being successfully weaned did not substantially help these patients. Fully 69.8% of the ward mortality patients signed DNR and DNI orders. Why did patients' families sign DNR/ DNI orders for these patients? Despite being successfully weaned from the mechanical ventilator, patients experienced suffering in their critical care with PMV support. This experience is a very shocking and painful one for patients. The patients are in poor health status or unconscious in the ward after successful weaning and cannot recover in the short term. Patients' families do not want their loved ones to go through that experience again. They believed that palliative therapy was a greater benefit for these patients. We have set up a shared decision-making program to address this situation (appendix). Through a medical decision-making program to help families understand the clinical course of PMV patients, the quality of medical treatment will improve, and long term medical care will be promoted. This is our goal for PMV patients.

Limitations of our study

We did not collect patient's laboratory data, respiratory parameters, APACHE II score, Glasgow Coma Scale, or other similar relevant variables. We were, therefore, unable to determine which of these measures, if any, may be related to the long term survival of successfully weaned PMV patients. The literature contains no discussion of successfully weaned PMV patients who died in the ward after successful weaning, nor studies of long term survival in successfully weaned PMV patients. Our

conclusions on the long term outcomes of successfully weaned PMV patients must be interpreted with care since they derive only from our retrospective single-unit study. We have no proper strategy to improve the survival rate of ward mortality patients. We expect that the addition of other clinical experiences and strategies to improve long term survival in successfully weaned PMV patients will yield additional insights.

Conclusions

In this study, 243 PMV patients were successfully weaned from invasive ventilation. The 1-year survival rate of successfully weaned patients was 32.5%. Fully 35.4% of weaned patients died in the ward before being discharged, which was due to a high percentage of signed DNR/ DNI orders in this group. Fully 81 patients (33.3%) in our study signed DNR/ DNI orders, meaning that, at most, 66.7% of survivors were willing to receive mechanical ventilation again. The end-of-life decision (signed DNR/ DNI orders) is one of the major influence factors of long term survival of successfully weaned prolonged mechanical ventilation patients. We have set up a shared decision-making program to address the needs of this population and their families. We expect to help patients' families understand the clinical course of PMV patients and improve the quality of medical treatment received by PMV patients.

Appendix:

If a family has successfully liberated from the ventilator when he/she suffers difficulty breathing again, does he/she need to receive endotracheal tube intubation and use an invasive ventilator?

Applicable patients:
a prolonged mechanical ventilation patient without tracheostomy who has successfully liberated from the invasive ventilator.

Introduction of invasive ventilator:
1. The use of an invasive ventilator by a patient is an emergency medical treatment. When the patient suffers difficulty breathing, the patient uses an invasive ventilator to assist ventilation, maintain life, and extend treatment duration.
2. When patients need to use an invasive ventilator, the patient must receive endotracheal tube intubation.

Four steps in decision-making program:

Step 1. Compare the advantages, risks, and treatment outcomes of each option

	Receive endotracheal tube intubation and use an invasive ventilator.	**Not receive endotracheal tube intubation.**	
		Oxygen therapy	**using a non-invasive ventilator**
Alleviate dyspnea	Alleviate dyspnea	Not alleviate dyspnea	Questionable alleviate dyspnea
Extend treatment duration	Extend treatment duration	Not extend treatment duration	Questionable extend treatment duration
Treatment outcome	Patient may cure	Most failure of treatment outcome	The patient's recovery is questionable
Patient’s comfort	The patient sustains discomfort for a long time	The patient bears short duration of discomfort before dying	The patient sustains mild discomfort for a long time
Patient’s life	May save the patient's life	The patient will die.	Not necessarily save a patient’s life
Clearing sputum effect	Good clearing sputum effect via endotracheal tube sputum suction	1. Poor clearing sputum effect 2. Rely on the patient's cough function	1.Poor clearing sputum effect 2. Rely on the patient's cough function
Supplying oxygen effect	Adequate supplying oxygen effect	Inadequate supplying oxygen effect	Adequate supplying oxygen effect is questionable

If a family has successfully liberated from the ventilator when he/she suffers difficulty breathing again, does he/she need to receive endotracheal tube intubation and use an invasive ventilator?

Step 2: when they chose a treatment, participants were asked about the factors they cared about and the degree to which they cared about each.
Please circle the following considerations: 0 is not important; 5 is most important.

Considerations	not important	less important	normal	important	very important	most important
Willingness of patient	0	1	2	3	4	5
Comfort of Patient	0	1	2	3	4	5
Alleviate of patient's difficulty breathing	0	1	2	3	4	5
Patient's treatment outcome	0	1	2	3	4	5
Patient's life	0	1	2	3	4	5
Clearing sputum effect	0	1	2	3	4	5
Supplying oxygen effect	0	1	2	3	4	5

Step 3: How much does the patient or family know about the treatment?

problems	right	wrong	unclear
1. Using an invasive ventilator will prolong the patient's discomfort	☐	☐	☐
2. After using an invasive ventilator, the patient's breathing difficulties can alleviate	☐	☐	☐
3. After using an invasive ventilator, the patient's life can be maintained and extend treatment duration	☐	☐	☐
4. Using invasive ventilators can decrease patient's mortality rate	☐	☐	☐
5. It can alleviate the patient's breathing difficulties without using an invasive ventilator.	☐	☐	☐
6. If not using an invasive ventilator, the patient may die.	☐	☐	☐
The following questions are about the using of non-invasive ventilators			
7. After using a non-invasive ventilator, the patient is less discomfort than using an invasive ventilator.	☐	☐	☐
8. After using a non-invasive ventilator, it maybe alleviates the patient's breathing difficulties.	☐	☐	☐
9. After using a non-invasive ventilator, the effect of clearing sputum effect and supplying oxygen effect is the same as using an invasive ventilator.	☐	☐	☐
10. After using a non-invasive ventilator, the rate of successful treatment outcome is the same as using an invasive ventilator.	☐	☐	☐

Step 4: Is the patient or family now confirming the treatment method?
☐ I (we) have confirmed the treatment method that I want - (the following one)
☐ Receive endotracheal tube intubation and use an invasive ventilator.
☐ Not receive endotracheal tube intubation and use oxygen therapy
☐ Not receive endotracheal tube intubation and use a non-invasive ventilator
☐ I (we) still can not decide which I want to treatment method–(the following one)
☐ I (we) want to discuss details with the attending physician or medical staff
☐ I (we) want to discuss the pros and cons with other relatives and friends
I (we) can make a decision about on _____ (date).
☐ For the above treatment methods, I (we) want to know more detail and my problems are:

Declarations

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Not applicable.

Funding:

There was no funding in this study.

Ethics approval and consent to participate:

The project was approved by Buddhist Dalin Tzu Chi general hospital research ethics committee. (Approved IRB No.: B10802009)

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

CH designed the study, collected the data, analyzed the data, wrote the manuscript, and reviewed the manuscript. All authors contributed to preparing the manuscript. All authors read and approved the final manuscript.

Consent for publication:

Not applicable.

Competing interests:

The authors declare that they have no competing interests

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