

European Respiratory Society Annual Congress 2013

Abstract Number: 2075

Publication Number: 388

Abstract Group: 2.1. Acute Critical Care

Keyword 1: Mechanical ventilation **Keyword 2:** Sepsis **Keyword 3:** Animal models

Title: Controlled mechanical ventilation in septic animals: Effects on diaphragm function

Dr. Karen 18927 Maes karen.maes@med.kuleuven.be¹, Ms. Debby 18928 Thomas debby.thomas@med.kuleuven.be¹, Ms. Cielen 18929 Nele nele.cielen@med.kuleuven.be¹, Dr. Smuder 18930 Asley asmuder@php.ufl.edu², Prof. Dr Powers 18931 Scott spowers@hhp.ufl.edu², Prof. Dr Hermans 18933 Greet greet.hermans@uzleuven.be³, Dr. Stamiris 18934 Angela angela.stamiris@muhc.mcgill.ca⁴, Prof. Dr Sabah 18935 Hussain sabah.hussain@muhc.mcgill.ca⁴, Prof. Dr Marc 18937 Decramer marc.decramer@uzleuven.be¹ and Prof. Dr Ghislaine 18951 Gayan-Ramirez ghislaine.gayan-ramirez@med.kuleuven.be¹. ¹ Department of Clinical and Experimental Medicine, KULeuven, Leuven, Belgium, 3000 ; ² Department of Applied Physiology and Kinesiology, University of Florida, Gainesville, FL, United States ; ³ Medical Intensive Care Unit, University Hospital, Leuven, Belgium, 3000 and ⁴ Department of Critical Care Medicine, McGill University, Montreal, Canada .

Body: Controlled mechanical ventilation (CMV) was shown to result in diaphragmatic dysfunction and atrophy in healthy animals. Whether mechanical ventilation results in more severe diaphragm dysfunction in animals with already weakened diaphragms is not known and was examined in septic animals. Male Wistar rats were either treated with lipopolysaccharide (5 mg/kg) to induce sepsis or with saline. After 12 hours they were divided into 3 groups: sepsis, sepsis+12hCMV and saline+12hCMV. The levels of IL-6 in plasma and in diaphragm were significantly increased in the sepsis+12hCMV group compared to the other groups. Diaphragm force was significantly lower in septic animals compared to saline+12hCMV with an additional decrease in the sepsis+12hCMV group compared to the sepsis group. mRNA expression of diaphragm MuRF1 and atrogin-1, markers of the proteasome system, were significantly higher in the sepsis+12hCMV group compared to the other groups. Diaphragm fiber dimensions and 4-HNE, a marker of oxidative stress, were similar in all groups. LC3B protein lipidation, used as an indirect assessment of autophagy, was increased in sepsis+12hCMV compared to the other groups. Similarly, protein levels of several autophagy-related genes including those involved in the initiation of autophagosome formation (ULK1, BECLIN1, PI3KC3), and targeting of the mitochondria by autophagosomes (SQSTM1, BNIP3 and PARKIN) were significantly increased in sepsis+12hCMV compared to the others. These data clearly show that CMV in septic animals further compromises diaphragm function, activates atrophic pathway and favors autophagosome formation. Supported by FWO-Flanders G.0893.11 and AstraZeneca Pharmaceuticals.