

Newborns as potential organ donors: a new perspective?

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Abstract

Demand for organ donation is increasing over the years in all age groups leading search for alternative sources. Donation pool expansion in newborns necessitates new approaches specifically for brain and circulatory death definition. The "dead donor rule" (the donor must be dead before organ removal starts) remains the cornerstone for organ procurement. Brain death definition and time determination of circulatory death need to be uniformly accepted by the scientific community. Technical advances, uniform protocols for death determination and new proceedings in surgical field can maximize donation pool along with establishment of end-of-life care standard procedures and persistent support of the family. Newborns can serve as multivisceral donors in the near future to meet the increasing demand for organs in this age group.

Keywords

Organ donation, newborns, brain death, cardio-circulatory death, dead donor rule.

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Introduction

In recent years, pediatric solid-organ transplantation has evolved into a well-established, usually successful procedure, with the gap between available organs and demand still growing. In newborns it is a subject of intense debate, opening this exciting new field for medical research and

therapy in end-stage organ diseases. Due to the fact that protocols for organ donation were developed for adults, potential pediatric donors are lost in the donation pool [1].

Organ donation primarily should be based on certain criteria for death. Death certification, ethical dilemmas and parental consent remain the most important issues for organ donation in children. Medical staffs' consistent/understandable information, emotional support and consequent parental consent seem to be prerequisites for expanding donation pool. It has been shown that supportive behaviors from medical staff based on training and educational programs, treating parents with dignity and respect are essential predictors for getting consent [2]. Consequently, hospital staff's ability to respond to families' informational and emotional needs can lead them more easily to decision making.

Additionally, interventions main focus should be strategies for parents to cope with less stress when organ donation matters emerge. Open and honest information in order to reduce parent's sense of loss of control due to their newborn's vulnerability and inability to claim their rights should be the primary policy for transplantation networks [3].

Donation pool for newborns are infants defined as dead, either meeting criteria for brain death (BD) or cardio-circulatory (or cardiovascular) death (CCD). Organ donation from anencephalic infants is no longer applied due to serious ethical, organ quality issues and BD diagnosis criteria [4]. It is essential for the organ donation process to apply the "dead donor rule", namely the declaration of death before organ removal [5, 6]. Consequently the precise moment for declaring time death (BD or CCD) is of extreme importance. However low quality data, lack of standardization, different policies among hospitals and scientific debate on this issue raise serious concerns.

Donation pool for cadaveric organs available in newborns is limited compared to adults because of incompatible organ size, restrictions for children donation, ethical dilemmas and BD definition in this age group. Consequently, limited organ availability causes high mortality in the wait list for transplantation. In the UK, British Pediatric Association (1991), in contrast to other Western countries, recommended that BD diagnosis in infants < 2 months could not be confirmed [7]. Due to the fact that infants classified as brain dead are few, definition of cardio-respiratory death becomes evenly important for the expansion of organ donation pool.

Procurement of organs is directly connected with permanent cessation (not returning) and irreversible cessation (could not return) of organs (heart and/or brain) function. Irreversible loss of function (with a failed attempt to reverse it) leads to permanent loss but the opposite does not always stand. Consequently, irreversibility is recognized as the persistent cessation of function after an observational period (for BD; irreversible cessation of brain functions) and/or trial of therapy (i.e. resuscitation) (for CCD; irreversible cessation of cardio-circulatory function).

Brain death and organ donation

BD is the permanent and irreversible loss of brainstem and cortical function [8]. Terms like brain stem, neocortical and whole brain death are not identical [9]. BD criteria in adults can be implemented for newborns (except for premature newborns < 37 weeks gestational age because of insufficient data) despite differences in brain function assessment (premature infants have not developed fully brainstem reflexes), resistance to hypoxia and aetiology of BD [10]. Common causes of BD in neonates are perinatal asphyxia, birth trauma, central nervous system infection, malformations, severe intracranial hemorrhage and metabolic diseases. There are disagreements and multiple tactics regarding definition and diagnosis. Still, BD diagnosis is not yet well documented. Guidelines are based on coma cause definition, higher brain function in addition to brain stem irreversible cessation, exclusion of reversible causes, clinical neurological examination criteria, neurodiagnostic tests (EEG, radio-nucleotide imaging) and suggestion of specific (according to age) observational periods. 1987's BD guidelines for children younger than 1 year of age in the USA were recently revised in 2011 by Nakagawa et al. [10]. Combination of neurologic examination, electro cerebral silence and no flow on CBF study in a newborn for 24 hours observational period is confirmatory of BD. BD diagnosis remains rare among newborns despite supporting literature [11, 12]. Still, there are discrepancies within and between countries for organ donation policies and changes on cultural, ethical and medical issues are needed; e.g., although BD criteria have not been established in the UK for infants < 2 months, donated hearts from Europe are allowed to be transplanted [13]. Consequently it is necessary to clearly define BD criteria for organ donation after BD (DBD) in children, specifically infants.

Cardiovascular death and organ donation

Diagnosis of CCD (previously called non-heart-beating death) is established according to cardio-respiratory criteria, with absent heart sounds, breath sounds, pupils fixed and dilated. CCD corresponds to newborns with severe and irreversible neurological impairment (not brain dead) who can be organ donors. Regarding the fact that the concept of brain death is still confused, clear definition of CCD criteria in neonates will create a wider reservoir of donors [6, 11].

Most organ donations after cardiac death (DCD) from children > 5 years old follow hypoxic-ischemic encephalopathy (HIE) or traumatic brain injury. Severe HIE renders the evolution from permanent to irreversible cessation of cardio-respiratory function. Labreque et al. supported donor pool expansion by qualifying newborns as DCD candidates [14]. He also suggested that weight > 3 kg and post conceptual age > 37 weeks should be prerequisites for considering donation. Ross and Frader reviewed the issue of the expansion of organ donation after determination of CCD in infants and emphasized the importance of quality of care for the infant-donor at the end of his life (quality end-of-life care) and those involved in it [11].

The key is determination of auto-resuscitation (the heart starting on its own) so that procurement of organs could proceed when permanent loss of function has occurred but before irreversible cessation [15].

Auto-resuscitation time beyond asystole with improbable self-resuscitation is the time needed to declare a newborn having CCD before organ removal for donation. Time suggested from the Maastricht Workshop was 10 minutes or 5 minutes after circulatory arrest (asystole) according to US Institute of Medicine (IOM) (2000) [16, 17]. In 2005 the USA adopted the recommendations of the Critical Care Medicine Society of 2 (to 5 maximum) minutes [6, 15]. Boucek et al. in a research protocol for heart donation process published in the *New England Journal of Medicine*, in three infants with brain damage auto-resuscitation time was significantly shortened. A period of 75 sec was estimated as appropriate, considering that the maximum period for auto-resuscitation was estimated at 60 sec [18]. Time for organ procurement should be minimized because of impending risk for warm ischemic damage to organs. Annas criticized Boucek's protocol pointing that heart transplantation in DCD donors violates the "dead donor rule" for irreversibility of heart function

[19]. Until more data for auto-resuscitation literature is provided, it is prudent to use for infants the proposed time of 5 minutes after circulatory arrest for declaration of CCD. DCD infants with severe HIE could expand donation pool for liver, small bowel, lung (organs resistant to warm ischemia) and even heart transplantation.

However, there are disagreements on several issues. Main issues still of concern are poorer prognosis compared to DBD donors or ethical dilemmas regarding time for confirmation of CCD. Still, the number of children recipients using organs from DCD donors is small.

Donated organs and contradictions

Organs procured from DBD infant donors is a clinical reality for heart, liver, bowel and even lung transplantation [20]. Heart donation from DCD infant donors, although feasible, is still highly controversial, liver is donated from infants > 15 kg and kidneys as well [11, 13]. Recently, a multivisceral transplantation using a neonatal donor was reported by Cauley et al. [21]. Poorer prognosis of grafts from CCD compared to BD donors, newborns' long auto-resuscitation, high incidence of dysfunction and complications (like hepatic artery strictures of liver grafts), logistical difficulties (need for major resources managed in order to meet organ donation requirements) hampers donation perspective for this age group. Additionally, uncertainty of established criteria for CCD diagnosis from medical staff and parents and ethical considerations comprise additional problems.

It is of major concern for NICUs participating in organ donation programmes that this procedure implemented by the transplantation team should be completely distinct from treatment withdrawal (to limit life-sustaining treatment) implemented by the NICU medical team. The "dead donor rule" has been challenged especially since BD and CCD definition have entirely differentiated the concept of death over the past years. DDR has been and still is the cornerstone for organ donation and transplantation despite different opinions [22, 23].

There is an urgent need to increase the number of available organs for newborns. The main reasons obstructing donation are medical contraindications, consent not requested by medical staff and consent denied by relatives. Medical contradictions to donation in newborns are mainly hematological malignancies, multisystem diseases (mitochondrial, metabolic disease), widespread asphyxia-related

organs damage and uncontrolled sepsis. Finally, clear definition of the term “devastating neurologic injury” for infant donors not being brain dead accordingly to Maastricht Workshop non-heart-beating-donor categories is of extreme importance [16].

Conclusions

Uniform opportunities for parental consent to donate across Europe should exist. European countries with no infant organ donation policies should be part of a network importing organs from other countries based on a mutual assistance process. Donation in newborns, although feasible, is still considered a “frontier” for transplantation as a rare or unattainable medical event in Western countries.

Organ transplantation procedure is necessary to follow the “dead donor rule” considering that exact time determination of permanent loss of circulation (regarding CCD) and irreversible loss of brain function (for BD) is extremely important. Despite effort and considerable success, there is still a growing gap between available organs and transplant recipients for children. Education of medical staff and well-established policies and practices from European Transplant Registry network for close coordination of European countries on common accepted guidelines could increase donation pool, including newborns as candidates. Hopefully, newborns with end-stage illness even though young and immature could serve as multivisceral donors in the future.

Declaration of interest

The Authors declare that there is no conflict of interest.

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