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Management of Acute and Chronic Hypercapnic Respiratory Failure in Severe Obesity-Hypoventilation Syndrome: A Case Study of Multi-Modal Therapy and Long-Term Weight Loss

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 53-year-old
Final Diagnosis: Obesity hypoventilation syndrome
Symptoms: Dynpnea
Clinical Procedure: —
Specialty: Pulmonology

Objective: Unusual clinical course

Background: Obesity-hypoventilation syndrome (OHS), also known as Pickwickian syndrome, is a respiratory consequence of morbid obesity, usually treated with non-invasive positive airway pressure (PAP) therapies and weight loss. This study reports a 53-year-old woman with a body mass index of 49 kg/m^2 who experienced acute hypercapnic respiratory failure due to OHS. Her treatment involved mechanical ventilation, home oxygen therapy, and long-term weight loss of >30 kg.

Case Report: A 53-year-old woman (109 kg) presented with acute hypercapnic respiratory failure due to OHS, which improved with mechanical ventilation and diuretics. After discharge from the hospital, she was treated with nocturnal non-invasive positive-pressure ventilation (NPPV) and home oxygen therapy. Over a 5-year period, following loss of >30 kg, she was re-evaluated for the discontinuation of NPPV and oxygen therapy. She was evaluated with various NPPV settings and oxygen doses, monitored by transcutaneous pressure of carbon dioxide ($PtcCO_2$). On NPPV, $PtcCO_2$ levels ≥55 mmHg were maintained within 10 min, indicating that the durations of $PtcCO_2$ ≥50 mmHg were too prolonged for her to be switched to continuous PAP therapy. Nonetheless, oxygen therapy was discontinued because the duration of peripheral blood oxygen saturation <90% was brief.

Conclusions: For patients with OHS treated with NPPV and oxygen therapy, weight loss alone may not improve hypoventilation and wean the patient from NPPV. Besides obesity, various factors influence respiratory compromise in OHS; hence, a comprehensive assessment of hypoventilation, including $PtcCO_2$ monitoring, is essential to determine whether NPPV withdrawal is possible after body weight loss.

Keywords: Diet, Reducing • Noninvasive Ventilation • Obesity Hypoventilation Syndrome • Oxygen Inhalation Therapy • Positive-Pressure Respiration

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Introduction

Obesity affects approximately 42% of adults in the USA and is associated with increased incidence of type 2 diabetes, cardiovascular disease, and premature death [1,2]. Furthermore, sleep disorders are remarkable complications associated with obesity [3,4]. Obesity-hypoventilation syndrome (OHS) is a sleep-related hypoventilation disorder observed in 8-20% of obese patients [5]. OHS is reported to occur in individuals with a lower BMI range in the Asian population [2]. The pathogenesis of OHS is multifactorial, involving reduced central respiratory stimulation, upper airway obstruction, and cardiovascular and respiratory abnormalities [2,6,7]. OHS is diagnosed when all 4 of the following conditions are met: 1) symptoms related to sleep hypoventilation, 2) body mass index (BMI) ≥30 kg/m^2, 3) arterial pressure of carbon dioxide ($PaCO_2$) ≥45 mmHg on awakening, and 4) no other disease causing alveolar hypoventilation [5]. OHS has a high mortality rate in untreated cases [8]. A 25-30% weight loss from the original weight and administration of positive airway pressure (PAP) ventilation therapy are recommended as treatments [9]. Continuous PAP (CPAP) is the first treatment choice if the symptoms are stable [9]. Furthermore, non-invasive positive pressure (NPPV) is recommended if the therapeutic effect and/or tolerability of CPAP is insufficient [10]. However, there are few reports on switching from NPPV to CPAP [11,12]. Therefore, which patients can transition to CPAP and which should remain on NPPV remains unclear.

This report presents the case of a 53-year-old woman with BMI of 49 kg/m^2 who developed acute hypercapnic respiratory failure due to OHS. She was managed with mechanical ventilation, home oxygen therapy, and long-term weight loss exceeding 30 kg.

Case Report

A female patient, who weighed 50 kg in her twenties, gained weight after childbirth, reaching 80 kg. At the age of 52 years, she developed hypothyroidism following radiotherapy for hyperthyroidism and began thyroid hormone supplementation. Her weight increased further, exceeding 100 kg. At the age of 53 years, she experienced edema and additional weight gain, leading to a diagnosis of severe hypercapnic (type-2) respiratory failure and subsequent hospitalization. Despite a month of treatment, her edema did not improve, and dyspnea developed, prompting a referral to a local hospital. While receiving NPPV and diuretics, her ventilatory failure worsened, and she was transferred to our hospital the following day.

On admission to our hospital, her height was 149 cm, weight was 109 kg, and BMI was 49.0 kg/m^2. Her vital signs were as follows: blood pressure 108/69 mmHg, pulse rate 83 beats/min, peripheral blood oxygen saturation (SpO_2) 40-60% in room air, and body temperature 38.0°C. Auscultation revealed decreased bilateral breath sounds in the chest. She had systemic edema. Blood examination results showed a D-dimer level of 5.1 μg/mL and a brain natriuretic peptide level of 108 pg/mL. Arterial blood gas analysis on room air showed type-2 respiratory failure (arterial pressure of oxygen [PaO_2] 31 mmHg, $PaCO_2$ 75 mmHg). Chest radiography revealed an overall decrease in permeability (**Figure 1A**). Echocardiography showed a slightly decreased ejection fraction but no pulmonary hypertension. Chest computed tomography showed bilateral lung congestion without features suggestive of other lung diseases or remarkable cardiac enlargement (**Figure 1B, 1C**). She was suspected of having OHS, which was accompanied by congestive heart failure triggered by an upper airway infection. On the day she was transferred to our hospital, she underwent intubation, and mechanical ventilation was initiated due to severe type-2 respiratory failure. She was also treated for right heart failure with diuretics and was extubated after $PaCO_2$ retention resolved on hospitalization day 4. From hospitalization days 4 to 9, NPPV was administered daily with inspiratory PAP (IPAP)/expiratory PAP (EPAP) 14/7 cmH_2O all day. On hospitalization day 9, she was switched to IPAP/EPAP 14/7 cmH_2O at night and oxygen therapy (3 L/min) during the day. A pulmonary function test on hospital day 21 showed a vital capacity (VC) of 1.59 L (58.6%) and forced expiratory volume in 1 second (FEV1) of 1.46 L (68.5%), indicating restricted ventilation failure. She was discharged with NPPV (IPAP/EPAP 12/7 cmH_2O) at night and home oxygen therapy (2 L/min at rest and 3 L/min during sleep) (**Figure 2**).

After discharge, she continued to lose weight under guidance of the Department of Endocrinology and Metabolism. However, approximately 4 years after discharge, her weight had not dropped below 90 kg. Subsequently, a continuous glucagon-like peptide 1 receptor agonist was administered, resulting in a weight loss of more than 30 kg over 5 years following discharge (**Figure 2**).

The patient was readmitted because withdrawal of NPPV and oxygen therapy was considered given the weight loss of more than 30% (BMI 49.0 kg/m^2 to 33.3 kg/m^2). Chest radiography and CT showed no findings suggestive of heart failure or other abnormalities in either lung field (**Figure 1D, 1E**). A respiratory function test also showed improvement in VC (1.96 L [79.0%]). Arterial blood gas analysis on room air showed that both hypoxia and hypercarbia had improved, while A-aDO_2 remained elevated (25.8 Torr). She was evaluated using various NPPV settings and oxygen doses (**Figure 3**). In the original NPPV and oxygen therapy settings (**Figure 3**, Setting 1: IPAP/EPAP 12/7 cmH_2O, frequency 15/min, O_2 3.0 L/min), SpO_2 was within an acceptable range, while duration of high

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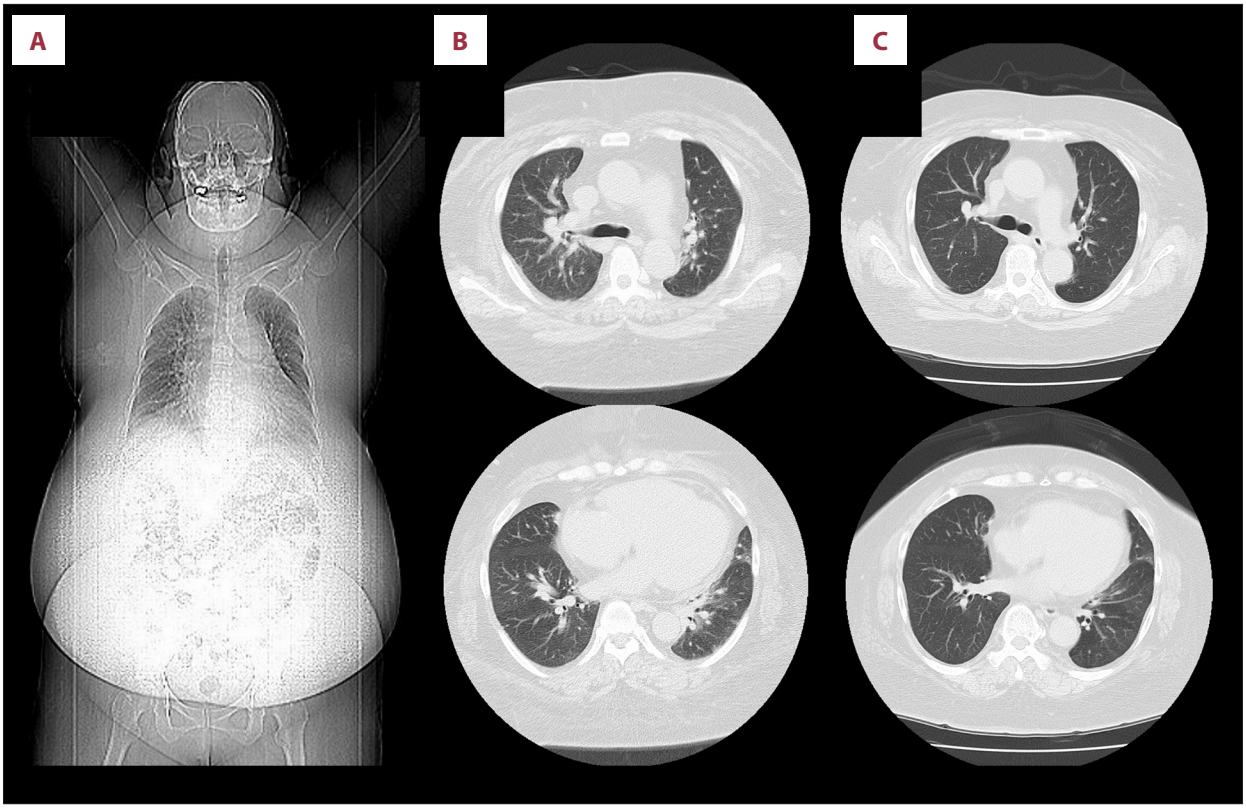

Figure 1. Changes in imaging findings over a 5-year period. (**A**) A scout image of a chest computed tomography (CT) at first admission demonstrates significant obesity. (**B**) A chest CT shows bilateral lung congestion without features suggesting other lung diseases and remarkable cardiac enlargement. (**C**) A CT showing no findings suggestive of heart failure or other abnormality in both lung fields when the patient lost more than 30 kg 5 years following her initial admission.

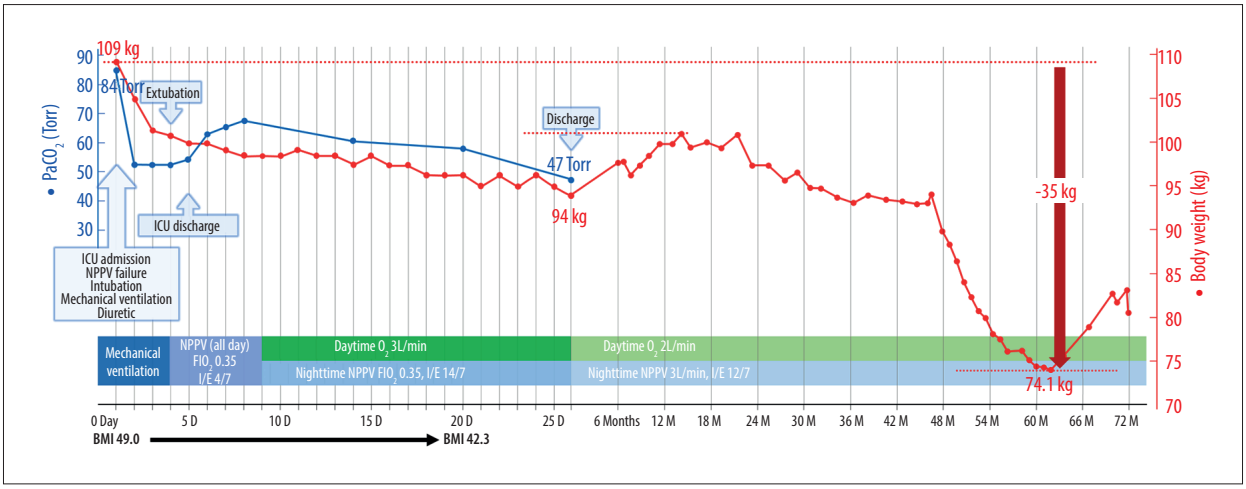

Figure 2. The clinical course of the patient and changes in body weight and $PaCO_2$ values. The weight of the patient initially decreased following the first hospitalization due to diuresis, while remained stable for approximately 2 years after discharge. However, over the subsequent 3 years, she achieved a weight loss of 30 kg. Regarding her respiratory status, although she initially required mechanical ventilation, her condition was successfully managed with NPPV and home oxygen therapy before discharge. BMI – body mass index; E – expiratory positive airway pressure; D – days; FIO_2 – fraction of inspiratory oxygen; I – inspiratory positive airway pressure; ICU – Intensive Care Unit; M – months; NPPV – non-invasive positive-pressure ventilation; $PaCO_2$ – arterial pressure of carbon dioxide. *This figure was created by MK and HK.*

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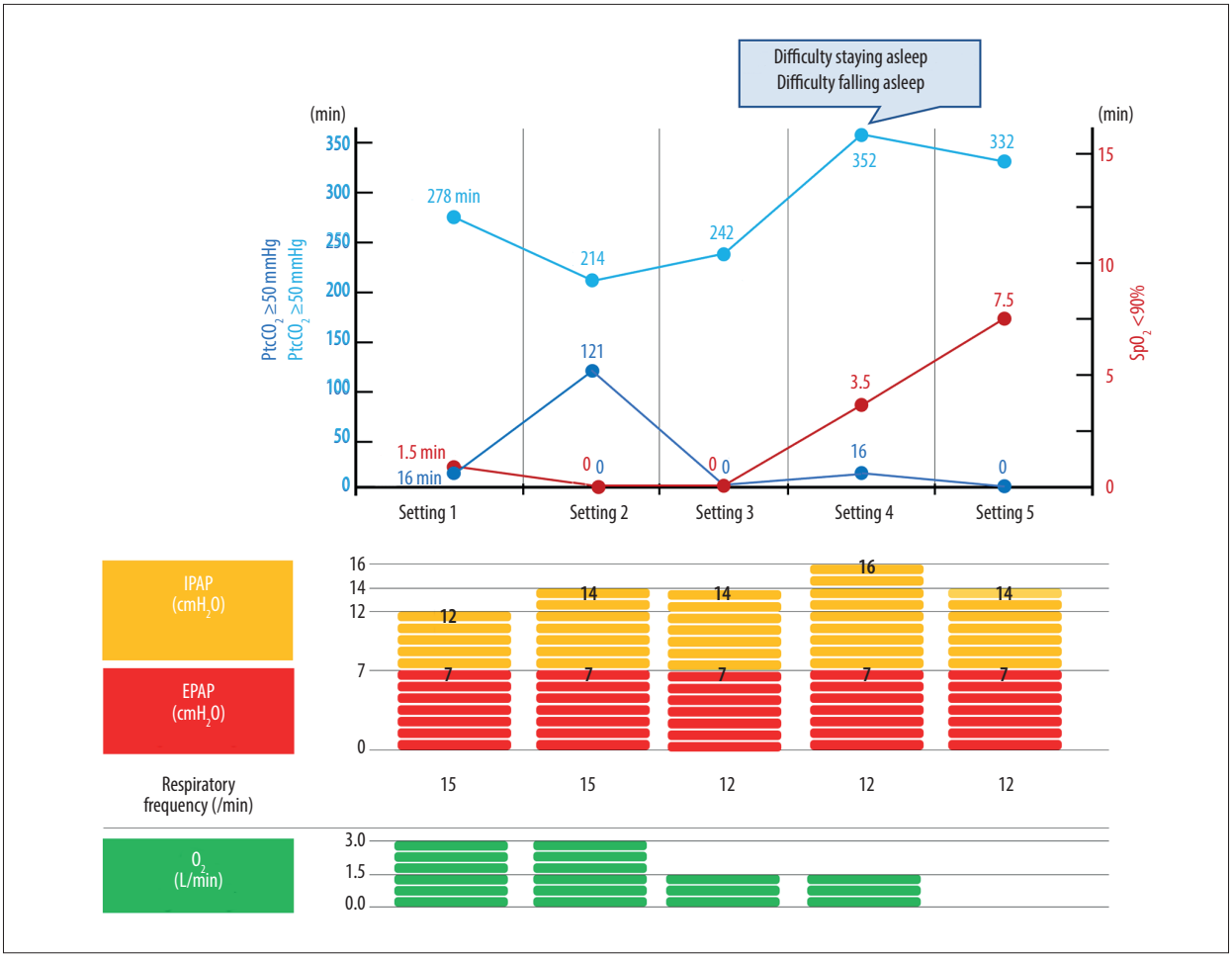

Figure 3. Respiratory status during various settings of non-invasive positive-pressure ventilation and oxygenation. All settings (1-5) resulted in an SpO_2 of less than 90% within an acceptable range; however, the duration of $PtcCO_2$ ≥50 mmHg remained prolonged. At setting 4, the patient experienced difficulty initiating sleep and reported nocturnal awakenings. At setting 5, although SpO_2 remained within the acceptable range, the extended duration of $PtcCO_2$ ≥50 mmHg prevented a transition to CPAP. EPAP – expiratory positive airway pressure; IPAP – inspiratory positive airway pressure; $PtcCO_2$ – transcutaneous pressure of carbon dioxide; SpO_2 – peripheral blood oxygen saturation. *This figure was created by MK and HK.*

transcutaneous pressure of carbon dioxide ($PtcCO_2$) remained long. In the increased IPAP setting, decreased respiratory frequency, and reduced oxygen dose (**Figure 3**, Setting 2-4), SpO_2 remained within an acceptable range, whereas the duration of high $PtcCO_2$ did not decrease. Furthermore, when the IPAP was increased to 16 cmH_2O (**Figure 3**, Setting 4), she had difficulty falling asleep and reported waking up in the middle of the night. Furthermore, the duration of high-concentration $PtcCO_2$ exposure was prolonged. On setting 5 (IPAP/EPAP 14/7 cmH_2O, frequency 12 times/min, O_2 0 L/min), $PtcCO_2$ ≥55 mmHg duration was within 10 min, while SpO_2 was within the acceptable range. However, $PtcCO_2$ ≥50 mmHg duration was too long to shift to CPAP. Nevertheless, she could be weaned off oxygen therapy because the duration of SpO_2 <90% was very short, even when oxygen administration was monitored. After discharge from the hospital, she was on NPPV (IPAP/EPAP 14/7) with no worsening of respiratory condition, and she planned to lose more weight.

Discussion

We present the case of a patient with OHS who achieved weight loss after stabilizing her respiratory status with NPPV and oxygen therapy. However, following a comprehensive assessment, including $PtcCO_2$ monitoring, she was weaned off oxygen therapy but not NPPV. This case report highlights 2 striking clinical findings regarding changes in hypoventilation status following weight loss in OHS. First, $PtcCO_2$ monitoring is useful for determining whether to continue or discontinue NPPV and oxygen therapy in patients with OHS whose respiratory status has stabilized with NPPV treatment and weight loss. Second, various

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factors other than obesity, such as central respiratory stimulus reduction, upper airway obstruction, and cardiovascular and respiratory disorders, can contribute to the respiratory status in OHS. Therefore, it is important to note that there are cases in which weight loss alone does not directly lead to improvement in hypoventilation that would allow withdrawal from NPPV.

In this case, $PtcCO_2$ monitoring was used to determine whether NPPV withdrawal was possible after weight loss. A reliable and practical method to identify hypoventilation during sleep is to continuously measure the CO_2 concentration during sleep by end-expiratory or transcutaneous monitoring [13]. End-tidal monitoring is simple; however, it requires that the patient has no unequal ventilation [13]; therefore, it may not be suitable for use in patients with OHS and unequal ventilation. In contrast, $PtcCO_2$ monitoring is non-invasive and allows continuous real-time monitoring over a 12-h period [14]. In this patient, $PtcCO_2$ ≥55 mmHg lasted less than 10 min during sleep, while $PtcCO_2$ ≥50 mmHg lasted longer than 3 h. Consequently, we were unable to wean her from NPPV because it was anticipated that further exacerbation of hypercapnia would occur when assisted ventilation was removed.

For the initial treatment of OHS, there are no significant differences between CPAP and NPPV in terms of mortality, cardiovascular events, healthcare resource use, and improvement in blood gases and sleepiness [10]. Therefore, CPAP is the first choice for stable OHS [10]. However, NPPV is recommended for unstable OHS [10]. Patients who become stable with NPPV and experience body weight loss can switch to CPAP [15]. As there are no clear guidelines for NPPV withdrawal or transition from NPPV to CPAP in OHS, evaluation with $PtcCO_2$ monitoring is valuable, even after remarkable weight loss has been achieved. In OHS, a weight loss of 25-30% is recommended for radical treatment [9]. Previous studies have reported that patients with OHS stable on NPPV for more than 3 months could be switched to CPAP, even if the patient had CPAP failure or severe type-2 respiratory failure at induction [12]. Characteristics of OHS that suggest a patient should not be switched from NPPV to CPAP include a mean $PtcCO_2$ ≥50 mmHg, SpO_2 <90% for at least 10 continuous minutes without apnea, and $PaCO_2$ ≥51 mmHg 4 h after the cessation of positive-pressure ventilation upon waking [12]. Orfanos et al also reported that a higher BMI is associated with the failure of transitioning from NPPV to CPAP in patients with OHS [11], but our patient exhibited a similarly elevated PCO_2 value, measured as $PtcCO_2$, but had a lower BMI of 33.3 kg/m^2. She was weaned from oxygen therapy but not from NPPV, despite a 32% weight loss. The mechanism of OHS is related to multiple factors, with the main 3 being: 1) decreased central respiratory stimulation, 2) upper airway obstruction, and 3) cardiovascular and respiratory abnormalities [6]. In this case, right heart failure improved after treatment on initial admission. Subsequent weight loss and positive-pressure ventilation improved the condition of the upper airway and respiratory system. However, central nervous system abnormalities might have persisted, affecting hypoventilation. Central nervous system abnormalities in OHS can be related to a high resistance to leptin, which has a stimulating effect on the respiratory center [16]. Leptin levels were not measured in this case, and the extent to which leptin contributed to hypoventilation remains unknown. It is also unclear whether leptin resistance persists even after weight loss. Further re-evaluation is needed to determine whether NPPV withdrawal is feasible after further weight loss.

Conclusions

In patients with OHS who are treated with NPPV and oxygen therapy, weight loss alone may not be sufficient to improve hypoventilation and wean the patient from NPPV. Aside from obesity, various factors influence respiratory compromise in OHS; hence, a comprehensive assessment of hypoventilation, including $PtcCO_2$ monitoring, can be essential to determine whether NPPV withdrawal is possible after body weight loss.

Institution Where Work Was Done

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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