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REVIEW

Cardio-pulmonary resuscitation of brain-dead organ donors: a literature review and suggestions for practice

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Dr Gardiner is deputy national clinical lead for organ donation in the UK for NHS Blood and Transplant.

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Summary

"Organ preserving cardiopulmonary resuscitation (OP-CPR)" is defined as the use of CPR in cases of cardiac arrest to preserve organs for transplantation, rather than to revive the patient. Is it ethical to provide OP-CPR in a brain-dead organ donor to save organs that would otherwise be lost? To answer this question, we review the literature on brain-dead organ donors, conduct an ethical analysis, and make recommendations. We conclude that OP-CPR can benefit patients and families by fulfilling the wish to donate. However, it is an aggressive procedure that can cause physical damage to patients, and risks psychological harm to families and healthcare professionals. In a brain-dead organ donor, OP-CPR is acceptable without specific informed consent to OP-CPR, although advance discussion with next of kin regarding this possibility is strongly advised. In a patient where brain death is yet to be determined, but there is known wish for organ donation, OP-CPR would only be acceptable with a specific informed consent from the next of kin. When futility of treatment has not been established or it is as yet unknown if the patient wished to be an organ donor then OP-CPR should be prohibited, in order to avoid any conflict of interest.

Introduction

Scarcity of organs in transplantation medicine has led to an international call for national self-sufficiency in organ supply to prevent transplant tourism and the exploitation of the vulnerable [1]. Several strategies have been developed to increase organ supply: better detection and management of brain-dead patients, use of expanded criteria donors, living donation, and donation after circulatory determination of death (DCDD). Despite strategies to improve brain-dead organ donor management [2–4] such as the "critical pathway" [5], cardio-vascular instability, hormonal changes [6,7], and inflammatory responses can result in cardiovascular collapse and cardiac arrest prior to organ donation [8,9].

The clinician in the situation of unexpected cardiac arrest in a brain-dead potential organ donor faces an ethical dilemma. If organ preserving cardiopulmonary resuscitation (OP-CPR) is not performed, transplantable organs are lost and potential recipients harmed by omission. On the other hand, performing OP-CPR can cause physical damage to the body of the patient, and risks psychological harm for professionals, and families. As we will show, guidelines and recommendations on brain-dead organ donor management barely mention the use of cardio-pulmonary resuscitation (CPR) in cases of cardiac arrest, and no consensus on the appropriateness of this intervention exists.

The purpose of this study is to establish whether OP-CPR is ethically acceptable, and if so, under which circumstances.

To answer this question, we review guidelines and recommendations on brain-dead organ donor management, ethical papers on transplantation, and the bioethical literature. We then conduct an ethical analysis and propose clinically applicable recommendations.

Concepts and definitions

Organ preserving CPR

We define OP-CPR as the use of CPR in cases of cardiorespiratory arrest, not to revive the patient or save the patient's life but with the motivation of preserving his or her organs for donation and transplantation by maintaining an oxygenated circulation in the body (Table 1). We deliberately avoid terminology such as "Elective" or "nontherapeutic," to prevent any confusion between the present discussion and other debates. In some literature, "Elective-Intensive care," "Nontherapeutic intensive care" [10–13], and "Elective mechanical ventilation" [14] refer to the use of intensive care or mechanical ventilation not for the patient's benefit but to preserve his or her organs for transplantation purposes, but the definitions of each of these modalities are often unclear.

Organ preserving cardiopulmonary resuscitation will usually involve one or more of the following interventions:

1 Chest compressions to maintain the circulation of blood,

2 Artificial ventilation (either mechanical or by a person) to replace the loss of spontaneous breathing,

3 Electrical defibrillation in cases of shockable heart dysrhythmias, and/or

4 The addition of drugs if necessary to support the resuscitation of the circulation.

Table 1. Definitions.

Organ preserving CPR (OP-CPR)	CPR used in cases of cardiac arrest in a potential organ donor, not to save the patient's life but to preserve his/her organs for transplantation purposes
Brain-dead patient	Formal brain death testing and confirmation of brain death
Not-yet tested brain-dead patient	Clinical belief of irreversible loss of brain function, but brain death tests have not been initiated or are yet to be completed
Not-yet brain-dead patient	Some degree of cerebral function but clinical belief that irreversible loss of brain function will occur in time
Consented organ donor	A person who was either registered to organ donation or for whom the family has given an informed consent to organ donation
Potential organ donor	A person considered by health professionals as a candidate for organ donation, before knowing her/his wish to donate
Organ donor	A person who has given her/his organs

It should be noted that some of these modalities are also used to maintain organ preservation in DCDD programs but such use falls outside the limits of this study. In our definition, it does not include other reanimation maneuvers, such as the use of extracorporeal support.

Organ preserving cardiopulmonary resuscitation will preserve the opportunity for organ donation by either rapidly reversing the cardiac arrest allowing the patient to be returned to the physiological state they were in prior to the arrest or by allowing organ function to be maintained via ongoing CPR, while the patient is transferred to the operating room for surgical organ recovery. This second possibility concerns DCDD Maastricht Category IV (i.e. DCDD after determination of brain death).

Literature review

Guidelines and case reports on OP-CPR after brain death

Our review established that very few guidelines on organ donor management or case reports mention the use of OP-CPR (see Table 2).

The International Guidelines (2000) for CPR and ECC (Emergency Cardiovascular Care) state that DNAR (do not attempt resuscitation) orders are replaced with standard deceased donor-care transplant protocols [15]. The Australian and New Zealand Intensive Care Society (ANZICS) guidance on donation appears to emphasize the use of CPR to restore the patient back to the pre-arrest physiology [16]. More specifically, the Los Angeles County Hospital's protocol recommends resuscitation of the donors in case of cardiac arrest, following normal resuscitation algorithms [17], while in Switzerland, chest compression is not recommended in cardiac arrest of a brain-dead organ donor [18]; however, defibrillation in case of shockable rhythm is left to the discretion of the physician in charge. The guidelines from Denmark, Canada, and the USA are silent on the use of OP-CPR, or it is left to physician preference [5,19,20].

We searched review articles, case reports, and surveys, using PubMed, Embase, Cochrane, and Google Scholar, with key words including: CPR, brain death, organ donors, resuscitation, and heart-beating donation. In a review of 39 randomized controlled trials assessing the efficiency of different strategies to manage brain-dead organ donors [3], while these strategies include fluid management, the use of vasopressors and hormonal therapy and other interventions; *OP-CPR was neither recommended, nor mentioned*.

Elsewhere in the literature, some authors do make mention of OP-CPR either supporting the use of CPR to restore the pre-arrest physiology in the potential donor [6,13,21–25] or supporting the use of OP-CPR without detailing the

Table 2. Current literature recommendations on organ preserving cardiopulmonary resuscitation (OP-CPR) after brain death.

	Recommendations on OP-CPR
Guidelines on organ donor management	
The International Guidelines (2000) for CPR and ECC (Emergency Cardiovascular Care) [15]	In a brain-dead consented organ donor: "previous DNAR (do not attempt resuscitation) orders are replaced with standard deceased donor-care transplant protocols until the organs have been procured."
Australian and New Zealand Intensive Care Society (ANZICS) [16]	"In the event of cardiac arrest, cardiopulmonary resuscitation may result in recovery of cardiac function and successful transplantation."
Los Angeles County Hospital's protocol [17]	In a potential organ donor: "cardiac arrest: Follow ACS [acute coronary syndrome] code guidelines."
The Swiss Foundation for Organ Donation [18]	Cardiac arrest in a brain-dead organ donor: chest compression not recommended; defibrillation left to the discretion of the physician.
Denmark [19]	No uniform guideline; decision regarding OP-CPR left to the physician in charge.
Canada [20]	No mention of OP-CPR.
The US "critical pathway" [5]	No mention of OP-CPR.
Review articles, case reports and surveys	
Rech *et al.* [3]	Review of 39 randomized controlled trials: No mention of OP-CPR.
Dösemeci *et al.* [22]; Turkey	Reported one case of OP-CPR (defibrillation) in 134 brain-dead patients
Chiu *et al.* [23]; Taiwan	Reported a case of OP-CPR
Jeong *et al.* [8]; Seoul	Reported 5 OP-CPR cases in 316 brain-dead potential organ donors
Hsieh *et al.* [36]; Taiwan	Case report of a not-yet tested brain-dead patient: OP-CPR for 1 h, followed by the implementation of ECMO
Other papers	
Wood *et al.* [6]	"In the event of cardiac arrest, standard advanced life support should be instituted, because the recovery of cardiac function in the potential donor can result in successful transplantation"
McKeown *et al.* [21]	"During the catecholamine storm, cardiovascular changes will be acute and transient, and active resuscitation, including cardiopulmonary resuscitation, may be required."
Tuttle-Newhall *et al.* [26]	In case of cardiac arrest in brain-dead patients, "aggressive treatment according to advanced cardiac life support guidelines should be instituted"
Tisherman *et al.* [27]	"Once brain death and family consent are confirmed, we continue to aggressively support potential organ donors, including the use of hemodynamic support, blood transfusion, and even cardiopulmonary resuscitation."

expected aim of the CPR beyond a general support of donation [8,26,27]. A retrospective analysis of the United Network for Organ Sharing from 1999 to 2011 revealed that 5.5% of all brain-dead organ donors sustained CPR previous to organ procurement [28]. CPR was performed either before the diagnosis of brain death, as a life-saving procedure or after the diagnosis of brain death, as OP-CPR. There was no significant difference in term of graft survival outcome.

The surprising lack of clinical effect on graft survival outcome is supported by a retrospective study carried out by Castleberry *et al.* [24] who showed that a reversible cardiac arrest in brain-dead organ donors resuscitated using CPR does not alter the outcome in lung transplant recipients. A similar study had similar results for heart transplantation [13]. A retrospective study, conducted by Ali *et al.* [25], concluded that "a period of cardiac arrest in the organ donor prior to cardiac procurement did not appear to have any negative influence on the post-operative course or clinical outcome following heart transplantation". Similar conclusions were reached by Sanchez-Lazaro *et al.* [29].

Ethics papers on OP-CPR

After an online search on PubMed and Scholar Google, adding the keywords "ethics," "moral," and "bioethics" to the keywords listed above, we were able to find only two articles discussing the ethics of OP-CPR. Cummings *et al.* [30] concluded that "because CPR is an invasive and potentially violent procedure—one that may be unacceptable to some families—we recommend families be explicitly informed of the possible need for such a procedure and their permission obtained during the discussion on organ donation". In Denmark, Gjerris *et al.* [19] conducted an opinion survey on physicians and nurses at nine intensive care centers. This revealed that some professionals are uncomfortable with resuscitating a brain-dead patient in cardiac arrest [31]. Gjerris commented that "staff may be able to make some progress by informing relatives that

CPR might be required as part of the organ preservation treatment" [31].

Ethical analysis

Brain-dead organ donors are in a vulnerable position because they cannot express their current wishes or change their mind. It is generally held that we have a duty to protect the dead by (i) respecting the body and by (ii) attempting to follow any wishes the deceased had previously expressed in life.

To decide whether OP-CPR is an acceptable ethical procedure we will start by describing its potential benefits and harms as applicable to different groups. For reasons of clarity, the ethical analysis will first concern, in some detail, the confirmed brain-dead and consented organ donor who has an unexpected cardiac arrest while awaiting organ removal. Thereafter, different, and increasingly complex, clinical scenarios will be considered.

OP-CPR in the brain-dead consented organ donor

Potential benefits and harms of OP-CPR to the brain-dead consented organ donor

Although the brain-dead consented organ donor cannot feel or be aware of any physical or psychological suffering, moral harm is nonetheless possible. The meaning and importance of the body, even after death, has cultural, religious and personal value. OP-CPR is an aggressive procedure, involving the use of chest compression, defibrillation, and augmented mechanical ventilation. CPR can physically damage the individual: ribs can be broken and mediastinal organs injured. However, it must be acknowledged that in brain-dead patients awaiting organ donation, surgical removal of their organs is already planned. This highly invasive operation has serious implications for bodily integrity, but is an action that the healthcare team, in agreement with the family, has already approved. The degree of physical damage in OP-CPR would not appear to carry the same level of insult against bodily integrity as the act of surgical organ recovery.

For some, OP-CPR might be seen as benefiting the patient by respecting her wish to be an organ donor, for without CPR in these circumstances the opportunity for donation will be lost. While others might see OP-CPR as against the wishes of the patient, who might have preferred to die "in peace" and "with dignity" (which includes treatment after death) instead of being subjected to interventions that require "interference" with her bodily integrity. Some patients might regard harm of this nature to the body after death as a genuine harm, even if they agreed to organ donation while alive.

Some brain-dead individuals will have "do not attempt resuscitation (DNAR)" orders, which specify that no attempts at CPR should be initiated. These might be thought to pose a problem for OP-CPR. There are two main motivations for DNARs: a wish not to be revived and a wish to avoid the intrusive procedure of CPR (both for oneself and for one's family). While the latter does raise problems for OP-CPR, the former does not, as the intention cannot be to revive the patient (who is already dead) but to preserve organs for transplantation.

It order to avoid any prejudice to the patient's interests, the values and wishes of the patient should always be established, ordinarily through discussion with those close to the patient.

Potential benefits and harms of OP-CPR to families

By fulfilling a personal wish to donate, OP-CPR might help families with the grieving process by facilitating donation [32]. Again there are some potential harms involved. First, if OP-CPR damages the patient's bodily integrity, this might be distressing for families. Families are not typically present in theater for organ recovery but are much more likely to be present on the intensive care and at the bedside of their relative when the cardiac arrest occurs. If the family is present while the cardiac arrest occurs, witnessing the CPR taking place might be distressing. However, even if the family is not physically present, it is unclear how they might view CPR.

Second, the concept of brain death can be difficult to understand for the general population. How can a life-saving procedure as CPR be performed on their relative, if he or she has already been declared dead? This issue might be able to be addressed through careful explanation.

Third, OP-CPR might be considered as interfering in death practices, by undue interference with the body or by reducing the time the family can spend with their loved one, particularly if CPR is continued up until organ recovery in the operating theater.

Potential harms and benefits of OP-CPR to health professionals

Organ preserving cardiopulmonary resuscitation can benefit professionals as a mean of facilitating organ donation, and thereby benefitting the end-of-life wishes of deceased patients, their families and patients in need of organs elsewhere in the healthcare system. However, there are also caveats.

The organ donation process in general can be a source of psychological suffering among professionals. First, their primary role is to take care of a patient; if the patient's life cannot be saved, treatment is withdrawn and comfort care is given. End-of-life care is part of the bereavement process for both professionals and families. The context of organ

donation changes this paradigm. Professionals now have to take care of an organ donor. This is known to cause a significant moral conflict for professionals and can induce psychological suffering [33,34]. For similar reasons, OP-CPR can be psychologically challenging for professionals.

Furthermore, it can be distressing for professionals, to use a practice that is normally used as life-saving procedure, on a brain-dead patient. Indeed, the notion of brain death is not always accepted among all professionals, some of whom struggle with the concept [35]. It is here important to emphasize that this kind of moral discomfort can lead to resistance, which could negatively affect organ donor programs.

Finally, if OP-CPR is conducted without a specific informed consent, professionals will not know if it is performed according to the patient's best interests, which is deeply problematic.

Potential benefits and harms of OP-CPR to recipients

Cardiac arrest causes warm ischemia and ischemia-reperfusion that can induce organ injury, making organs unsuitable for transplantation. However, the literature confirms that a brain-dead patient who sustains cardiac arrest can still offer organs that are suitable for transplantation [13,24,25,28,29]. It is not an exaggeration to say that in some cases patients who would otherwise have died could be saved by organs whose donation was facilitated via OP-CPR.

However, recipients are concerned about how organ donors and their family are treated and this should be taken into consideration.

Weighing the potential benefits of OP-CPR against the potential harms

Do the benefits of facilitating organ donation justify the potential harm induced by OP-CPR? The whole process of organ donation by its nature damages bodily integrity and interferes with typical death practices in hospitals. Most societies allow organ donation despite this because transplantation can save or improve the lives of many patients.

To assess whether this risk of harm is justifiable because of the benefits of transplantation, it is useful to compare the harm induced by OP-CPR with the harm induced by other procedures that are indispensable to the organ donation process. As discussed above, OP-CPR is obviously a much less invasive procedure than organ removal itself. If OP-CPR is not worse than organ removal, and organs removal is a procedure already generally accepted as ethical, it might follow that OP-CPR is also ethically acceptable.

A utilitarian might claim that "if the invasiveness of CPR is acceptable for patients who experience life afterward, it can hardly be ethically unacceptable for those who can never experience any pain or suffering because of it." However, the organ donation and transplantation programs of most countries are not structured on utilitarian grounds. Instead, they are structured around strong ethical norms that direct practice; most importantly, the dead donor rule and the need for consent of some approved kind to make organ donation and transplantation legal.

A solution might be to obtain either specific informed consent to OP-CPR when people join in life any organ donor register. However, this does not seem realistic. Apart from the necessity of a complicated and large public education campaign for a rare event in organ donation, in the UK, for example, only 41% of organ donors are on the organ donor register [36]. An alternative solution is to obtain a specific informed consent to OP-CPR from families. The informed consent process should be conducted carefully, as it can distress family members. Indeed, it is additional information for the family to receive on top of processing the death of their loved one by neurological criteria, giving their consent for organ donation if the brain-dead patient was not known to wish to be an organ donor, and then giving their consent for OP-CPR, an event only rarely likely to occur.

On balance, we feel that even when a specific informed consent to OP-CPR has not been yet obtained, our opinion is that OP-CPR should be performed on a brain-dead consented organ donor where unexpected cardiac arrest occurs, although advance discussion with next of kin regarding this possibility is strongly advised.

Different clinical situations

The not-yet tested brain-dead potential organ donor

This clinical situation has two distinctive issues: (i) an issue of uncertainty regarding the brain death of the patient and (ii) a legal issue with a patient that is not formally confirmed dead.

The medical uncertainty regarding brain death gives rise to an uncertainty about any residual functions of the brain. Does the brain still have some function? And if so, does this function enable the patient to feel and experience any kind of suffering?

Because of this uncertainty, and because of the legal issue, we propose to include the not-yet tested brain-dead organ donor in the category that follows: the not-yet brain-dead organ donor.

The not-yet brain-dead potential organ donor

A not-yet brain-dead potential organ donor, contrary to the brain-dead organ donor, can experience physical or psychological suffering, even if minimal, in addition to moral harm, because he has some cerebral function. It can be argued that the patient's clinical condition during

OP-CPR is so close to death that his ability to experience any kind of physical or psychological suffering is close to zero. However, once circulation returns after successful CPR, the patient could return to a state where he can experience a certain amount of physical or psychological suffering. Not-yet brain-dead potential organ donors are often denied any kind of sedative or opioid analgesics, to avoid confounding any future brain death tests.

For not-yet brain-dead organ donors, OP-CPR can be compared with other procedures in organ donor management, such as specific vasopressor infusion or hormonal therapy. These procedures are often commenced before death has been declared and the patient consented for organ donation. OP-CPR is a more aggressive procedure than either of these and could induce more harm. Because of the risk of harming a living patient, we think that OP-CPR is justifiable only if it is performed in accordance with the patient's values, necessitating specific informed consent from the family. We specify here that we speak about OP-CPR, that is, CPR performed for the only purpose of preserving organ and not of reviving life. This means that OP-CPR concerns only not-yet brain-dead patients for whom futility of care has been established between health professionals and family members, and who are known to be willing organ donors. Thus, outside the context of organ donation, withdrawal of treatment would be proposed, but because of the possibility of organ donation, patient's care is continued.

We are aware that in practice, when clinicians manage patients with catastrophic brain damage, the line between a patient who has some chances of recovery and a patient who has no hope of recovery (and thus for whom futility of care has been determined) is not clearly defined. However, we caution that it is the duty of each clinician to avoid any conflict of interest. If futility of treatment has not yet been established, any discussion or action should be directed toward the patient's care and not toward organ donation, to avoid an evident and dangerous conflict of interest.

If the patient is for full and active management, he should be reanimated with standard ACLS, including CPR, as a life-saving treatment. If the patient has a DNR order, he should not be reanimated, and OP-CPR should not be performed, because organ donation should not enter into consideration.

Patient not consented for donation

If the patient is not known to be a willing organ donor and an informed consent on organ donation has not been yet obtained from the family, we do not recommend provision of OP-CPR.

Our recommendations are summarized in Table 3.

Conclusion

Cardiac arrest in a brain-dead consented organ donor is a challenging situation, but OP-CPR can facilitate organ donation which otherwise would need to be abandoned. Very few guidelines recognize this possibility, and there is very little guidance for clinicians.

The principal limitation of our study is that guidelines and recommendations were extracted only from a web research (Cochrane, Pubmed, etc.), which will miss local protocols unpublished online. It would be interesting to search for different local protocols on brain-dead organ donor management around the globe, as well as to conduct an opinion survey among healthcare professionals on OP-CPR. A further limitation may be within our ethical analysis, which should be taken as our argued opinion.

Our ethical review suggests that OP-CPR can be ethically justified in some circumstances but not all.

We conclude that OP-CPR can benefit patients and families by fulfilling the wish to donate. However, it is an aggressive procedure that can cause physical damage to patients, and risks psychological harm to families and healthcare professionals.

In a confirmed deceased (brain-dead) consented organ donor, OP-CPR is acceptable without specific informed consent to OP-CPR, although advance discussion with next of kin regarding this possibility is strongly advised. In a patient where brain death is yet to be determined, but there is either consent for donation or knowledge that organ donation is something the patient would have wished for after death, CPR might well be being initiated by the treating team with the goal of reviving the patient for ongoing prognostication and treatment, and this would be acceptable, but if OP-CPR is the primary justification, then this would only be acceptable with specific informed consent from the next of kin (or unusually an advance statement from the patient). When futility of treatment has not been established or it is as yet unknown if the patient wished to

Table 3. Recommendations on organ preserving cardiopulmonary resuscitation (OP-CPR).

Brain-dead consented organ donor	Acceptable without specific informed consent; specific informed consent preferred
Not-yet tested brain-dead potential organ donor	Acceptable with a specific informed consent
Not-yet brain-dead potential organ donor	Acceptable with a specific informed consent
Futility of treatment not yet established	Not recommended
Not known as a consented organ donor	Not recommended

be an organ donor, then OP-CPR should be prohibited, in order to avoid any conflict of interest.

We hope this study will generate discussion and enable the development of formal guidelines that reflects ethical consensus.

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