10.5 ± 1.3 (range, 8–12 cm H2O). In contrast, one patient breathed exclusively through the mouth. OSA was abolished at 17 cm H2O of CPAP. Among the patients who breathed predominantly through the nose (n = 11), the percentage of oronasal plus oral breaths was similar during awake versus sleep (8.8% [1.0–17.4%] vs. 1.5% [0.2–4.5%]; P = 0.11) and non-REM versus REM sleep (1.9% [0.3–5.0] vs. 0% [0–0.9%]; P = 0.08). Among patients who slept in both supine and lateral positions (n = 8), percentage of oronasal plus oral breaths was not significantly affected by position supine versus lateral while awake (10.1 [1.8–17.5] vs. 4.9 [1.3–23.8]; P = 0.94) and during sleep (0.8 [0–9.2] vs. 0.3 [0–2.4]; P = 0.31) (Figure 2).

Discussion
Our study reconciles previous physiological studies indicating that CPAP delivered by oronasal mask is less effective to treat OSA when the patient breathes predominantly through the mouth with the clinical observation that several patients are well adapted to oronasal CPAP (8). We confirmed the hypothesis that successful oronasal CPAP titration is associated with predominantly nasal breathing in 11 out of 12 patients. The only patient who breathed exclusively through the mouth required a CPAP of 17 cm H2O, well above the remaining patients (8–12 cm H2O). We speculate that in this patient, lung hyperinflation, induced by the high level of CPAP, was sufficient to stabilize airway patency owing to tracheal tug. The patient who breathed exclusively through the mouth only slept in the supine position. Unfortunately, he refused to return for a second study. We have recently reported one patient with OSA on oronasal mask for whom CPAP titration was successful in the lateral position but ineffective in the supine position. This observation raised the hypothesis that oral breathing may increase in the supine position, resulting in CPAP failure (9). In our study, breathing pattern was not significantly influenced by position and sleep stage. However, no reliable conclusion is possible because the number of observations was small, as the patients breathed predominantly through the nose at all times (Figure 2). We also showed that oral expiration, which can be associated with palatal prolapse, was rare (10). We are particularly concerned with widespread use of oronasal CPAP to treat OSA after the recent evidence that the acute transition from nasal CPAP to oronasal CPAP during flow limitation resulted in airway obstruction even in patients breathing exclusively through the nose (6). However, future studies are necessary to test the hypothesis that nasal-breathing patients benefit from switching from an oronasal to a nasal mask.

Conclusions
Patients with OSA who are well adapted to oronasal CPAP breathe predominantly through the nose. Our findings suggest that a nasal mask may be suitable for many patients using an oronasal mask.

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circGSAP: A New Clinical Biomarker for Idiopathic Pulmonary Hypertension?

To the Editor:

We read with interest the recent paper published by Yuan and colleagues (1). They find that lower circGSAP (circular
γ-secretase activating protein) level is associated with the occurrence and poor prognosis of idiopathic pulmonary hypertension (IPAH). circGSAP may be an emerging biomarker for the diagnosis and prognosis of IPAH. We first congratulate the authors for clarifying the correlation between them for the first time, which provides a new direction for our diagnosis and treatment of IPAH. This is an important field, but the relationship between them has not yet been fully studied.

As we all know, patients with PAH have a poor prognosis if they do not receive an early diagnosis and adequate treatment (2). However, the current main approach for the diagnosis and treatment of IPAH is based on invasive hemodynamics and subjective parameters (3). This brings great inconvenience to the diagnosis and treatment of IPAH in many places and even delays the condition of IPAH. In addition, in current clinical practice, there are only three drugs for PAH, including nitric oxide–cyclic guanosine monophosphate pathway, prostacyclin pathway, and endothelin pathway, and the efficacy is not ideal (2). The research results of Yuan and colleagues provide a new direction for solving this problem, and we affirm the authors’ contribution in this regard (1). With the development of high-throughput sequencing technology and bioinformatics, more and more data show that circular RNA (circRNA) plays an important role in regulating gene expression (3).

The expression profile of circRNA has been analyzed in the context of many diseases such as tumors, hypertension, cardiovascular disease, pulmonary fibrosis, pulmonary tuberculosis, and acute lung injury, which has a great impact on the diagnosis and treatment of these diseases (3). As far as we know, circRNA is a kind of epigenetic modifier, and their disorder is related to the pathogenesis of the disease. It has attracted extensive attention as a biomarker or therapeutic target (3–5). From the experimental results at the clinical, cellular, and animal levels, the studies of Yuan and colleagues have well proved that the lower circGSAP level is related to the occurrence and poor prognosis of IPAH (1). Therefore, the relationship between circRNA and IPAH is worthy of further study.

However, there are still some problems in the research of Yuan and colleagues (1). The comparison between the control group and the experimental group in the clinical baseline of the patient did not list the P value, and it is not known whether the statistical difference is significant. To minimize the influence of other factors, we should try to match common demographic characteristics, and even control related covariates in multivariate regression analysis.

In a word, although the research of Yuan and colleagues still has some limitations, it is undeniable that their research has opened a new situation for our diagnosis and treatment of IPAH (1). We suggest that the authors perform enrichment analysis on the differential expression screened in the article to provide relevant signal pathways, which will provide great convenience for the subsequent research on mechanisms and therapeutic targets. In addition, the authors have calculated the receiver operating curve area of circGSAP, but its predictive value is not very high. It can be combined with other meaningful indicators to build a model, and even machine learning methods can be used to analyze and choose a more appropriate model to predict IPAH, which may make this research more meaningful. Finally, we suggest expanding the sample size and conducting a multicenter study to provide further evidence for clinical practice.

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