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## Cardiac contractility modulation provides improved ventilatory efficiency and reduces oscillatory breathing pattern

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**Introduction:** Cardiac Contractility Modulation (CCM) is a treatment for patients with heart failure with reduced ejection fraction (HFrEF) providing improved myocardial molecular and biochemical characteristics and thus improved exercise tolerance and quality of life by application of electrical signals during the absolute refractory period.

Cardiopulmonary exercise testing is an integrative method to assess exercise tolerance in heart failure patients providing insights in circulatory, respiratory and metabolic reactions during exercise. The VE/VCO2-Slope (minute ventilation/carbon dioxide production) and an oscillatory breathing pattern have widely been demonstrated to have strong prognostic value for patients with chronic heart failure.

**Methods:** Between February 2017 and January 2019 15 patients (mean age 64.4±7.9 years, NYHA 2.93±0.58) with standard indication for CCM-therapy have been enrolled in a single center in Germany. Prior to implantation of the Optimizer Smart System, symptom-limited cardiopulmonary exercise testing was performed using a bicycle ramp protocol (25W+10W/min). The Follow-up was conducted 6 weeks post implantation. The control group consisted of 45 patients (mean age 64.8±7.9 years, NYHA 2.2±0.72) with stable systolic heart failure and reduced ejection fraction. Statistical Analysis was performed by paired and unpaired t tests.

**Results:** 6 weeks after CCM-implantation the VE/VCO2-Slope showed a significant decrease (39.6±11.1 vs. 36.6±8.9, p<0.05) showing changes in

ventilatory efficiency whereas the control-group showed stable measurements with even an increasing tendency (33.6±7.4 vs. 34.2±7.4, p=0.43). The absolute change of the VE/VCO2-Slope between the CCM-group and control-group highlights the improvement after the intervention (–2.99±5.07 vs. 0.63±4.79, p<0.05). The number of patients presenting an oscillatory breathing pattern markedly decreased with CCM-therapy (11 of 15 vs. 6 of 15, p<0.05), whereas even one additional patient of the control group showed an oscillatory breathing pattern at follow up (15 of 45 vs. 16 of 45). In contrast, subjects showed no significant changes in watt-measurements (72.67 W  $\pm$  19.2 W vs. 76.57 W  $\pm$  18.5 W) or maximal oxygen uptake (1034 ml/min  $\pm$  247 ml/min vs. 1104 ml/min  $\pm$  256 ml/min) compared to baseline. Similarly, the control-group showed stable measurements for external load (79.9 W  $\pm$  16.4 W vs. 77.1 W  $\pm$  17.5 W) and peak oxygen uptake (1097 ml/min  $\pm$  225 ml/min vs. 1116 ml/min  $\pm$  330 ml/min).

**Conclusion:** Cardiac Contractility Modulation provides improved ventilatory efficiency measures by VE/VCO2-slope and reduces oscillatory breathing pattern during exercise at follow up. As the low ventilatory efficiency observed in patients with heart failure constitutes an important predictor of cardiovascular mortality these results provide an interesting insight of therapeutic effects of Cardiac Contractility Modulation apart from VO2-measurements.