



Protocols for Uncontrolled Donation after Circulatory Death: International & Comprehensive Analysis

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Cardiac Arrest, Resuscitation and Organ Donation: Joint Venture for Saving Lives One Way or Another

Determination of death, the exact moment that a person's death occurs, has been a constant challenge throughout human being history. What we already know is that death usually does not occur abruptly, at a specific time and for all parts of the body simultaneously. Human resistance to degradation by lack of oxygen varies depending on the type of cell and organ. It is possible, for example, for successful cornea transplants from deceased individuals as many as seven days after death. Actually, the absolute absence of any residual vital activity in the body after cessation of circulatory function can only be confirmed once the putrefaction process is fully established and completely widespread throughout the corpse. It is not feasible logically, however, to wait until that point to declare death, due to safety and public health reasons.

Another obvious reason to of life of certain patients, thanks to organ donation and transplantation processes [1]. On the one hand, harvesting vital organs from living people, causing their death, is currently unacceptable worldwide [2] but, on the other hand, waiting too long after declaring death to begin the organ extraction could compromise the quality and quantity of organs retrieved and consequently, declare the death of an individual as soon as possible is the possibility of saving lives or improving the quality and outcomes in terms of long term graft and recipient survival.

Both theoretical and practical problems of determination of death in the context of organ donation are rooted in this kind of tug of war game between obtaining organs in optimum conditions without affecting the goal of providing quality care at the end-of-life stage for potential donors, still patients.

The laws of a large number of countries around the world support the determination of death of an individual in the clinical setting according to two alternative conditions [3]:

1. After declaring the irreversible cessation of cardiorespiratory functions (the so-called cardiac or circulatory death), or
2. After declaring the irreversible cessation of the brain function (the so-called neurologic or brain death)

However, according to the legal definition of death criteria in all

these countries, it is not required for both of these conditions to occur simultaneously for the patient to be considered dead and, therefore, to be a potential organ donor. In other words, either criteria, when fulfilled separately, is sufficient for the patient to be declared legally dead and thus become a deceased donor. It is not necessary for both criteria to be met at the same time [4].

In this way, legally declared brain dead individuals can maintain circulatory function (heart-beating donors) and, supported by ventilation assistance, respiratory function can be artificially maintained. In such cases brain function does not exist, and the patient is declared legally dead, but simultaneous loss of circulatory function does not occur. These so called heart-beating deceased donors can provide an important quantity of organs. In fact, the circulation of oxygenated blood throughout the body is precisely what preserves the organs in good condition, pending the authorization that must be given by the next-of-kin of the patients, unless their wills were registered before the organ removal begins.

The rest of the deceased donors are therefore individuals declared dead according to circulatory criteria, after considering that loss of pulse is irreversible. The so-called non heart-beating donors are not necessarily assessed by a neurologic exam demonstrating a total and irreversible loss of brain function because, as we said, the law does not consider it mandatory. To be fair, in France, a simple neurologic exam is mandatory according to the law [5]. In other countries, the absences of respiratory and circulatory function after resuscitation attempts are enough to judge the cardiac arrest as irreversible. Therefore, organ donors whose determination of death is certified according to circulatory criteria may pose the following basic physiological questions:

When and why we can say that cardiac arrest is really irreversible? and

What is the status of their cognitive functions that is their brain function, along the process of preservation and retrieval of vital organs for transplantation?

When May we Consider that Cardiac Arrest is Irreversible?

Most people who die are declared dead according to circulatory criteria after confirming the absence of pulse. Thanks

to cardiopulmonary resuscitation (CPR), certain patients suffering cardiac arrest are reversed from the episode, and if ensured adequate perfusion of the brain during the process, reducing the so called no flows period and low flow period as much as possible, some individuals have a complete recovery with good quality of life. Unfortunately, most of the time, a return of spontaneous circulation does not occur, or is not followed by a complete neurologic recovery, and results in different disabilities [6,7].

In any case, it is clear that if resuscitation maneuvers are not performed and the function of the heart is not restarted, or if the intrinsic contractile function of the heart is not resumed either, this dying and hopeless person will be irreversibly dead in a short period of time.

But, how long exactly should we attempt to resuscitate a patient before deciding that efforts are futile? When can we be sure that nothing more can be done for this patient? When can we be sure that death is irreversible? When is 'enough' enough? Even for professionals dealing with resuscitation, these questions have no simple and evident answer [8]. International recommendations have agreed to set a standard time of 30 minutes of advanced cardiopulmonary resuscitation. Following such a standard period, if the patient does not recover signs of circulation, so effective pulse, efforts can be interrupted [6,7]. Then, a death certificate is signed, and a corpse can be conveyed to a morgue.

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The best and most current and updated medical evidence encourages professionals from emergency medicine in general, and from prehospital emergency medical services in particular, to provide a case-by-case based resuscitation to certain unexpected cardiac arrests [9]. Accordingly, the last international guidelines on Resuscitation [6,7] call upon an ideal resuscitation that should be minimally interrupted, of high quality, and guided by the primary cause that originated cardiac arrest, until offering the patient specific treatments that can reverse or treat the process, if feasible. Different groups, in several countries, have obtained promising results in terms of survival with an excellent neurologic recovery (Cerebral Performance Category score, CPC 1-2) after sudden cardiac arrest, after the implementation of programs for non-conventional CPR. [10-15].

Different approaches of non-conventional resuscitation are currently active worldwide including procedures, techniques and treatments such as:

- a) On arrival at catheterization laboratory, coronary angiography and/or percutaneous coronary intervention are performed during ongoing resuscitation, when coronary disease is diagnosed or suspected as the actual cause of cardiac arrest
- b) Life support with extracorporeal circulation is provided by trained teams when refractory cardiogenic shock is identified, while the primary cause of the process is being resolved
- c) thrombolytic treatment, during resuscitation maneuvers, when cardiac arrest is secondary to a cardiopulmonary thromboembolism
- d) Echocardiography performed under disrupted resuscitation may identify the trigger of cardiac arrest and physicians are able to focus on this reversible cause.

Donation After Circulatory Determination of Death from the Prehospital Setting

Mainly in Spain and France, but increasingly spreading to other countries and continents, there are Emergency Medical Services with portfolios including protocols for transport from the prehospital setting for patients who have not recovered from cardiac arrest.

After 30 minutes of standard resuscitation, transfer is begun to a hospital with a deceased organ donation program available. The transplant team is pre-alerted to the arrival of the potential donor. During transport, and supported by automated compressor devices and ventilators, organ preservation is initiated. From this moment, nothing more is attempted for restoring circulation and preserving organs to protect the interests of a future recipient becomes the priority [1,5,9,16].

On arrival at the hospital, the organ preservation procedures already initiated during the transfer are interrupted for at least five minutes [5,16]. If the potential donor does not resume effective pulse spontaneously during this hands-off period, a death certificate is signed and the individual large vessels are cannulated. Then, the potential donor is connected to an extracorporeal machine that assures continued and more effective organ preservation, reducing the ischemic process. If the family does not reject the donation, the harvesting team immediately proceeds to the retrieval of organs [5,16].

According to some published series, around 6% of the patients transferred to the hospital as donors had return of spontaneous circulation [17], which obviously invalidated the donation option. At least one case reported a complete full recovery of a patient without any neurological sequelae [17]. Such cases, albeit exceptional, question the standard approach to resuscitation at least for some individuals, and suggest that certain interventions that are made solely for purposes of preservation of organs could be focused on saving lives and initiated as soon as possible, instead of the standard resuscitation in the field. Moreover, at least in some patients, the decision to initiate the transport under ongoing resuscitation, must be taken earlier in time, with a clear therapeutic end goal [18]. Of course, the option of these interventions depends on the quality of life that can be expected case-by-case, which is crucial to ensuring, as much as possible, any neurological damage. Furthermore, a validated predictive model [19] is the keypoint that underpins this approach. In fact, it allows to select from all patients in cardiac arrest those who would benefit from certain unconventional -but available and already used- resuscitation techniques, increasing the chances to reverse some sudden cardiac arrest considered irreversible until now [13,20]. At the same time, such an approach to considered refractory cardiac arrest is aligned with the goals of the most updated international guidelines on resuscitation, so would avoid existing conflicts of interest [1,9,20,21]. Such a conflicts are difficult to manage by health professionals who are faced with both the families of patients and the concerns of society as a whole [1,9,16,20,21]. Joining both strategies [1,9,20,22,23] and subordinating the eligibility as donor to the futility or failure of unconventional resuscitation in a case-by-case based decision, we could increase survival with quality of life in certain patients who have been considered medically hopeless, and this in itself is a clear improvement. Moreover, even when certain individuals receiving these techniques and treatments would not have been saved, or if pulse was restored resulting in extensive neurological damage due to prolonged ischemia, the option for organ donation would still remain [15,22,23]. This option could be offered either after declaring death by neurological criteria, if that is the case, or after declaring death from circulatory criteria after considering the option of withdrawal of life support. Both options are currently being used worldwide.

In places where a case-by-case cause based approach to refractory cardiac arrest have already been implemented, both of the final goals of the process have increased in quantitative and qualitative terms: firstly, there has been an increase in survival rates with good neurological recovery and, secondly, in non-survivors and survivors with extended neurologic damage there has been an increase in the number of potential deceased donors, where deceased organ donation programs were implemented [22-24].

Does a more efficient way to treat patients with refractory cardiac arrest exist, according with best evidence? Is there any fairer possible use of the means we have? By trying to save hopeless patients' lives, and when this is not possible, by increasing availability of organs for

transplant, we will be providing near to excellent care to patients suffering refractory cardiac arrest in the field, and saving more lives one way or the other: Throughout high-quality resuscitation, and when really impossible despite of doing our best, throughout donation and transplantation after declaring death [25].

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