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Critical appraisal of organ procurement under Maastricht 3 condition☆,☆☆,☆☆☆

Analyse critique du prélèvement en condition M3 de Maastricht

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ABSTRACT

The ethics committee of the French Society of Anesthesia and Intensive Care (Sfar) has been requested by the French Biomedical Agency to consider the issue of organ donation in patients after the decision to withdraw life-supportive therapies has been taken. This type of organ donation is performed in the USA, Canada, the United Kingdom, the Netherlands and Belgium. The three former countries have published recommendations formalizing procedures and operations. The French Society of Anesthesia and Intensive Care (Société française d'anesthésie et de reanimation [Sfar]) ethics committee has considered this issue and envisioned the different aspects of the whole process. Consequently, it sounded a note of caution regarding the applicability of this type of organ procurement in unselected patients following a decision to withdraw life-supportive therapies. According to French regulations concerning organ procurement in brain-dead patients, the committee stresses the need to restrict this specific way of procurement to severely brain-injured patients, once confirmatory investigations predicting a catastrophic prognosis have been performed. This suggests that the nature of the confirmatory investigation required should be formalized by the French Biomedical Agency on behalf of the French parliamentarians, which should help preserve population trust regarding organ procurement and provide a framework for medical decision. This text has been endorsed by the Sfar.

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RÉSUMÉ

Le comité d'éthique de la Société française d'anesthésie et de réanimation (Sfar) a été sollicité par l'Agence de la biomédecine sur la question des prélèvements d'organes après arrêt des thérapeutiques actives (ATA). Ce type de prélèvement est autorisé et pratiqué aux États-Unis, au Canada, au Royaume-Uni, aux Pays-Bas et en Belgique. Les trois premiers pays ont rédigé des recommandations concernant ce type de prélèvement. Ces recommandations fixent pour l'essentiel une procédure ou une conduite à tenir opérationnelle, une fois l'ATA validé. Le comité a délibérément cadré sa réflexion selon un champ plus large et global que celui qui prévaut dans l'approche anglo-saxonne. Cette analyse qui envisage toutes les étapes d'un tel prélèvement, nous a conduits à émettre des réserves quant à l'applicabilité de ce type de prélèvement à tout patient chez qui une décision d'ATA aurait été validée. Dans un souci de cohérence par rapport aux pratiques du prélèvement d'organes chez des patients en mort encéphalique qui prévalent en France, nous avons souligné la nécessité de n'envisager l'ATA-M3, pour le moment, que chez les patients cérébrolésés chez qui un très mauvais pronostic neurologique pouvait être prédit avec un niveau de certitude élevé, au moyen d'examens paracliniques. Dans notre esprit, les éléments de preuve doivent être fixés et assumés par la collectivité, représentée par l'Agence de la biomédecine, et pas par le médecin en charge du malade. Ils doivent être opposables au cas où l'on s'interrogerait sur la qualité de la pronostication neurologique. Ce texte a été endossé par le conseil d'administration de la Sfar.

1. Introduction

In this article, the ethics committee of the French Society of Anesthesia and Intensive Care (Sfar), named ICARE, presents the fruit of a collective reflection on the principle of organ donation performed under MIII conditions of the Maastricht classification[1] (MIII: organ procurement after death by circulatory arrest following a life-supportive therapy withdrawal [LSTW] decision) [1]. To our knowledge, this practice already exists in five western countries: the United States, Canada, the United Kingdom, the Netherlands and Belgium. Three of these countries have published recommendations regarding MIII procedures: the United States [2], Canada [3] and the United Kingdom [4].

This article aims at explaining the medical considerations of these situations as understood by the professionals taking part in the committee. This reflection is based on the law of April 22, 2005, which governs the withholding and withdrawal of life-supportive therapy. In the case of MIII, compliance with this law and with the terms of its application is crucial. Indeed, ensuring the independence of the LSTW decision from the consideration of procurement under MIII conditions constitutes a key issue in the following reflection.

The National Consultative Ethics Committee (CCNE) expressed this necessity for independence in an opinion published in April 2011, titled: "Ethical issues in connection with organ harvesting and donation for transplanting".[2] This opinion puts forward seven recommendations, including: *Exercise the utmost caution in the event of an ethical debate concerning Maastricht category III: the long awaited April 22, 2005 law, referred to as the Leonetti law, on the curtailment and discontinuation of treatment is not the equivalent of an authorisation to remove organs in such a situation. This law can only be freed of any suspicion as to its intentions if it is fully understood.* In addition to this recommendation, which is important to keep in mind when considering procurement in Maastricht category III patients, the CCNE stresses the need both to inform the public on the legal requirements for organ procurement on brain-dead patients and to encourage people to consider this option and to communicate their wishes to their relatives. It also highlights the necessity to maintain a strict separation between the intensive care and procurement teams.

With these points in mind, we centred our reflection on the description of the difficulties raised by the principle of organ procurement in Maastricht category III patients, even though, legally speaking, such procurement is conceivable within the current legal framework[3,4] following the amendment of the protocols enacted by the Biomedicine Agency.[5] Rather than proposing an operating procedure, which seemed premature considering the many issues raised by the very principle of procurement under MIII conditions, we offer in this article an analysis of issues and potential challenges as foreseen by professionals.

2. Differences between LSTW and LSTW followed by MIII procurement

LSTW-MIII is a particular type of LSTW that impacts the logic, procedure and factors of the "usual" LSTW. This is all the more important given that the process and approval of life-supportive therapy withholding and withdrawal have been long to emerge.

2.1. "Usual" LSTW in the Intensive Care Unit (ICU)

"Usual" LSTW refers to an LSTW that is not followed by MIII. In order to be credible and bearable both in the eyes of relatives and of civil society, LSTW decisions must imperatively respect the spirit of

[1] An international classification named the "Maastricht classification" has organized into groups the different theoretical situations, defining 4 categories of individuals: (1) Maastricht category I: individuals who suffered cardiac arrest outside of any sort of medical care. Under these circumstances, organ procurement can only be considered if attempts at resuscitation have been made within the 30 minutes following the cardiac arrest; (2) Maastricht category II: individuals who suffered cardiac arrest in the presence of qualified assistance capable of performing efficient cardiopulmonary resuscitation, but which failed to achieve haemodynamic recovery; (3) Maastricht category III: individuals who suffered cardiac arrest in a hospital after the decision to withdraw life-supportive therapy in the intensive care unit had been taken due to a particularly unfavourable prognosis; (4) Maastricht category IV: brain-dead individuals who suffer irreversible cardiac arrest while being treated in an intensive care unit.

[2] Available on http://www.ccne-ehique.fr.

[3] Article R1232-4-1, Code of Public Health. Organ procurement on a deceased individual can only be performed if the said deceased individual is assisted by mechanical ventilation and retains haemodynamic function. However, in the case of organs appearing on a list established by order from the minister in charge of public health, made after a proposal from the Biomedicine Agency, procurement can be performed on a deceased individual with persistent cardiac or respiratory arrest.

[4] Article R1232-4-2, Code of Public Health. The procurements mentioned in the second subparagraph of article R1232-4-1 are performed in compliance with the protocols enacted by the Biomedicine Agency. These protocols determine, in particular, the situations in which these procurements can be performed as well as the conditions under which they are to be performed.

[5] Report on the application of the law on bioethics of August 6, 2004. http://www.genopole.fr/IMG/pdf/rapport-bilan-LB-oct2008.pdf.

the aforementioned "Leonetti" law of April 22, 2005. One can summarize it as the will to restrain from unreasonable obstinacy towards a patient whose treatment has become futile. The issue is then to lead the patient back onto the path to a "natural" death, thus allowing for accompaniment within a palliative care approach. Following this logic, curative medicine gives way to a medicine meant for comfort. The patient's relatives lie at the heart of this accompaniment approach and are allowed back into the patient's intimate space, while physicians and caregivers stay in charge of the *care*, taking over from the *cure*.

LSTW in the ICU is often considered by medical and paramedical caregivers, and sometimes by the patient's relatives. The decision is medical and is based on the conviction that treatments are useless, as they have indeed, given the prognosis, "become futile". This conviction, issued by a "collegial procedure", takes into account the clinical assessment, the patient's evolution considering the treatments undertaken, the paraclinical data, the physical and moral suffering of the patient, as well as the relatives' opinion, if known. These elements are not formally organized into a hierarchy, and can neither be absolutely certain nor totally irrefutable. The collegial medium of the decision, as well as the act of informing the family of the LSTW decision, which generally leads to the postponing of such a decision if the family gives a constant refusal, are all precautions to limit abuses and errors. Nevertheless, the LSTW procedure cannot be totally freed from subjectivity, as is true of any medical procedure. In that sense, reflection on LSTW does not differ from therapeutic decision-making in general: the issue is to choose what is best within a range of possibilities. This explains why LSTWs are identical in terms of implementation procedures, while they differ from one patient to the other, and sometimes one centre to the other, in terms of the elements justifying them. This diversity is a component of the ethical questioning process, and guarantees adaptation to the complexity of each situation. To the extent that LSTW is aimed at stopping treatments and favouring palliative care, it cannot be suspected of exploitation for other purposes, since the patient represents the only subject of the decision.

2.2. LSTW followed by procurement (LSTW-MIII)

The fact that the patient can die following LSTW, and thus give way to procurement, muddles the principle and expectations of "usual" LSTWs. Caregivers collectively accept a double intentionality: the stopping of treatments which have become futile, and the following procurement. Moreover, LSTW-MIII involves third parties in the procedure: society, the procurement team, the receiver and his relatives.

Furthermore, a strong temporality exists: LSTW-MIII is no longer a question of returning the patient to the unpredictable course of his destiny once the powerful influence of intensive care is removed. In LSTW-MIII, this destiny is in some way "modified": the physicians in charge of procurement, as well as society and receivers, all implicitly exert a pressure for the death to occur early enough to enable procurement and transplantation. These expectations surrounding the death impose the patient's transfer either to the operating theatre where extubation will be performed, or, if extubation is done in the ICU, with urgency to the operating theatre after circulatory arrest. These requirements generate a strong tension for the relatives, in contrast with the palliative approach prevailing in "usual" LSTWs, which is free from any temporal constraints.

With the idea of optimizing grafts in mind, the issue of the legality and legitimacy of organ-protecting treatments, which are administered once LSTW is decided (vasopressors, or even invasive supportive techniques such as normothermic regional circulation), is raised. These treatments have nothing in common with palliative care.

Finally, sedation for comfort purposes, which is desirable in "usual" LSTWs, often poses problems when agonalagonal symptoms arise such as gasps, airway obstruction and respiratory tract congestion. Physicians' approaches diverge in such situations. Some choose to deepen sedation in order to limit these symptoms. In that case, treatment for palliative purposes ensures the patients' and relatives' comfort (suppression of agonal symptoms) to allow a peaceful death, less traumatizing for all involved. There is no possible confusion on the fact that sedation "benefits" only the patient and possibly the relatives. When applied to LSTW-MIII, however, this approach is questionable. One can indeed fear that this sedation might also be a way to ensure that the patient will certainly die within a time frame compatible with procurement.

Two other points deserve comment:

- extubation is far from common to all "usual" LSTWs. Approaches diverge and some teams maintain artificial ventilation or intubation. Furthermore, extubation of LSTW-MIII could be difficult for some to accept;
- the teams will be forced to settle back into their ICU bed LSTW-MIII patients who have not died within a time frame compatible with procurement. This situation could be hard for relatives to bear and difficult for caregivers to manage. It constitutes a potential factor for abuses such as resorting to massive sedation to avoid this possibility.

Before performing LSTW-MIII, it is therefore necessary to explain the entire procedure to the relatives, as well as the potential impossibility of achieving procurement, and its consequences.

3. Specificities of the LSTW-MIII

3.1. Context

LSTW-MIII implies cardiac arrest (followed by procurement) after extubation of the patient. For purposes of coherence and clarity of the procedure, extubation in LSTW-MIII must be performed by the physician responsible for the LSTW decision. Extubation can lead to procurement if the patient dies within a time frame compatible with the maximal duration of warm ischemia (duration varies for each organ: from 1 to 2 hours, depending on the protocol, for kidneys; 30 minutes for the liver). Warm ischemia corresponds to the elapsed time between the moment when arterial pressure is below a certain threshold (mean arterial pressure <60 mmHg in the United States or systolic arterial pressure <50 mmHg and/or SpO_2 $<70\%$ in the United Kingdom), and the moment when the cold perfusion of the organs is in place. The death will be declared by the physician responsible for the LSTW decision. If death does not occur, comfort treatments will be continued as envisaged in "usual" LSTW.

Extubating in the operating room means performing this act in an environment not intended for it. This presents certain challenges such as:

- facing a lack of understanding from the operating room staff, who has neither experience in intensive care, nor knowledge of the procedures and methods, in a place where the culture of surgery prevails;
- breaking the continuity of nursing care. The relatives leave the nursing staff who has been caring for the patient since the beginning of hospitalization in the ICU, and with whom they have built a relationship of trust. They are then confronted, without proper transition, with the operating room environment, with no one to speak to other than the procurement team and the physician responsible for LSTW;

- lacking the appropriate space to perform extubation and wait for cardiac arrest. Using the operating rooms for this purpose would lead to strong pressure, the possible temptation being to prepare the intervention before cardiac arrest has occurred. The recovery room is hardly suitable either, even though in some centres recovery rooms are not exclusively devoted to the reception of postoperative patients (for example, some function as emergency rooms, or intermediate care units...);
- not being able to properly care for the families who would want to accompany the patient to the end. For anyone familiar with the operating theatre, its dressing room, and the diversity of actors working there, it is easy to assume that families will, at best, feel uneasy in this highly technical context, where no space is provided for relatives to be alone and in peace at the patient's side;
- the fact of dying in the operating room during surgery is seen as a tragic event by its staff, and LSTW-MIII could fall outside the scope of what is expected and acceptable within this environment.

Finally, from an organizational perspective, circulatory arrest "must" lead to procurement surgery without delay. This explains why, in countries performing such procurements, a majority of teams have chosen to perform extubation in the operating room. If it were instead performed in the ICU, the patient in a circulatory arrest situation would have to be taken to the operating theatre as fast as possible. This is difficult to achieve in hospitals located in pavilion-type buildings, or even within one building, and is psychologically questionable when considering the peace in which the relatives should be left.

3.2. The question of predicting the time frame in which cardiac arrest occurs after extubation

Two studies have confirmed criteria for predicting cardiac arrest after extubation. UNOS criteria (United Network for Organ Sharing), which are predictive of rapid circulatory arrest following extubation, could be used [5] (Table 1).

Other criteria have been put forward by the University of Wisconsin [6] (Appendix A). They take into account the subject's dependence on oxygen and vasopressors, as well as spontaneous ventilation, age, Body Mass Index and tracheal access type.

3.3. The question of standardization of the sedation procedure accompanying extubation

Sedation surrounding extubation can be questioned. Indeed, who should be treated (the patient, the relatives, the staff?), what to treat (possible residual physical or moral pain, agonal symptoms?) and up to what point (tolerating a circulatory arrest from respiratory depression corollary to the suppression of agonal gasps?)? In this context, sedation must remain within the usual scope of palliative treatments. The optimal level of sedation should be reached by titration so as not to surpass the level required for the patient's comfort [7].

In the United States, gasps are avoided and prevented through sedation with anxiolytic dose titration [8,9], directed by institutional guidelines. Anxiolytic dose titration is presented as a safeguard against terminal sedation abuse. This titration does not seem to influence the time of cardiac arrest after LSTW [10,11]. The following arguments can be made in favour of formalized sedation both before LSTW and before extubation:

- it would limit physicians' and staff's decision-making leeway, thus providing them with a framework for action in a practice whose boundaries are unclear, as pointed out above. Such restrictions would prevent potential suspicions of goal-oriented sedation to ensure rapid and certain death;
- it would preserve the palliative care approach, by requiring, at the very least, the continuation of comfort-oriented sedation undertaken before extubation, even adapting it in relation to the patient's requirements[6];
- it would avoid agonal symptoms which would be difficult for the team to endure and possibly uncomfortable for the patient.
- it would reassure the families of the absence of any suffering.

Table 1
United Network for Organ Sharing (UNOS) criteria.

Characteristics at time of withdrawal of life-sustaining treatments	n (%) or median (25th and 75th percentiles) $n = 505$ patients	Association with death ≤60 minutes	
		Relative risk[a]	P-value
Demographics			
Male	261 (52%)	0.95	NS
Age (years)	67 (54, 77)		
<60	171 (34%)	1.00	NS
60-70	117 (23%)	1.03	
>70	217 (43%)	0.87	
Race			
White	389 (77%)	1.00	NS
Black	107 (21%)	1.08[b]	
Other race	6 (1%)		
Disease processes			
Central nervous system failure	279 (55%)	1.43	0.001
Status post-cardiac arrest	116 (23%)	1.15	NS
Circulatory failure	244 (49%)	1.72	0.001
Respiratory failure	486 (96%)	1.64	NS
Renal failure	152 (30%)	1.01	NS
Hepatic failure	56 (11%)	0.99	NS
Overwhelming infection	107 (21%)	1.28	0.028
Hemorrhage and shock	42 (8%)	0.83	NS

From Devita et al. [5].
[a] Rate of death within 60 minutes for the entire sample of $n = 505$ patients is 45%.
[b] RR of death within 60 minutes for Black or other race versus White race.

One can make the following arguments against such a method:

- a "typical sedation" will not take into account the specificity of the patient, including at the pharmacologic level (tachyphylaxy), and will therefore rarely be appropriate;
- titration would involve standardizing beforehand the patient's (or the relatives'?) pain symptoms assessment, which does not rely on supported knowledge or practices. Even when imperfectly codified, however, assessment of the patient's supposed suffering constitutes a routine practice leading to empirical titration, which usually allows for alleviated agonal symptoms and for an end of life characterized by a "gradual decline" whose unpredictable duration varies from one patient to the other.

In the end, the patient's rapid death following extubation is an essential condition for organ procurement, while also being important for the perception of the event by the relatives, who have agreed to the procedure. This scenario is the one envisioned and expected by the team as well. A patient enduring an endless agony would invite two types of dangers: the temptation to force the hand of destiny through drastic sedation to allow for MIII and thereby rescue medical logic, *or* discouraging the teams to engage in LSTW-MIII from fear that death would not occur and thus discredit their medical word, despite its sincerity.

[6] Sédation pour détresse en phase terminale et dans les situations spécifiques et complexes. Société française d'accompagnement et de soins palliatifs (SFAP), 2009.

One solution to these paradoxical constraints would be to require that the physicians explain the whole procedure to the relatives. This would include explaining the scenario in which circulatory arrest does not occur [10] within the prescribed time frame, thus resulting in the patient's transfer back to the ICU, if extubation had been performed in the operating theatre. One alternative option would be to apply the procedure only to patients with a high probability of cardiac arrest within a time frame compatible with procurement. Along those lines, one could consider procurement under MIII conditions only in patients presenting at least two UNOS criteria or a Wisconsin score $\geq$15.

4. Types of diseases compatible with LSTW-MIII

The type of patients for whom LSTW is considered and who would be eligible for an MIII-type procurement can be determined through two contradictory approaches. To include all LSTWs without obvious contraindications to procurement would ensure that no disparity exists in the way LSTW is considered in ICU patients. The ethical concept of providing all patients with equal chances for a given decision (LSTW) would thus be preserved. Conversely, to restrict MIII eligibility to patients suffering from specific diseases and presenting precise medical criteria so as to predict that death will occur within the hour following extubation would limit the risk of repeated failures. Such failures could, indeed, discourage teams from continuing with what they would consider to be hazardous MIII procedures.

4.1. Brain-damaged patients

In France, the decision for LSTW in the acute stage of a severe neurological disease is based essentially on medical reflection, centred on the patient's neurological prognosis and on the treatments undertaken, since it is rare that the patient has left any advanced directives. Furthermore, since such directives serve only an advisory function, medical arguments still play the greatest role in the decision. This does not rule out the necessity to use all available means to know the patient's wishes and values. Moreover, when one considers the factors leading to an LSTW decision, severe neurological diseases differ from one another.

4.1.1. Head trauma

Regarding head trauma patients, the moment an LSTW-MIII decision is made directly determines the time frame in which cardiac arrest will occur following extubation. Indeed, any severe intracranial hypertension (which disappears during the third week at the latest) will lead to rapid death after extubation. Yet at that stage, uncertainty regarding the prognosis is usually very high and LSTWs are thus difficult to imagine. Conversely, extubation after the intracranial hypertension stage will most likely not induce rapid cardiac arrest, though far less uncertainty remains concerning the patient's future. This major temporality issue does not allow for composed and double-free consideration of MIII in severe head trauma patients.

4.1.2. Anoxic coma

Cerebral anoxia, on the contrary, allows for an early determination of the prognosis, especially since it is supported by tests such as NSE or S100 dosage, evoked potentials or multimodal MRI. Indeed, intracranial hypertension is exceptional in anoxic patients (less than 10% of patients fall into a brain-dead state). This allows for a rapid withdrawal of sedation (between day 3 and day 5) and for a clinical examination without confounding factors within the first week. Predictive algorithms have been validated which combine elements of a clinical (GCS at 3 or 4, pupil unreactivity, absence of corneal reflex), biological (NSE superior to threshold value) and electrophysiological (N_2 absence on somesthetic evoked potentials) nature, or of mismatch negativity (MMN) on the evoked related potentials of EEG [12] (Fig. 1). This type of algorithm, once updated due to the recourse to hypothermia and MRI, could be used within the MIII procedure. Moreover, multimodal MRI will constitute a key test in the short-term as it is very specific of a bad neurologic outcome. This condition will be discussed further in the article.

4.1.3. Severe stroke

The issue of LSTW-MIII in severe stroke patients first brings up the question of the criteria motivating LSTW in the course of this condition. Yet no study has tackled this specific issue. Though the neurological outcome, often described as "catastrophic", seems to justify certain non-resuscitation instructions during the evolution of severe strokes, and therefore justify LSTW as well, it remains difficult to define. Similarly, the notion of "unacceptable handicap", as it is sometimes called, raises the question of quality of life, which is difficult to predict, as quality of life does not systematically correlate to the handicap [13]. Therefore, in this domain, the idea of handicap can be projected into many different representations. Such subjectivity in prediction can lead to self-fulfilling prophecies, which have been clearly demonstrated in the case of cerebral haemorrhage, and imposes a certain amount of caution in life-supportive therapy withholding or withdrawal decisions [14].

4.2. Other diseases

4.2.1. ARDS

Though LSTWs predominantly affect patients whose condition is incompatible with organ procurement (for example cancer, malignant haemopathy, multiple organ failure syndrome), acute respiratory distress syndrome (ARDS) is considered compatible with MIII in some American centres. This approach does not correspond to French practice, in which ARDS is addressed as a curable and reversible syndrome.

4.2.2. Chronic neuromuscular or respiratory diseases

The case of patients in the terminal stage of a chronic neuromuscular or respiratory disease (myopathy, ALS...) who are conscious and demand treatment withdrawal poses a tough question. In this context, the time frame for cardiac arrest under sedation and after extubation is unknown. The impact of demands for extubation in patients having previously accepted intubation is not known either, but these demands seem to be isolated cases in France.

5. Implications of MIII

Aside from the "technical" aspects mentioned earlier, it is necessary to discuss the implications of, and risks, which could result from, the promotion of organ procurement under Maastricht category III conditions compared to other consensual and codified procurement procedures currently performed in France.

5.1. Procurement on brain-dead patients and LSTW implementation procedures should not be undermined

In France, organ procurement on brain-dead patients currently constitutes the main source of grafts (there were 3,049 brain-dead patients in France in 2010, among which 1,477 were donors; 1,405 kidney donors enabled 2,617 kidney transplantations). This type of procurement is based on a definite clinical diagnosis controlled by

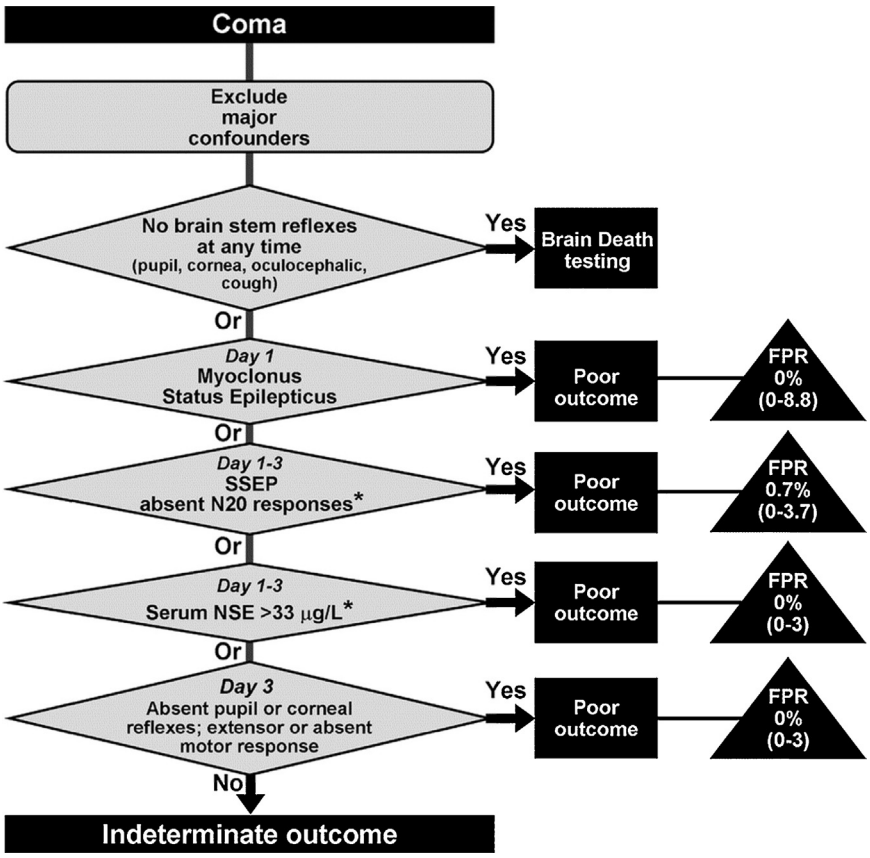

Fig. 1. Non-clinical criteria to assess the false positive rate for a poor prognosis [12].

compulsory complementary tests. Its practice is carefully codified. Despite these precautions, this procedure is still subject to suspicions and fears from part of the population. Furthermore, the context in which organ donation is presented to relatives is a painful one, tolerating no ambiguity regarding the medical approach and implementation procedure. Procurement rate on brain-dead patients in France (about 23 per million inhabitants [pmi][7]) places it within the top range of western countries.[8] Such is not the case for the United Kingdom (13 pmi) nor the Netherlands (16 pmi), which have developed MIII procurement the most, in large part to compensate for the imbalance between organ need and availability.

Any new procurement method, if it became dysfunctional, could discredit the entire organ donation process and affect all procurement methods. Furthermore, a dysfunction occurring within the context of MIII could also bring the LSTW approach into question.

Consequently, an MIII-type procedure must not contradict the three following principles:

- preserve the patient's will as expressed during his lifetime or reported by his relatives;
- preserve the patient's interests during the LSTW procedure (no obstinacy, substitute palliative care for life-supportive therapy when such therapy is considered futile);
- refrain from twisting the principles of and justifications for LSTW decisions.

Finally, as mentioned earlier, the act of considering an MIII-type procurement after LSTW leaves this procedure open to abuse. Only a distinct separation of these two decisions can make the medical intentionality perfectly clear.

5.2. Coherence with procurement in brain-dead patients should be maintained

Brain death diagnosis implies that all signs of brainstem activity have disappeared. In France, however, this diagnosis must be confirmed through compulsory paraclinical exams if procurement is to be considered. This is the prevailing logic in southern European countries, as opposed to Anglo-Saxon countries.

Maastricht category III procurement occurs after the patient's death following an LSTW decision. Such a decision is based on the "collegial" conviction that treatments are "futile" for a particular patient.

Procurement thus originates, in the case of brain death, from a definite diagnosis, and in the case of LSTW-MIII, from a chain of events leading to the acknowledgement of the futility of treatments and to the LSTW decision, none of these events being based on a standardized diagnosis. One may worry that such uncertainty could limit the practice of MIII, for fear that one day an LSTW-MIII patient would survive after extubation or even come out of their coma. Should such an event arise, relatives and even caregivers might find the situation difficult to comprehend and handle.

Two options exist therefore:

- accept the possibility that cardiac arrest may not occur after extubation and attempt to lessen the impact of such an event by informing the relatives in a clear way, with no extra procedural elements compared to standard LSTW;

[7] Annual report from the Biomedicine Agency (2010). http://www.agence-biomedecine.fr/agence/le-rapport-annuel.html.

[8] La greffe en Europe (Transplantation in Europe). http://www.dondorganes.fr/La-greffe-en-Europe.html.

- accept as eligible for LSTW-MIII only a subgroup with a very high probability of bad neurological outcome, which could include patients suffering from severe anoxia for whom LSTW is decided and who present several criteria for irreversible coma defined through complementary exams. Indeed, prognosis for severe anoxia is supported by evoked potentials, NSE dosage and probably soon multimodal MRI [15–17]. These exams possess a very high positive predictive value for irreversible prognosis and, supposedly, for rapid death following extubation:
  - these exams would support the clinicians' firm conviction, which prevails in an LSTW decision. They would be useful in limiting a double error risk:
    - an error risk in predicting the neurological outcome,
    - an error risk in predicting whether circulatory arrest will occur within the time frame required for organ procurement,
  - this procedure would in fact be similar to that surrounding brain death in France. Exams would be required when MIII procurement is considered after an LSTW decision and would not be necessary when it is not considered.[9]

Following this logic, several similarities would be maintained between both scenarios:

- the principle of presumed consent for donation shall apply similarly in the case of LSTW-MIII as it does in brain death;
- contraindications to procurement shall remain the same;
- the procurement team shall intervene only after the LSTW decision is made. Indeed, its role must not differ from the role it plays during brain death. The team shall intervene in the ICU when the time comes to discuss the possibility for donation with the relatives and obtain donation consent;
- normothermic Regional Circulation cannot be set up before death is declared in LSTW-MIII, no more than in brain death.

6. Prerequisites for MIII procurement in France

At present, after reviewing the literature and reflecting upon various practical and ethical aspects, it seems difficult to imagine LSTW-MIII in all diseases, even those deemed potentially eligible.

Indeed, in most diseases, prognostic criteria (in particular the prediction of the "irreversibility" of the neurological condition) do not seem reliable enough to allow for an LSTW-MIII decision. Furthermore, in most of the situations discussed earlier, the probability of rapid death following extubation (a necessary condition for procurement) is unknown, though likely to be low (less than 25% of patients in neurointensive care) [18]. These two arguments justify the choice to favour, in the beginning at least, and after a feasibility study, only one category of patients: those in a coma due to cerebral anoxia.

In other words, the search for conceptual simplicity (to include all LSTWs) clashes with pragmatism (to include only a subgroup with the most predictable paraclinical diagnosis for coma irreversibility and probability for rapid cardiac arrest following LSTW) and with the concern to respect the logic of procurement in brain-dead patients. The pragmatic option seems preferable to us, even though the idea of considering MIII only in a sub-category of brain-damaged patients can be debated on a formal level for ethical reasons (risk of selecting potential organ donors rather than other patients).

[9] Indeed, in the case of brain death, no angioscan or EEG are used in the decision to withdraw ventilation in a *clinically brain-dead patient* who cannot be procured (for example because of cancer history). The clinical diagnosis for brain death and the hypercapnia test are considered to be sufficient.

6.1. Preliminary prospective analysis of LSTW in post-anoxic coma patients

Before going any further, it seems necessary to conduct a feasibility study enumerating, in a prospective fashion, the prognostic criteria and time frame for the occurrence of circulatory arrest during LSTW in patients suffering from post-cardiac arrest cerebral anoxia. This study would be conducted in centres authorized for multiorgan procurement (the only types of centres in which MIII would be authorized). It would allow for the redefinition of UNOS criteria in light of French practices and of this specific condition.

6.2. Registry

The logical consequence of the uncertainties evoked earlier is that MIII, if it were considered, should be implemented during a probation period (of 3 years for example), combined with the implementation of a registry making a list of all LSTW-MIII cases and of the procedure followed for their execution. The resulting analysis of acquired experience would inform any decision to continue or not with this approach.

7. Conclusion

Life-supportive therapy withholding and withdrawal criteria are as of yet insufficiently studied and require further specification before post-LSTW organ procurement can be considered. All of the challenges discussed above deserve consideration, as the point of view they express contrasts with the opinions that undoubtedly governed the elaboration of recommendations in Anglo-Saxon countries. Such a contrasting situation can but bring to mind the major difference regarding the definition and confirmation of brain death between Anglo-Saxon and southern European countries. Besides, as the issue of MIII procurement exceeds the scope of medicine and directly affects civil society, it is the representatives of said civil society who should choose from the various options presented here. Nevertheless, once the uncertainties described earlier have been removed and a feasibility study carried out, the danger of MIII for patients, caregivers and society will hopefully be minimized and its implementation able to be considered. The MIII procedure, still quite uncertain and complex, must not delay or postpone the other approaches likely to enable organ procurement through readily available channels and methods. Finally, the decision to launch MIII would require more preparation and discussion than for organ procurement on patients who died after cardiac arrest (categories I and II of the Maastricht classification).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix A. Wisconsin University criteria

Criteria	Assigned points	Patient score
Spontaneous respirations after 10 minutes		
Rate >l2	1	
Rate <l2	3	
TV >200 cc	1	
TV <200 cc	3	
NIF >20	1	
NIF <20	3	
No spontaneous respirations	9	

Appendix A (*Continued*)

Criteria	Assigned points	Patient score
BMI		
<25	1	
25–29	2	
>30	3	
Vasopressors		
No vasopressors	1	
Single vasopressor	2	
Multiple vasopressors	3	
Patient's age		
0–30	1	
31–50	2	
51+	3	
Intubation		
Endotracheal tube	3	
Tracheostomy	1	
Oxygenation after 10 minutes		
O_2 Sat >90%	1	
O_2 Sat 80–89%	2	
O_2 Sat <79%	3	
	Final score	
Date of extubation	Time of extubation	
Date of expiration	Time of expiration	
	Total time	

From Lewis et al. [6].
Scoring: 8–12: high risk for continuing to breathe after extubation; 13–18: Moderate risk for continuing to breathe after extubation; 19–24: low risk for continuing to breathe after extubation.
TV: tidal volume; NIF: negative inspiratory force.

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