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# Cardiopulmonary resuscitation – When to start, when to stop

BY PETER G. BRINDLEY, MD, FRCPC

**Cardiopulmonary resuscitation (CPR) has the power to prevent premature death. Sadly, however, it can also prolong inevitable death, family duress, patient suffering in the short-term and unacceptable disability in the long-term. Each year, there are an estimated 370,000 to 750,000 attempted resuscitations following cardiac arrest in the United States.[1] Cost-estimates vary greatly, but several authors agree that the cost of futile resuscitative efforts is over 1 billion dollars US per annum.[2-5] Extrapolating data to other countries is complicated by different healthcare models and population factors; however, even crude estimates emphasize that CPR is an issue of daily relevance. This is especially true if resuscitation is attempted on anyone without explicit documentation to the contrary.[6] While discussions must focus on whether CPR is appropriate therapy for an individual patient, it is also essential to justify the best use of scarce resources.**

**For physicians, there is a complicated "balancing act" that demands aggressive and immediate, but considered and compassionate life-saving efforts. Decisions made during a time of stress can impact patient and family well-being, resource consumption, and even healthcare worker morale. It is typically difficult to predict with certainty who will survive or the quality of that survival. As such, in order to practice sound medicine and counsel families, it is essential to review the existing evidence pertaining to the likelihood of survival following attempted resuscitation. Currently, patient and cardiopulmonary arrest factors (Table 1), rather than therapeutic interventions, have the greatest influence upon survival, and these are the focus for this issue of *Critical Care Rounds*.**

## Patient factors

### *Age and gender*

Despite frequent misconceptions, increased patient age is not consistently associated with decreased survival or a lower quality of survival following cardiac and respiratory arrest. While several studies have shown an association,[7-10] just as many have not.[6,11-16] While the elderly may well have a lower life expectancy overall, they do not have decreased survival, at least not for the 3-month period following a cardiac and respiratory arrest (Table 2).[6] Likewise, gender has not been shown to be significantly associated with lower survival. Although women may have an increased rate of initial resuscitation, the female survival advantage disappears by the time of hospital discharge and therefore, in women, death is essentially delayed rather than averted.[17,18] Overall, there is insufficient evidence to recommend basing resuscitative protocols on age or gender alone.



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**Table 1: Characteristics of cardiopulmonary arrest patients[6]**

| Variable | % |
|---|---|
| **Survived** | |
| Initial resuscitation | 36.8 |
| To hospital discharge | 13.4 |
| Able to return to independent living | 11.3 |
| **Hour of cardiopulmonary arrest** | |
| 07:01-15:00 h | 35.6 |
| 15:01-23:00 h | 24.7 |
| 23:01-07:00 h | 39.7 |
| **Type of arrest** | |
| Respiratory | 11.7 |
| Cardiac Subtypes | |
| Asystole | 37.2 |
| Pulseless electrical activity (PEA) | 24.3 |
| Ventricular fibrillation (VF) | 16.6 |
| Pulseless ventricular tachycardia (pVT) | 10.1 |
| **Age (in years)** | |
| ≤50 years | 18.9 |
| 51-60 | 10.3 |
| 61-70 | 23.6 |
| 71-80 | 29.6 |
| >80 | 17.3 |

VT = ventricular tachycardia; VF = ventricular fibrillation;
PEA = pulseless electrical activity


**Table 2: Predictors of failure to be discharged home amongst patients undergoing cardiopulmonary arrest[6]**

| Variable | Odds ratio | 95% CI | P-value |
|---|---|---|---|
| **Age (years)** | | | |
| ≤50 years | 1.0 | – | – |
| 51-60 | 0.5 | 0.1-2.4 | 0.39 |
| 61-70 | 0.8 | 0.2-3.0 | 0.72 |
| 71-80 | 1.5 | 0.4-6.3 | 0.55 |
| >80 | 7.4 | 0.3-1.9 | 0.52 |
| **Gender** | | | |
| Female | 1.0 | – | – |
| Male | 0.7 | 0.3-1.9 | 0.52 |
| **Arrest type** | | | |
| Respiratory | 1.0 | – | – |
| Pulseless VT/VF | 3.9 | 1.4-10.9 | 0.010 |
| Asystole/PEA | 20.3 | 6.2-67.2 | <0.0001 |
| **Hour of cardiopulmonary arrest** | | | |
| 07:01-15:00 | 1.0 | – | – |
| 15:01-23:00 | 1.7 | 0.6-4.8 | 0.35 |
| 23:01-07:00 | 3.2 | 1.0-10.1 | 0.045 |

VT = ventricular tachycardia; VF = ventricular fibrillation;
PEA = pulseless electrical activity


## Cardiopulmonary arrest factors

### *Time of arrest*

Several large trials examining out-of-hospital arrest have observed an increased incidence of myocardial infarction (MI) and cardiac arrest in the early morning. This is commonly attributed to the catecholamine and cortisol surge associated with awakening.[19-22] It is less clear if this is duplicated by in-patients where the circadian influence may be minimized. However, a recent small retrospective study of only in-hospital arrests also resported more early morning cardiac arrests and worse survival during this time period. In addition, there was an increased percentage of pulseless electrical activity and asystole arrests in the early morning. It is quite likely that the poor survival and increased percentage of asystole arrests are due to more arrests progressing unwitnessed to what are considered "terminal" arrests. Alternatively, there may simply be more malignant arrest types in the early morning. Either way, it is ironic that hospitals typically have a lower staff-to-patient ratio during the hours associated with the largest number of arrests.

### *Cardiac arrest type*

Numerous studies have demonstrated that there is a very significant association between arrest type and survival. The lowest rates/percentages are associated with asystole, with survival rates increasing for pulseless electrical activity, then pulseless ventricular tachycardia, and finally, ventricular fibrillation with the highest rate of survival.[6,7-10,14-16,23-26] No published study disputes this order of the least reversible to the most reversible arrest type and several authors have argued to end attempted resuscitations following asystole.[7,8] It is also noteworthy that the highest survival rate following ventricular fibrillation was actually reported from a casino and not from a hospital. Presumably, the high survival rate was due to particularly close observation of individuals and a rapid response,[27] which introduces the discussion of "witnessed" as compared to "unwitnessed" arrests.

### *Witnessed versus unwitnessed arrests*

A recent retrospective review of Canadian cardiac and respiratory arrests revealed that, of all arrests, whether they were witnessed or not:

- roughly 1 in 3 survived the initial resuscitation
- roughly 1 in 7 survived to discharge, and
- roughly 1 in 10 were able to return to independent living (Table 3).

When divided into witnessed and unwitnessed arrests, clearly, survival was significantly lower following an unwitnessed arrest.[6] As a result, these arrests should be considered separately. For all witnessed arrests, spontaneous circulation was regained in roughly 1 in 2 arrests, 1 in 3 survived to 24 hours, 1 in 4 survived to discharge, and 1 in 5 were able to return home. In stark contrast, for unwitnessed arrests, roughly 1 in 5 were initially resuscitated, but only 1 patient survived to discharge (Table 4). Of note, over 40% of arrests were unwitnessed.[6] There was such a

**Table 3: Type of arrest and percentage survival following cardiopulmonary arrest[6]**

| All ages | Survived initial resuscitation independently | Discharged from hospital | Able to live |
|---|---|---|---|
| **All arrest types** (n=247) | 36.8% (n=91) | 13.4% (n=33) | 11.3% (n=28) |
| **Respiratory** (n=29) | 93.1% (n=27) | 55.2% (n=16) | 44.8% (n=13) |
| **All cardiac** (n=218) | 29.4% (n=64) | 8.0% (n=17) | 7.0% (n=15) |
| **Pulseless VT/VF** (n=66) | 39.4% (n=26) | 18.2% (n=12 | 15.2% (n=10) |
| **Asystole/PEA** (n=152) | 25.0% (n=38) | 3.3% (n=5) | 3.3% (n=5) |

VT = ventricular tachycardia; VF = ventricular fibrillation;
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co-linearity between whether an arrest was witnessed and the arrest type (with a strong correlation between asystole/pulseless electrical activity arrests and unwitnessed arrests), that multivariant analysis was not able to distinguish these 2 variables.

The arrest type and whether the arrest is witnessed measure a similar construct, namely the "irreversibility of an arrest." However, despite this co-linearity and the dismal survival rate following an unwitnessed arrest, mandating "do-not-resuscitate (DNR)" orders for unwitnessed arrests may be more difficult than mandating orders based on arrest type. Forbidding resuscitation following an unwitnessed arrest may simply encourage families to insist upon admission to a monitored bed and this could put unreasonable strains on critical care and emergency departments.

### *Respiratory versus cardiac arrests*

Primary respiratory arrests have significantly higher survival rates than cardiac arrests of any type.[6] As suggested above, this may be because the arrest is halted before it progresses to a full cardio-respiratory collapse. Regardless, it is often appropriate to discuss resuscitation plans for respiratory and cardiac arrests separately. For some patients, chest compressions and intubations are appropriate, but for others, neither is appropriate. For still others, it may be sensible to offer intubation and ventilatory support if there is a good chance of recovery, whereas full CPR would be withheld if the patient is very unlikely to survive to discharge. If respiratory and cardiac arrests are considered synonymous and treatment options as merely "all-or-none," it is likely that some families will insist on a "full-code" because they fear that the patient will otherwise be neglected. Knowing that treatment is not "all-or-none" may decrease family dissatisfaction, enable

**Table 4: Type of arrest and percentage survival following cardiopulmonary arrests stratified by whether arrest was witnessed or unwitnessed[6]**

| All ages | Survived initial resuscitation | Discharged from hospital | Able to live independently |
|---|---|---|---|
| **Witnessed arrests** | | | |
| All arrest types (n=143) | 48.3% (n=69) | 22.4% (n=32) | 18.9% (n=27) |
| Respiratory (n=27) | 96.3% (n=26) | 55.6% (n=15) | 44.4% (n=12) |
| All cardiac (n=116) | 37.1% (n=43) | 14.7% (n=17) | 12.9% (n=15) |
| Pulseless VT/VF (n=47) | 38.3% (n=18) | 25.6% (n=12) | 21.3% (n=10) |
| Asystole/PEA (n=69) | 36.2% (n=5) | 7.2% (n=5) | 7.2% (n=5) |
| **Unwitnessed arrests** | | | |
| All arrest types (n=104) | 21.2% (n=22) | 1.0% (n=1) | 1.0% (n=1) |
| Respiratory (n=2) | 50.0% (n=1) | 50.0% (n=1) | 50.0% (n=1) |
| All cardiac (n=102) | 20.6% (n=21) | 0% (n=0) | 0% (n=0) |
| Pulseless VT/VF (n=19) | 42.1% (n=8) | 0% (n=0) | 0% (n=0) |
| Asystole/PEA (n=83) | 15.7% (n=13) | 0% (n=0) | 0% (n=0) |

VT = ventricular tachycardia; VF = ventricular fibrillation;
PEA = pulseless electrical activity



the setting of appropriate limits, and ensure that a DNR does not come to mean, cynically, "do-not-respond." There may be concerns that resuscitative wishes will become too complex or resemble "picking from a menu." However, the marked survival discrepancy between respiratory and cardiac arrests makes it difficult to discuss these arrest types as if they were a single entity. Over 40% of respiratory arrest patients (those that require intubation, but not chest compressions), as opposed to <10% of cardiac arrest patients, survive to be able to return home.[6] Offering therapies known to be of potential benefit, but withholding those that are unlikely to be beneficial, is no different for patients suffering an arrest than for any number of medical problems.

### *Length of attempted resuscitation*

First, unless hypothermia, electrical shock, or drug overdose is involved, numerous authors have stated that resuscitation efforts should not continue in-hospital if they have been unsuccessful in the prehospital setting.[2,28,29] The survival rate of patients who fail to respond to advanced life support in the field has never been shown to improve in-hospital and, to quote the 2000 Advanced Cardiac Life Support (ACLS) guidelines, "does not justify high-speed potentially dangerous transportation to hospital."[29] In a Canadian multivariate analysis of in-hospital arrests, return of spontaneous circulation within 20 minutes of resuscitation was significantly associated with increased survival.[30] In 2001, a review of out-of-hospital arrests by Eisenberg stated that CPR should not exceed 10 minutes for an unwitnessed asystole.[1] ACLS guidelines recommend rapid instigation of CPR, intubation, treatment of rapidly reversible factors, followed by early withdrawal if no rapid improvement is seen.[29] No author has recommended prolonged resuscitative efforts for asystole;[1,29] others have found that resuscitation following asystole is successful in <1 out of 100 attempts and therefore, fulfills the definition of quantitative futility.[1,7,8,31] While complete discussions of futility clearly include consideration of more than just crude survival percentage, the onus rests considerably on justifying the continuation, rather than the discontinuation, of resuscitation following asystole.

### *Effect of comorbidities upon survival*

It was stated above that age does not have a clear enough association with survival to dictate resuscitation plans. This raises the adage familiar to clinicians of the contrast between "the *good* 80-year-old" and "the *bad* 80-year-old," and introduces the potential influence of comorbidities upon survival. Unfortunately, this assumption is not clearly borne out in the current literature. Many studies have found an association between being house-bound/functionally dependant and significantly decreased survival following arrest.[16,30-32] In addition, Bedell et al did find an association between decreased survival and renal failure, congestive heart failure, sepsis, hypotension, pneumonia, and cancer.[16] However, there is considerable disagreement. Other research has revealed an association only with sepsis[31] and a recent Canadian multivariate analysis failed to find a significant association between survival and the presence of malignancy, sepsis, myocardial infarction, pneumonia, renal failure, or hypotension.[30] The lack of a clear association between comorbidities and survival duplicates the findings of another Canadian study performed a decade earlier.[25] Furthermore, there is a common assumption that those with cardiac illness who suffer a primary cardiac event are more likely to survive than those with noncardiac illness who suffer a cardiac arrest.[11-13,26] Despite the apparent common sense that single-organ disease patients are likely to do better than those with multi-organ dysfunction, the literature again raises potential doubt. In a prospective study, Doig et al found that survival is not significantly lower in patients with 4 or more active medical problems versus those with 3 or less.[30] Definitive conclusions are likely complicated by differing study designs and disease definitions, but disappointingly, there is insufficient evidence to accurately predict the outcome of resuscitation based on pre-existing illness.

### *End-tidal carbon dioxide levels during attempted resuscitation*

During cardiac arrest, end-tidal carbon dioxide levels ($ETCO_2$) reflect cardiac output and these levels have been used to predict both mortality and the adequacy of resuscitation.[4,5]

In a study performed between 1991-95, Levine suggested that while $ETCO_2$ cannot be used to predict those who will achieve long-term survival, it can predict those who will not, and therefore, when resuscitative efforts should cease. He found that although there was no association between initial $ETCO_2$ levels and survival, an $ETCO_2$ <10 mm Hg after 20 minutes predicted mortality with 100% sensitivity, specificity, positive predictive value, and negative predictive value.[4] This study suggests that $ETCO_2$ levels cannot be used to make predictions before 15 minutes and, as such, does not assist in making the decision to cease resuscitation earlier. Extrapolation is also complicated because the study was restricted to out-of-hospital arrests brought to the emergency room, included only pulseless electrical activity rather than all cardiac or respiratory arrests, and had a sample size of only 150. Furthermore, although a level <10 mm Hg is predictive of mortality, a level >10 mm Hg does not predict survival or the quality of that survival and, even though a level of 18 was achieved in all cases where spontaneous circulation was restored, two-thirds of these patients (19/35) still died in hospital.

Other studies suggest that a threshold $ETCO_2$ level exists between 10 and 18 mm Hg and somewhere between 14 and 20 minutes of resuscitation.[4,5] However, Levine felt that physicians would expect a 100% predictive value in order to terminate efforts and this is why he chose <10 mm Hg following 20 minutes of resuscitative efforts. He believed that using the conservative threshold of 10 mm Hg would permit withdrawal in >75% of arrests without any decrease in restoration of spontaneous circulation, let alone survival to discharge. It was further estimated that this guideline would save roughly 1 billion dollars annually in the United States without any change in survival.

In a less well-known US study, Ahrens et al[5] examined 127 patients, including those with in-hospital arrests and all types of arrest rhythms. The study concluded that an $ETCO_2$ of <10 mm Hg at any time (0, 5, 10, 15, 20 minutes) predicted non-survival to discharge. While it was a smaller sample, this study does suggest that $ETCO_2$ could be used earlier and in a plethora of arrest types. Ahrens et al found that those who survived initial resuscitation, but died in hospital constituted >10% of all arrest patients and they remained in intensive care for an average of 20 days. With a conservative estimate of $1000 per patient per day, the estimated savings using an $ETCO_2$ value of <10 mm Hg to terminate resuscitative efforts were far in excess of 1 billion dollars per annum for the US. Again, this is without any decrease in survival to discharge. As mentioned, precise extrapolations for other healthcare systems are difficult. However, the ability to reduce the strain on limited resources, to possibly save millions of dollars per year and, most importantly, to reduce the potential suffering of patients, means that $ETCO_2$ monitors represent a cost-effective and appropriate addition to the code cart.

## Conclusion

There is a vast body of literature concerning resuscitation, but with a few exceptions, it is composed of retrospective data and small studies of no more than several hundred patients. As such, this typically represents type IIb evidence at best. However, despite disagreement about the influence of some pre-arrest characteristics, the 3 factors that are repeatedly shown to have the greatest impact on survival are the arrest type, whether that arrest is witnessed, and whether it can be halted within 10 minutes.[6,30,33] Understandably, many physicians will be reluctant to stop CPR based on a single criterion, but a study of over 1000 Canadian patients between 1989 and 1995 suggests that the combination of these 3 factors predicts mortality with 100% sensitivity.[33] Add to this, the 100% sensitivity of an $ETCO_2$ <10 mm Hg after 20 minutes,[4] then physicians can predict with some confidence which patients will not survive to be discharged.

The concept of CPR was introduced 40 years ago.[34] While inpatient populations may well be older and sicker than in the past, survival rates have not changed appreciably.[6,30] This is despite remarkable advances over the last 4 decades that include ubiquitous training in CPR and the concept of modern critical care units. With the exception of rapid defibrillation, no therapeutic interventions have been shown to unequivocally improve outcome following CPR, and this includes the drugs used for ACLS.[35,36] In the 2000 ACLS guidelines, new therapies such as vasopressin and amiodarone were recommended but, unfortunately, although these interventions may increase the chances of initial resuscitation, they do not clearly increase discharge from hospital.[29,35,36] That being the case, such therapies might only increase the numbers of patients in intensive care, raise potential duress, and compound strained resources.

The greatest increase in patient survival continues to be "who" is resuscitated[6,11-13] and "when" resuscitation is terminated,[4,5,25,26] and that is why these factors are the focus of this review. Having stated that, research into better resuscitation must continue. Recently, post-arrest hypothermia has been shown to be a putative method to increase both the likelihood and quality of survival following ventricular fibrillation.[37] However, no intervention has been shown to improve outcome following asystole or pulseless electrical activity arrests and they constitute as many as two-thirds of all in-hospital arrests.[6,33] Therefore, it is imperative not to focus all our energy on novel therapies at the expense of relatively mundane, but vitally important, pre-arrest and peri-arrest characteristics.

Sadly, many physicians are reluctant to preemptively address resuscitation. In a study of 5 US teaching hospitals, investigators found that nearly half of all physicians did not know the code status of their patients, nearly half of all DNR orders has been written within 2 days of death, and an intensive education program did not change this significantly.[38] In Canada, only 16.8% of in-patients who arrested in a major Calgary hospital had a physician's order addressing the intensity of medical care to be delivered. This was despite a policy that mandated otherwise.[30] The need for informed dialogue is only heightened by studies suggesting that the public may believe survival rates are 2-fold higher than any published data. Popular medical dramas that minimize the long-term consequences of resuscitation do not help this perception.[39] Overall, it is essential to appreciate that for some patients, CPR represents a life-saving intervention, while for others, it represents futility, unnecessary suffering, and squandered resources. It is vital for physicians to take ownership of this increasingly important issue.

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