Intensive Care Med (2016) 42:117–118
DOI 10.1007/s00134-015-4132-3

EDITORIAL

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Optimizing apnea testing to determine brain death

Received: 25 September 2015
Accepted: 28 September 2015
Published online: 10 November 2015
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The final step in the diagnostic process to establish a diagnosis of brain death (BD) in a potential organ donor (POD) with catastrophic brain injury is the apnea test (AT). The whole brain death concept, which is adhered to in most countries, dictates that apnea is the final and most definitive proof of total loss of brain function including the brain stem. This situation is then legally representative of a deceased patient, in spite of intact cardiac function, which allows subsequent organ procurement because this would not be ethically and legally acceptable in a patient considered still "alive". However, the apnea test, which aims to establish apnea in spite of a significant rise of CO_2 in the blood (which would always trigger respiratory effort in neurologically intact persons without medical suppression of breathing), cannot always be completed due to the fact that hemodynamic instability and/or desaturation may ensue due to interruption of mechanical ventilation and inadequate oxygenation in apnea. To minimize the risk of hypoxia and the subsequent need for interruption of the AT, a common practice is to apply the oxygen-diffusion method (i.e. apneic oxygenation) during the apnea period, after adequate preoxygenation. This method has a very high success rate with very low percentages of desaturations that require abortion of the AT [1].

In a large series of patients ($n = 142$) tested for brain death and undergoing ATs, including the largest cohort of patients on veno-arterial extra-corporeal membrane oxygenators (VA-ECMO, $n = 25$) reported to date, Giani et al. recently evaluated the success rate of recruitment maneuvers before, and the maintenance of positive-end expiratory pressure (PEEP) during, the apnea after separation from the ventilator [2]. Of note, Italian legislation requires a total of three ATs for BD diagnosis. During the AT, PEEP was established with an AMBU bag with an adjustable PEEP valve connected with 8 L/min of oxygen. The main findings of this investigation were that AT abortions did not occur with this strategy in non-ECMO patients (except for one patient with hemodynamic instability not related to the AT) and that AT in patients on VA-ECMO was feasible in all included patients. In almost all patients, hemodynamic stability was maintained during the AT. Of note, however, hypoxia, defined as pO_2 <40 mmHg (5.3 kPa), occurred in 2.7 % in non-ECMO and in 6.4 % in ECMO patients (and in 11.1 vs. 4.8 % of all patients with vs. without baseline hypoxia

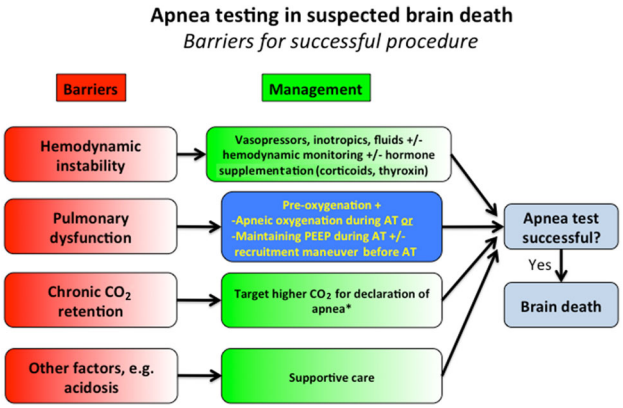

Fig. 1 Barriers for successful completion of the apnea test to establishing brain death diagnosis in patients with catastrophic brain injury who are potential organ donors, and key issues in management of these barriers. * In some countries chronic CO_2 retention precludes the apnea test and alternative proof of brain death is needed, e.g., absent cerebral circulation

defined as a paO_2/FiO_2 ratio <200 mm Hg). The authors did not provide data on oxygen saturation levels.

An important question is whether and how the results of this study may impact our clinical practice of determination of BD, especially regarding the AT. To address this question, several issues need to be scrutinized. First, the data do not suggest that using recruitment and PEEP in AT are superior to previously published results for ATs using the oxygen-diffusion method, since abortion occurred in one study using this method in 4.8 % (10/207) of the patients in whom hypoxia was the main reason for AT abortion [1]. These hypoxia rates seem comparable to the study by Giani et al., although hypoxia was not precisely defined. Therefore, one is left wondering whether the recruitment and PEEP application is worthwhile. Second, exact AT abortion criteria were not given by the authors, and the data provided even suggest that some level of hypoxia was accepted, whereas hypoxia defined as oxygen saturation of <90 % may be an abortion criterion for the AT in other countries, for instance in the Netherlands [3]. In that sense, comparability of studies on abortion rates is seriously hampered when exact definitions of aborting criteria are not provided, as was the case in this study. Third, it is not entirely clear why the authors chose to apply recruitment and PEEP in all patients, because most patients without pulmonary dysfunction will easily pass an AT with pre-oxygenation and subsequent apneic oxygen-diffusion method. Recruitment and PEEP application may theoretically even bear some risks in such patients, for instance by causing pneumothorax, although this was reported not to be the case in this paper. However, it feels more appropriate to select patients with pre-AT hypoxia for recruitment and PEEP, instead of a "one-size-fits-all" strategy. Furthermore, the data provided do not allow conclusions on the comparative effectiveness of either recruitment or PEEP since both were applied in all patients. Fourth, although this is the largest published cohort on BD patients on VA-ECMO to date, the study may not also be applicable to patients with veno-venous ECMO, which may be regarded as a limitation of the study. Finally, AT is just one of the steps in BD diagnosis, and optimizing the AT may not be sufficient to optimize the entire BD diagnostic process (Fig. 1).

Two messages seem to stand out from the results provided: (1) recruitment and PEEP application before and during AT seem quite safe, although the additive value of this strategy compared with the apneic oxygen-diffusion technique cannot be derived from this study, and (2) BD testing including AT in VA-ECMO patients seems feasible, rendering these patients suitable for organ procurement. For clinical practice, intensivists may, based on these results, feel more confident when they want to use recruitment and/or PEEP for ATs in selected patients in whom desaturation during an AT is anticipated or expected, or who are on VA-ECMO. The authors are to be applauded for these clinically relevant data that may help optimizing ATs for the declaration of brain death. However, whether the strategy described really contributes to increased numbers of organ procurements remains to be established.

Compliance with ethical standards

Conflicts of interest The authors report no conflict of interest.

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