中枢性睡眠時無呼吸症用デバイスは心不全の死亡率を上昇させる(ESC2015 Presentation＃5063)

慢性心不全患者における中枢性睡眠時無呼吸症の治療に関して、実際の診療を変化させるガイダンスがスタディにより提供された

Study provides practice-changing guidance for the treatment of central sleep apnea in patients with chronic heart failure

適応補助換気（ASV）は死亡率を増加させるため、心駆出率の低下した心不全患者の中枢性睡眠時無呼吸症の治療には使用すべきでない、との研究結果が2015年ESC Congressで発表され同時に*New England Journal of Medicine*に掲載された。SERVE-HFトライアルにおいて、心駆出率の低下した慢性心不全患者1325人が、ガイドラインベースの薬物管理のみ（コントロール群）または推奨されている夜間5時間週7回のASVを加える群にランダムに割り付けられた。追跡期間中央値31か月後、ASVは中枢性睡眠時無呼吸症の治療には有効であったが、一次エンドポイントである総死亡、救命のための心血管インターベンション、または心不全悪化による予定外入院の合計である一次エンドポイントにおいて効果がなかった。一次エンドポイントのイベント率はASV群の54.1%に対し、コントロール群では50.8%であった（ハザード比[HR]1.13；p=0.10）。さらに、ASVを標準治療に追加しても、QOL、6分間歩行距離、または症状などの機能的計測値において有益な効果が認められなかった。しかし、総死亡率および心血管系死亡率はASV群でコントロール群よりも高かった（34.8% 対29.3%；HR 1.28；p=0.01および29.9%対24.0% HR 1.34；p=0.006）。

Full Text

Adaptive servo-ventilation (ASV) therapy increases mortality and should not be used to treat central sleep apnea in heart failure patients with reduced ejection fraction, the SERVE-HF trial shows.

The Hot Line study, presented at ESC Congress 2015, and published simultaneously in the New England Journal of Medicine, "provides practice-changing guidance for the treatment of chronic heart failure (CHF)," said Martin Cowie, MD, co-principal investigator of the study, from Imperial College London, in London, UK.

"This study has changed our understanding of sleep-disordered breathing in systolic heart failure – the text books will have to be rewritten," he commented. "Doctors now know that treatment of central sleep-disordered breathing by mask therapy is not helpful for these patients and might be harmful. Lives will be saved by the findings of this new study."

Professor Cowie emphasized that patients in the study had reduced ejection fraction and predominantly central sleep apnea, and therefore the results cannot be generalized to patients with preserved ejection fraction or obstructive sleep apnea.
Unlike obstructive sleep apnea, central sleep apnea (CSA) is caused by the brain failing to trigger breathing during sleep.

ASV is designed to detect significant variation in breathing and deliver pressure through a facemask in order to maintain a normal breathing pattern.

In SERVE-HF (which stands for The Treatment of Sleep-Disordered Breathing With Predominant Central Sleep Apnoea by Adaptive Servo Ventilation in Patients With Heart Failure) 1,325 chronic heart failure patients with a reduced ejection fraction who were randomized to receive either guideline-based medical management alone (control group), or with the addition ASV for a recommended 5 hours per night, 7 days a week.

After a median follow-up of 31 months ASV effectively treated central sleep apnea but had no effect on the primary end point, which was a combination of all-cause death, life-saving cardiovascular intervention, or unplanned hospitalization for worsening heart failure.

The event rate for the primary outcome was 54.1% in the ASV group compared to 50.8% in the control group (hazard ratio [HR] 1.13; P=0.10). Moreover, the addition of ASV to standard care had no beneficial effect on functional measures, including quality-of-life, six-minute walk distance, or symptoms.

However, all-cause mortality and cardiovascular mortality were higher in the ASV group than in the control group (34.8% versus 29.3%; HR 1.28; P=0.01 and 29.9% versus 24.0%; HR 1.34; P=0.006).

"The early and sustained increase in cardiovascular mortality seen with ASV was unexpected, and the reasons for this effect remain unclear," said Professor Cowie, noting that the SERVE-HF results are contrary to findings from some previous studies.

One possible explanation for this is that central sleep apnea may actually be a compensatory mechanism in some heart failure patients, he suggested.

"Potentially beneficial consequences of central sleep apnea in these patients could be that it rests respiratory muscles, and modulates excessive sympathetic nervous system activity, and by diminishing this effect ASV may be detrimental for patients with heart failure."

Although SERVE-HF did not meet its primary endpoint, "it was a well-designed and executed study," concluded Professor Cowie, "and because of it we now know that ASV therapy is contraindicated in this subset of chronic heart failure patients."

The SERVE-HF study was funded by ResMed Ltd.Professor Cowie receives research funding and consultancy fees from ResMed Ltd.

Conference News