**Introduction:**
Intrinsic positive end-expiratory pressure (PEEPi) may substantially increase the inspiratory effort during assisted mechanical ventilation. Our purpose of the study was to assess whether electrical activity of the diaphragm (EAdi) can be reliably used to estimate PEEPi in patients undergoing conventional pneumatically-controlled pressure support (PSP) ventilation and neutrally-controlled pressure support (PSN) and whether PSN was beneficial in comparison with PSP in patients affected by PEEPi.

**Methods:**
Twelve intubated and mechanically ventilated COPD patients with static PEEPi $\geq$5cm H2O underwent PSP and PSN at different levels of extrinsic PEEP (PEEPe) (at 0%, 40%, 80%, and 120% of static PEEPi, for 12 minutes at each level on average), at matching peak airway pressure. We simultaneously recorded EAdi, airway, esophageal pressure, and flow. Tracings were analyzed to measure dynamic PEEPi (decrease in esophageal pressure to generate inspiratory flow), and intrinsic-EAdi (EAdi value at the onset of inspiratory flow), and IDEAdi (inspiratory delay between the onset of EAdi and the inspiratory flow).

**Results:**
Mean airway pressure was comparable for PSP and PSN at same target levels. The pressure necessary to overcome PEEPi, intrinsic-EAdi, and IDEAdi was significantly lower in PSN as compared with PSP, decreased with increase in PEEPe, although the effect of external PEEP was less pronounced in PSN. Intrinsic-EAdis at different PEEPe in PSP were tightly correlated with dynamic PEEPi ($r^2 =0.46$, $r^2 =0.56$, $r^2 =0.71$, $r^2 =0.62$, respectively).

**Conclusion:**
In COPD patients with PEEPi, PSN compared with PSP, led to a decrease in the pressure necessary to overcome PEEPi, which could be reliably monitored by the electrical activity of the diaphragm before inspiratory flow onset (intrinsic-EAdi) in PSP.