Prearrest Predictors of Survival Following In-Hospital Cardiopulmonary Resuscitation: A Meta-analysis

Mark H. Ebell, MD
Athens, Georgia

Background. The success rate of cardiopulmonary resuscitation (CPR) varies with the patient population studied. Prearrest variables have been used to identify groups of patients with a particularly low rate of survival following CPR. The purpose of this study was to use the technique of meta-analysis to identify prearrest variables associated with a decreased rate of survival to the time of discharge following CPR of hospitalized patients.

Methods. The MEDLINE database was searched using the following key words: *resuscitation*, *survival*, and *1980–1991*. The bibliographies of studies identified in the computerized search as well as those of appropriate studies in the author's personal files were reviewed. The following inclusion criteria were used: study published since 1980 (data collected after 1975), in-hospital resuscitation, retrospective or prospective design, consecutive adult patients from both the general wards and intensive care units, an end-point of survival to hospital discharge, and data reported for at least one variable measured before cardiac arrest. Of the 22 studies initially identified, 14 met the above criteria. Data were taken directly from the published reports. In two cases where no specific survival data were reported but the studies met all other criteria for inclusion, the authors were contacted and agreed to supply the necessary information. Two-way variables were combined across studies using the Mantel-Haenszel statistic.

Results. The following prearrest variables were associated with a decreased rate of survival to discharge following CPR ($P < .005$): age over 70 years, serum creatinine >130 μmol/L, serum creatinine >220 μmol/L, homebound lifestyle, presence of cancer or metastatic cancer, and a primary diagnosis of sepsis or pneumonia. A primary diagnosis of myocardial infarction was associated with an increased rate of survival to discharge following CPR ($P = .005$). Based on these results, modifications to the Pre-Arrest Morbidity Index initially devised by George and colleagues have been proposed.

Conclusions. The identification of prearrest variables that are associated with decreased survival following CPR will assist clinicians when they counsel their patients regarding do-not-resuscitate (DNR) orders. In addition, the further refinement of a predictive tool such as the modified Pre-Arrest Morbidity Index can help clinicians to identify patients for whom CPR is futile. Such an instrument must be validated on an independent data set before it can be considered for clinical application.

Key words. Resuscitation; survival; heart arrest.
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Cardiopulmonary resuscitation (CPR) of hospitalized patients is a technique with widely varying effectiveness, with rates of survival to discharge following CPR ranging from 7%[1] to 24%.[2] Certain subgroups of patients, such as those admitted for a cardiovascular diagnosis, have comparatively high survival rates of 21% to 27%.[3,4] Others, such as patients with metastatic cancer, do very poorly, with no survivors to discharge following CPR reported in the literature.[5]

Previous studies have examined numerous variables and their relationship to survival following CPR. Of particular interest to clinicians are prearrest variables, since they may permit the prospective identification of patients with a particularly low rate of survival to discharge should cardiopulmonary arrest occur. Once identified, these factors could form the basis for discussions between physicians and patients regarding the risks and benefits of resuscitative efforts.

In previous studies that have analyzed survival following CPR by diagnosis or by other clinical variables,

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From the Athens Regional Medical Center, Athens, Georgia. Requests for reprints should be addressed to Mark H. Ebell, MD, 310 Snapfinger Dr, Athens, GA 30605.

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most patient subpopulations did not contain enough patients to avoid a type 2 error. A type 2 error is defined as the error of falsely stating that a statistically significant difference does not exist between two groups when they actually are different, usually because there are not enough patients in each group.[6] If one defines a negligible rate of survival to discharge as less than or equal to 1%, and the average rate of survival following CPR is 13%, a study must have sufficient statistical power to detect this difference in order to identify factors associated with a negligible rate of survival to discharge. Using the technique of power analysis described by Arkin and colleagues,[7] one finds that the study and control groups must each contain approximately 110 patients to avoid a type 2 error.

Type 2 errors may be responsible for conflicting results between studies. For example, while some workers have found a significant relationship between age and survival following CPR,[1,8] others have not.[9–11] Similarly, while Bedell found no survivors among patients with pneumonia,[3] smaller studies have failed to duplicate this finding.[9,12]

The technique of meta-analysis uses specialized statistical techniques to combine data from several similar studies.[13,14] It is a useful way to resolve conflicts between studies that may suffer from type 2 statistical errors. It has been applied successfully to analyze a number of medical questions, including the effect of aspirin on pregnancy-induced hypertension,[15] the effect of estrogen replacement therapy on the risk of breast cancer,[16] and the effect of beta-blockade on myocardial infarction.[17]

In this study the technique of meta-analysis has been applied to the question of survival to discharge following cardiopulmonary resuscitation. The variables studied are all measured before the onset of cardiac arrest. The particular goal of this work is to identify factors associated with patient subpopulations having negligible rates of survival. With this information, physicians can give more accurate prognostic information to patients about the potential utility of various treatments and the implications for do-not-resuscitate (DNR) orders.

Methods

Identification and Selection of Studies

A combination of computerized and manual searches was used to identify studies for meta-analysis. The MEDLINE database was searched for the following key words: *resuscitation*, *survival*, and *1980–1991*. Of the 80 studies that met all three criteria, 71 were discarded. These dealt with out-of-hospital resuscitation (n = 28), specific diagnoses or rhythms (n = 11), pediatric resuscitation (n=7), or other issues unrelated to survival following in-hospital cardiopulmonary resuscitation. The bibliographies of the 9 remaining studies were carefully searched, in addition to the author's personal reference files, for further appropriate references. Twenty-one potential references were identified. In addition, data from a recent retrospective study by the author on the effect of prearrest variables on survival following CPR were included in the analysis (M. H. Ebell, P. S. Preston, unpublished data, 1991).

The following inclusion criteria were used: study published after 1980 (data gathered after 1975), in-hospital resuscitation, retrospective or prospective design, consecutive adult patients from both the general wards and intensive care units (ICUs), and an end-point of survival to hospital discharge. To be useful for meta-analysis, studies had to report data on at least one prearrest variable such as age, diagnosis, or renal function. Studies were allowed to exclude inappropriate calls for resuscitation in which no chest compressions or rescue breathing were used, as well as patients who had syncope, seizure, or simple airway obstruction that was mistaken for cardiac arrest.

Eight studies were rejected because they did not meet the above inclusion criteria. Three used survival to either 3 or 6 months after hospital discharge as their criterion for success,[18–20] and another used excessive exclusion criteria in selecting patients for the study, such as the presence of chronic illness or malignancy.[21] Two studies only analyzed patients from the general wards in detail, and either excluded[18] or did not provide adequate information[22] for patients resuscitated in the ICUs. Another collected data from 1971 through 1976, which was too early to meet our criteria.[23] One study only recorded the rate of survival to discharge, and did not collect data on diagnosis or any other clinical variables.[24] Two studies collected data for prearrest variables but did not report specific rates of survival to discharge.[2,25] The authors of both studies were contacted and agreed to submit more detailed data so that the studies qualified to be used in the meta-analysis.

A total of 14 studies* met criteria for inclusion in the meta-analysis.[1–4,9–12,25–29] Because each study reported information about a different set of prearrest variables, the number of studies analyzed for each variable ranged from a minimum of three for renal function to a maximum of 10 for a diagnosis of cancer.

**Including M. H. Ebell, P. S. Preston, unpublished data, 1991.*

Quality Assessment

Each of the studies included in the meta-analysis consisted of a consecutive series of patients. None of the studies were blinded. Seven of the studies were prospective,[2–4,11,12,26,27] and seven* were retrospective chart reviews.[1,9,10,25,28,29] Although each study provided some information about inclusion criteria, four did not clearly state any exclusion criteria.[12,26,27,29] Regarding diagnosis, nine studies* presented survival data for all diagnoses recorded,[2,4,9,12,25–28] four only reported survival data for diagnoses with a statistically significant relationship to survival following CPR,[1,3,11,29] and one did not report any survival data by diagnosis.[10]

Statistical Analysis

Analysis was performed with the Systat 4.0 computer program.[30] A 2 × 2 table was generated for each categorical variable within each study, using survival to discharge as the outcome measured. These tables for each variable were combined using the Mantel-Haenszel statistic, which removes the effect of variability across studies. An overall probability value, as well as an odds ratio and its corresponding 95% confidence interval, were then calculated for each prearrest variable. An odds ratio where one of the cell items was equal to zero was estimated using Depid, a public-domain statistics package from the University of Michigan.

In the event that studies used different criteria to define a two-way variable, the studies that used the most common criteria were evaluated using the Mantel-Haenszel statistic. Advanced age was thus defined as age greater than 70 years, and poor renal function was defined as a serum creatinine level greater than 130 μmol/L or 200 μmol/L.

Results

The studies used in the meta-analysis are summarized in Table 1. The number of patients in each trial ranged from 48 to 470, with a total of 2643 in all 14 studies. There were twice as many men as women studied. The average age ranged from 59 to 79 years. The rate of survival to discharge following CPR ranged from 6.6% to 24.3%.

The effect of selected demographic variables is presented in Table 2. Patients older than 70 years (n = 254, P = .003, odds ratio [OR] = 1.4) and patients of dependent functional status (n = 345, P < .001, OR = 5.0) were significantly less likely to survive to discharge following CPR. Patients admitted from a nursing home were also less likely to survive, although this did not achieve statistical significance (P = .054). Only 47 nursing home patients were identified in the meta-analysis, however, which is less than the 110 necessary to avoid a type 2 error as discussed earlier. The patient's sex had no effect on survival to discharge (P=.180).

The association between renal function and left ventricular function on survival following CPR is summarized in Table 3. Each of the four studies that reported the effect of renal function found that it was a significant negative predictor of survival following CPR. Diminished renal function was significantly associated with decreased survival to discharge following CPR when defined by a serum creatinine level of > 130 μmol/L (n = 225, P < .001, OR = 5.44) as well as when defined by a serum creatinine level of >220 μmol/L (n = 106, P < .001, OR = 5.8).

Table 4 is a summary of the effect of the primary diagnosis on survival following CPR. The following diagnoses were associated with a significantly lower rate of survival: cancer (n = 276, P < .001, OR = 3.1), metastatic cancer (n = 141, P < .001, OR = 44.9), pneumonia (n=131, P < .001, OR = 2.9), and sepsis (n = 158, P < .001. OR = 6.9). A diagnosis of myocardial infarction was associated with a significantly higher rate of survival to discharge (n = 215, P = .005, OR = 0.53).

Discussion

The primary goal of this analysis was to identify prearrest variables that significantly affect the rate of survival to discharge following CPR. Dependent functional status, a serum creatinine level greater than 130 μmol/L or 220 μmol/L, the presence of cancer or metastatic cancer, age over 70 years, and primary diagnoses of sepsis and pneumonia were all associated with failure to survive to discharge following CPR. Conversely, a diagnosis of myocardial infarction was associated with an increased rate of survival to discharge following CPR.

If one accepts the premise that a survival rate of 0% is futile and does not support the use of CPR, only the diagnosis of metastatic cancer was associated with futility. However, only 141 (6.2%) of the 2285 patients who did not survive to discharge had metastatic cancer. To improve the sensitivity of predictions of failure to survive following CPR, it is therefore necessary to look at other prearrest variables, or more than one variable at a time.

One approach is to utilize the Acute Physiologic and Chronic Health Evaluation (APACHE) II score,[31] which uses easily measured clinical characteristics to generate a score reflecting the severity of illness. It may not be the

*Including M. H. Ebell, P. S. Preston, unpublished data, 1991.

Table 1. Methods Summay for Studies Included in the Meta-analysis

Study	Institutional Setting	Number of Patients	Average Age (y)	Sex	Inclusion Criteria	Exclusion Criteria
Arena et al (1980)[27]	Tertiary cancer center (New York)	48	59.1	M: 32 F: 16	Consecutive adult patients	None noted
Bedell et al (1983)[3]	University hospital (Boston)	294	70.0	M: 164 F: 134	Consecutive adult patients (wards, ICUs, ER)	CPR before admission to hospital, subsequent arrests
Scaff et al (1984)[25]	Large community hospital (Corpus Christi, Texas)	242	NR	NR	Consecutive adult patients (wards, ICUs)	CPR in OR, ER
Sowden et al (1984)[12]	Acute care hospitals (2) (Bristol, England)	108	65.8	M: 83 F: 25	Consecutive adult patients	None noted
Kelly et al (1986)[11]	District general hospital (Worcester, England)	62	NR	M: 39 F: 23	Consecutive adult patients (wards, ICUs)	Inappropriate calls, ie, patient not pulseless or apneic (2)
Urberg and Ways (1987)[9]	Large community hospital (Detroit)	121	67.5	M: 63 F: 58	Consecutive adult patients (wards, ICUs)	CPR in OR, ER, or catheterization laboratory
Taffet et al (1988)[1]	Veterans hospital (Houston)	329	62.6	M: 327 F: 2	Consecutive adult patients (wards, ICUs, ER if arrived in prearrest state)	CPR in OR
Rozenbaum and Shenkman (1988)[26]	General hospital (Kfar Saba, Israel)	71	67	M: 42 F: 29	Consecutive adult patients (internal medicine ward, medical ICU)	None noted
George et al (1989)[2]	Large teaching hospital (Nashville)	140	NR	M: 91 F: 49	Consecutive adult patients (wards, ICUs)	CPR in OR, ER, or catheterization laboratory
Keatinge (1989)[29]	General hospital (London, England)	156	NR	M: 107 F: 49	Consecutive adult patients (age >16 y, wards, ICUs)	None noted
Murphy et al (1989)[10]	University and community hospitals (5) (Boston)	259	79	M: 108 F: 151	Consecutive adult patients (age >69 y, wards, ICUs, ER if seen by physician)	Syncope, seizure, airway obstruction from food, elective intubation
Tortolani et al (1990)[28]	University hospital (Manhasset, New York)	470	68.3	M: 276 F: 194	Consecutive adult patients (wards, ICUs, ER)	Uncomplicated respiratory arrest, syncope, patients with multiple arrests (49)
Lazzam and McCans (1991)[4]	University hospital	125	NR	M: 83 F: 42	Consecutive adult patients (wards, ICUs, ER, OR)	None noted
Ebell and Preston (unpublished data, 1991)	Community hospital (Athens, Georgia)	218	68.1	M: 133 F: 85	Consecutive adult patients (wards, ICU, initial arrest only)	Inappropriate calls, ER, OR

CPR denotes cardiopulmonary resuscitation; ICU, intensive care unit; ER, emergency room; NR, not reported; OR, operating room.

best predictor of survival following CPR, however, since it does not adequately take into account either the diagnosis or the patient's physiologic reserve. Additionally, it includes variables such as temperature and heart rate, which have not been shown to predict survival following CPR. The advantage of the APACHE II score is that it is widely used, and may therefore be available for clinical decision making. The recently developed APACHE III score may be a better predictor of individual patient outcome, although its relationship to survival following CPR has not been evaluated.[32]

An instrument specifically designed to predict failure to survive following CPR has been developed by George and colleagues.[2] The Pre-Arrest Morbidity (PAM) index evaluates the severity of illness of patients before cardiopulmonary arrest, and assigns a value of 1 or 3 points to each of 15 clinical characteristics (Table 5). A score greater than 8 was not compatible with survival following CPR in the authors' experience with 140 patients.

The clinical characteristics selected for inclusion in the PAM index were based largely on the study by Bedell and colleagues[3] and the clinical experience of George et al. Based on the results of this meta-analysis, I would suggest a simplified scheme, with the elimination of some variables that were not found to be significantly associated with survival to discharge following CPR, and with increased weight given to factors that are associated with especially low rates of survival (Table 5). Using the odds

Table 2. Effect of Selected Demographic Variables on Survival to Discharge Following Cardiopulmonary Resuscitation

	Survival Rate Following CPR Number (% Surviving to Time of Discharge)								
Study	All Paitents	Age < 70 y	Age ≥ 70 y	Female Patients	Male Patients	Dependent Functional Status	Independent Functional Status	Nursing Home Resident	Lives at Home
Arena et al (1980)[27]	48 (14.6)	NR	NR	NR	NR	NR	NR	NR	NR
Bedell et al (1983)[3]	294 (13.9)	NR	NR	134 (19.4)	160 (9.4)	137 (4.4)	128 (27.3)	NR	NR
Scaff et al (1984)[25]	242 (14.0)	NR	NR	NR	NR	NR	NR	NR	NR
Sowden et al (1984)[12]	108 (21.3)	NR	NR	25 (16.0)	83 (22.9)	NR	NR	NR	NR
Kelly et al (1986)[11]	62 (17.7)	NR	NR	NR	NR	NR	NR	NR	NR
Urberg and Ways (1987)[9]	121 (10.7)	NR	NR	58 (10.3)	63 (11.1)	62 (3.2)	59 (18.6)	31 (3.2)	90 (13.3)
Taffet et al (1988)[1]	329 (6.7)	261 (8.0)	68 (0.0)	2 (0.0)	327 (6.4)	NR	NR	NR	NR
Rozenbaum and Shankman (1988)[26]	71 (18.3)	NR	NR	29 (10.3)	42 (23.8)	NR	NR	NR	NR
George et al (1989)[2]	140 (24.3)	75 (29.3)	65 (18.5)	49 (26.5)	91 (23.1)	33 (12.1)	107 (28.0)	2 (50.0)	138 (23.9)
Keatinge (1989)[29]	156 (10.9)	NR	NR	NR	NR	38 (0.0)	102 (16.7)	NR	NR
Murphy et al (1989)[10]	259 (6.6)	NR	NR	NR	NR	56 (5.4)	149 (8.1)	NR	NR
Tortolani et al (1990)[28]	470 (14.7)	NR	NR	194 (17.5)	276 (12.3)	NR	NR	NR	NR
Lazzam and McCans (1991)[4]	125 (18.4)	NR	NR	42 (21.4)	83 (16.9)	19 (5.3)	105 (20.9)	NR	NR
Ebell and Preston (unpublished data, 1991)	218 (15.6)	97 (19.6)	121 (12.4)	85 (12.9)	133 (17.3)	NR	NR	14 (0.0)	204 (16.7)
All studies (%)	2643 (13.5)	<70 y: 62/433 (14.3) ≥70 y: 27/254 (10.6)		Female: 106/618 (17.1) Male: 164/1258 (13.0)		Dependent: 16/345 (4.6) Independent: 127/650 (19.5)		NH: 2/47 (4.3) Not in NH: 49/432 (11.3)	
Mantel-Haenszel test		$P = .003$		$P = .180$		$P < .001$		$P = .054$	
Odds ratio (95% CI)		1.41 (.87–2.27)		1.38 (1.06–1.80)		4.99 (2.92–8.55)		5.67 (1.35–23.83)	

CPR denotes cardiopulmonary resuscitation; NR; not reported; NH, nursing home; CI, confidence interval.

Table 3. Effect of Selected Clinical Variables on Survival to Discharge Following Cardiopulmonary Resuscitation

Study	Renal Function (Serum Creatinine Before Arrest, Survivors/Total)	Renal Function (Serum Creatinine Before Arrest, Survivors/Total)	Left Ventricular Function
Bedell et al (1983)[3]	NR	>220 μmol/L: 3/64 ≤220 μmol/L: 38/214	On admission: NYHA class I or II: 14/25 NYHA class III or IV: 7/88 ($P < .001$)
Murphy et al (1989)[10]	>130 μmol/L: 0/96 ≤130 μmol/L: 15/108	NR	NR
Lazzam and McCans (1991)[4]	>130 μmol/L: 3/47 ≤130 μmol/L: 17/54	NR	NR
Ebell and Preston (unpublished data, 1991)	>130 μmol/L: 7/82 ≤130 μmol/L: 27/130	>220 μmol/L: 1/42 ≤220 μmol/L: 33/170	Echocardiography within 3 months before cardiac arrest: Ejection fraction < 0.35: 6/24 Ejection fraction ≥ 0.35: 17/58 ($P = .620$)
Aggregate results (%)	>130 μmol/L: 10/225 (4.4) ≤130 μmol/L: 59/292 (20.2)	>220 μmol/L: 4/106 (3.8) ≤220 μmol/L: 71/384 (18.5)	Unable to analyze
Mantel-Haenszel test	$P < .001$	$P < .001$	
Odds ratio (95% CI)	5.44 (2.72–10.91)	5.78 (2.06–16.23)	

Note: 130 μmol/L = 1.5 mg/dL and 220 μmol/L = 2.5 mg/dL.
NR denotes not reported; NYHA, New York Heart Association (classification of heart disease); CI, confidence interval.

Table 4. Effect of Selected Diagnoses on Survival to

Study	Cancer		Metastatic Cancer		Survival Rate Following CPR, Cardiovascular Disease*	
	Yes	No	Yes	No	Yes	No
Arena et al (1960)[27]	45 (15.6)	3 (0.0)	23 (0.0)	25 (28.0)	NR	NR
Bedell et al (1983)[3]	59 (6.8)	236 (15.7)	NR	NR	165 (20.6)	118 (5.9)
Scaff et al (1984)[25]	4 (25.0)	238 (13.9)	3 (0.0)	239 (14.2)	60 (23.3)	196 (10.2)
Sowden et al (1984)[12]	11 (0.0)	97 (23.7)	NR	NR	80 (25.0)	28 (10.7)
Kelly et al (1986)[11]	7 (0.0)	55 (20.0)	NR	NR	NR	NR
Urberg and Ways (1987)[9]	8 (0.0)	113 (11.5)	NR	NR	66 (15.1)	55 (5.4)
Taffet et al (1988)[1]	89 (0.0)	240 (8.7)	63 (0.0)	266 (7.9)	NR	NR
Rozenbaum and Shenkman (1988)[26]	5 (0.0)	66 (19.7)	5 (0.0)	66 (19.7)	NR	NR
George et al (1989)[2]	16 (18.7)	123 (25.2)	NR	NR	98 (11.2)	42 (5.5)
Keatinge (1989)[29]	NR	NR	21 (0.0)	135 (12.6)	NR	NR
Tortolani et al (1990)[28]	NR	NR	NR	NR	231 (13.0)	239 (15.9)
Lazzam and McCans (1991)[4]	NR	NR	NR	NR	70 (27.1)	47 (6.4)
Ebell and Preston (unpublished data, 1991)	32 (3.1)	186 (17.7)	26 (0.0)	192 (17.7)	65 (21.5)	153 (13.1)
All studies (%)	Yes: 16/276 (5.8) No: 215/1356 (15.8)		Yes: 0/141 (0) No: 126/923 (13.6)		Yes: 152/835 (18.2) No: 117/878 (13.3)	
Mantel-Haenszel test	$P < .001$		$P < .001$		$P = .030$	
Odds ratio (95% CI)	3.08 (1.82–5.20)		44.9 (9.53–211.5)		.69 (.53–.90)	

**Cardiovascular disease: myocardial infarction, congestive heart failure, unstable angina, admission to rule out myocardial infarction, valvular disease, arrhythmia, and pericardial effusion.*

NOTE: In all studies with the exception of Bedell, Kelly, Taffet, and their colleagues, and Keatinge, survival for all major diagnostic categories was reported. In the aforementioned four studies, survival data were reported only for diagnoses with a statistically significant relationship between diagnosis and survival to discharge following CPR (cardiopulmonary resuscitation). NR denotes not reported; CI, confidence interval.

ratio for each variable as a general guideline and simplifying the scale where possible, metastatic cancer is assigned 10 points, dependent functional status and a diagnosis of sepsis are assigned 5 points each, a serum creatinine greater than 130 μmol/L and diagnoses of cancer and pneumonia are assigned 3 points each, and age over 70 years is assigned 2 points. Since patients admitted with a diagnosis of myocardial infarction had a higher rate of survival to discharge, this characteristic is assigned a negative value of −2 points. The maximum possible score is 25 points (only the primary admitting diagnosis was used, and the presence or absence of malignancy was considered in addition to the admitting diagnosis).

The original PAM index identified 24 of 106 nonsurvivors in the study by George and co-workers,[2] a sensitivity of 22%. The modified PAM index described above was applied to the group of 218 patients studied by the author (M. H. Ebell, P. S. Preston, unpublished data, 1991), and identified 37 patients (20.1%) with a score greater than 8, none of whom survived. To validate the modified PAM index and to determine whether it is more sensitive and specific than the original, both must be tested on an independent set of data, ideally in a prospective fashion.

As in any meta-analysis, subtle differences in the patient populations and selection criteria can affect the validity of the results. For example, none of the studies established specific diagnostic criteria. Future studies should endeavor to be more specific regarding inclusion and exclusion criteria, and more carefully define the variables studied.

A common criticism of meta-analysis is the so-called file drawer effect first articulated by Rosenthal.[33] Since there is a tendency for journals to publish trials with positive results, it is theorized that studies that detect negative results have a tendency to end up in the researcher's file drawer. One way to address this problem is to calculate the number of unpublished studies with negative results needed to nullify the results of the meta-analysis.[34] This calculation was performed for each prearrest variable found to be significantly associated with a decreased rate of survival to discharge following CPR: serum creatinine >130 μmol/L (24 unpublished negative studies needed), dependent functional status (43 studies), age >70 years (4 studies), cancer (60 studies), metastatic cancer (23 studies), pneumonia (23 studies) and myocardial infarction (103 studies).

Another limitation of the technique of meta-analysis is that it is confined to univariate analysis. Multivariate analysis of the data from a large patient population could assist in further refining or validating the modified PAM index, although such a study would be quite difficult owing to the relative rarity of the event (CPR) being studied.

Discharge Following Cardiopulmonary Resuscitation

Number (% Surviving to Time of Discharge)									
Myocardial Infarction		Respiratory Disease†		Pneumonia		Sepsis		Neurologic Disease ††	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	NR	NR	58 (0.0)	236 (17.4)	42 (0.0)	243 (16.0)	NR	NR
NR	NR	13 (15.4)	231 (13.9)	5 (0.0)	237 (14.3)	NR	NR	4 (25.0)	238 (13.9)
69 (26.1)	39 (12.8)	7 (28.6)	101 (20.8)	4 (50.0)	104 (20.2)	2 (0.0)	60 (18.3)	8 (0.0)	100 (23.0)
27 (29.6)	35 (8.6)	NR	NR	NR	NR	NR	NR	3 (0.0)	59 (18.6)
23 (26.1)	98 (7.1)	6 (16.7)	115 (10.4)	6 (16.7)	115 (10.4)	15 (6.7)	106 (11.3)	0 (0.0)	121 (10.7)
NR	NR	NR	NR	NR	NR	73 (1.4)	256 (7.8)	NR	NR
41 (22.0)	30 (13.3)	NR	NR	4 (0.0)	67 (19.4)	4 (0.0)	67 (19.4)	NR	NR
37 (18.9)	103 (26.2)	57 (17.5)	83 (28.9)	24 (16.7)	111 (27.0)	14 (7.1)	123 (26.8)	8 (25.0)	132 (24.2)
NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
NR	NR	116 (17.2)	354 (13.6)	NR	NR	NR	NR	29 (20.7)	441 (14.1)
NR	NR	NR	NR	9 (0.0)	116 (19.8)	NR	NR	NR	NR
18 (27.8)	200 (14.5)	39 (10.3)	179 (16.8)	21 (9.5)	197 (16.2)	8 (12.5)	214 (15.9)	9 (11.1)	209 (15.8)
Yes: 53/215 (24.6) No: 75/505 (14.8)		Yes: 39/238 (16.4) No: 167/1063 (15.7)		Yes: 9/131 (6.9) No: 206/1183 (17.4)		Yes: 4/158 (2.5) No: 161/1065 (15.1)		Yes: 10/61 (16.4) No: 217/1237 (17.5)	
$P = .005$		$P = .738$		$P < .001$		$P < .001$		$P = .90$	
.53 (.36–.79)		.98 (.66–1.43)		2.86 (1.43–5.72)		6.86 (2.51–18.76)		.96 (.48–1.93)	

†Pulmonary disease: pneumonia, pneumothorax, chronic obstructive pulmonary disease, asthma, cystic fibrosis, pulmonary embolism. ††Neurological disease: cerebrovascular accident, intraventricular hemorrhage, other neurologic diagnosis.

Table 5. Suggested Modifications to the Pre-Arrest Morbidity (PAM) Index

Clinical Characteristic	Original PAM Index	Modified PAM Index
Malignancy	3	
Metastatic	—	10
Nonmetastatic	—	3
Sepsis*	1	5
Dependent functional status	3	5
Pneumonia*	3	3
Creatinine > 130 μmol/L†	3	3
Age > 70 y	—	2
Acute myocardial infarction*	1	−2
Hypotension (systolic ≤ 90 mm Hg)	3	—
Heart failure (NYHA class III or IV)	1	—
Angina pectoris	1	—
S3 gallop	1	—
Oliguria (<300 mL/d)	1	—
Mechanical ventilation	1	—
Recent cerebrovascular event	1	—
Coma	1	—
Cirrhosis	1	—

Note: Patients with a score greater than 8 are unlikely to survive to discharge following cardiopulmonary resuscitation.
**Admitting diagnosis.*
†130 μmol/L = 1.5 mg/dL.
NYHA denotes New York Heart Asociation (classification of heart disease).

Conclusions

The identification of prearrest variables that are associated with a decreased rate of survival to discharge following CPR will assist clinicians when they counsel their patients regarding DNR orders. Furthermore, the development of a predictive tool such as the modified PAM index can help identify a subset of patients for whom CPR is futile. Physicians have no obligation to submit patients to futile medical interventions, as Faber-Langendoen eloquently argued in her essay on the attempted resuscitation of patients with metastatic cancer.[5] When a physician decides that it is appropriate to withhold the medical intervention of CPR because it is futile, that decision should be communicated to the patient or the family or both in a compassionate, timely, and sensitive manner. The patient and family should especially be assured that the decision to withhold CPR does not affect other decisions about the patient's medical care, and that the patient's comfort needs will always be met. In the event of a conflict between the medical team and patient or family that cannot be resolved by further discussion, it is recommended that care be transferred to another physician or medical team.

Further work remains to be done to improve the sensitivity of predictive instruments such as the modified PAM index, and to validate them on independent data sets. Such studies require an adequate number of patients to avoid a type 2 error, should be prospective in design, and should carefully define diagnoses and other prearrest variables for maximum reproducibility. Once validated, such a predictive instrument will be a valuable adjunct to the DNR-order decision-making process.

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References

1. Taffet GE, Teasdale TA, Luchi RJ. In-hospital cardiopulmonary resuscitation. JAMA 1988; 260:2069–72.
2. George AL, Folk BP, Crecelius PL, Campbell WB. Pre-arrest morbidity and other correlates of survival after in-hospital cardiopulmonary arrest. Am J Med 1989; 87:28–34.
3. Bedell SE, Delbanco TL, Cook EF, Epstein FH. Survival after cardiopulmonary resuscitation in the hospital. N Engl J Med 1983; 309:569–75.
4. Lazzam C, McCans JL. Predictors of survival of in-hospital cardiac arrest. Can J Cardiol 1991; 7:113–6.
5. Faber-Langendoen K. Resuscitation of patients with metastatic cancer: is transient benefit still futile? Arch Intern Med 1991; 151:235–9.
6. Young MJ, Bresnitz EA, Strom BL. Sample size nomograms for interpreting negative clinical studies. Ann Intern Med 1983; 99: 248–51.
7. Arkin CF, Wachtel MS. How many patients are necessary to assess test performance. JAMA 1990; 263:275–8.
8. Takeda Y, Mifune J, Taga K, et al. Survival after sudden cardiac arrest in hospital. Jpn Heart J 1989; 30:645–53.
9. Urberg M, Ways C. Survival after cardiopulmonary resuscitation for an in-hospital cardiac arrest. J Fam Pract 1987; 25:41–4.
10. Murphy DJ, Murray AM, Robinson BE, Campion EW. Outcomes of cardiopulmonary resuscitation in the elderly. Ann Intern Med 1989; 111:199–205.
11. Kelly CA, Watson D, Hutchinson CM, Pole JM. Prognostic factors in cardiac arrest occurring in a district general hospital. Br J Clin Pract 1986; 40:251–3.
12. Sowden GR, Robins DW, Baskett PJ. Factors associated with survival and eventual cerebral status following cardiac arrest. Anesthesia 1984; 39:39–43.
13. Sacks HS, Berrier J, Reitman D, Ancona-Berk VA, Chalmers TC. Meta-analysis of randomized controlled trials. N Engl J Med 1987; 316:450–5.
14. Cunningham AS. Meta-analysis and methodology review: what's in a name? J Pediatr 1988; 113:328–9.
15. Imperiale TF, Petrulis AS. A meta-analysis of low-dose aspirin for the prevention of pregnancy-induced hypertensive disease. JAMA 1991; 266:260–4.
16. Steinberg KK, Thacker SB, Smith SJ, et al. A meta-analysis of the effect of estrogen replacement therapy on the risk of breast cancer. JAMA 1991; 265:1985–90.
17. Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomized trials. Prog Cardiovasc Dis 1985; 27:335–71.
18. Bayer AJ, Ang BC, Pathy MS. Cardiac arrests in a geriatric unit. Age Ageing 1985; 14:271–6.
19. Skovron ML, Goldberg E, Suljaga-Petchel K. Factors predicting survival for six months after cardiopulmonary resuscitation: multivariate analysis of a prospective study. Mt Sinai J Med 1985; 52:271–5.
20. Suljaga-Petchel K, Goldberg E, Strickon P, Berger M, Skovron ML. Cardiopulmonary resuscitation in a hospitalized population: prospective study of a factors associated with outcome: Resuscitation 1984; 12:77–95.
21. Gulati RS, Bhan GL, Horan MA. Cardiopulmonary resuscitation in old people. Lancet 1983; 2:267–9.
22. Hershey CO, Fisher L. Why outcome of cardiopulmonary resuscitation in general wards is poor. Lancet 1982; 2:31–4.
23. DeBard ML. Cardiopulmonary resuscitation: analysis of six years' experience and review of the literature. Ann Emerg Med 1981; 10:408–16.
24. Dans PE, Nevin KL, Seidman CE, McArthur JC, Kariya ST. Inhospital CPR 25 years later: why has survival decreased? South Med J 1985; 78:1174–8.
25. Scaff B, Munson R, Hastings DF. Cardiopulmonary resuscitation at a community hospital with a family practice residency. J Fam Pract 1984; 18:561–5.
26. Rozenbaum EA, Shenkman L. Predicting outcome of in-hospital cardiopulmonary resuscitation. Crit Care Med 1988; 16:583–6.
27. Arena FP, Perlin M, Turner AD. Initial experience with a "code–no code" resuscitation system in cancer patients. Crit Care Med 1980; 8:733–6.
28. Tortolani AJ, Risucc DA, Rosati RJ, Dixon R. In-hospital cardiopulmonary resuscitation: patient, arrest and resuscitation factors associated with survival. Resuscitation 1990; 20:115–28.
29. Keatinge RM. Exclusion from resuscitation. J R Soc Med 1989; 82:402–5.
30. Systat: the system for statistics for the PC. Sherman Ill: Systat Inc., 1989.
31. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985; 13:818–29.
32. Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991; 100:1619–36.
33. Rosenthal R. The 'file drawer problem' and tolerance for null results. Psychol Bull 1979; 86:638–41.
34. Rosenthal R. Judgement studies: design, analysis and meta-analysis. Cambridge, England: Cambridge University Press, 1987: 223–5.