Ventilator Autocycling and Delayed Recognition of Brain Death

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Abstract

Background Improvements in technology play an important role in caring for critically ill patients. One example is the advance in ventilator design to facilitate triggering of mechanical breaths. Minimal changes in circuit flow unrelated to respiratory effort can trigger a ventilator breath and may mislead caregivers in recognizing brain death.

Methods We observed patients with devastating brain injuries in a mixed medical/surgical intensive care unit (ICU) with a high clinical suspicion for brain death including the absence of cranial nerve function with apparent spontaneous breathing during patient-triggered modes of mechanical ventilation. Further clinical observation for spontaneous respirations was assessed upon removal of ventilatory support.

Results Nine patients with brain injury due to multiple etiologies were identified and demonstrated no spontaneous respirations when formally assessed for apnea. Length of time between brain death and its recognition could not be determined.

Conclusion When brain-dead patients who are suitable organ donors are mistakenly identified as having cerebral activity, the diagnosis of brain death is delayed. This delay impacts resource utilization, impedes recovery and function of organs for donation, and adversely affects donor families, potential recipients of organs, and patient donors who may have testing and treatment that cannot be beneficial. Patients with catastrophic brain injury and absent cranial nerve function should undergo immediate formal apnea testing.

Keywords Brain death determination · Apnea test · Brain death · Flow triggering · Organ donation

Abbreviations

PSV Pressure support ventilation
ICU Intensive care unit
PCO2 Partial pressure of carbon dioxide
PO2 Partial pressure of oxygen
HCO3 Bicarbonate
DCD Donation after cardiac death

Introduction

Technological advances serve many roles in caring for the critically ill patient. Advances in organ support techniques improve survival for the critically ill patients. Organ transplantation allows both survival and improved quality of life for recipients. We describe a series of patients where technology, in the form of improved mechanisms for triggering mechanical ventilation, hindered the ability to recognize brain death and organ donation. Recognition of this potentially confounding mechanism of simulated spontaneous respirations is necessary as one considers the importance of diagnosing brain death by critical care practitioners, neurologists, neurosurgeons, and other members of the team responsible for identifying and treating potential organ donors.

Identifying potential donors is impacted by technology designed to maintain viability. The demand for donated organs far exceeds the supply: 73,479 patients added to the
Waiting list in 2009 and the first half of 2010, with 9,217 dying in the same period and 108,123 candidates awaiting transplant as of July 2010 [1]. Increasing organ donations is a societal goal.

**Methods**

We identified a series of patients in the medical/surgical intensive care unit (ICU) of Baystate Medical Center with absent cranial nerve function secondary to catastrophic neurologic injury. Baystate Medical Center is a 750-bed teaching affiliate of Tufts University School of Medicine where all care is directed by a dedicated staff of full-time intensivists. We selected patients with high clinical suspicion for brain death, the absence of cranial nerve function, and presumed spontaneous breathing activity on pressure support ventilation (PSV) for formal apnea testing off of the ventilator.

The Institutional Review Board at Baystate Medical Center evaluated our submission and determined that the data we analyzed for the patients included in this case series were already brain-dead. Therefore, they did not meet the definition of human subject research under the common rule and formal IRB review was not required. Similarly, informed consent for this observation was not obtained.

**Index Case and Results**

A 66-year-old man post-orthotopic liver and kidney transplantation was admitted to the hospital with a diagnosis of healthcare-associated pneumonia and bleeding from an arterio-venous fistula in the right arm. During his hospitalization, the bleeding resulted in episodic hypotension and associated diaphoresis related to myocardial ischemia demonstrated by electrocardiogram changes. Forty-eight hours after admission, the patient suffered asystolic arrest. After 10 mins of cardiopulmonary resuscitation, spontaneous circulation was restored. Twenty-four hours following this event, cranial nerve function was absent. Specifically, the patient had no pupillary reflex, no doll’s eye reflex, no corneal reflex, no ocular response to ice water in either ear canal, and no cough or gag reflexes.

The patient was on PSV and appeared to be triggering the ventilator with a spontaneous respiratory rate of 18–20 breaths/min and a tidal volume of 500–600 cc. PSV requires the patient to initiate respiratory activity, recognized by the ventilator as either a change in pressure or flow in the ventilator circuit. This change in flow or pressure initiates a high flow of gas at the preset pressure. Inspiration is terminated when the flow reaches a percent decrement relative to the peak flow of each cycle. No patient respiratory effort was noted in this patient despite a respiratory rate of 18–20 breaths/min. On inspection, the patient had a hyperdynamic precordium. He was switched from flow trigger at 1.5 l/min to pressure trigger at 2 cm of water and maintained in the PSV mode. No respirations were noted after this change. The patient was then placed back on flow trigger mode with increasing flow required to trigger the ventilator in 1 l increments from 1–4 l/min; spontaneous ventilation was presumed at each level of flow trigger with a rate varying between 16 and 20 breaths/min and a tidal volume of 500–600 cc. PSV of 10 mmHg was maintained during the interval change in flow triggering from 1 to 4 l/min. When returned to the pressure triggering mode, there were no spontaneous breaths.

At this point, given the constellation of findings, it was decided that an apnea test should be performed, and the patient was prepared in the assist-control mode for a blood gas reading. The values were pH 7.4; partial pressure of carbon dioxide (PCO₂) 42 torr; partial pressure of oxygen (PO₂) 470 torr (fraction of inspired oxygen 100%); and bicarbonate (HCO₃) 26 mEq/l. The patient was then disconnected from mechanical ventilation, and examination for apnea was initiated. During this observation period, no respiratory effort or movement of the chest was noted. The precordium remained hyperdynamic. The values for blood gas at the end the apnea test were pH 7.28; PCO₂ 55 torr; PO₂ 111 torr; and HCO₃ 26 mEq/l, which suggested that the patient was brain-dead. Clinical examination 2 hours later confirmed the initial findings and, upon informing the family, it was agreed to withdraw life-supporting measures, and the patient expired.

Since identification of this patient, eight additional patients over a 15 month period demonstrated similar phenomena, ultimately delaying the diagnosis of brain death. This likely represents the minimum number, as no systematic approach exists to identify patients presumed to be taking spontaneous respirations when they are in fact brain-dead. Our ICU declares brain death in 50 patients per year, on average, suggesting an incidence of at least 10–12% in our institution.

Case #2 was a “spontaneously” breathing traumatic brain injury patient whose endotracheal tube was removed in the operating room in preparation for donation after cardiac death (DCD). After removal of the endotracheal tube, the patient failed to demonstrate any respiratory efforts, suggesting that he was in fact brain-dead, and cardiac arrest occurred. Donation using the non-heart beating protocol was utilized but could have been avoided [2]. This case further demonstrates how ventilator mechanics can easily masquerade as patient effort, which impacts both treatment and patient outcome. Table 1 is a summary of all nine brain-dead patients in our ICU mistakenly identified as having spontaneous breathing activity.
Discussion

Our series represents a convenient sample of patients identified by the authors secondary to astute clinical suspicion and some awareness of the problem of autocycling. As no systematic approach was undertaken, it is likely these numbers represent the absolute minimum occurrence of this phenomenon in our ICU. Indeed, many of these patients had the absence of cranial nerve function with the preservation of “spontaneous breathing activity” for 24 h or more before assessment by the authors.

The reasons why patients were unable to donate generally fall into one of the three categories in our ICU. Either consent could not be obtained or the organs were ultimately deemed unsuitable for transplantation due to damage caused by the physiologic instability that accompanies brain death [3]. In addition, the surgeon performing the recovery of organs, based on gross abnormalities or occult masses, may reject their utilization.

As the authors did not evaluate this systemically, the reason for some patients being unable to donate remains unclear. Awareness and recognition of the interaction between patients and mechanical ventilation in the setting of brain death, based on the experience in our ICU, remains poor.

The observations of the cases demonstrate the potential misdiagnosis of cerebral activity related to self-cycle triggering (autocycling) of mechanical ventilation in a brain-dead patient. This phenomenon has been recognized previously in pharmacologically paralyzed patients [4]. However, except for reports in specialty journals in anesthesiology and neurology [5, 6] and nursing publications [7], such events have not been well described in the critical care or general medical literature [8]. Our series represents the largest number of cases reported and further emphasizes that this phenomenon is likely more common than appreciated.

The potential reasons for autocycling in brain death depend on the method of ventilator-triggering applied for the detection of spontaneous breathing [4, 9]. The two most common modes of triggering a ventilator breath utilize changes in airway circuit pressure or flow. With pressure triggering, a change in pressure must be generated to reach the inspiratory threshold pressure in order for the ventilator to deliver a breath. Autocycling in this mode is possible and has been reported with an endotracheal tube cuff leak [10] or a large bronchopleural fistula causing the pressure change [11–14].

When flow triggering is used, the ventilator monitors a continuous flow of gas through the ventilator circuit, and a breath is initiated when the return flow is less than the delivered flow. Patient’s effort required to initiate a breath is more effectively reduced with this mode, decreasing the overall work of breathing [15]. Cardiogenic oscillations are known to generate pulsatile gas flow in lobar and segmental bronchi as measured during routine bronchoscopy [16]. These changes in gas flow are capable of triggering mechanical breaths, mimicking spontaneous breathing during mechanical ventilation in paralyzed patients following cardiac surgery [4] and implantation of total artificial hearts [9]. Patients exhibiting this ventilator-triggering phenomenon tend to be hyperdynamic with larger cardiac size and have a more compliant respiratory system relative to those in whom it is not seen [4]. Flow triggering of a mechanical breath is directly related to the amount of inspiratory flow generated by the cardiac oscillation and can be abolished by setting the flow trigger above this threshold value. Although flow was not directly measured in our index patient, inspiratory flow generated by cardiac oscillation was above 4 l/min, the upper limit for this trigger on the ventilator, necessitating a switch to pressure triggering and ultimately withdrawal of the ventilator completely to demonstrate a lack of respiratory effort as is necessary for the diagnosis of brain death.

Table 1 Formal apnea test results and organ donation outcome for patients evaluated for brain death while ventilated with PSV, a patient-initiated mode of mechanical ventilation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mechanism of injury</th>
<th>Response to apnea test</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>66-year-old male (index case)</td>
<td>Anoxic brain injury from cardiac arrest</td>
<td>No spontaneous respirations</td>
<td>Unable to donate</td>
</tr>
<tr>
<td>27-year-old male (case #2)</td>
<td>Traumatic brain injury from motor vehicle collision</td>
<td>No spontaneous respirations once extubated in OR</td>
<td>Donated organs via DCD</td>
</tr>
<tr>
<td>42-year-old male</td>
<td>Gunshot wound to head</td>
<td>Positive</td>
<td>Donated organs</td>
</tr>
<tr>
<td>73-year-old male</td>
<td>Traumatic brain injury due to fall</td>
<td>Positive</td>
<td>Donated organs</td>
</tr>
<tr>
<td>52-year-old female</td>
<td>Intracranial hemorrhage</td>
<td>Positive</td>
<td>Unable to donate</td>
</tr>
<tr>
<td>56-year-old female</td>
<td>Anoxic brain injury from cardiac arrest</td>
<td>Positive</td>
<td>Donated organs</td>
</tr>
<tr>
<td>43-year-old male</td>
<td>Gunshot wound to head</td>
<td>Positive</td>
<td>Donated organs</td>
</tr>
<tr>
<td>44-year-old male</td>
<td>Intracranial hemorrhage</td>
<td>Positive</td>
<td>Unable to donate</td>
</tr>
<tr>
<td>57-year-old female</td>
<td>Anoxic brain injury from cardiac arrest</td>
<td>Positive</td>
<td>Unable to donate</td>
</tr>
</tbody>
</table>

DCD donation after cardiac death
Although DCD is a possibility in such patients, this pathway is rarely used (4 out of 41 donors at our institution in 2008) and limits the ability to harvest organs [17]. This pathway may not even be considered for patients with otherwise normal lungs who are thought to be spontaneously breathing as they would not meet the Wisconsin protocol, which stipulates a short period of time from withdrawal of support to death [18, 19]. Vasopressor withdrawal or severe hypoxia without supplemental oxygen is often the mechanism of death for these patients.

The most likely clinical scenario that would be followed in similar cases would consist of withdrawal of medical interventions, including mechanical ventilation, followed by rapid cessation of circulation and subsequent pronouncement of death. This would be done without any awareness that the patient had actually expired earlier and precludes the recovery of organs for transplantation. It is clear to the authors that this has occurred at our institution.

The loss of potential donor organs due to lack of appreciation for these mechanisms of ventilator autocyling is tragic for both recipients and donors alike. Typically, multiple recipients receive organs from a single donor; these are patients who otherwise will die waiting for organs if the latter are not available. A gift of donated organs often provides needed comfort for donor patients’ families dealing with the death of a loved one. Both of these benefits are lost if brain death is not recognized in a timely manner. Maintaining organ viability in this group of patients is often challenging before the declaration of death and typically becomes more difficult following cessation of brain activity [3, 20]. Any delay in the diagnosis of brain death, therefore, threatens successful organ retrieval and outcome of transplant [21].

Prolonging the interval between death and its recognition has a negative impact on many levels, beyond the sometimes fatal outcome for potential organ recipients. It extends suffering for families during an interminable wait for death that always occurs. Families may be further stressed when asked for decisions in planning for DCD when that is unnecessary. Caregivers spend time continuing to provide therapies that cannot be helpful when they could be directing their efforts elsewhere. Thus, these delays also affect resource utilization, thereby increasing costs [7]. Appreciation of the unintended negative impact of technology improvement, in this instance, decreasing the patient’s effort to obtain a breath is critically important.

In the limited data available on the potential incidence of autocyling with newer ventilators, a range of 5–50% has been reported [4, 6, 9]. Although the overall incidence of misdiagnosis of brain activity is not known, clinical experience in our ICU suggests that this clinical scenario is not rare. Based on our observations, we conclude that there is no substitute for careful clinical observation at the bedside of the critically ill. The team approach employed in most academic units, consisting of residents, nurses, and respiratory therapists all providing input on patient care, could easily lead to the alternative scenario described with delayed recognition of death and prolongation of ICU care. Indeed, considering battlefield triage commonly employed in many ICUs [22], intensivists are quick to move away from patients who cannot be successfully treated to care for those who can benefit from medical intervention.

The remedy is clear, and we recommend that it should immediately be adopted for assessing apparent spontaneous breathing activity in suspected brain-dead patients. If cranial nerve function is absent and the only perceived brain activity is breathing above the ventilator set rate or spontaneously, the patient should be observed for spontaneous breathing activity off the ventilatory circuit. If there is none, then a formal apnea evaluation should be performed promptly and adherence to the most recent guidelines for determination of brain death [23].

No substitute exists for careful clinical observation at the patient bedside which ultimately led to the correct yet delayed diagnosis of brain death in our patients. Advances in technology, in this case, minimizing patients’ work during mechanical ventilation, have significant unintended consequences with broad impact. Maintaining organ support and medical interventions for patients beyond cessation of brain activity causes unnecessary suffering for patients’ families and unnecessary resource utilization. For those awaiting transplant, the potential for death is real. The shortage of donor organs could be mitigated to some degree by recognition of this phenomenon and prompt performance of an apnea test off the ventilator once cranial nerve function is absent. This simple proposal will result in rapid improvement in this difficult process with tangible benefits for organ donors and recipients, their families, the healthcare team, and resource utilization.

1. Barriers to organ donation may include lack of recognition of brain death.
2. Ventilator technology utilized in caring for the critically ill may inadvertently delay the diagnosis of brain death.
3. Clinicians should make every effort to rapidly identify brain-dead patients, including formal apnea testing even when there appears to be spontaneous respiration in the absence of other evidence of cerebral function.

Conclusions

Demand for organ donation continues to exceed supply. Any delay in recognition of suitable donors compounds this problem. Present ventilator technology has the unintended consequence of potentially obscuring the diagnosis of brain

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death, and clinicians must consider formal apnea testing in all patients with the absence of brain stem function following a devastating brain injury regardless of the appearance of potential spontaneous breathing activity.

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