The authors respond

To the Editor:

We thank Drs Bonorino and Cani for their interest in our study and for the important points they raised regarding our research.[1] The first point was the great number of excluded patients and the small sample size. Of 113 eligible patients, we included only 8. We agree that this small sample does not necessarily represent all the subjects admitted to a clinical-surgical ICU, and it limits the external validity of our results. We stated this limitation in the original article and discussed that the small sample size may have hindered the inference of the impact of early exercise on subject-ventilator asynchrony. Moreover, it may also have limited the inference of the impact of asynchrony on clinical outcomes, such as duration of mechanical ventilation, ICU length of stay, or mortality. We did not describe the characteristics of the excluded patients because we followed the STROBE statement for observational studies.[2] According to STROBE, we should report the number of subjects at each stage of the study, give reasons for nonparticipation at each stage, and use a flow diagram to clearly show these steps. To our knowledge, those steps were followed.

The second point that was raised was the necessity of a standardized analgesia to avoid asynchrony caused by pain or discomfort during the exercise period. In our ICU, we follow a strict analgesic protocol for pain management, and before the exercise sessions subjects were comfortable. Pain or discomfort may have occurred during exercise and may have contributed to asynchrony. However, other signs, such as tachycardia and increase in arterial pressure, which would be expected in the presence of pain or discomfort, were not observed. Moreover, the aim of our study was to identify the occurrence of asynchrony during and after passive exercise, regardless of their possible causes.

The third point was about the limitation of using waveforms to detect asynchrony. Although they are not the most accurate method to detect asynchrony, waveforms are commonly used at bedside for this purpose. Different studies measuring the accuracy of waveforms to detect asynchrony have shown a wide range of results.[3,4] Colombo et al[5] reported low sensitivity and positive predictive value for detecting asynchrony with waveforms (22% and 32%, respectively), results that improved to some extent (55% and 44%, respectively) in cases in which asynchrony were frequent (asynchrony index > 10%). However, in the study cited by Drs Bonorino and Cani, Chacón et al[6] reported that trained nurses could detect asynchrony based on waveforms with high accuracy (ie, 92.5% sensitivity and 95.4% positive predictive value, not 22% and 32%, respectively, as stated in the letter).

The fourth point was about the possible occurrence of reverse-triggering, a type of asynchrony that could have been misdiagnosed as insufficient flow. Reverse-triggering is the muscular effort triggered by passive insufflation of the lungs and occurs primarily around the transition phase from inspiration to expiration.[7] In reverse-triggering, the breath is triggered by the machine, and signs of subject's effort, such as airway pressure decrease and flow increase, are not seen in the waveforms.[8,9] The cycles with insufficient flow that we identified in our study were triggered by the subject (Fig. 3A in our article), which allowed us to rule out reverse-triggering. The same be-havior was found in the cycles with double-triggering, another type of asynchrony that could have been mistaken for reverse-triggering.

Finally, the authors stated that insufficient flow, one of the most frequent types of asynchrony observed in our study, typically occurs during volume controlled ventilation, whereas our subjects were ventilated in the pressure controlled mode. Although insufficient flow is more common in the volume controlled mode with a fixed flow pattern, it can also occur in modes with a variable flow, including pressure controlled ventilation. During pressure controlled ventilation, the flow generated by the ventilator depends on the level of the adjusted pressure and the rise time. When these parameters are adjusted below the subject's demand, the subject may contract their inspiratory muscles more vigorously. This contraction can lead to a decrease of the airway pressure with a simultaneous change of the decelerate pattern of the inspiratory flow, a marker of this type of asynchrony.[10]

Our study, despite the limitations that we stated in the discussion and others raised by Drs. Bonorino and Cani, indicates that different types of asynchrony can occur during passive exercise in deeply sedated subjects. However, further studies are necessary for better understanding of these asynchronies.

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