A systematic review of autoresuscitation after cardiac arrest*

K. Hornby, MSc; L. Hornby, MSc; S. D. Shemie, MD

Objective: **There is a lack of consensus on how long circulation must cease for death to be determined after cardiac arrest. The lack of scientific evidence concerning autoresuscitation influences the practice of organ donation after cardiac death. We conducted a systematic review to summarize the evidence on the timing of autoresuscitation.**

Data Sources: **Electronic databases were searched from date of first issue of each journal until July 2008.**

Study Selection: **Any original study reporting autoresuscitation, as defined by the unassisted return of spontaneous circulation after cardiac arrest, was considered eligible. Reports of electrocardiogram activity without signs of return of circulation were excluded.**

Data Extraction: **For each study case, we extracted patient characteristics, duration of cardiopulmonary resuscitation, terminal heart rhythms, time to unassisted return of spontaneous circulation, monitoring, and outcomes.**

Data Synthesis: **A total of 1265 citations were identified and, of these, 27 articles describing 32 cases of autoresuscitation were included (n = 32; age, 27–94 yrs). The studies came from 16 different countries and were considered of very-low quality (case reports or letters to the editor). All 32 cases reported autoresuscitation after failed cardiopulmonary resuscitation, with times ranging from a few seconds to 33 mins; however, continuity of observation and methods of monitoring were highly inconsistent. For the eight studies reporting continuous electrocardiogram monitoring and exact times, autoresuscitation did not occur beyond 7 mins after failed cardiopulmonary resuscitation. No cases of autoresuscitation in the absence of cardiopulmonary resuscitation were reported.**

Conclusions: **These findings suggest that the provision of cardiopulmonary resuscitation may influence autoresuscitation. In the absence of cardiopulmonary resuscitation, as may apply to controlled organ donation after cardiac death after withdrawal of life-sustaining therapies, autoresuscitation has not been reported. The provision of cardiopulmonary resuscitation, as may apply to uncontrolled organ donation after cardiac death, may influence observation time. However, existing evidence is limited and is consequently insufficient to support or refute the recommended waiting period to determine death after a cardiac arrest, strongly supporting the need for prospective studies in dying patients. (Crit Care Med 2010; 38:1246–1253)**

KEY WORDS: organ donation; cardiac arrest; donation after cardiac death; withdrawal of life support; cardiopulmonary resuscitation; autoresuscitation

The physiologic transition from life to death is a complex process. The determination of death affects all physicians regardless of specialty, and modern, sophisticated medical technology has complicated rather than facilitated this process. The availability of life-sustaining interventions, such as cardiopulmonary resuscitation (CPR), mechanical ventilation, extracorporeal life support, ventricular assist devices, and other organ support or replacement technologies, has obscured our ability to distinguish between the seemingly discrete states of life and death. Yet, the practices of organ donation and transplantation necessitate this distinction. The ethical norm for organ donation is the "dead donor rule," which states that "vital organs should only be taken from dead patients and, correlatively, living patients must not be killed by organ retrieval" (1). For organ transplantation to be successful, the arrest of circulation and resulting warm ischemic injury (which occur at death and during organ procurement and transplantation) must be minimized. This conundrum is partially overcome when death is determined using neurologic criteria, because the brain-dead donor remains on a ventilator and circulation is maintained until surgical removal of organs.

Organ donation from brain-dead donors continues to be the preferred source of organs for transplantation; however, one of the responses to the persistent shortage of organs has been the re-emergence of donation after cardiocirculatory death (donation after cardiac death [DCD], which is also referred to as nonheart-beating organ donation). With advances in both transplant surgery and organ preservation techniques, the practice of DCD has progressively increased. DCD programs have developed throughout the world and now account for the largest incremental increase in organ donation in active programs in the United States (2, 3). There is an ongoing, focused attempt in the United States to increase the number of DCD donors (4). Accompanying this renewed emphasis on DCD is the requirement to determine death as rapidly as possible after cardiac arrest to minimize any loss of circulation to the organs. This time pressure has forced the identification of a precise waiting period that is long enough to ensure the person has died but short enough to maintain organ viability for transplantation.

Death is generally understood to be based on the irreversible cessation of either brain function or circulatory and respiratory functions and the determination of death is a clinical matter that should be made according to widely ac-

***See also p. 1377.**

From Division of Critical Care (KH, LH, SDS), Montreal Children's Hospital, McGill University, Montreal, Quebec, Canada; Bertram Loeb Research Consortium in Organ and Tissue Donation (KH, LH), Bertram Loeb Chair in Organ and Tissue Donation (SDS), University of Ottawa, Ottawa, Canada.

Given the nature of this study, it was exempt from requiring approval of the Institutional Review Board of the McGill University Health Centre.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: sam.shemie@mcgill.ca

DOI: 10.1097/CCM.0b013e3181d8caaa

cepted guidelines established by expert medical groups (5). In the absence of organ donation, accepted medical practice for determining death after cardiac arrest has not included standardized diagnostic criteria or a specific time period of observation. In the setting of DCD, although recommendations exist for diagnostic criteria, there is a lack of consensus on how long circulation and respiration must cease for a person to be determined dead (6–9). Internationally, this time period varies from 2–10 mins (10). The historical influences on these timeframes include the 1995 International Maastricht Workshop (10 mins) (11), the 1992 Pittsburgh protocol (2 mins) (12), the 1997 US Institute of Medicine report (≥5 mins) (13), and the 2001 Report of the Ethics Committee, American College of Critical Care Medicine, and Society of Critical Care Medicine (≥2 mins but not >5 mins) (14). In a recent DCD pilot project in the United States, hearts from three severely brain-injured newborns were removed for transplantation soon after cardiac arrest (3 mins in the first case and 75 secs in the other two cases) (15). This variability in wait times required to determine death after a cardiac arrest, in part, reflects a lack of scientific evidence concerning autoresuscitation (AR) (16, 17).

AR is the phenomenon of the heart being able to restart spontaneously and generate anterograde circulation (18). Electrical activity of the heart (as measured by an electrocardiogram [ECG]) is essential to generate the contractile activity required for the heart to produce circulation. However, simply detecting the presence of some form of electrical activity is not an indication of contractile activity or of effective circulation. The determination of death after cardiac arrest is based on indirect measurements of circulatory arrest, including absent heart sounds, absent pulse, absent blood pressure, and cessation of breathing and neurologic function. Terminal ECG activity may persist in the absence of circulation and does not preclude the diagnosis of death (10, 19–23).

Given these considerations, if AR can occur, then the termination of circulation is not yet irreversible and the patient is not dead. The time limits of AR are uncertain. Therefore, we conducted a systematic review of the AR literature to answer the following question: how long after cardiac arrest can AR still occur? The primary objective of this review was to summarize the evidence on the timing of AR. We hypothesized that insufficient evidence exists to define the time limits of AR and the provision of CPR confounds these limits.

MATERIALS AND METHODS

Definitions

For the purposes of this review, irreversibility of circulatory and respiratory functions is defined as a state in which these functions cannot return on their own and will not be restored by medical interventions (24, 25). CPR was defined as any resuscitative intervention that could reestablish circulation, such as the administration of artificial respiration, cardiac compressions, cardiac resuscitation medications, and external or internal pacemakers. We defined AR as the unassisted return of spontaneous circulation (ROSC) after a cardiac arrest. The ROSC was defined as one or more of the following signs: heart sounds, pulse (detected by palpation or Doppler), blood pressure (detected by invasive or noninvasive methods), oxygenation (detected by pulse oximetry), opening of the aortic valve (detected by echocardiography), and resumption of breathing or neurologic function. Therefore, reports solely documenting the presence of ECG activity without reporting any of these signs of ROSC were excluded.

AR can occur during two very different situations: after failed CPR, first described by Linko et al (26) and subsequently called the "Lazarus phenomenon" by Bray (27), and when no CPR has been attempted before the unassisted ROSC. In the remainder of this report, we use AR to refer to the phenomenon in a general sense. "AR after failed CPR" refers to cases of AR that occur after the cessation of failed CPR, and "AR without CPR" refers to cases in which no CPR has been attempted. A further distinction is necessary to understand the implications of our findings for DCD. There are two main types of DCD, controlled and uncontrolled. Controlled DCD follows a planned withdrawal of life-sustaining therapy and no provision of CPR, whereas uncontrolled DCD follows failed CPR. Thus, the phenomenon of AR without CPR is relevant to controlled DCD, and AR after failed CPR is relevant to uncontrolled DCD.

Search Strategy and Selection of Studies

Three narrative reviews summarizing case reports of AR after failed CPR have been published (28–30). In addition, DeVita (19) has published a narrative review of AR. None of these publications was considered to be systematic reviews of the form described by Pai et al (31). Therefore, we conducted a systematic review of the AR literature.

Any original study that reported on the phenomenon of AR was considered eligible for this review. To identify all eligible studies, the following electronic databases were searched (from date of first issue of each journal until July 22, 2008): MEDLINE using PubMed, EMBASE using OVID, Web of Science, and the Cochrane Library. The study language was limited to English, French, German, and Spanish. We consulted a health sciences librarian to develop our search strategies for each database (Appendix 1). All citations fulfilling the search criteria were compiled and duplicate citations were eliminated. Citation titles and abstracts were scanned independently by two reviewers (KH and LH) to identify original and review articles reporting occurrences of AR. The full texts of these articles were retrieved and independently reviewed to assess study eligibility. In addition, the reference lists of these articles were independently examined to identify additional relevant articles. All disagreements were resolved by consensus. Studies that were excluded were tracked and reasons for their exclusion were recorded.

We included all types of original studies, regardless of the study type or quality. Language restrictions were based on our ability to read English and French, as well as previous knowledge of studies from Germany and Spain. When an English or French version of a study was not available, we attempted to contact the study authors to obtain relevant information. A reminder was sent if no response was received after a 2-wk period. An in-house translation was performed if no response was obtained after this reminder.

Data Extraction

A data extraction spreadsheet was designed and pilot-tested by two reviewers (KH and LH). We independently extracted data from each of the studies included in the final review, with disagreements resolved by consensus. The data extracted included the following information: study type, study population, number of people in study, and time period of the study. In addition, for each study case the following information was extracted: age, gender, case scenario, length of time CPR was performed, last heart rhythm before AR, time from cardiac arrest or failed CPR to unassisted ROSC, method in use to monitor vital signs at time of AR, if there was a return of consciousness, and the final outcome.

Grading Quality of Evidence

The quality of the studies included in this systematic review was assessed according to the Grading of Recommendations Assessment, Development and Evaluation system (32, 33), which categorizes study quality into one of four levels: high, moderate, low, or very low. This categorization is based on the study design but also takes into consideration other factors, such as study limitations and publication bias (which may decrease the quality level) and the magnitude of the intervention effect (which may increase quality level).

Assessment of Heterogeneity and Statistical Analysis

We anticipated some heterogeneity in the primary outcome measure (timing of AR) based on the age of the participant, the scenario of the AR (AR without CPR vs. AR after failed CPR), and the quality of the study. However, because of the nature of the studies (and data) included in this review, no assessment of heterogeneity was possible, nor were we able to calculate confidence intervals; therefore, only point estimates are provided for the primary outcome. Data analysis consisted of a tabulation of study characteristics (year, setting, study design, and quality) and outcomes.

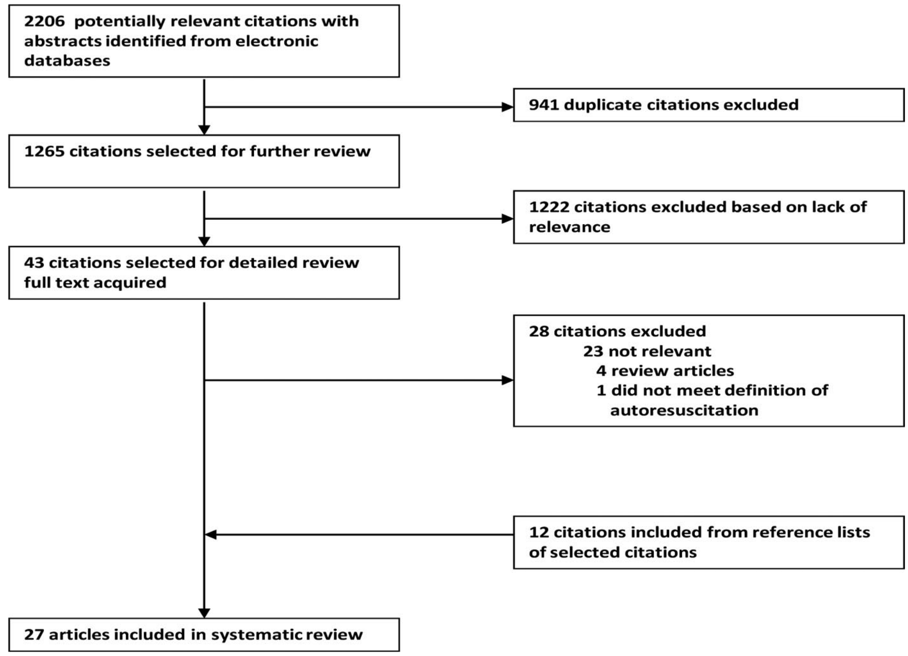


Figure 1. Study process.

RESULTS

A total of 1265 unique citations were identified from our search of the literature (Fig. 1). Of these, 43 citations were selected for full-text review but 28 of which were excluded because 23 were not relevant, four were review articles, and one did not meet our definition of autoresuscitation in that all resuscitative interventions were not stopped before the reported ROSC (34). The reference lists of the 43 “fully reviewed” studies were scanned and 12 additional citations were included from these lists. We attempted to contact the lead authors of six studies that were only available in German or Spanish. Only two of these authors provided the requested information. Therefore, three in-house translations were completed and one study could not be included because we were unable to obtain a full copy for translation (35). Consequently, a total of 27 articles were included in the final review. For all studies screened, rejected, and accepted, there was excellent agreement between the two reviewers with respect to study selection (kappa, 0.78; confidence interval, 0.68–0.88).

The 27 included studies reported a total of 32 cases of AR (26–28, 36–59). The studies came from 16 different countries, the majority of which were from Germany (5; 19%) and the United States (5; 19%). All the studies were either case reports (18; 67%) or letters to the editor (9; 33%). Therefore, based on the Grading of Recommendations Assessment, Development and Evaluation system (32, 33), they were all considered as being of very low quality.

The characteristics of the study subjects are contained in the Table 1. All of the subjects were adults (median age, 68 yrs; range, 27–94 yrs) and 66% were male (gender and age were not reported in one study of three subjects). There were no cases reported in children. All 32 cases reported AR after failed CPR. There were no cases identified in which AR was reported when CPR was not provided. The duration of CPR ranged from approximately 6 to 88 mins, with three studies (five cases) failing to report this time period. Asystole was the most frequently reported (19; 63%) heart rhythm before AR. The duration of time from failed CPR to unassisted ROSC for the cases ranged from “a few seconds” to 33 mins. However, for the eight studies (36, 37, 40, 43, 48, 49, 57, 58) that reported ECG monitoring and exact times, AR did not occur beyond 7 mins (Fig. 2). Of the 20 cases for which information on the patient’s level of consciousness was available, 14 (70%) reported a return of consciousness, eight of which recovered fully, with follow-up information ranging from 18 days to 6 months. Of the 27 cases for which information on the patient’s final outcome was available, most (18; 67%) died.

DISCUSSION

The principle findings of this review are: 1) the existing evidence documenting the timing of AR is of low quality and limited in scope; 2) AR after failed CPR has been reported in 32 patients, with times ranging from a few seconds to 33 mins; however, AR did not occur beyond 7 mins in studies reporting exact times and appropriate monitoring; 3) there are no reported cases of AR without CPR; and 4) there are no reported cases of AR in children. The following discussion elaborates on these principle findings, our study limitations, and the implications of our findings for clinical practice and DCD.

Existing Evidence

Our study hypothesis was confirmed in that there is insufficient evidence to define the limits of autoresuscitation. The only evidence available is that of case reports and letters to the editor, which are deemed to be low-quality evidence. Despite repeated calls by the Institute of Medicine (16, 17) and others (60, 61) to undertake studies designed to investigate the occurrence of AR, no such studies have been performed. One small observational study by Wijdicks (18) has been performed to monitor ECG activity after asystole after withdrawal of mechanical ventilation in 12 comatose patients with catastrophic neurologic injury. Results of the ECG monitoring demonstrated that after cardiac arrest, ECG recordings of short duration were detected up to 10 mins after the arrest. These recordings consisted of

Table 1. Subject characteristics

Author, Year, Country, Reference	Age, yr	Gender	Length of Cardiopulmonary Resuscitation, min	Last Heart Rhythm Before AR	Time From Failed Cardiopulmonary Resuscitation to Unassisted ROSC, min	Method in Use to Monitor Vital Signs at Time of AR	Return of Consciousness	Final Reported Outcome
Abdullah, 2001, United States (36)	93	F	≈6	NR	5	ECG	NR	NR
Al-Ansari et al, 2005, Saudi Arabia (37)	63	F	≥12	Asystole	3	ECG	Yes	D (12 days)
Ben-David et al, 2001, United States (38)	66	M	17	Asystole	10	None	Yes	RF (5 wks)
Bradbury, 1999, United Kingdom (39)	59	M	6 loops and 3 mins	EMD	≈2	None	No	D (30 min)
Bray, 1993, United States (27)	75	M	23	Asystole	≈5	None	No	D (several days)
Casielles Garcia et al, 2004, Spain (40)	94	F	40	Pulseless electrical activity	5	ECG, arterial line	Yes	D (21 days)
De Salvia et al, 2004, Italy (41)	81	F	13	Asystole	A few mins later	None	NR	D (20 hrs)
Duck et al, 2003, Germany (42)	81	M	25	Asystole	2–3	ECG, arterial line	Yes	D (33 days)
Frolich, 1998, Germany (43)	67	F	43	Asystole	5	ECG	Yes	D (9 days)
Fumeaux et al, 1997, Switzerland (44)	54	F	≈20	EMD	A few secs	NR	Yes	RF (93 days)
Gomes et al, 1996, Portugal (45)	66	M	30	Ventricular fibrillation	Moments	NR	Yes	Recovered but with neurologic impairments (length of follow-up NR)
	71	M	35	Asystole	Moments	NR	Yes	RF (NR)
Kamarainen et al, 2007, Finland (46)	47	M	26	Ventricular fibrillation	15	None	Yes	D (3 mos)
Lapinsky et al, 1996, Canada (47)	NR	NR	NR	EMD	NR	NR	NR	NR
	NR	NR	NR	EMD	NR	NR	NR	NR
	NR	NR	NR	EMD	NR	NR	NR	NR
Letellier et al, 1982, France (48)	80	M	20	Asystole	5	ECG	Yes	RF (35 days)
Linko et al, 1982, Finland (26)	67	M	20	Asystole	Some mins	NR	NR	D (15 days)
	68	F	NR	Asystole	≈20	None	Yes	RF (3 months)
	84	M	10	Asystole	NR	None	NR	D (6 days)
MacGillivray, 1999, United Arab Emirates (49)	76	M	30	Asystole	5	ECG	NR	D (24 hrs)
Maeda et al, 2002, Japan (50)	65	M	35	Asystole	≈20	None	No	D (5 days)
Maleck et al, 1998, Germany (28)	80	M	30	Asystole	≈5	ECG, arterial line	No	D (2 days)
Martens et al, 1993, Belgium(51)	87	F	>15	Other	Unknown	ECG	NR	D (12 days)
Monticelli et al, 2006, Austria (52)	78	M	25	Asystole	Unknown	NR	No	D (19 hrs)
Mutzbauer, 1997, Germany (53)	35	M	88	NR	Soon after	NR	NR	NR

Table 1. —*Continued*

Author, Year, Country, Reference	Age, yr	Gender	Length of Cardiopulmonary Resuscitation, min	Last Heart Rhythm Before AR	Time From Failed Cardiopulmonary Resuscitation to Unassisted ROSC, min	Method in Use to Monitor Vital Signs at Time of AR	Return of Consciousness	Final Reported Outcome
Püschel et al, 2005, Germany (54)	83	F	17	Asystole	33	None	No	D (4 hrs)
Quick et al, 1994, United States (55)	70	M	34	Asystole	8	NR	Yes	RF (3 wks)
Rogers et al, 1991, United States (56)	64	M	20	EMD	15	NR	NR	D (1 hr)
Rosengarten et al, 1991, Australia (57)	36	F	18	EMD	5	ECG	Yes	RF (6 mos)
Voelckel et al, 1996, Austria (58)	55	M	30	Asystole	7	ECG	NR	D (3 days)
Walker et al, 2001, United Kingdom (59)	27	M	25	Asystole	≈1	ECG	Yes	RF (18 days)

ECG, electrocardiogram; EMD, electromechanical dissociation; NR, not reported; RF(#), recovered fully and no neurologic impairment (length of follow-up); D (#), died (duration of survival).

bizarre complexes that were unlikely to generate a meaningful contraction. Two patients with arterial line monitoring did not show any circulatory activity associated with the ECG activity. No ROSC was measured and thus AR did not occur and this study was not included in our review.

AR After Failed CPR

The cases reported in this review pertain to AR after failed CPR and describe an unassisted ROSC from a few seconds to 33 mins after what was thought to be the death of the patient. It is uncertain whether some of these reports reflect errors in the diagnosis of death, a lack of continuous monitoring after "death," or the actual time period beyond which AR after failed CPR can still occur. We did not define the criteria for "cardiac arrest" in the inclusion criteria. Therefore, in the 11 cases that did not demonstrate asystole by ECG (Table), it is impossible to confirm that circulatory arrest had actually occurred. In the case reports that did include ECG monitoring before cardiac arrest and continuous monitoring by ECG after cardiac arrest (28, 36, 37, 40, 42, 43, 48, 49, 51, 57–59), AR after failed CPR did not occur beyond 7 mins.

Weise et al (34) report on a possible case of AR that we did not include in our review. This study reports on the case of a patient who experienced cardiac arrest during surgery and because of a poor prognosis did not receive "CPR;" however, his pacemaker continued to work and he was receiving high-dose catecholamine infusions. After the arrest, the catecholamine infusions were discontinued and a 6-min period of apnea and cessation of circulation were recorded by arterial line and ECG. We did not include this case in our review because it did not meet our inclusion criteria regarding the definition of AR. Given that the pacemaker was not stopped, all resuscitative measures were not terminated before the observed return of circulation.

AR Without CPR

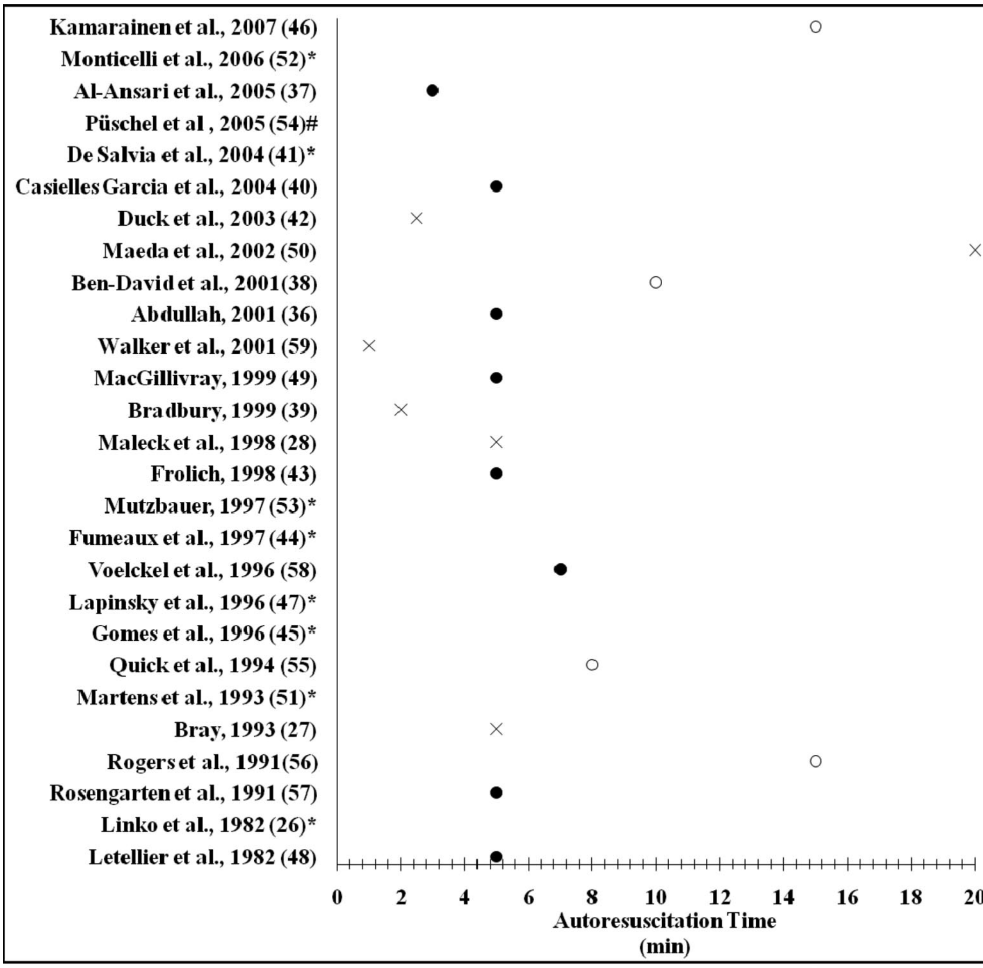
We did not find any studies that reported the occurrence of AR in the absence of CPR. Our review excluded the studies reported on by DeVita (19) in his narrative review of AR. Although the information from these studies continues to be reported as evidence that AR without CPR will not occur beyond 65 secs (14, 61), these studies described terminal cardiac electrical activity without any confirmation of ROSC and are therefore not examples of AR (17). For the purposes of our review, AR was clearly defined as the demonstrable return of circulation. ECG activity is necessary but not sufficient for circulation to resume.

Impact of CPR

Our findings suggest that the provision of CPR influences the occurrence of AR. Sudden death after unexpected cardiac arrest is distinct from an expected death after withdrawal of life-sustaining therapy. Unexpected cardiac arrests generally occur after a primary myocardial event, often attributable to an arrhythmia. CPR in this setting often includes ventilation with 100% oxygen, administration of high-dose catecholamines, and chest compressions. These patients are more likely to be monitored when CPR is discontinued. CPR has been reported to cause dynamic lung hyperinflation and tamponade of venous return and heart function that may give the false appearance of circulatory arrest (49, 56, 57). In contrast, after a planned withdrawal of life-sustaining therapy in a critically ill intensive care unit patient who is often comatose, cardiac arrest occurs because of progressive hypoxemia and CPR is not applied. These patients may have diminished levels of monitoring; withdrawal of oxygen, ventilator, and hemodynamic supports; and they may be palliated with analgesia and sedation. This distinct clinical and physiologic picture may explain the absence of AR in these cases.

Study Limitations

The main limitation of our systematic review is the exclusion of studies that were not reported in English, French, German, or Spanish. It is possible that we missed a report of AR that was published in a lan-



*no numerical time given.
Püschel study reported 1 case at 33 minutes. This was not included in the graph.

● Exact time and electrocardiogram monitoring reported.

○ Exact time reported, monitoring not reported.

x Approximate time reported.

Figure 2. Time from failed cardiopulmonary resuscitation to unassisted return of spontaneous circulation as a function of study date.

guage other than these. In addition, as for any systematic review, we cannot entirely rule out the possibility of having missed a reported case of AR because of our search methods. Despite these limitations, we feel that it is unlikely that our search strategy failed to include any existing publications of observational studies designed specifically to determine how long one must wait after cardiac arrest to ensure AR is no longer possible.

CONCLUSIONS

There will continue to be a shortage of organs for transplantation for the foreseeable future. As such, it is anticipated that the present interest in DCD programs will continue to grow. A threat to the appropriate implementation or expansion of DCD programs is the lack of consistency in the recommended waiting period (2–10 mins) between cardiac arrest and the determination of death. These recommendations, in general, are based on studies examining the pathophysiologic limits to the reversibility of cerebral ischemia during cardiac arrest (62), expert opinion (14), and commentary (19).

The existing data are of insufficient quality to support or refute the recommended waiting period to determine death after a cardiac arrest in the context of DCD. Autoresuscitation, as defined by an unassisted ROSC after cardiac arrest, has not been reported in the absence of CPR. This has implications for controlled DCD. Autoresuscitation has been reported to occur from a few seconds to 33 mins after failed CPR. However, in studies reporting exact times and appropriate monitoring, AR did not occur beyond 7 mins after failed CPR. In addition, we were unable to find any reports of AR in children. This has implications for uncontrolled DCD programs, because the provision of CPR may confound the time period after which death can be determined after a cardiac arrest. The limitations of the existing data in this field strongly support the need for additional potential methods of evaluating the “time to death” question after withdrawal of life support. Such methods might include the implementation of prospective observational studies of the determinants of death after cardiac arrest in patients after withdrawal of life-sustaining therapy, the establishment of a registry for cases of autoresuscitation in DCD programs, and/or the development of a global consensus statement regarding the recommended time period of observation for the determination of death after cardiac arrest, which would include international experts in the fields of critical care medicine, resuscitation medicine, and organ donation.

ACKNOWLEDGMENTS

We are grateful to Drs. Sam Parnia, Sonny Dhanani, and Michael DeVita for providing critical reviews of this manuscript.

REFERENCES

1. Youngner SJ, Arnold RM: Ethical, psychosocial & public policy implications of procuring organs from NHB cadaver donors. *JAMA* 1993; 269:2769–2774
2. Abt PL, Fisher CA, Singhal AK: Donation after cardiac death in the US: History and use. *J Am Coll Surg* 2006; 203:208–225
3. Leichtman AB, Cohen D, Keith D, et al: Kidney and pancreas transplantation in the United States, 1997–2006: The HRSA Breakthrough Collaboratives and the 58 DSA Challenge. *Am J Transplant* 2008; 8(4 Pt 2):946–957
4. Shafer TJ, Wagner D, Chessare J, et al: US organ donation breakthrough collaborative increases organ donation. *Crit Care Nurs Q* 2008; 31:190–210
5. World Medical Association Statement on Human Organ Donation and Transplantation: Adopted by the 52nd WMA General Assembly in Edinburgh, Scotland during October 2000 and Revised by the WMA General Assembly, Pilanesberg, South Africa, October 2006. Available at: http://www.wma.net/en/30publications/10policies/wma/index.html Accessed February 24, 2010
6. Curfman GD, Morrissey S, Drazen JM: Cardiac transplantation in infants. *N Engl J Med* 2008; 359:749–750
7. Veatch RM: Donating hearts after cardiac death—Reversing the irreversible. *N Engl J Med* 2008; 359:672–673
8. Truog RD, Miller FG: The dead donor rule and organ transplantation. *N Engl J Med* 2008; 359:674–675
9. Bernat JL: The boundaries of organ donation after circulatory death. *N Engl J Med* 2008; 359:669–671
10. Shemie SD, Baker AJ, Knoll G, et al: National recommendations for donation after cardiocirculatory death in Canada: Donation after cardiocirculatory death in Canada. *CMAJ* 2006; 175:S1
11. Kootstra G: Statement on non-heart-beating donor programs. *Transplant Proc* 1995; 27: 2965
12. DeVita MA, Snyder JV: Development of the University of Pittsburgh Medical Center policy for the care of terminally ill patients who may become organ donors after death following the removal of life support. *Kennedy Inst Ethics J* 1993; 3:131–143
13. Herdman R, Beauchamp TL, Potts JT: The Institute of Medicine's report on non-heart-beating organ transplantation. *Kennedy Inst Ethics J* 1998; 8:83–90
14. Ethics Committee American College of Critical Care Medicine, Society of Critical Care Medicine: Recommendations for nonheart-beating organ donation. A position paper by the Ethics Committee, American College of Critical Care Medicine, Society of Critical Care Medicine. *Crit Care Med* 2001; 29: 1826–1831
15. Boucek MM, Mashburn C, Dunn SM, et al: Pediatric heart transplantation after declaration of cardiocirculatory death. *N Engl J Med* 2008; 359:709–714
16. Institute of Medicine: Non-Heart-Beating Organ Transplantation: Medical and Ethical Issues in Procurement. Washington, DC, National Academy Press, 1997
17. Institute of Medicine: Non-heart-beating organ transplantation: Practice and protocols. Report 0-309-06641-7. Washington, DC, National Academy Press, 2000
18. Wijdicks EF, Diringer MN: Electrocardiographic activity after terminal cardiac arrest in neurocatastrophes. *Neurology* 2004; 62: 673–674
19. DeVita MA: The death watch: Certifying death using cardiac criteria. *Prog Transplant* 2001; 11:58–66
20. Willius FA: Changes in the mechanism of the human heart preceding and during death. *Med J Rec* 1924; 119(Suppl):44–50
21. Enselberg CD: The dying human heart; electrocardiographic study of forty-three cases, with notes upon resuscitative attempts. *AMA Arch Intern Med* 1952; 90:15–29
22. Robinson GC: A study with the electrocardiograph of the mode of death of the human heart. *J Exp Med* 1912; 16:291–302
23. Rodstein M, Bornstein A: Terminal ECG in the aged. Electrocardiographic, pathological, and clinical correlations. *Geriatrics* 1970; 25: 91–100
24. Cole DJ: The reversibility of death. *J Med Ethics* 1992; 18:26–30
25. Youngner SJ, Arnold RM, DeVita MA: When is "dead"? *Hastings Center Report* 1999; 29: 14–21
26. Linko K, Honkavaara P, Salmenpera M: Recovery after discontinued cardiopulmonary resuscitation. *Lancet* 1982; 1:106–107
27. Bray JG Jr: The Lazarus phenomenon revisited. *Anesthesiology* 1993; 78:991
28. Maleck WH, Piper SN, Triem J, et al: Unexpected return of spontaneous circulation after cessation of resuscitation (Lazarus phenomenon). *Resuscitation* 1998; 39:125–128
29. Adhiyaman V, Adhiyaman S, Sundaram R: The Lazarus phenomenon. *J R Soc Med* 2007; 100:552–557
30. Adhiyaman V, Sundaram R: The Lazarus phenomenon. *J R Coll Physicians Edinburgh* 2002; 32:9–13
31. Pai M, McCulloch M, Gorman JD, et al: Systematic reviews and meta-analyses: An illustrated, step-by-step guide. *Natl Med J India* 2004; 17:86–95
32. Guyatt GH, Oxman AD, Kunz R, et al: What is "quality of evidence" and why is it important to clinicians? *BMJ* 2008; 336:995–998
33. Guyatt GH, Oxman AD, Vist GE, et al: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; 336:924–926
34. Wiese CH, Stojanovic T, Klockgether-Radke A, et al: [Another case of "Lazarus phenomenon" during surgery? Spontaneous return of circulation in a patient with a pacemaker.] *Anaesthesist* 2007; 56:1231–1236
35. Klockgether-Radke A: Monitoring im Rettungsdienst. *Notarzt* 1987; 3:85–88
36. Abdullah RS: Restoration of circulation after cessation of positive pressure ventilation in a case of "Lazarus syndrome." *Anesth Analgesia* 2001; 93:241
37. Al-Ansari MA, Abouchaleh NM, Hijazi MH: Return of spontaneous circulation after cessation of cardiopulmonary resuscitation in a case of digoxin overdosage. *Clin Intensive-Care* 2005; 16:179–181
38. Ben-David B, Stonebraker VC, Hershman R, et al: Survival after failed intraoperative resuscitation: A case of "Lazarus syndrome." *Anesth Analgesia* 2001; 92:690–692
39. Bradbury N: Lazarus phenomenon: Another case? *Resuscitation* 1999; 41:87
40. Casielles Garcia JL, Gonzalez Latorre MV, Fernandez AN, et al: [Lazarus phenomenon: Spontaneous resuscitation.] *Revista Espanola de Anestesiologia y Reanimacion* 2004; 51:390–394
41. De Salvia A, Guardo A, Orrico M, et al: A new case of Lazarus phenomenon? *Forensic Sci Int* 2004; 146(Suppl):S13–S15
42. Duck MH, Paul M, Wixforth J, et al: [The Lazarus phenomenon. Spontaneous return of circulation after unsuccessful intraoperative resuscitation in a patient with a pacemaker.] *Anaesthesist* 2003; 52:413–418
43. Frolich MA: Spontaneous recovery after discontinuation of intraoperative cardiopulmonary resuscitation: Case report. *Anesthesiology* 1998; 89:1252–1253
44. Fumeaux T, Borgeat A, Cuenoud PF, et al: Survival after cardiac arrest and severe acidosis (pH = 6.54). *Intensive Care Med* 1997; 23:594
45. Gomes E, Araujo R, Abrunhosa R, et al: Two successful cases of spontaneous recovery after cessation of CPR. *Resuscitation* 1996; 31: S40
46. Kamarainen A, Virkkunen I, Holopainen L, et al: Spontaneous defibrillation after cessation of resuscitation in out-of-hospital cardiac arrest: A case of Lazarus phenomenon. *Resuscitation* 2007; 75:543–546
47. Lapinsky SE, Leung RS. Auto-PEEP and electromechanical dissociation. *N Engl J Med* 1996; 335:674
48. Letellier N, Coulomb F, Lebec C, et al: Recovery after discontinued cardiopulmonary resuscitation. *Lancet* 1982; 1:1019
49. MacGillivray RG: Spontaneous recovery after discontinuation of cardiopulmonary resuscitation. *Anesthesiology* 1999; 91:585–586

50. Maeda H, Fujita MQ, Zhu BL, et al: Death following spontaneous recovery from cardiopulmonary arrest in a hospital mortuary: "Lazarus phenomenon" in a case of alleged medical negligence. *Forensic Sci Int* 2002; 127:82–87
51. Martens P, Vandekerckhove Y, Mullie A: Restoration of spontaneous circulation after cessation of cardiopulmonary resuscitation. *Lancet* 1993; 341:841
52. Monticelli F, Bauer N, Meyer HJ: Lazarus phenomenon: current resuscitation standards and questions for the expert witness. *Rechtsmedizin* 2006; 16:57–63
53. Mutzbauer TS: Compression-decompression (ACD)-CPR. *Prehosp Disaster Med* 1997; 12: S21
54. Puschel K, Lach H, Wirtz S, et al: Ein weiterer Fall von "Lazarus-Phanomen"? *Notfall Rettungsmedizin* 2005; 8:528–532
55. Quick G, Bastani B: Prolonged asystolic hyperkalemic cardiac arrest with no neurologic sequelae. *Ann Emerg Med* 1994; 24:305–311
56. Rogers PL, Schlichtig R, Miro A, et al: Auto-PEEP during CPR. An "occult" cause of electromechanical dissociation? *Chest* 1991; 99: 492–493
57. Rosengarten PL, Tuxen DV, Dziukas L, et al: Circulatory arrest induced by intermittent positive pressure ventilation in a patient with severe asthma. *Anaesth Intensive Care* 1991; 19:118–121
58. Voelckel W, Kroesen G: Unexpected return of cardiac action after termination of cardiopulmonary resuscitation. *Resuscitation* 1996; 32:27–29
59. Walker A, McClelland H, Brenchley J: The Lazarus phenomenon following recreational drug use. *Emerg Med J* 2001; 18:74–75
60. The President's Council on Bioethics: Controversies in the determination of death: A white paper by The President's Council on Bioethics, December 2008, Available at http://www.bioethics.gov/reports/death/index.html. Accessed February 24, 2010
61. Bernat JL, D'Alessandro AM, Port FK, et al: Report of a national conference on donation after cardiac death. *Am J Transplant* 2006; 6:281–291
62. Safar P: Resuscitation of the ischemic brain. *In:* Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives. Albin MS (Ed.). New York, NY, McGraw Hill, 1997, pp 560–560

APPENDIX: SEARCH STRATEGIES FOR ELECTRONIC DATABASES

MEDLINE Using PubMed

Search terms used: (autoresuscitation OR auto-resuscitation) OR ((lazarus[TI]) OR ("lazarus phenomenon")) OR ((discontin* OR Suspend* OR Terminat* OR Cessat* OR Halt*) AND (resuscitat* OR reanimat* OR cpr OR "cardiopulmonary resuscitation" OR "cardiopulmonary resuscitation"[Mesh]) AND (ROSC OR SROC OR (Circulation AND Spontaneous AND (Recover* OR Restor* OR Return*)))) OR ((ROSC OR SROC OR (Circulation AND Spontaneous AND (Recover* OR Restor* OR Return*))) AND (("electromechanical dissociation" OR "ventricular fibrillation" OR asystole OR "pulseless electrical activity" OR ((Arrest* OR cessat*) AND (cardiac OR cardiorespiratory OR cardiocirculatory OR cardiopulmonary OR circulation))) OR ("Ventricular Fibrillation"[Mesh] OR "Heart Arrest"[Mesh]))) AND ((Humans[Mesh]) AND (English[lang] OR French[lang] OR German[lang] OR Spanish[lang]))

EMBASE (1974–1979) and (1980–2008 Week 28) and EMBASE Classic (1947–1973), All Using OVID

Searched on key words with limit on humans, no language restrictions. Search terms used: (autoresuscitation OR auto-resuscitation) OR ("lazarus phenomenon") OR ((discontin* OR Suspend* OR Terminat* OR Cessat* OR Halt*) AND (resuscitat* OR reanimat* OR cpr OR "cardiopulmonary resuscitation") AND (ROSC OR SROC OR (Circulation AND Spontaneous AND (Recover* OR Restor* OR Return*)))) OR ((ROSC OR SROC OR (Circulation AND Spontaneous AND (Recover* OR Restor* OR Return*))) AND (("electromechanical dissociation" OR "ventricular fibrillation" OR asystole OR "pulseless electrical activity" OR ((Arrest* OR cessat*) AND (cardiac OR cardiorespiratory OR cardiocirculatory OR cardiopulmonary OR circulation)))))

Web of Science

Searched on "topic" using same strategy as EMBASE (but no limit to human) but limited to Science Citation Index.

Cochrane Library

Used the advanced search option (searching on title, abstract, or key words in Cochrane Central Register of Controlled Trials) with the same strategy as EMBASE but with no limits.