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Clinical paper

Organ donation after resuscitation from cardiac arrest

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Abstract

Background: We compared the characteristics and outcomes of post-arrest donors to those of other donors, described the proportion of post-arrest decedents who donated, and compared their characteristics to post-arrest decedents who did not donate.

Methods: We performed a retrospective cohort study including patients who died at a single academic medical center from January 1, 2010 to February 28, 2019. We linked our registry of consecutive post-arrest patients to donation-related data from the Center for Organ Procurement and Recovery (CORE). We used data from CORE to identify donor eligibility, first person designation, family approaches to seek consent for donation, and approach outcomes. We determined number of organs procured and number transplanted, stratified by donor type (brain death donors (BDD) vs donors after circulatory determination of death (DCD)).

Results: There were 12,130 decedents; 1525 (13%) were resuscitated from cardiac arrest. CORE staff approached families of 836 (260 (31%) post-arrest, 576 (69%) not post-arrest) to request donation. Post-arrest patients and families were more likely to authorize donation (172/260 (66%) vs 331/576 (57%), $P = 0.02$), and more likely to be DCDs (50/146 (34%) vs 55/289 (19%), $P < 0.001$). Overall, 4.1 ± 1.5 organs were procured and 2.9 ± 1.9 transplanted per BDD, which did not differ by post-arrest status, 3.2 ± 1.2 organs were procured and 1.8 ± 1.1 transplanted per DCD. Number of organs transplanted per DCD did not differ by post-arrest status. Unfavorable arrest characteristics were more common among post-arrest organ donors compared to non-donors.

Conclusion: Patients resuscitated from cardiac arrest with irrecoverable brain injury have excellent potential to become organ donors.

Keywords: Cardiac arrest, Organ donation, Brain death, Resuscitation

Introduction

Most organs transplanted in the United States are procured after determination of death by neurological criteria (brain dead donors (BDD)) or planned withdrawal of life-sustaining therapy and donation after circulatory determination of death (DCD).[1] Sudden cardiac arrest is common, and many patients hospitalized after resuscitation from cardiac arrest will die after progression to brain death or withdrawal of life-sustaining therapy.[2–4] Thus, post-arrest patients represent an important population of potential organ donors.[4,5] Concerns about ischemia-reperfusion injury at the time of initial cardiac arrest, post-arrest organ dysfunction and preexisting medical comorbidities in this patient population may temper enthusiasm for pursuing organ procurement from post-arrest patients.[5,6] Despite these concerns, growing evidence suggests long-term graft function of organs procured from post-arrest patients is comparable to organs procured from other deceased donors.[5,6]

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We, and others, have reported the yield of organs per post-arrest donor using data now nearly a decade old.[7,8] Transplantation science has steadily advanced, with improvements in preoperative donor management,[9,10] better ex vivo organ support tools,[11,12] and expanding criteria for both donor and recipient eligibility.[13,14] Thus, we aimed to report the updated experience of our medical center in the modern transplantation era. Specifically, we sought to compare the characteristics and outcomes of post-arrest donors to those of other donors, describe the proportion of post-arrest decedents who become organ donors, and compare their characteristics to post-arrest decedents who do not donate.

Methods

Ethical approval

We performed a retrospective cohort study including patients who died at a single academic medical center from January 1, 2010 to February 28, 2019. Research involving only deceased subjects is not consider human subjects research under United States law (45 CFR 46.102(f)). Thus, most aspects of the present study were deemed exempt from Institutional Review Board (IRB) oversight. The IRB approved all aspects of the research involving living subjects (e.g. post-arrest registry data collection and allograft outcomes).

Setting

In the United States, 58 federally designated Organ Procurement Organizations (OPOs) operate under supervision of multiple government agencies including the Centers for Medicare and Medicaid Services (CMS), and the United Network for Organ Sharing (UNOS). The Association of Organ Procurement Organizations (AOPO) and CMS accredit each OPO based on performance across multiple standards. Federal regulations require acute care hospitals to refer all patients with impending death, determined based on defined clinical triggers, to their local OPO to determine potential for organ donation. In the United States, organs may be procured after determination of death by neurological criteria (BDD) or after determination of death by circulatory criteria (DCD). Criteria for determination of death by neurological criteria are established by state governments and typically conform to the 1981 Uniform Determination of Death Act. DCD cases generally fall into Maastricht Category III (controlled DCD)[15] and occur after planned palliative extubation with subsequent apnea and circulatory arrest.

In our region, OPO staff complete an initial screening evaluation by phone that is primarily focused on identifying clinical factors that unequivocally preclude donation. These factors include patients who are not mechanically ventilated; those with known active malignancy; severe multisystem organ failure; abdominal sepsis; or positive human immunodeficiency virus (HIV) sero-status (prior to passage of the HIV Organ Policy Equity Act). An organ procurement coordinator (OPC) completes a detailed evaluation of all remaining patients to further determine suitability for donation. All OPCs in our area have clinical expertise, by virtue of either specialized graduate education, or professional licensure as a Registered Nurse or Respiratory Therapist. No single set of criteria is applied to determine eligibility for donation among patients who screen in as potential donors. Patient factors such as age, past medical and social history, current illness severity including recent laboratory and imaging results, organ dysfunction, and anticipated warm ischemia time (for DCD) factor into the OPCs' evaluation. These factors do not typically include cardiac arrest-specific historical factors (e.g. arrest duration, initial rhythm, etc). In equivocal cases, clinical information is presented to local transplant surgeons to query their assessment of suitability or formal offers are made following standard organ allocation regulations set by UNOS. Procurement only proceeds if at least one organ is accepted for transplantation. An OPC approaches the legally authorized representative of patients determined to have potential as organ donors to request their authorization for donation. In the state of Pennsylvania, first person donor designation (for example, as indicated on a driver's license) is a legal advanced directive and is honored. Among patients without first-person designation, the legally authorized representative must agree to donation on the potential donor's behalf.

Our hospital is a 798-bed tertiary care center and a CMS-accredited transplant center. Our Post-Cardiac Arrest Service (PCAS), the structure and function of which we have previously described in detail, cares for most patients resuscitated from cardiac arrest.[16,17] Among other responsibilities, a PCAS attending physician coordinates the initial resuscitation of post-arrest patients and meets with patients' families on arrival and daily during acute illness. Early work by our group, using data collected when PCAS involvement in post-arrest care was less uniform than it is currently, demonstrated a positive association between PCAS care and organ donation.[8] Several intensivists in our Department of Critical Care Medicine staff a dedicated Organ Donor Support Team (ODST).[18] ODST staff provide supportive care to both BDD and DCD from the time of authorization for donation until organ procurement. We have previously reported ODST management is associated with an increase in the number of organs procured per donor.[18]

Data sources

Our PCAS maintains a prospective registry of consecutive patients treated by the service after resuscitation from cardiac arrest. The registry includes identifiable demographic, clinical and outcomes data. These data elements generally follow the recommended Utstein template for reporting,[19] but the registry also includes more detailed clinical information that is beyond the scope of the Utstein template. The Center for Organ Recovery and Education (CORE) is the OPO responsible for the evaluation and procurement of organs from deceased donors in our region. CORE staff and OPCs enter demographic, clinical information, process and outcome information for all referred patients into a web-based electronic health record (TrueNorth™, LifeLogics Inc., Nottingham, MD, USA), which is designed specifically for OPO use and meets AOPO accreditation standards. In parallel, our hospital generates a daily list of patient deaths pulled from multiple sources including billing, physician documentation and bed flow data. This list is later reconciled against CORE referral information to ensure hospital compliance with referral requirements and identify and remediate any referral process breakdowns. During this reconciliation, patient records are manually linked using the hospital's medical record number and a unique CORE referral number based on multiple patient identifiers. We merged these data sources with PCAS registry data using patients' names, medical record numbers, sex and date of admission with perfect linkage.

Variable definitions

We defined post-cardiac arrest status by inclusion in our PCAS registry. We use standard Utstein template definitions for cardiac arrest-specific demographic and treatment characteristics within this registry,[19] and

abstract data from both the prehospital and in-hospital medical records. We determined arrest etiology as previously described.[20] We used data from TrueNorth to identify patients meeting donor eligibility criteria on initial screening criteria and subsequent OPC chart review, first person donor designation, family approaches by OPCs and approach outcomes. Reasons for ineligibility after OPC evaluation are often multifactorial and not consistently documented, so were not available for analysis. For authorized donors, we determined donor status (BDD vs DCD) as status at the time of death (i.e. a donor initially authorized for DCD that progressed to brain death prior to procurement was considered BDD) and did not differentiate between extended criteria and standard criteria BDD. We further determined whether or not organs were procured from each donor, which organs were procured and which organs were transplanted. Standard definitions used to determine organ yield changed several times during the study period. For purposes of this analysis, we considered right and left lungs and kidneys each to be two organs whether or not they were procured en bloc or separately, and whether or not they were transplanted into a single or multiple recipients. We considered split liver transplants to be a single transplanted organ. We were unable to retrospectively differentiate non-transplanted organs that were procured with the *a priori* intent for research from those that were procured with the intent to transplant but were found to be unsuitable for transplantation, so reasons for non-transplantation of procured organs could not be determined.

Statistical analysis

We used descriptive statistics to summarize population characteristics and present raw numbers with corresponding percentages for categorical variables, means with standard deviation for normally distributed continuous variables and medians with interquartile ranges for skewed continuous variables. We used Chi2 tests to compare categorical variables across post-arrest status, and t-tests or rank sum tests to compare continuous variables, as appropriate. We explored potential secular trends during the study period by testing for a linear change in the proportion of overall donors annually with an antecedent cardiac arrest or proportion of post-arrest patients annually who became organ donors, and comparing post-arrest donor characteristics from 2010 to 2014 and 2015 to 2019. We used Stata version 14 (StataCorp, College Station, TX) for all analyses.

Results

Overall, there were 12,130 decedents from January 2010 to February 2019, of whom 1,525 (13%) were resuscitated from cardiac arrest and treated by our Post-Cardiac Arrest Service (Fig. 1). On initial screening, 2771 were deemed to have no potential for organ donation. Among the remaining 9,359, 8,523 (1,108 post-arrest patients and 7,415 not post-arrest) were deemed unsuitable to be organ donors after evaluation by an OPC. OPCs approached families of the remaining 836 patients (260 (31%) post-arrest and 576 (69%) not post-arrest) to seek authorization for organ donation. Thus, 260 of 1,525 post-arrest decedents (17%) were approached for donation and 576 of 10,605 decedents without cardiac arrest (5%) were approached seeking authorization for donation ($P < 0.001$).

Approach outcomes are listed in Table 1. Post-arrest patients and families were significantly more likely to authorize donation (172/260

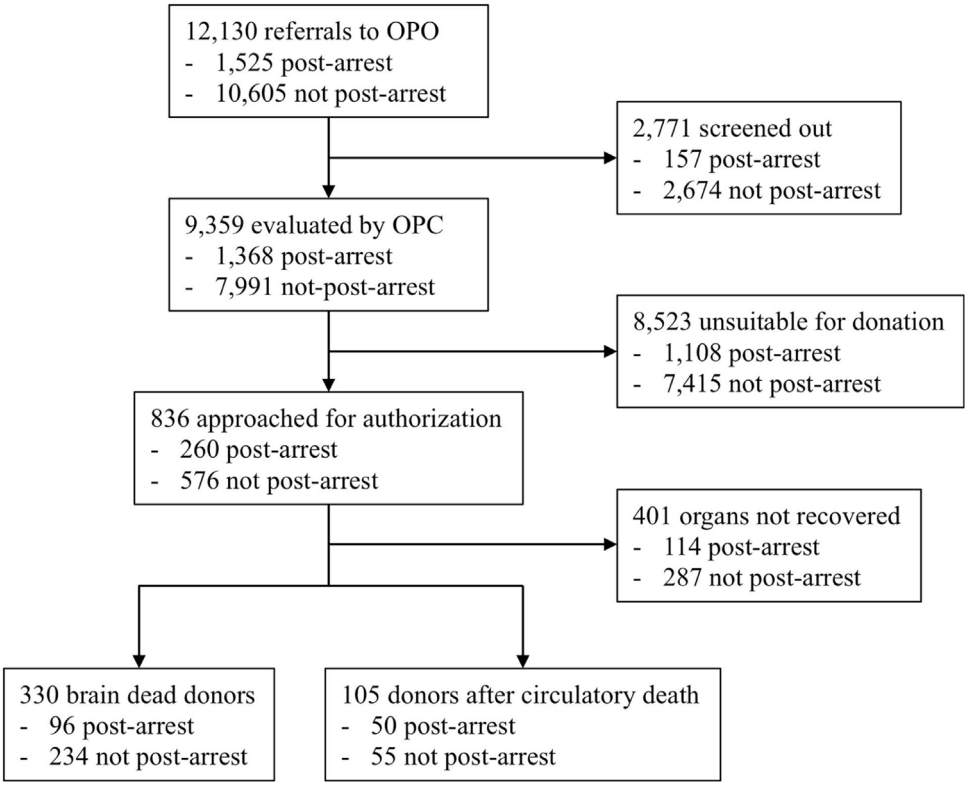

Fig. 1 – STROBE diagram detailing reasons for non-donation among all in-hospital decedents referred to the organ procurement organization, stratified by post-arrest status.
Abbreviations: OPO - Organ procurement organization; OPC - Organ procurement coordinator.

Table 1 – Outcomes of family approaches to authorize organ donation by CORE organ procurement coordinators.

Approach outcome	Post-arrest (n = 260)	Not post-arrest (n = 576)
Family declines donation	79 (30)	195 (34)
Determined during approach to have no donor potential	9 (3)	50 (9)
Authorized donation	172 (66)	331 (57)
First-person donor designation[a]	88 (34)	162 (28)
Organs not procured[a]	26 (15)	42 (13)
Organs recovered[a]	146 (85)	289 (87)

Data are presented as raw numbers with corresponding percentages.
[a] Expressed as a percentage of authorized donor.

(66%) vs 331/576 (57%), P = 0.02). There was no significant difference in the proportion of post-arrest patients who had first person (drivers license or other advanced directive) donor designation compared to other patients. Post-arrest patients were approached to authorize donation significantly later after admission than other patients (median 2.7 [IQR 1.7–4.6] days vs 1.7 [IQR 1.1–3.9] days, P = 0.001). Of 503 authorized donors, organs were not procured in 68 (14%) because no recipients were identified, the donor arrested before procurement or DCD was attempted but the patient did not die in within the pre-specified maximum warm ischemic time after palliative extubation in the operating room. This proportion did not differ by post-arrest status.

Organs were procured from 435 individuals. Overall, 4.1 ± 1.5 organs were procured and 2.9 ± 1.9 were transplanted per BDD, and 3.2 ± 1.2 organs were procured and 1.8 ± 1.1 were transplanted per DCD. Of the 435 donors, 146 (34%) were post-arrest patients, and this proportion did not change over time. Post-arrest patients were more likely to donate after circulatory determination of death (50/146 (34%) vs 55/289 (19%) donors, P < 0.001). For BDDs, the number of organs procured and transplanted did not differ between post-arrest and other donors. (4.1 ± 1.4 vs 4.1 ± 1.6 organs procured, respectively; 2.8 ± 1.6 vs 2.9 ± 1.9 transplanted, respectively). Significantly fewer organs were procured from post-arrest DCDs than other DCDs (2.9 ± 0.9 vs 3.4 ± 1.3, respectively, P = 0.03). However, the number of organs actually transplanted per DCD did not differ by post-arrest status (1.8 ± 1.0 vs 1.8 ± 1.2, respectively). Organ-specific short-term outcomes are listed in Table 2.

Among 1,525 post-arrest decedents, 146 (10%) became organ donors compared to 289 of 10,605 (3%) of other decedents (P < 0.001). The proportion of post-arrest decedents who donated organs did not change over time. Compared to post-arrest decedents who did not donate, post-arrest donors were younger, more likely to have arrested out-of-hospital and were more likely to have arrived at our hospital via interfacility transfer (Table 3). Unfavorable arrest characteristics including initial asystole, unwitnessed collapse, longer arrest duration and more epinephrine doses administered were all significantly more common among organ donors (Table 3). The distribution of characteristics did not change over the study period. Drug overdose accounted for a substantial minority (33%) of arrest etiologies among donors, and progression to brain death was more common among donors. Of 133 out-of-hospital arrest patients who became organ donors, 32 (24%) had unwitnessed arrests with initial asystole on EMS arrival; 22 (17%) were never shocked, did not have arrest witnessed by emergency medical service providers and did not regain pulses before hospital arrival.

Discussion

At our center, one in ten patients hospitalized after cardiac arrest that did not survive to discharge donated organs, with an average of 2.5 organs transplanted per post-arrest donor. In the United

Table 2 – Donor outcomes, stratified by type of donor (brain dead donor (BDD) or donation after circulatory determination of death (DCD)) and post-arrest status.

Organ outcome	BDD (n = 330)		DCD (n = 105)	
	Post-arrest (n = 96)	Not post-arrest (n = 234)	Post-arrest (n = 50)	Not post-arrest (n = 55)
Heart procured	34 (0.35)	85 (0.36)	–	–
Heart transplanted	24 (0.25)	71 (0.30)	–	–
Lungs procured	77 (0.80)	286 (0.79)	12 (0.24)	39 (0.71)
Lungs transplanted	29 (0.30)	102 (0.43)	0 (0)	8 (0.15)
Liver procured	92 (0.96)	220 (0.94)	26 (0.52)	32 (0.58)
Liver transplanted	72 (0.75)	192 (0.82)	17 (0.34)	16 (0.29)
Kidneys procured	180 (1.89)	424 (1.81)	100 (2.0)	108 (1.96)
Kidneys transplanted	139 (1.45)	298 (1.27)	74 (1.48)	74 (1.35)
Intestine procured	0 (0)	7 (0.03)	–	–
Intestine transplanted	0 (0)	5 (0.02)	–	–
Pancreas procured	12 (0.13)	47 (0.20)	3 (0.06)	4 (0.07)
Pancreas transplanted	5 (0.05)	20 (0.09)	1 (0.02)	0 (0)
Total organs procured	395 (4.11)	969 (4.14)	143 (2.86)	189 (3.34)
Total organs transplanted	269 (2.80)	688 (2.94)	92 (1.84)	98 (1.78)

Data are expressed as raw number of organs and average yield per donor of that type.

Table 3 – Demographics and arrest characteristics of organ donors after cardiac arrest compared to non-donor decedents.

Characteristic	Organ donors (n = 146)	Non-donors (n = 1379)	P value
Age, years	41 ± 13	62 ± 16	<0.001
Female sex	67 (46)	568 (41)	0.27
Arrest location			<0.001
Out-of-hospital	133 (91)	909 (66)	
Emergency department	8 (5)	150 (11)	
In-hospital	5 (3)	320 (23)	
Transferred from another facility	119 (82)	846 (61)	<0.001
Initial rhythm			<0.001
VT/VF	16 (11)	276 (20)	
PEA	38 (26)	570 (41)	
Asystole	70 (48)	412 (30)	
Unknown	22 (15)	121 (9)	
Defibrillated during CPR	43 (29)	504 (36)	0.09
Witnessed collapse	68 (51)	622 (70)	<0.001
Lay person CPR	106 (80)	614 (69)	0.01
Arrest duration	26 ± 20	20 ± 18	<0.001
Epinephrine boluses administered	4 [2–5]	3 [1–5]	<0.001
Prehospital ROSC[a]	90 (68)	609 (68)	0.93
Arrest etiology			<0.001
Cardiac causes	13 (9)	286 (21)	
Overdose	48 (33)	117 (8)	
Other	40 (41)	522 (38)	
Unknown	25 (17)	454 (33)	
Proximate cause of death or care limitations[b]			<0.001
Rearrest or intractable shock	7 (5)	474 (34)	
Brain death	89 (61)	73 (5)	
Withdrawal for non-neurologic reasons	5 (3)	197 (14)	
Withdrawal for neurologic reasons	45 (31)	635 (46)	

[a] Percentages reflect the proportion of those with arrest out-of-hospital.
[b] Seven patients were authorized as DCD donors after family requested withdrawal of life-sustaining for neurological or non-neurological causes then progressed to brain death prior to organ procurement.

States, over 100,000 patients annually survive to hospital care after resuscitation from in- or out-of-hospital cardiac arrest, of which approximately 65% (65,000 patients) do not survive to discharge.[2,3,21–24] The current proportion of deceased donors hospitalized after cardiac arrest is unknown, however replication of our center's performance nationally might result in over 16,000 organs transplanted annually, or roughly half of the total transplant volume nationally.[1] It is likely that actual donor and transplant volumes from post-arrest patients is far lower. Indeed, our findings demonstrate a significant improvement over both our own historical data and reports from other systems of care internationally.[4,7,8,25] Several aspects of our system of care may optimize our performance. Engagement of a dedicated PCAS physician in initial post-arrest resuscitation and ongoing family communication may both minimize secondary organ injury after return of spontaneous circulation and help explain the observed higher rates of authorization for donation from surrogate decision makers.[8] There may also be a volume-outcome relationship, as has been observed in other aspects of post-arrest care.[26] In parallel, specialty physician care after authorization for donation may increase the yield of organs procured per donor.[18]

Multiple sources of variability in care and outcomes have been documented after cardiac arrest, including decisions by prehospital providers to initiate resuscitation,[27] application of decision rules to terminate resuscitation attempts among patients unlikely to survive,[28] rates of return of spontaneous circulation,[29,30] and survival to discharge.[22] Whether post-arrest patients benefit from transfer to high-volume centers for specialty care is another actively debated topic.[26] Our results demonstrate that such sources of variability and policy decisions may have a substantial impact on the supply of organs available for transplant. For example, a significant minority of the post-arrest donors in our study would have met validated criteria for prehospital termination of resuscitation.[31] Not coincidentally, these rules closely reflect those that might be used to identify patients with ongoing resuscitation efforts who may be appropriate for uncontrolled DCD.[32] As calls to develop national standards, regionalization and accreditation for post-arrest centers of excellence grow,[24,26,33] policy makers must consider not only benefits to survival and favorable recovery but also the implications of their decisions on the potential for organ donation and transplantation.

We found many significant differences between post-arrest patients who donated organs and those who did not, several of which deserve additional consideration. A full third of donors arrested after recreational drug overdose, virtually all of which we have previously reported are due to opioids.[34] This is consistent with national trends, and overdose status does not appear to affect transplant survival.[35] Overall, 11% of post-arrest decedents progressed to brain death and slightly more than half brain dead patients donated organs, both of which are consistent with the results of prior meta-analyses.[4] Organ donors had several unfavorable arrest characteristics compared to post-arrest patients who did not donate, including significantly lower rates of shockable initial rhythms, fewer witnessed arrests and more epinephrine

administration. This is perhaps unsurprising since donation after brain death occurs only after devastating neurological injury. Even planned donation after circulatory determination of death requires neurologic or cardiopulmonary illness to be sufficiently severe that apnea and pulselessness are predicted to occur rapidly after palliative extubation. While each of these unfavorable prognostic characteristics is associated with greater initial illness severity,[36] differential susceptibility of certain organ systems to ischemia reperfusion injury and/or varied ability of organ function to recover after initial cardiac arrest appears to result in sufficient sparing of extracerebral organ systems to allow transplantation. Thus, while such unfavorable arrest characteristics may inform prognostication of recovery potential, their role in predicting donor potential is unclear.

Our study has several important limitations. By design, this was a single center study performed at a hospital with systems of care expected to be associated with high performance. As such, we interpret our results as demonstrating the potential for organ donation after cardiac arrest with robust systems of care, but do not view our experience as reflective of current outcomes in other settings nationally or internationally. Procured organs not suitable for transplantation may be used for biomedical research. We could not determine retrospectively whether organs were procured with the *a priori* intent to transplant or for research, nor could we reliably determine which non-transplanted organs contributed substantively to research efforts. Moreover, most organ donors can also donate tissue, which has the potential to benefit many additional recipients. As such, our focus on transplanted organs underestimates the overall benefit derived from these donors to both individuals and society. Finally, data pertaining to long-term graft function and recipient outcome were not available for analysis, limiting our analysis to short-term outcomes such as organ yield.

In conclusion, our findings add to the evidence that patients resuscitated from cardiac arrest with irrecoverable brain injury have excellent potential to become organ donors, with no difference in the yield of transplantable organs from these patients compared to other deceased donors. Future work to quantify and improve quality of post-arrest care should consider not only patient recovery but also donation-specific outcomes among decedents.

Disclosures

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