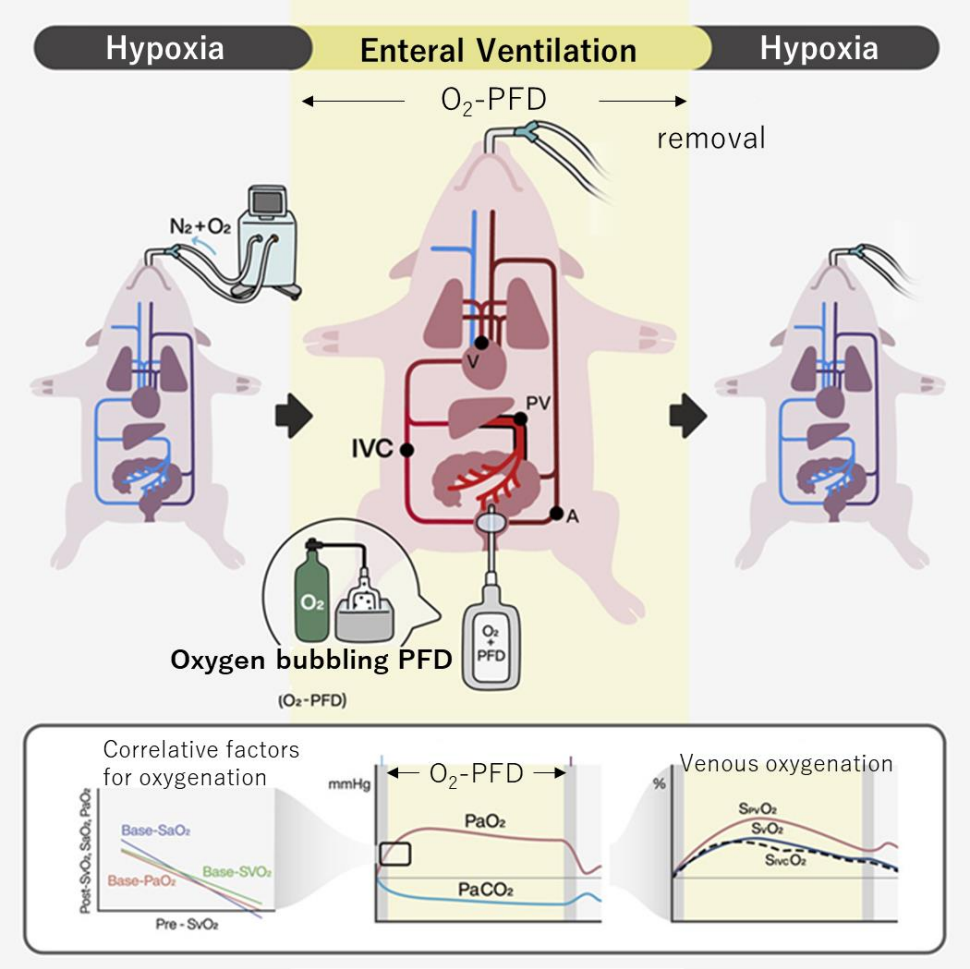
News Release

Title: Enteral ventilation with liquid breathing leads to improvement of hypoxia

Summary

A research group consists of Professor Takanori Takebe (Institute of Research, Tokyo Medical and Dental University), Lecturer Tasuku Fujii and Professor Kimitoshi Nishiwaki (Department of Anesthesiology, Nagoya University Graduate School of Medicine), and Professor Toyofumi Yoshikawa (Department of Respiratory Surgery, Nagoya University Graduate School of Medicine), have demonstrated that liquid breathing using the distal intestine, i.e., enteral ventilation, provided oxygenation and ventilation effects in a hypoxic pig model. Based on this research, it is expected to develop a new respiratory support system that does not depend on lung function for patients with respiratory failure. This work was supported by funding from AMED for the Research Projects on COVID-19 (JP20fk0108278, 20fk0108506h0001, 21fk0108491h0001), and JSPS KAKENHI Grant Number JP21H04822 (Principal Investigator: Takanori Takebe). The research finding will be published in the international scientific journal, *iScience* (volume26 Issue3) on March 17, 2023.



Research Background

Oxygen therapy is commonly used for patients with respiratory failure, such as COVID-19. For severe respiratory failure, mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO) are used. However, these therapies can cause serious complications, including lung damage due to mechanical ventilation, bleeding and thrombosis in vital organs, and systemic infections. In addition, the shortage of medical equipment and human resources will become a problem during a pandemic of respiratory infections. Therefore, there is an urgent need to develop a new respiratory support system that is safer, less invasive, and more convenient to provide oxygenation and ventilation effects. A research group led by Professor Takanori Takebe (Institute of Research, Tokyo Medical and Dental University) focused on intestinal respiration performed by aquatic organisms such as the loach, and showed that mammals such as mice also have a respiratory function using the distal intestine. This research group is aiming to apply the enteral ventilation clinically.

Research Results

Initially, they established a hypoxic pig model of respiratory failure, highly extrapolation to humans, by controlled mechanical ventilation with a muscle relaxant under general anesthesia. They conducted experiments using a rectal catheter and perfluorodecaline (PFD) which are already used as medical devices. This research method is to validate the oxygenation and ventilation effects of distal intestinal mediated respiratory support by administration of oxygen-bubbled PFD (O_2-PFD) into the rectum through a catheter like an enema.

As a result of this research, they found that enteral ventilation has both oxygenation effect (increased in oxygen of systemic blood) and ventilation effect (decreased in carbon dioxide of systemic blood) (Fig. 1). They also showed that enteral ventilation oxygenated the systemic blood through the oxygenation of local venous blood in distal intestine. In addition, there were no serious side effects such as adverse effects on hemodynamics (blood pressure and pulse rate) during the enteral ventilation and significant pathological changes in the distal intestine and spleen.

Research Summary and Future Perspective

This study demonstrates for the first time in the world that enteral

ventilation, a new medical concept, provides efficacy and safety in a large hypoxic animal model. We can have hope that the enteral ventilation will be used in the clinical practice in the future. Enteral ventilation is expected to be used in the following situations: insufficient medical resources of oxygen therapy due to respiratory infection pandemic, transporting patients with respiratory failure to other medical facilities, ensure time to prepare for mobilization of medical staff and oxygen therapy upgrade for the progress of respiratory failure.

Although it will be necessary to confirm the effectiveness and safety in human clinical trials in order to clinically adapt to the enteral ventilation, it is highly expected that this simpler and safe new respiratory support system that does not depend on the pulmonary function can provide treatments that contribute to the prognosis of patients.

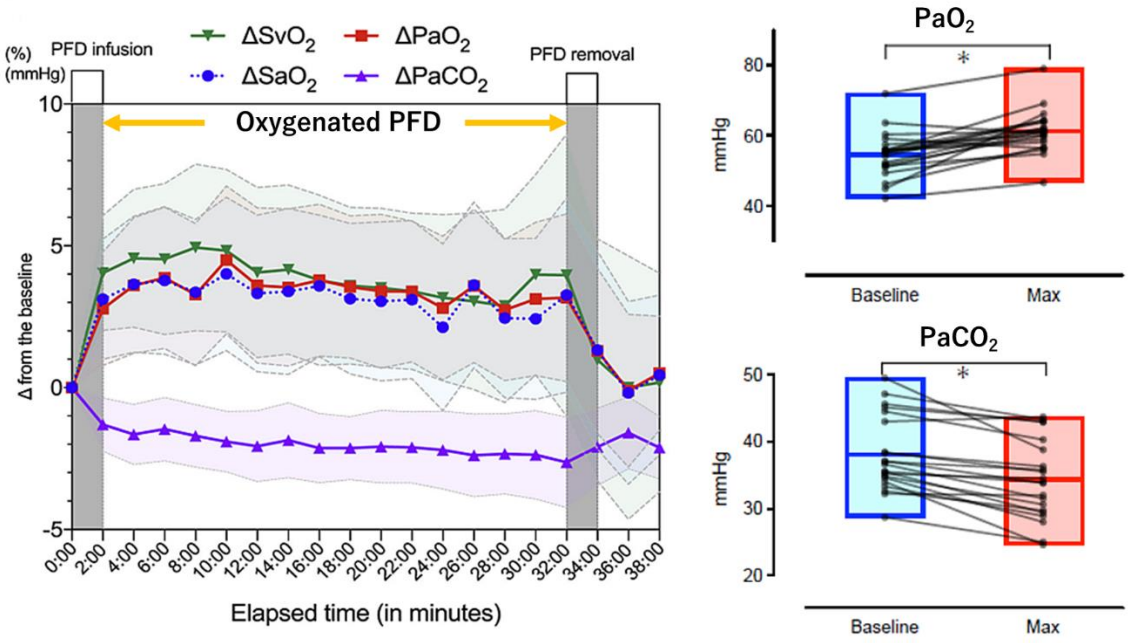


Fig.1：Systemic oxygenation and ventilation effects by enteral ventilation

While the oxygen bubbling PFD (Oxyganated PFD, O_2-PFD) was stored in the distant intestine, there was an oxygenization effect (increase in SaO_2, PaO_2, SvO_2) and a ventilation effect (decrease in $PaCO_2$). Then, after removing the O_2-PFD from the distant intestine, these effects are canceled.

Publication

The article, “Enteral liquid ventilation oxygenates a hypoxic pig model” was published in iScience. DOI：https://doi.org/10.1016/j.isci.2023.106142

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