

## Réanimation respiratoire : translationnel

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### Impact of subject-ventilator dyssynchrony on diaphragm function and structure

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#### Position du problème et objectif(s) de l'étude:

Subject-ventilator dyssynchrony following prolonged controlled mechanical ventilation (CMV) is common and associated with extubation failure, extended ICU length of stay and mortality (1,2). The direct impact of dyssynchrony on diaphragm after prolonged CMV is unknown. Our aim was to assess the effect of dyssynchrony after CMV on diaphragm function and structure in a piglet model of eccentric contraction (assimilated to ineffective efforts) and overdistension (assimilated to double triggering).

#### Matériel et méthodes:

The Institutional (University of Montpellier, France) and the Regional (CEEA-LR-36) Ethics Committees for Animal Research and Care, and the French Ministry of Agriculture (Paris, France) approved the study protocol (APAFIS #15866 2018070509081002). In this experimental study, 10 Large-White piglets were sedated and maintained under totally CMV during 72h followed by 2 hours of dyssynchrony with ineffective efforts and double triggering patterns. Diaphragm function (as previously described (3) supramaximal diaphragm force assessed by negative tracheal pressure (Ptrach) after phrenic nerve transvenous stimulation) was recorded at baseline (start of sedation), after 72h of CMV and after additional 2h of dyssynchrony. Diaphragm structure (sarcomeric injuries) was evaluated by electronic microscopy from biopsies harvested after 72h of CMV and after additional 2h of dyssynchrony.

#### Résultats & Discussion:

Of all the piglets, initially healthy, one died of sudden cardiac arrest following severe ARDS and was therefore excluded. The others 9 piglets completed the experiment. Supramaximal diaphragm force decreased by 22% from  $69.9 \pm 12.7$  to  $54.9 \pm 19.7$  cmH<sub>2</sub>O ( $p=0.025$ ) after 72h of CMV attesting the ventilatory-induced-diaphragm-dysfunction (VIDD). It dropped by an additional 29% from  $54.9 \pm 19.7$  to  $38.9 \pm 15.5$  cmH<sub>2</sub>O ( $p<0.005$ ) after the additional 2h period of dyssynchrony (figure 1), with a  $54 \pm 15\%$  rate of dyssynchronous cycles. Diaphragm sarcomeric injuries accounted for  $13 \pm 10\%$  of the total micrograph area after 72h of CMV and increased to  $24 \pm 19\%$  ( $p<0.001$ ) after the additional 2h of dyssynchrony (figure 2).

#### Conclusion:

Two hours of subject-ventilator dyssynchrony in pre-existing ventilatory-induced-diaphragm-dysfunction are associated with further impairment of diaphragm function and additional damage to the diaphragm structure in this experimental piglet model.

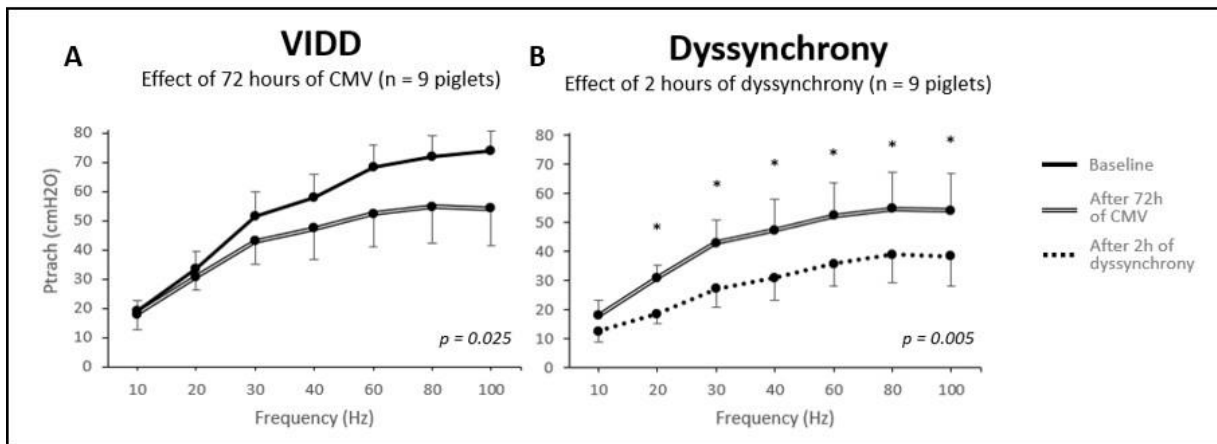
#### Références bibliographiques:

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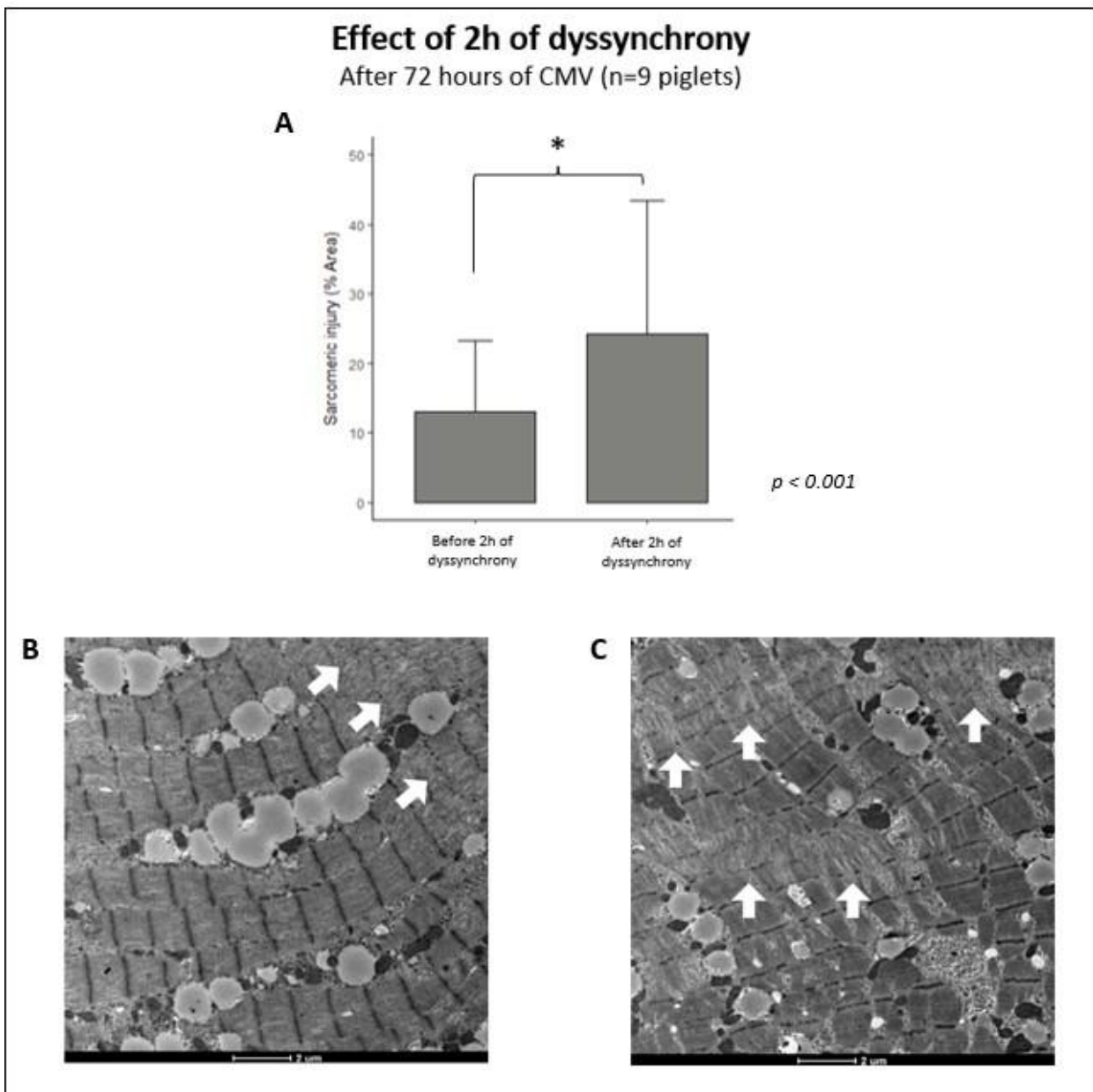
P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. *Intensive Care Med.* 2006;32(10):1515-22. 3. Jaber S, Jung B, Sebbane M, Ramonatxo M, Capdevila X, Mercier J, et al. Alteration of the Piglet Diaphragm Contractility In Vivo and Its Recovery after Acute Hypercapnia: *Anesthesiology.* 2008;108(4):651-8.

**Figure 1:** diaphragmatic force frequency curves (A) at baseline versus after 72 hours of totally controlled mechanical ventilation (CMV), (B) and after 72 hours of CMV versus after additional 2 hours of dyssynchrony, for the same piglets (n=9).



VIDD: Ventilatory-Induced-Diaphragm-Dysfunction. CMV: Totally controlled mechanical ventilation. Ptrach: tracheal pressure. Posted p-values between two periods were obtained after two-way ANOVA. \*  $p < 0.01$  between two periods using paired t-test with Bonferroni correction for post hoc analysis.

**Figure 2:** (A) percentage area of diaphragm sarcomeric injury after 72 hours of totally controlled mechanical ventilation (CMV), before versus after additional 2 hours of dyssynchrony. Representative electron microscopy images of longitudinal ultrathin sections obtained from the diaphragms after 72 hours of CMV (B) before and (C) after additional 2 hours of dyssynchrony. White arrows show disorganization of sarcomeric structure.



CMV: Totally controlled mechanical ventilation. Posted  $p$ -values between two periods was obtained after paired  $t$ -test. \*  $p < 0.05$  between two periods.

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