Sleep Science and Practice

CASE REPORT

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Case report: fast reversal of malignant obesity hypoventilation syndrome after noninvasive ventilation and pulmonary rehabilitation

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Abstract

Background: Malignant obesity hypoventilation syndrome (MOHS) is described as a subtype condition of OHS, characterized by extreme obesity, obese-related hypoventilation, and multiorgan dysfunction. Because of low awareness and inadequate treatment, MOHS leads to high morbidity and mortality.

Case presentation: A 53-year-old man was diagnosed with MOHS evidenced by extreme obesity and multiorgan abnormalities. After taken noninvasive ventilation (NIV) treatment, he was rescued. And at the end of the six-month pulmonary rehabilitation (PR) program, improvement in terms of respiratory parameters, BMI, apnea-hypopnea index (AHI), and pulmonary hypertension were observed in the patient. Two years later, the patient was still in good condition.

Conclusions: This case highlights the awareness and proper use of NIV to rescue MOHS patients. Furthermore, the benefits of PR were explored in this case, which has not been considered within the therapeutic options for MOHS patients.

Keywords: Malignant obesity hypoventilation syndrome, Noninvasive ventilation, Pulmonary rehabilitation

Background

Obesity has risen inexorably worldwide in the past 4–5 decades and is now one of the most significant contributors to poor health in most countries (Swinburn et al., 2019). In China, the rapid lifestyle changes associated with urbanization are characterized by high caloric intake and reduced physical activity, putting Chinese people at a high risk of obesity (Yin et al., 2016). Obesity can result in obesity hypoventilation syndrome (OHS), of which the prevalence is increasing proportionally to the prevalence of obesity. Furthermore, OHS brings patients with many complications, involving obstructive sleep apnea (OSA), metabolic and cardiac disorders.

Malignant obesity hypoventilation syndrome (MOHS) was recently described as a severe form of OHS (Marik, 2012). It is defined as a patient with a body mass index (BMI) greater than 40 kg/m^2 with awake hypercapnia ($PaCO_2$>45 mmHg), metabolic syndrome (central obesity, hypertension, hyperlipidemia, and insulin resistance), and multiorgan dysfunction related to obesity (Munoz et al., 2013). At the same time, the awareness about MOHS among physicians is limited, and the evidence on therapy and outcomes are sparse (Sunwoo & Mokhlesi, 2018); moreover, the patients with MOHS are often not diagnosed, and the morbidity is high, because of complications, rapid change, and progression (Raveendran et al., 2017). Therefore, it is more important than ever to diagnose and aware of the phenotype accurately and

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explore the appropriate treatment of MOHS. Here, we present a case from our institute, in which a severely obese patient presenting with breathlessness was found to have respiratory failure, metabolic syndrome, OSA, and cardiac dysfunctions. After receiving a diagnosis of MOHS and treatment of average volume-assured pressure support (AVAPS), the patient was fast recovered from respiratory failure. Post-discharge pulmonary rehabilitation (PR) was taken for 6 months, and improvement in terms of respiratory parameters, BMI, AHI, and pulmonary hypertension were observed in the patient.

Case presentation

A 53-year-old smoking Chinese man was admitted to Obesity Medicine of Zhongshan Hospital for obesity and difficulty breathing. Clinical history showed that he had suffered from snoring and weight gain (around 4 kg per year) for 30 years since he was 20 and had daytime sleepiness and witnessed apnea in the recent 10 y. He had systemic hypertension treated since 2009. Four months ago, the patient was diagnosed with COPD in another hospital by pulmonary function testing (post-bronchodilator forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC) =69%, FEV1 = 43.71% of predicted value), and he received inhale treatment of salmeterol/fluticasone and tiotropium bromide.

On arrival, his arterial blood gas (ABG) showed a pH of 7.45, $PaCO_2$ of 91 mmHg, PaO_2 of 63.0 mmHg, and SaO_2 of 93% (Fig. 1a) indicating a type II respiratory failure. He was 153 cm tall, with a weight of 118 Kg, BMI 50.4 kg/m^2; his waist- to- hip ratio is 1.019 (131.5 cm waistline, 129 cm hip). A chest radiograph revealed cardiomegaly and peribronchial thickening. A cardiac echocardiogram showed a dilated right ventricle with reduced ejection fraction, as well as dilated left atrium, left ventricular hypertrophy, and pulmonary hypertension (40 mmHg). Fatty liver was diagnosed by an ultrasound test. Bloodwork indicated insulin residence. Consequently, he underwent polysomnography to look for OSA. A 6-lead electroencephalographic (EEG: F3-M2, F4-M1, C3-M2, C4-M1, O1-M2, O2-M1), submental electromyographic, and bilateral electromyographic recording was performed according to the AASM guidelines (Malhotra et al., 2018). His AHI was 61.4 events /hour, indicating severe OSA (Fig. 2a). Based on the medical evidence, he was diagnosed with MOHS.

Ten hours after admission, he had the aggravation of dyspnea suddenly with cyanosis. ABG showed an

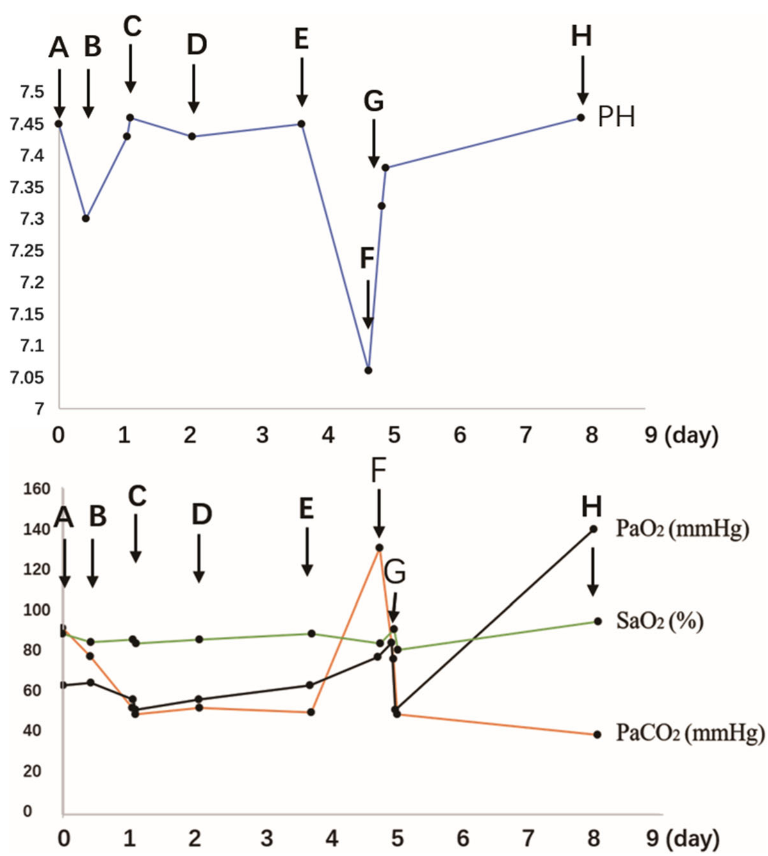

Fig. 1 Changes in PH, PaO_2, and SaO_2 were detected by ABG

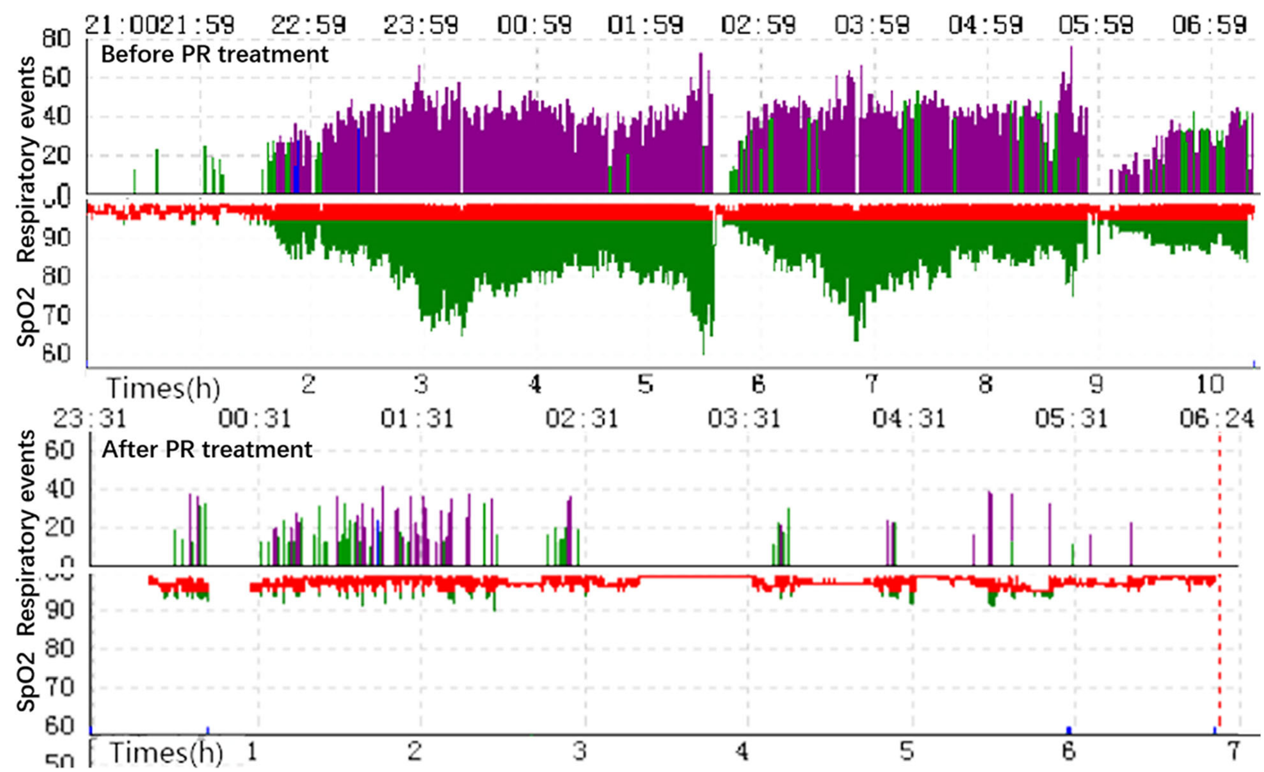

Fig. 2 Polysomnogram analysis obtained before and after pulmonary rehabilitation treatment

obvious decrease of $PaCO_2$ (from 91 mmHg to 77.4 mmHg), SaO_2 (from 93 to 88.9%), and PH (from 7.45 to 7.30) (Fig. 1b). For treatment, noninvasive ventilation (NIV) was started with a mode of auto-bilevel positive airway pressure (BiPAP). The 90% actual inspiratory positive airway pressure (IPAP) level was set at 13.6 cm H_2O, and 90% expiratory positive airway pressure (EPAP) was at 10.1 cm H_2O. However, after 16-h treatment, ABG showed continued deterioration in PaO_2 (from 64.3 to 51 mmHg) and SaO_2 (from 88. 9 to 88.0%) (Fig. 1c). Following 24-h NIV treatment with oxygen therapy, improvements in ABG were still not obvious (Fig. 1d). Therefore, 90% IPAP and 90% EPAP were respectively improved to 15 cm H_2O and 11.5 cm H_2O. Then after 36 h, ABG showed slightly improvement in PaO_2 (from 56 to 63 mmHg), SaO_2 (from 90 to 93%) and $PaCO_2$ (from 52 to 50 mmHg) (Fig. 1e). However, 24 h thereafter, he was found foaming from the mouth and conscious disturbance. ABG identified his $PaCO_2$, and pH drastically deteriorated to 130 mmHg and 7.06 (Fig. 1f). Then, Drager BiPAP was used instead of auto-BiPAP. During titration, the IPAP level ranged between EPAP and 20 cm H_2O under a constant rate of 18 breaths per minute (bpm). EPAP was set at 10 cm H_2O with a 40% inspired fraction of oxygen (FiO_2) for further therapy; after 1 h, ABG analysis showed improvement in PaO_2 (84 mmHg) and $PaCO_2$ (76 mmHg) (Fig. 1g). Because of low tidal volume and obvious abdominal

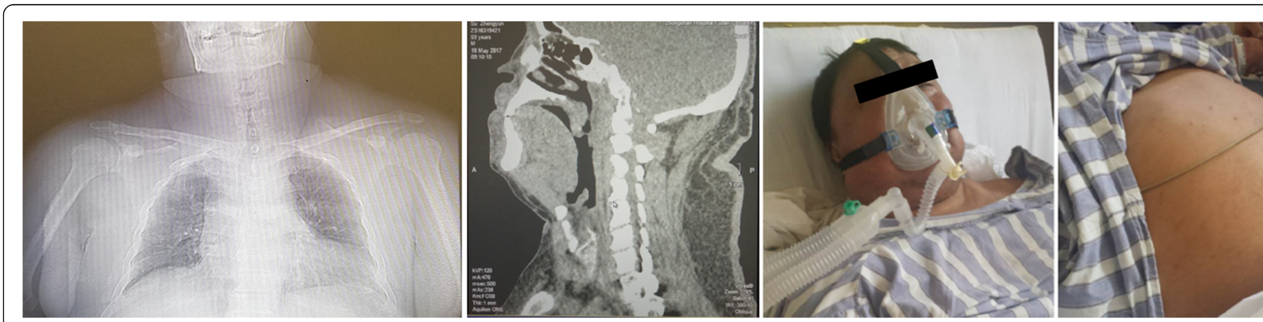

Fig. 3 Abdominal distension limited the use of Drager BiPAP

distension (Fig. 3), he received AVAPS. The $IPAP_{min}$, $IPAP_{max}$, and EPAP were set at 10, 24, 7 cm H_2O respectively, to ensure adequate tidal volume (700 mL) under a constant rate of 18 bpm. The patient was rescued after 3 - day AVAPS, with an improvement in ABG (Fig. 1h) and clinical symptoms.

After discharge, an educational assessment to determine how to manage the patient's conditions was performed. He underwent a PR program of aerobic and resistance training exercises per day up to 30 min each, for 6 months. For the aerobic training, the work rate began at 50% of his maximum heart rate on a treadmill, with a speed of 2.5 km per hour and 0% of a slope. The workload and duration of exercise were increased by 10% when the patient reached the level of exercise at 10 min without intolerable dyspnea, measured as Borg rating of dyspnea < 5. For his respiratory muscles training, progressive exercise was employed, which consisted of diaphragmatic breathing and inspiratory muscle training at 40 to 50% of his initial maximal inspiratory pressure. Our patient took oxygen therapy to maintain SpO_2 >90% during exercise. Physicians also encouraged the patient to lose weight and designed restricted calorie meal planning for him. He was acclimatized to training with BiPAP during sleep (the IPAP and EPAP were set at 30 and 8 cm H_2O respectively). At the end of the PR program, improvement in terms of BMI, respiratory parameters and polysomnography were observed in the patient (Table 1). However, the changes in chest radiograph and pulmonary hypertension were not provided in the case report, because the absence of the examination after PR.

Discussion and conclusions

This case presented with a complex of signs/symptoms consistent with the descriptions of MOHS, with a BMI greater than 40 kg/m^2 and a $PaCO_2$ in the context of respiratory failure, RV dysfunction, pulmonary hypertension, OSA, insulin resistance, and liver abnormality. As far as we know, this is the first case report of MOHS in China; otherwise, this patient was fast revealed after proper NIV treatment and was able to remain his BMI reduction and recovery of lung function and pulmonary hypertension by post-hospital PR.

MOHS patients before discharge are often erroneously diagnosed with COPD because of respiratory issues. As the case in our patient, COPD was also previously diagnosed, although a diagnosis of OSA and OHS is better supported by the clinical picture. And after discharge PR, the lung function of the patient was completely returned to normal. Physicians should be more vigilant for the diagnosis of OHS or OSA in obese patients with a respiratory abnormality.

Although the effect of applying NIV in MOHS has been proven, the patient in the case presentation slightly improved in ABG by BiPAP, and his condition deteriorated after 3-day treatment of NIV in the mode of BiPAP. After applying AVAPS, his gas exchange and clinical symptoms were significantly improved. AVAPS is an additional mode for a bilevel pressure ventilation device, and some trials have identified that AVAPS provides more benefits on ventilation quality in OHS patients, resulting in a more efficient decrease of the mean transcutaneous partial pressure of carbon dioxide ($PtcCO_2$) and rapid recovery of consciousness when compared to traditional BiPAP (Storre et al., 2006; Ciftci et al., 2017; Briones Claudett et al., 2013). Notably, our

Table 1 Results of respiratory and clinical tests before and after a pulmonary rehabilitation in the patient

Test	Items	Before PR treatment	Post PR treatment
	Height (m)	155	155
	Weight (kg)	110	83
	BMI (kg/m^2)	50.4	34.55
Respiratory functional tests	FEV1/FVC	69	78.74
	FEV1 (% of predicted value)	43.71	104.17
	FVC (% of predicted value)	46.12	101.35
Polysomnography	AHI (events/hour)	61.4	20.7
	Hyponea	87	47
	OSA	481	44
	CSA	3	1
	MSA	0	0
	Total	571	92
	Lowest O_2 saturation (%)	60	90.2

Abbreviations: *PR* Pulmonary rehabilitation, *BMI* body mass index, *FEV1/ FVC* post bronchodilator forced expiratory volume in 1 s/ forced vital capacity, *AHI* apnea-hypopnea index, *OSA* obstructive sleep apnea, *CSA* central sleep apnea, *MSA* mixed sleep apnea patients were also improved after treatment with AVAPS. Physicians should have an awareness of applying AVAPS in MOHS patients, which has received little attention in the literature (Murphy et al., 2012; Masa et al., 2019).

Management after discharge is essential for patients with chronic diseases. Weight loss is the most crucial element in the management of OHS (Kakazu et al., 2020); however, it is often difficult to achieve and maintain weight loss by medical management. Bariatric surgery is reported to effectively making a more substantial degree of weight loss and maintaining this loss over more extended periods in OHS patients (Schauer et al., 2012; Sjostrom et al., 2007). While MOHS patients usually combine multiorgan disabilities, especially cardiovascular and respiratory failure, which undoubtedly increase the risk and difficulty of surgery. Perhaps this may partly explain why there are few reports on bariatric surgery in MOHS patients.

Recent evidence showed that treatment of chronic respiratory failure with NIV was associated with weight loss and a decrease in sedentary time. A multidisciplinary rehabilitation program, in addition to NIV, can bring OHS patients' effects in terms of enhanced weight loss and improved exercise capacity (Mandal et al., 2018). PR is an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased activities of daily living. Based on the evidence, we evaluated whether a patient with MOHS, an illness that has not yet been considered for PR, can benefit from PR. In this case, PR was designed with an aerobic retraining program and exercise training, nutritional education, restricted calorie meal planning, encouragement for weight loss, psychological support, and training with and acclimatization to NIV. In the literature, there are no reports on the efficacy of PR in MOHS patients, in contrast with other lung diseases such as COPD or pulmonary hypertension where clinical studies have demonstrated the benefits of PR (Sahni et al., 2015; Arena, 2011). Further studies are needed to clarify the benefits of PR among MOHS patients. Notably, clinically relevant improvements and long-term benefits were demonstrated in this report as a result of a PR. Although clinical studies on long-term effects within a large patient population are required for definitive conclusions, our observations suggest that PR would be beneficial for patients with MOHS.

Abbreviations

MOHS: Malignant obesity hypoventilation syndrome; AVAPS: Average volume-assured pressure support; PR: Pulmonary rehabilitation; AHI: Apnea-hypopnea index; NIV: Noninvasive ventilation; OHS: Obesity hypoventilation syndrome; COPD: Chronic obstructive pulmonary disease; OSA: Obstructive sleep apnea; BMI: Body mass index; ABG: Arterial blood gas; BiPAP: Auto-bilevel positive airway pressure; IPAP: Inspiratory positive airway pressure; EPAP: Expiratory positive airway pressure; FiO_2: Inspired fraction of oxygen; $PtcCO_2$: Partial pressure of carbon dioxide

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Not applicable.

Authors' contributions

S.Y. Hao and L.L. Pang collected the patients' information and wrote the initial draft of the paper; L. Xie and X. Wu interpreted the results; S.Q. Li conceived the idea of the study; All authors contributed to the writing and revisions. The author(s) read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are available and included in this published article.

Declarations

Ethics approval and consent to participate

This case was approved by the institutional ethics board of Zhongshan Hospital Affiliated to Fudan University, China; oral and written consent was obtained from the patient involved before data collection.

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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References

Arena R. Exercise testing and training in chronic lung disease and pulmonary arterial hypertension. Prog Cardiovasc Dis. 2011;53(6):454–63. https://doi.org/10.1016/j.pcad.2011.02.003.

Briones Claudett KH, Briones Claudett M, Chung Sang Wong M, Nuques Martinez A, Soto Espinoza R, Montalvo M, et al. Noninvasive mechanical ventilation with average volume assured pressure support (AVAPS) in patients with chronic obstructive pulmonary disease and hypercapnic encephalopathy. BMC Pulm Med. 2013;13:12.

Ciftci F, Ciledag A, Erol S, Oz M, Acar D, Kaya A. Evaluation of the feasibility of average volume-assured pressure support ventilation in the treatment of acute hypercapnic respiratory failure associated with chronic obstructive pulmonary disease: a pilot study. J Crit Care. 2017;39:232–7. https://doi.org/10.1016/j.jcrc.2016.12.023.

Kakazu M, Soghier I, Afshar M, Brozek J, Wilson K, Masa J, et al. Weight loss interventions as treatment of obesity hypoventilation syndrome. A Systematic Review. 2020;17(4):492–502.

Malhotra RK, Kirsch DB, Kristo DA, Olson EJ, Aurora RN, Carden KA, et al. Polysomnography for obstructive sleep apnea should include arousal-based scoring: an American Academy of sleep medicine position statement. J Clin Sleep Med. 2018;14(7):1245–7. https://doi.org/10.5664/jcsm.7234.

Mandal S, Suh ES, Harding R, Vaughan-France A, Ramsay M, Connolly B, et al. Nutrition and exercise rehabilitation in obesity hypoventilation syndrome (NERO): a pilot randomised controlled trial. Thorax. 2018;73(1):62–9. https://doi.org/10.1136/thoraxjnl-2016-209826.

Marik PE. The malignant obesity hypoventilation syndrome (MOHS). Obes Rev. 2012;13(10):902–9. https://doi.org/10.1111/j.1467-789X.2012.01014.x.

Masa JF, Mokhlesi B, Benítez I, Gomez de Terreros FJ, Sánchez-Quiroga M, Romero A, et al. Long-term clinical effectiveness of continuous positive airway pressure therapy versus non-invasive ventilation therapy in patients with obesity hypoventilation syndrome: a multicentre, open-label, randomised controlled trial. Lancet (London, England). 2019; 393(10182):1721–32.
Munoz S, Nowzaradan Y, Varon J. Extreme obesity in the intensive care unit: the malignant obesity hypoventilation syndrome. J Intensive Care Med. 2013; 28(2):134–5. https://doi.org/10.1177/1559827612445707.
Murphy PB, Davidson C, Hind MD, Simonds A, Williams AJ, Hopkinson NS, et al. Volume targeted versus pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomised controlled trial. Thorax. 2012;67(8):727–34. https://doi.org/10.1136/thoraxjnl-2011-201081.
Raveendran R, Wong J, Singh M, Wong DT, Chung F. Obesity hypoventilation syndrome, sleep apnea, overlap syndrome: perioperative management to prevent complications. Curr Opin Anaesthesiol. 2017;30(1):146–55. https://doi.org/10.1097/ACO.0000000000000421.
Sahni S, Capozzi B, Iftikhar A, Sgouras V, Ojrzanowski M, Talwar A. Pulmonary rehabilitation and exercise in pulmonary arterial hypertension: an underutilized intervention. J Exerc Rehabil. 2015;11(2):74–9. https://doi.org/10.12965/jer.150190.
Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med. 2012;366(17):1567–76. https://doi.org/10.1056/NEJMoa1200225.
Sjostrom L, Narbro K, Sjostrom CD, Karason K, Larsson B, Wedel H, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007; 357(8):741–52. https://doi.org/10.1056/NEJMoa066254.
Storre JH, Seuthe B, Fiechter R, Milioglou S, Dreher M, Sorichter S, et al. Average volume-assured pressure support in obesity hypoventilation: a randomized crossover trial. Chest. 2006;130(3):815–21. https://doi.org/10.1378/chest.130.3.815.
Sunwoo BY, Mokhlesi B. Obesity hypoventilation syndrome: will early detection and effective therapy improve long-term outcomes? J Clin Sleep Med. 2018; 14(9):1455–7. https://doi.org/10.5664/jcsm.7310.
Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The Global Syndemic of Obesity, Undernutrition, and Climate Change. The Lancet Commission report. Lancet (London, England). 2019;393(10173):791–846.
Yin J, Kong AP, Chan JC. Prevention and care programs addressing the growing prevalence of diabetes in China. Curr Diab Rep. 2016;16(12):130. https://doi.org/10.1007/s11892-016-0821-8.

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