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Are terminally ill patients dying in the ICU suitable for non-heart beating organ donation?

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Abstract *Objective:* To evaluate the feasibility of implementing a program of controlled non-heart beating organ donation, in patients undergoing the withdrawal of intensive care treatment. *Design and setting:* Prospective observational study. Medical and Surgical ICUs in a tertiary university hospital. *Patients:* Consecutive patients younger than 70 years dying in the ICU after treatment withdrawal for dire neurological prognosis. *Measurements and results:* We analyzed prospectively collected data from the ICU clinical information system. Seventy-three of 516 ICU deaths (13%) were identified, equally distributed among traumatic, stroke, and anoxic brain injury. The management and the course in these three diagnostic categories were similar. All patients underwent withdrawal of mechanical ventilation and half were extubated. Median time to death was of 4.8 h (IQR 1.4–11.5). In 70% of cases the patient received analgesia and 30% sedation. Such treatment was not related to earlier death. Hypotension was observed in 50% of patients during the 30 min preceding cardiac death. *Conclusions:* With our current management of terminal patients controlled non-heart beating organ procedure may be difficult due to the duration and variability of the dying process. This observation suggests that we can perform better by evaluating this process more closely.

Keywords Coma · Terminal care · Treatment withdrawal · Organ donation · Non-heart beating organ donor

Introduction

Insufficient procurement of organs from brain-dead donors is the principle factor limiting access to solid organ transplantation. There is evidence that some patients not developing brain death criteria but ending in cardiac death may be suitable for donation of kidney and in certain situations liver or lung [1, 2], a process called non-heart beating donation (NHBD). In the intensive care unit (ICU) when the prognosis (in particular neurological) is unambiguously dire, life-support treatments are futile and should be withdrawn. In such situations controlled NHBD

can be considered suitable [2]. This refers to the fact that in such circumstances a treatment plan of palliative care can be carefully explained to the next of kin. Once they have understood and accepted this line of treatment, sufficient time should be given for quiet communication with the relatives so as to seek consent for NHBD before cardiac death, or the relatives may spontaneously propose organ donation. Continuous monitoring enables to pronounce death following the cardiac arrest, in which case a surgical team on standby can retrieve the organs immediately.

Patients presenting catastrophic neurological patholo-gies are usually perceived as the most suitable for this ap-proach by the healthcare team [3]. Although communica-tion, ethical, and juridical barriers to this approach may appear difficult, and in many countries, including our own, certain of these obstacles have not yet been resolved, there is emerging evidence that in favorable circumstances such a procedure is feasible and can increase the number of available organs for transplantation [4]. From published literature [5, 6], it appears that the timing of the process is vital to limit warm ischemia time. The lack of informa-tion regarding the practical aspects of patient management led us to investigate our own data on the process of with-drawing treatment [7].

We studied a group of critically ill, preterminal patients perceived as potential candidates for NHBDs to estimate the feasibility of implementing an NHBD program at our institution. We specifically evaluated the management and the timing of death in patients undergoing the withdrawal of supportive intensive care treatment for dire neurological prognosis.

Method

Patient management

We analyzed all 516 patients suffering catastrophic brain injury, defined as acute brain illness and unresponsive to maximal medical and surgical treatment. Intensive care treatment was withdrawn according to the recommen-dations of the Swiss Academy of Medical Sciences [8], a national committee issuing bioethical recommendations. Due to patient incompetence the next of kin are informed of the situation, of the focus on palliative care, and of the plan to withdraw life-sustaining therapy. Oral consent by the family is documented in the patient's notes. Firstly, vasoactive agents (if any) are withdrawn, followed by withdrawal of mechanical ventilation, with discretionary extubation. Sedative-analgesic drugs are administered to relieve perceived respiratory distress, vegetative reactions, and disturbing movements if deemed appropriate by the attending physician and nurses. Family members are encouraged to accompany their beloved one during this period and to seek the assistance of a chaplain if required. This procedure reflects current professional conduct and

complies with the local ethical and legal standards. There are no existing institutional recommendations for this process at present, apart from the recommendations of the Swiss Academy of Medical Sciences [8].

Study design

In this observational study we considered patients under the age of 70 years who were dying in the ICU between 1 January 2002 and 31 December 2004. The prospective data were entered and analyzed in the computerized clin-ical information system (CIS) of our medical and surgi-cal ICUs. The CIS provides on-line information on patient management and medical history. Physiological variables from the monitors, ventilators, and laboratory results are automatically entered every minute and validated by the nurses and physicians. During end-of-life in the ICUs the vital signs are usually not displayed on the monitors sur-rounding the patient but are continuously recorded in the database of the CIS. Administered drugs, procedures and care are selected manually from a predefined scroll down list. The CIS constitutes the nurses' observation chart, and this part of patient's file is paperless.

Our institution's ethics committee waived the require-ment of informed consent for analysis of these data and the anonymous publication of results. A nurse certified in intensive care extracted the data while an attending ICU physician validated and analyzed it. For each patient we recorded: the diagnosis, Glasgow Coma Scale (GCS) score at the time of treatment withdrawal, pharmacological treat-ment, management of mechanical ventilation, and survival time following treatment withdrawal. The total doses of se-dation/analgesia administered (intravenous bolus and con-tinuous perfusion) were divided by the duration of the ter-minal phase and expressed as micrograms per kilogram per hour. Hemodynamic values (mean arterial pressure and heart rate) and SpO_2 were recorded.

Descriptive statistics were calculated using JMP Sta-tistical software version 5.1.2 (SAS Institute, Cary, N.C., USA). Data are presented as a mean $\pm$ SD or as median (interquartile range, IQR). Comparisons between diagnos-tic groups and between patients receiving or not receiving analgesia or sedation, extubated or not were carried out by the Wilcoxon test. Differences at the level of $p < 0.05$ were considered statistically significant.

Results

Of the 516 patients dying in the ICU 73 fulfilled the above criteria (Fig. 1); their characteristics are presented in Table 1. There were 21 (29%) with traumatic brain injury, 25 (37%) anoxia, and 25 (34%) stroke (either ischemic, subarachnoidial hemorrhage or cerebral hematoma). In addition to the fact that head trauma patients were signif-
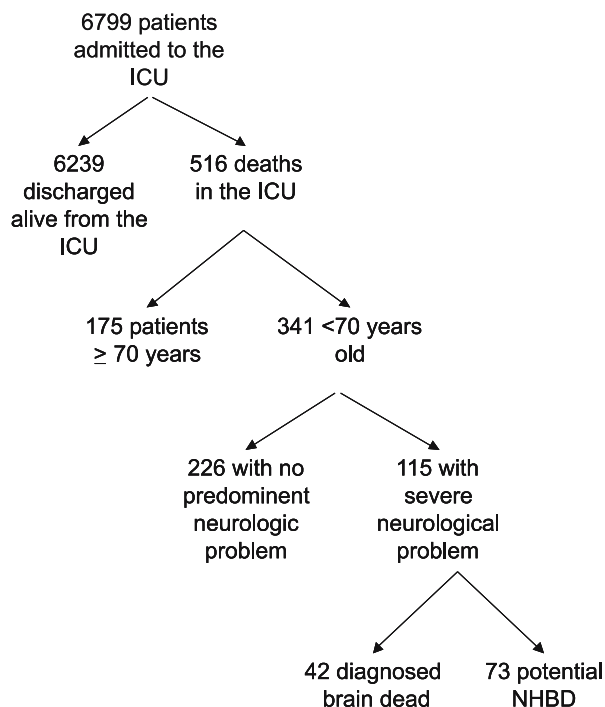
Patient selection

Fig. 1 Patient selection from the general population of ICU patients (2002–2004). Seventy three (13% of all ICU deaths) were identified as potential non-heart beating donors

icantly younger, there were no differences between the diagnostic groups. At the time of treatment withdrawal, a GCS of 3 was recorded in 7 patients, 4 in 55, and 5 in 11, confirming the severity of the neurological disorder.

All patients were mechanically ventilated. Four patients were treated with norepinephrine, which was interrupted as the first measure. Mechanical ventilation was withdrawn in all the other patients, followed by extubation of 53%. Overall survival was 4.8 h (IQR 1.4–11.5). In 22% of cases the patient died during the first hour and in 31% after 2 h. Extubated patients survived significantly

longer, 9.4 h (3.3–15.3) vs. 3.1 h (1.2–6.6; $p < 0.01$; see Electronic Supplementary Material, S.F1). These patients died 7.6 h (1.5–13.6) after extubation (S.F2).

Analgesia was administered to 70% of the patients, mainly as a morphine drip at an hourly dose of 75 µg/kg (32–134). Sedation was administered to 26%, principally midazolam at 81 µg/kg per hour (54–145). Analgesia was administered to patients with a more protracted course, and these patients therefore survived significantly longer [6.6 h (2.8–13.2) vs. 1.9 h ([0.6–5.0), $p < 0.04$], but survival time did not differ between patients receiving or not receiving sedation [6.1 h (3.3–9.9) vs. 3.8 h (1.2–11.8), $p = 0.6$].

Hemodynamic instability was frequent in all three groups. Hypotension, defined as having a mean arterial pressure lower than 60 mmHg, was observed in 80% of patients 10 min before death. One-half of patients (52%) were already hypotensive 30 min before death, and one-third (37%) during their last hour of life (S.T1, S.F3). Likewise, hypoxia defined as SpO_2 below 90% was present in 67% of patients 10 min before death, 71% at time minus 30 min, and 75% 1 h before (S.T1, S.F4). We could not identify factors statistically correlated with the occurrence of hypotension, hypoxia, or the duration of agony.

Discussion

Withdrawal of life-support treatment in patients presenting an unequivocally poor prognosis is considered a duty for intensive care practitioners in most countries. This not only allows the patient to die with dignity but also promotes efficient ICU bed use [9]. This approach is well established and has been socially accepted in our country for many years [8]. Harvesting organs from NHBD is a far more complex problem. This approach is based on a utilitarian attitude, believing that organ procurement, a good and useful action, enables some aspects of the death process to be manipulated. Ethical issues have been discussed in detail [1, 10], some aspects of which are still controversial. Policies and regulations vary from country to country and institution to institution depending on the emphasis put

Table 1 patients characteristics

	Traumatic brain injury ($n = 21$, 29%)	Stroke ($n = 25$, 34%)	Anoxic brain injury ($n = 27$, 37%)	All patients ($n = 73$)
Age (years)	42 ± 14	53 ± 11	55 ± 12	50 ± 13
Survival time (h)	6.1 (2.4–12.5)	3.9 (1.3–11.5)	3.6 (1.0–9.8)	4.8 (1.4–11.5)
Died within 1 h	4 (19%)	5 (19%)	7 (26%)	16 (22%)
Died within 2 h	5 (24%)	8 (31%)	10 (37%)	23 (31%)
Extubation	11 (52%)	15 (60%)	13 (48%)	39 (53%)
Sedation	9 (42%)	4 (16%)	6 (22%)	19 (26%)
Dose of midazolam ($\mu g^{-1} kg^{-1} h^{-1}$)	81 (42–125)	134 (70–161)	77 (47–343)	81 (54–145)
Analgesia	16 (76%)	18 (72%)	17 (63%)	51 (70%)
Dose of morphine ($\mu g^{-1} kg^{-1} h^{-1}$)	77 (33–195)	72 (28–113)	77 (34–138)	75 (32–134)

on respecting the integrity of a dying patient or on maximizing organ procurement.

The time course of withdrawing life-sustaining treatment and cardiac arrest is entirely in accord with the result of a large European study on unselected ICU patients [9] and those of a study in the United States on patients suffering neurological disaster [11]. We therefore believe that a median survival time of several hours should be expected in such circumstances, and we were not able to identify patient characteristics that would predict the precise time of death, in particular with the use of sedation and analgesia, or tracheal extubation. During agony, hypotension and hypoxia were frequently observed, although the tolerability for transplanted organ viability is not settled yet.

Such an extent and variability in the time while awaiting death can raise problems. It is difficult to establish a NHBD program with a complete surgical team waiting on standby, in some situations up to 1 day, for the cardiac death of a potential organ donor. Hemodynamic instability and hypoxia were frequently observed during agony, although their effect on organ function could not be evaluated. To overcome this problem and have a better control of the process one could decide for example, limiting the time between treatment withdrawal and cardiac death to 1 h. Such a decision, from our analysis would result in a decrease in this donor pool by 80%. It is equally worth weighing the arguments for and against the setting up of such a program for which there is only a 20% chance of it actually happening. In addition to ethical, legal, and logistical aspects, family care and communication related to organ donation request should be considered, as well as the negative consequences of a failed NHBD. Recent evidence shows that the death of a family member is a major determinant of posttraumatic stress disorder for the next of kin, and that sharing end-of-life decisions further increases the risk of anxiety and depression [12]. The impact of controlled NHBD on relatives of the deceased patient should hence be carefully evaluated.

Actively accelerating the dying process could conceivably resolve many issues. This would simplify the organization and minimize hemodynamic instability before death. High doses of opiates and sedation would most likely accomplish this goal. Outside the context of NHBD this practice was in fact documented in a European observational study, with a significant shortening of the dying process in 6.5% of ICU end-of-life situations [9]. The use of high doses of sedation for the purpose of "improving" NHBD goes far beyond the classical "double-effect" in the use of medication to alleviate suffering. Such practice has been proposed in an opinion paper highlighting the limited harm to the dying patient compared to the benefit for the receiver [3]. It has even been suggested, along these lines, that the perfect process for controlled NHBD would be to harvest organs without even bothering to wait for cardiac arrest, since the patient is dying anyway and that he had given his consent.

There are obviously numerous objections to this approach, based on the principle of beneficence. The use of terminal sedation to deliberately accelerate death is explicitly condemned by the ethical recommendations in our country [8]. Indeed, in our setting analgesia or sedation was administered only when the family or the healthcare workers felt uneasy, in particular when the patient presented signs of dysautonomy that suggest suffering or abnormal movements that were distressing. If terminal sedation is necessary to facilitate controlled NHBD, this issue should be openly addressed and debated by ethics committees. It is necessary to reach ethical, legal, and social consensus before this approach can be implemented.

With our current management of terminal patients controlled NHBD organ procedure may be difficult due to the duration and variability of the dying process. This observation suggests that we can perform better by evaluating this process more close. On the other hand, actions aiming to accelerate dying, such as the administration of high doses of sedation or analgesia, raise vast ethical questions.

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