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Simulation Studies for Device Evaluation—Reply

In Reply:

Mr Chatburn begins his letter explaining what should be simulation in medicine. Many of the ventilator bench studies published before are only bench tests, as our study, and not a simulation of a more complex reality. The goal of this study was to test transport ventilators under conditions similar to those used in previous studies and to assess their performance limits. Moreover, we have pointed out that bench studies are not for commercial advertising. In our study,[1] we were not interested in giving any awards for a particular ventilator, and we had no interest in any of the manufacturers. This is not the case for Mr Chatburn, who is paid consultant for a testing device company (which he cites in his letter) and three manufacturers of ventilators that we have studied in this work.

We have tried to show that there has been major improvement in the field of transport ventilators in comparison with older technology. Therefore, we implemented the same experiment as that performed in an older study (10 y ago)[2] using the same parameters for the static portion; used the same dynamic experiments as used in many previous bench studies.[3-8]

In addition, we showed that the most recent turbine transport ventilators are a breakthrough in the field of transport ventilators even if they have some limitations, and their performances are close to those of ICU ventilators.

Choice of Lung "Simulator"

Mr Chatburn criticizes the choice of the Training and Test Lung (TTL) simulator (Michigan Instruments, Grand Rapids, Michigan) instead of the ASL 5000 lung simulator (IngMar Medical, Pittsburgh, Pennsylvania). Unfortunately, we do not have this device. To our knowledge, there are no scientific studies proving that this device is more "realistic" than the TTL simulator in passive conditions. The ASL 5000 lung simulator is probably very interesting to test in dynamic conditions. Studies using a TTL simulator are numerous,[3-8] and Mr Chatburn cites only three recent studies using the ASL 500 simulator. To allow better comparison with these more numerous studies carried out using all types of ventilators (transport, home, and ICU), we used the TTL simulator.

Choice of Parameters

Mr Chatburn criticizes our choice of parameters. He argues that the studied parameters are not "realistic." Our answer is that the main goal of this study was to compare this generation of ventilators with the former[2]; we used parameters introduced in the previous studies conducted by well respected teams versed in this topic. Note that one goal is to know the limits of operation of the tested devices. It is not completely absurd to push ventilators to extreme conditions such as resistance (R) = 50 cm H_2O/L/s.

Concerning the definition of a normal compliance, there is no consensus. It is difficult to define what a "normal" value of compliance is because it is different depending on the situation: intubated versus nonintubated subjects, young versus old, etc. Several previous bench studies have used the value used in our work.[2,4,9] One can find this value also in some physiological articles.[10] Azarian et al[11] found a wide range for compliance in healthy volunteers (from 100 to 200 mL/cm H_2O). In their article, they proposed the following formula for the compliance of the respiratory system (C_{RS}): $C_{RS}\,(L \cdot kPa^{-1}) = 3.56 \times \text{height}\,(m) - 4.86$ (± 0.23). This value is 1.548 $L \cdot kPa^{-1}$ for 1.80 m (154 mL/cm H_2O). It is certainly too high for a ventilated patient, but it gives an order of magnitude of what a normal compliance is for a subject who has healthy lungs and has not been ventilated for many days. This value is found also in physiological books.[12] A study published in this Journal went as far as 120 mL/cm H_2O in evaluating performances of ventilators.[13]

We agree that ICU patients rarely have such a compliance value. Some of our patients in our ambulances are in this category (isolated neurotrauma in the first hours, for example). We would like to stress that if we take the formula given by Mr Chatburn in his letter, a young healthy man who is 18 y old and 180 cm tall has a compliance of 95 mL/cm H_2O.

Mr Chatburn cites studies using parameters that seem to him more suitable or advisable. We found several studies with the same resistance parameters,[2,8,14,15] compliance,[2] and tidal volume (V_T)[2,8,14-17] as in our study. Here again, there is no formal scientific evidence that the parameters presented by Mr Chatburn are more "realistic."

We do not want to explain again why V_T = 800 mL was used (previous studies and limits of use). We rarely ventilate patients with V_T = 800 mL, and it is rare to have R = 50 cm H_2O/L/s. We are in agreement with this. It is an extreme functioning of the ventilator, but it was tested in older studies.[2,8,14-16] It is interesting to us to know what a transport ventilator can do or not do in extreme conditions.

The limit of parabolic resistors is well known, but linear resistors are not easily available. Indeed, ventilators are not tested in very similar conditions.

We were aware that Dräger Carina and Hamilton Medical ventilators operate in a pressure control mode, but it is identified as "VAC+" (a dual mode). In this mode, the pressure is controlled by a feedback loop to deliver the V_T set by the clinician. Emergency physicians are not very familiar with these modes. We knowingly tested all of the ventilators in the VAC mode because it is the reality of their use in the field.

The age of the pediatric patients ranged from 0 to 18 y. The transport ventilators tested in our studies are not intended for neonates, who have weak lung compliance and high chest wall compliance. We showed above that the compliance of a 18-y-old boy who is 180 cm tall using the formula recommended by Mr Chatburn was ~100 mL/cm H_2O. We think that Mr Chatburn made a calculation error. A 13-y-old child measures ~160 cm (63 inches), not 63 cm; thus, his lung compliance is near 80 mL/cm H_2O, not 47. We found no study addressing the compliance measurements of teenagers, but we can infer the results of healthy young volunteers. Teenagers may have relatively high respiratory system compliance. In our article, we pointed that there is a problem with highly compliant lung in low volume for one specific ventilator. We had a patient with C = 100 mL/cm H_2O, and one should know this limitation.

We apologize that the equation used to calculate the relative error was not provided in our article. Note that the reviewers did not ask us to correct this. The equation can be found elsewhere, and it is

classic in measurement theory: % error = (V_T measured − V_T set)/V_T set. These relative errors could of course be negative or positive.

Correction of Gas Condition

Ambient temperature and pressure saturated (ATPS)/body temperature and pressure saturated (BTPS) conditions are a well known problem in such studies. Some of the ventilators compensate for BTPS conditions, whereas others do not. Only the Elisée 350 ventilator (ResMed, San Diego, California) allows the operator to turn the compensation on and off manually. We turned it off. The Medumat (Weinmann Medical Technology, Hamburg, Germany), Osiris 3 (Air Liquide Medical System, Paris, France), and Monnal T60 ventilators (Air Liquide Medical System) have no compensation. The Oxylog and Carina ventilators (Dräger Medical, Lübeck, Germany) compensate their display. The Hamilton-T1 and Hamilton-C1 ventilators (Hamilton Medical, Reno, Nevada) are based on the volume, and the readings are in BTPS. As stated in the letter, these devices are not operated with a heated humidifier, and they are for ATPS conditions. The Elisée 350, Monnal T60, Medumat transport, and Osiris 3 ventilators are for ATPS conditions.

The calibration of the pneumotachograph was a flow calibration, with the Puritan Bennett 840 ventilator operating in ATPS conditions as stated in our article. We checked that it was consistent with the Super Syringe measurement (we had < 1% discrepancy). Thus, we measured volume in ATPS. We used the Puritan Bennett 840 ventilator (Puritan Bennett, Dublin, Ireland) with and without BTPS correction, and we recorded for each V_T (300, 500, and 800 mL). We extracted a calibration for BTPS conditions. We agree that it depends on the Puritan Bennett 840 algorithm of compensation, which seems to be precise and efficient.[14] Thus, we corrected the readings of the Hamilton-T1 and Hamilton-C1 ventilators, and we corrected the set V_T of the Carina and Oxylog 3000 ventilators accordingly to the calibration. The difference observed between ATPS and BTPS calibration was < 5% in our study. This discrepancy is explained by the condition of the experiment: it was carried out at an environmental temperature of 30°C for practical reasons (summertime and small non-air-conditioned room).

In addition, is 10% really clinically the problem for a transport ventilator? Ventilators with a severe dysfunction in this study are well above that. We did not study specifically the BTPS/ambient temperature and pressure dry problem in this research, and maybe some interested teams could research this for transport ventilators, as has been done for ICU ventilators.[17] Indeed, without a heated humidifier, the real pressure and temperature of the gas administered to the patient are not known, and more studies are needed.

Conclusion

In this study, we utilized extensively used experimental setups for comparison with older generation transport ventilators or ICU ventilators. Many of the criticisms expressed by Mr Chatburn could have been applied to all of the previous studies. There is no consensus on respiratory parameters or testing devices, and no one can be certain about the realistic parameters for testing such devices. To stay pragmatic and comparative, we used the same parameters as in the previous studies. We found that there has been a major improvement in transport ventilator performance, especially with turbine technology. All have limitations, but the clinical relevance of these limitations remains uncertain.

Bench studies are not strictly simulation studies but are performed to better understand the devices we use every day and their limitations. No tests are perfect, but the lack of testing or partial company testing is undesirable. Independent clinicians should carry on these studies to improve our knowledge of the technology we use, leading to improvements for a new generation of ventilators.

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Near-Infrared Spectroscopy with Vascular Occlusion Test May Not Be the Adequate Tool to Explore Microcirculation in Pulmonary Arterial Hypertension

To the Editor:

Dimopoulos et al[1] likened the microcirculation of stable patients with pulmonary arterial hypertension (PAH) and congestive heart failure (CHF) and matched normal subjects. They found an effect on the microcirculation, measured by near-infrared spectroscopy with vascular occlusion test (NIRS-VOT), in patients with PAH and CHF and a deleterious action of hyperoxia (performed in the PAH group). Despite a very meticulous work and a conclusion that seems fair and pragmatic, their results should be interpreted carefully. I would like to raise several issues.

First, the authors did not comment on the role of hypoxemia in patients with PAH in their study. A partial means of moderating this would have been to assess the extraction of tissue oxygen (O_2) as a surrogate of microcirculatory function.[2] Elevation of the extraction before VOT would indicate microcirculatory dysfunction with decreased O_2 supply to tissue in local demand-supply dependence. This value can be obtained noninvasively and calculated as follows: microvascular oxygen extraction rate (μOER) = $(S_{pO_2} - S_{tO_2})/0.5 \times S_{pO_2}$ (where S_{tO_2} is muscle tissue oxygenation). When fit for S_{pO_2}, μOER values were 33.6, 31, 28, and 20.3 for PAH in the basal state and hyperoxia, CHF, and normal subjects, respectively. A discussion of these results (yet more abnormally high values in PAH) and the role of chronic tissue hypoxia would have been interesting. Accordingly, a decrease in O_2 consumption is seen in tissue with chronic hypoxia, termed conformance.[3] Are we confronted with a paradoxical response to hypoxia (greed for O_2, opposite what is expected with conformance) or microvascular dysfunction? Nevertheless, the paucity of data on cardiac output and the role of chronic hypoxia make this derived value questionable. One can also imagine a different behavior of cells in chronic hypoxia, further amending the dynamic curves (ie, O_2 consumption rate, reactive hyperhemia time, and time interval) compared with the princeps work during sepsis.[4]

Accordingly, elevated venous pressure has been related to impaired microvascular tissue perfusion.[5] Thus, a possible modification of post-capillary venous vessel capacitance would obscure NIRS-VOT-derived values. In PAH patients, the role of such a right-sided outflow obstruction has been overlooked in this study. Moreover, from several intrinsic technological limiting factors, NIRS-VOT explores a derivative of the values of tissue oxygenation and may be dependent on the diffusion of O_2 in the context of hyperoxia.

I think that it may be reasonable to conclude that those patients with PAH likely had a microcirculatory dysfunction, potentially exacerbated by hyperoxia. However, a validation of NIRS-VOT to explore the microcirculation is required in this context of chronic hypoxemia and right-sided overpressure before more formal conclusions can be made. A joint (or with replacement of NIRS) assessment by sidestream dark field imaging would be interesting.

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Near-Infrared Spectroscopy With Vascular Occlusion Test May Not Be the Adequate Tool to Explore Microcirculation in Pulmonary Arterial Hypertension—Reply

In Reply:

We thank Dr Champion for his particular interest in our study and his thorough comments. However, we would like to share our concerns related to his comments.

In our point of view, we should use the microvascular oxygen extraction rate with caution, as it is not yet a valid accurate index to use. This index does not take into account all of the factors that influence oxygen delivery, such as cardiac output, serum hemoglobin levels, and hemoglobin dissociation curve, and to the best of our knowledge, it has not been investigated previously in patients with chronic hypoxemia.

Resting tissue oxygen saturation (S_{tO_2}) values depend mainly on the ratio of tissue oxygen delivery to tissue oxygen extraction. In our study,[1] pulmonary arterial hypertension (PAH) patients presented with a relatively normal cardiac index (median value of 2.5 L/min/m^2) and normal serum hemoglobin levels (median value of 16 g/dL) with mild hypoxemia (S_{pO_2} median value of 94%), the latter being a possible factor that might slightly decrease tissue oxygen supply. However, tissue oxygen delivery de-