ORIGINAL ARTICLES

Predicting Survival from In-hospital CPR:

Meta-analysis and Validation of a Prediction Model

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Objective: To better clarify patient factors that predict survival from in-hospital cardiopulmonary resuscitation (CPR), using two methods: 1) meta-analysis and 2) validation of a prediction model, the pre-arrest morbidity (PAM) index.
Design: Meta-analysis of previously published studies by standard techniques. Retrospective chart review of validation sample.
Setting: University-affiliated teaching hospital.
Patients/participants: Meta-analytic sample of 21 previous studies from 1965–1989. The validation sample consisted of all patients surviving resuscitation from the authors' hospital during the period September 1986 to January 1991. A matched sample of patients who did not survive from the same time period was used as the comparison group.
Interventions: None.
Measurements and main results: The strongest negative predictors of survival, by meta-analysis, were renal failure ($r = 0.088$, $p < 0.0002$), cancer ($r = 0.08$, $p < 0.0002$), and age more than 60 years ($r = 0.063$, $p < 0.006$). Sepsis ($r = 0.046$, $p < 0.02$), recent cerebrovascular accident (CVA) ($r = 0.038$, $p < 0.04$), and congestive heart failure (CHF) class III/IV ($r = 0.036$, $p < 0.05$) were weaker negative predictors. Presence of acute myocardial infarction (AMI) was a significant positive predictor of survival ($r = 0.15$, $p < 0.0001$). The PAM score was highly predictive of survival in a logistic regression model ($p < 0.0003$, $R^2 = 9.6\%$). No patient who survived to discharge had a PAM score higher than 8.
Conclusion: Meta-analysis reveals that the most significant negative predictors of survival from CPR are renal failure, cancer, and age more than 60 years, while AMI is a significant positive predictor. The PAM index is a useful method of stratifying probability of survival from CPR, especially for those patients with high PAM scores, who have essentially no chance of survival.
Key words: cardiopulmonary resuscitation; meta-analysis; pre-arrest morbidity index; survival; prediction.
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SINCE the description of closed-chest cardiac massage in 1960,[1] the scope and techniques of cardiopulmonary resuscitation (CPR) and advanced cardiac life support have undergone many changes. Originally intended as a life-saving technique for those suffering sudden cardiac collapse, its use has extended to a much wider spectrum of hospitalized patients. Unlike other invasive techniques, CPR need not be ordered by a physician; rather, the withholding of this procedure requires explicit and detailed documentation and planning by the medical personnel.[2-10] Because of the medical, emotional, and legal implications of either performing or withholding CPR inappropriately, it is extremely important to determine which patients receive the most benefit from this technique. Recently several studies have attempted to construct prediction models toward this end.[11,12]

During the past 25 years, numerous other investigators, in varied settings, have evaluated outcomes from CPR.[13-18] Studies examining in-hospital CPR have generally found a low percentage of survivors to discharge, ranging from 3.8% to 24%.[19-43] Although the reasons for low survival from CPR are complex and not entirely understood, it is possibly due in part to inappropriate selection of patients who receive in-hospital CPR. It has been suggested that certain patient groups, for example, those with cancer, those with pneumonia, and the elderly, have a negligible chance of survival and should not be offered CPR.[31,44,45] However, due to variations in patient population, variations in definitions, and the low number of survivors in general, findings have not been consistent across studies,[44,46-48] and generalizable recommendations have been difficult to make.[6-8,10,49,50]

In 1983, Bedell et al.[45] reported a carefully controlled, prospective study on this tropic. From this study, 15 patient factors were identified that had a significant relationship to survival from in-hospital CPR. Building on these results, George et al.[51] developed the pre-arrest morbidity (PAM) index, a composite score based on factors that can be identified prior to cardiac arrest and designed to stratify patients as to their likelihoods of being discharged from the hospital alive. The PAM index individually evaluates 14 patient morbidities, each assigned a specific point score, in order to arrive at a single value that reflects PAM. George et al.[51] showed that the PAM index was predictive of survival from CPR. Use of the PAM index, if valid, could be a very helpful adjunct in deciding whether to perform CPR.

This study seeks to further define and quantify characteristics of hospitalized patients that predict success or failure from CPR. We first chose 15 patient variables that prior research suggested might influence outcome from in-hospital CPR.[45,51] These included the 14 variables from the PAM index plus age. Next, we

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TABLE 1

Predictor Variables (Weights in Pre-arrest Morbidity Index)

- Age > 60 years (0)
- Malignancy (3)
- Pneumonia (3)
- Homebound lifestyle (3)
- Azotemia (3)
- Hypotension (3)
- Angina (1)
- Oliguria (1)
- Sepsis (1)
- Congestive heart failure class III/IV (1)
- Acute myocardial infarction (1)
- Coma (1)
- Cirrhosis (1)
- Cerebrovascular accident (recent) (1)
- Mechanical ventilation (1)

conducted a meta-analysis of 21 studies that considered some or all of the 15 patient variables in order to determine to what extent each variable predicts success or failure from CPR. Finally, we validated the PAM index as a predictive instrument using a sample of patients from our hospital.

METHODS

Table 1 lists the 15 variables chosen for our meta-analysis and the number of points that each receives in the computation of the PAM index. Age was not scored in the original PAM study because the authors felt that age was not an independent predictor of outcome, but rather was highly correlated with other morbidities. All of these variables can be assessed prior to an arrest.

MEDLINE was searched using the key word *resuscitation* from 1965 to the present in the English-language database. Bibliographies from 38 articles in our possession were also searched for relevant citations. Any article that contained raw data for survival to discharge, or from which the raw data could be calculated for at least one predictor variable listed in Table 1, was included in the study. Twenty-one studies, representing a total of more than 7,500 patients, met these criteria. Not every study used in the meta-analysis contained all 15 patient factors. For example, data for mechanical ventilation, cirrhosis, coma, and oliguria were available from only one study, and therefore were not eligible for meta-analysis. Two variables, homebound lifestyle and hypotension, did not meet the criteria for homogeneity.[52] Although age more than 65 years was used in the original formation of the PAM index, age was found to be stratified by decade in most other studies. The cutoff used for this meta-analysis was age more than 60 years.

The meta-analysis was conducted according to standard techniques.[52] We employed the product-moment correlation coefficient (r) as our estimate of effect size. Combined effect sizes were calculated using Stouffer's procedure. Each variable was tested for homogeneity, and failsafe values were computed. The failsafe value indicates the number of studies with opposite effect that would invalidate the results shown.

Quality reviews of all 21 studies were conducted by two board-certified internists (GJM and MJA) who were blinded to both author and journal. Both internists independently rated the studies, using a nine-point Likert scale ranging from "highest quality" (1) to "lowest quality" (9), on seven quality criteria. Study characteristics rated were: 1) design of study clearly defined; 2) definition of CPR clear and logical; 3) inclusion and/or exclusion criteria for individual patients clearly defined; 4) patient factors (e.g., age, cancer, renal failure) clearly defined; 5) sample size sufficient to support conclusions made; 6) study group generalizable to other medical centers; and 7) overall quality. The interrater reliability of the quality ratings was calculated by the Pearson correlation.

To determine whether the results of poorly designed studies had influenced the overall results obtained, meta-analysis of the 11 studies that received the highest-quality scores was then conducted. These results were compared with results from the meta-analysis of all 21 studies. The results reported refer to those obtained from analysis of all 21 studies.

To validate the PAM index, a list of all patients who received resuscitation charges after admission to a large Midwestern university-affiliated hospital from September 1986 to January 1991 was obtained from the automated billing records of the study hospital. All charts for patients who received resuscitation charges and survived to discharge were reviewed, and an assessment of whether the application of "immediate life-sustaining resuscitation" had occurred was made. For the purpose of PAM validation, the definition of immediate life-sustaining resuscitation was that death would be imminent, within minutes, if life support were not instituted. This definition was felt to more accurately reflect the application of life-sustaining treatment than would other definitions of CPR. As in the original PAM study, patients requiring only electrical countershock for the conversion of ventricular tachyarrythmias or ventricular fibrillation were excluded.

These charts were then abstracted in accordance with the method described by George et al.[51] and PAM scores were obtained. Each survivor was then randomly matched by year with a patient who received CPR but did not survive to discharge. Matching by year was done to compensate for potential temporal differences in the deliveries of CPR. The PAM score was also obtained for the matched control patient.

RESULTS

Meta-analysis

Table 2 provides a summary of the studies included in the meta-analysis. A wide variety of study types, medical centers, and factors examined are included, spanning a large time period. There is approxi-

TABLE 2

Studies Included in the Meta-analysis

Study*	Year	Institution	No. Patients	Factors Examined	Quality Score†	Percentage of Survival to Discharge
Broadhurst et al.[25]	1963	Royal Victoria Hospital, Montreal	126	Renal failure, acute myocardial infarction (AMI), age	6.5	13.5
Stemmler[28]	1965	Hospital of the University of Pennsylvania, Philadelphia	103	Coronary artery disease (CAD), AMI, age	7.0	4.9
Johnson et al.[34]	1967	Royal Victoria Hospital, Montreal	552	Pneumonia, malignancy, renal failure, CAD	6.0	14.9
Saphir[21]	1968	Buffalo General Hospital	123	Renal failure, sepsis, congestive heart failure (CHF), AMI, age, cerebrovascular accident (CVA)	6.5	8.0
Hollingsworth[23]	1969	University of Virginia Hospital, Charlottesville	368	Pneumonia, renal failure, CAD, sepsis, CVA	5.5	8.2
Stiles et al.[39]	1971	Hospital of the Good Samaritan, Los Angeles	302	Pneumonia, malignancy, sepsis, CHF, AMI, CVA	7.0	15.0
Wildsmith et al.[38]	1972	Edinburgh Royal Infirmary	536	Age		11.9
Tweed et al.[27]	1980	Health Science Center, Winnipeg, Manitoba	971	CAD, age	5.0	12.5
Peatfield et al.[37]	1977	Central Middlesex Hospital, Great Britain	1,063	Pneumonia, malignancy, sepsis, CHF, AMI, CVA	7.0	8.7
Coskey[36]	1978	St. Joseph Hospital, Burbank, California	1,155	AMI	6.0	24.0
Debard[19]	1981	St. Elizabeth Medical Center, Dayton, Ohio	925	Pneumonia, CAD, CVA	3.5	24.0
Scott[30]	1981	Radcliff Infirmary, Oxford	78	AMI, age	5.0	14.0
Gulati et al.[33]	1983	Oldham General Hospital, Great Britain	52	Homebound lifestyle, age	6.0	17.3
Bedell et al.[45]	1983	Beth Israel Hospital, Boston	294	Pneumonia, malignancy, homebound lifestyle, renal failure, hypotension, CAD, sepsis, CHF, age, CVA	1.5	14.0
Scaff et al.[22]	1984	Memorial Medical Center, Corpus Christi, Texas	242	Age	5.0	14.0
Sowden et al.[29]	1984	Frenchey Hospital, Bristol, Great Britain	108	Pneumonia, malignancy, sepsis, CHF, AMI, CVA	6.0	21.3
Skovron et al.[35]	1985	Beth Israel Medical Center, New York	208	CAD	4.0	12.0
Kelly et al.[32]	1986	Newcastle General Hospital, Great Britain	62	Malignancy, renal failure, hypotension	5.5	18.0
Urberg and Ways[24]	1987	Grace Hospital, Detroit	121	Pneumonia, malignancy, homebound lifestyle, CHF, AMI	4.5	11.0
Taffet et al.[20]	1988	VA Medical Center, Houston	329	Malignancy, sepsis, age	3.5	16.0
Murphy et al.[31]	1989	Hebrew Rehabilitation Center for Aging, Boston	503	Homebound lifestyle, renal failure	4.0	3.8

*For complete reference citations, see the reference list.
†Computed as the mean of two independent reviewers' judgments of overall quality of study design on a 1–9 scale (1 = highest quality, 9 = lowest quality).

TABLE 3
Meta-analysis Results

	Number of Studies	Combined r	p<	Failsafe N
Azotemia	6	−0.088	0.0001	24
Cancer	8	−0.080	0.0002	29
Age > 60 years	9	−0.063	0.006	13
Sepsis	7	−0.046	0.02	4
Cerebrovascular accident	7	−0.038	0.04	2
Congestive heart failure	7	−0.036	0.05	1
Acute myocardial infarction	7	0.149	0.0001	80
Pneumonia	6	0.032	0.0002	1
Coronary artery disease	5	0.032	0.14	3
*Hypotension	2	−0.137	0.0005	6
*Homebound lifestyle	4	−0.126	0.0001	1

*Failed to meet homogeneity criteria.

mately a sixfold difference in the percentages of survivors to discharge among the studies examined.

Table 3 contains a summary of the meta-analysis results. Combined r represents the strength of effect, which is a measure of how strongly the factor of interest was related to outcome. A negative value for combined r predicts death and a positive value predicts discharge alive from the hospital. Azotemia, cancer, and age more than 60 years were the strongest predictors of negative outcome, followed by sepsis, cerebrovascular accident (CVA), and congestive heart failure (CHF). The presence of an acute myocardial infarction (AMI) correlated relatively strongly with survival. Pneumonia was significantly associated with survival, although with a smaller r and a low failsafe. This low failsafe value of 1 indicates a weak association, in that a single study with opposite results would neutralize the findings obtained here. Hypotension and lifestyle, although not meeting the criteria for homogeneity, showed a strong tendency toward predicting an unfavorable outcome.

Blinded quality reviews of all studies were tabulated as described previously. The quality scores reported in Table 2 represent the mean of the two reviewers' scores for overall quality, ranging from 1 (highest) to 9 (lowest). The interrater reliability of the quality ratings was $r = 0.73$, $p < 0.001$. Meta-analysis was repeated using only studies receiving moderate to high quality ratings (11 studies, quality score cutoff = 5.5). Using only these high-quality studies, similar results were obtained, and in general the strength of effect was increased.

Validation of PAM Index

The PAM index was calculated for 43 patients receiving CPR who survived to hospital discharge and 43 who did not survive. Figure 1 shows the distributions of the PAM indexes by discharge status. Although there is substantial overlap between the two groups, at the low end there is a larger proportion of patients who survived, while at the high end of the scale, a threshold is reached where all of the patients died. The mean overall PAM score was 4.5 (SD = 3.0). Those patients who were discharged alive had a mean PAM score of 3.4 (SD = 2.0), while those who died had a mean of 5.9 (SD = 3.2). The difference between means of these

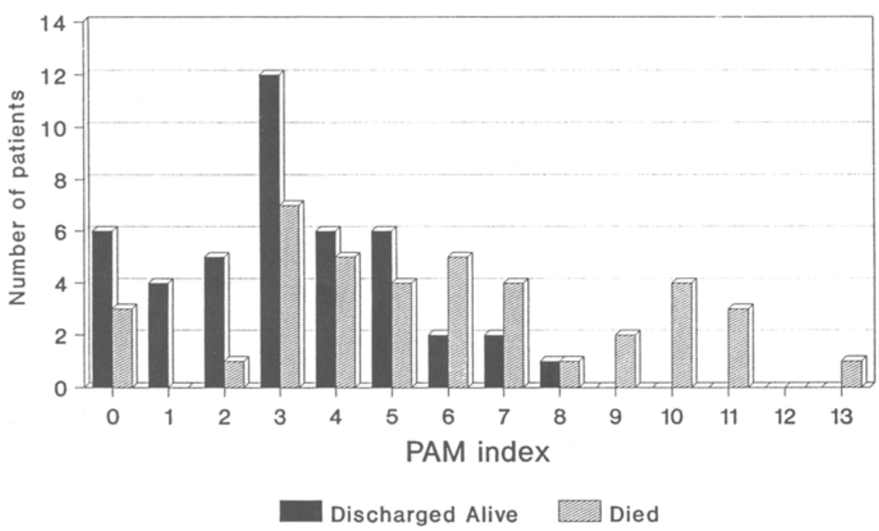

FIGURE 1. Pre-arrest morbidity (PAM) index distribution by discharge status.

two independent groups is statistically significant by t-test ($p < 0.001$).

To further examine PAM's ability to predict outcome from CPR, we used a logistic regression model with outcome as the dependent variable and the PAM score as an independent variable. In this model the PAM index was highly predictive of outcome ($p < 0.0003$, $R^2 = 9.6\%$). The odds ratio for the PAM score was 1.49, meaning that each one-point increase in PAM increased the chance of dying 1.49 times. The relatively low R^2 value indicates that the majority of the variation in outcome is explained by factors other than those in the PAM index.

Our final goal was to estimate the percentage of patients who received CPR that would not have been expected to benefit from the intervention. As suggested by George et al.,[51] there exists a threshold in the PAM score above which the probability of survival to discharge approaches 0. This value was proposed as higher than 7 in the earlier study, since 7 was the highest PAM score of any patient who survived to discharge. In the present study, one patient with a PAM score of 8 survived to discharge, while no patient with a PAM score higher than this survived. Using the PAM cutoff point of higher than 8, 14.6% of our sample fell into the category of having an extremely small chance of survival. Applying a PAM score of higher than 7, as proposed by George et al., 19.5% of the patients in our sample had very little chance of benefiting from CPR.

DISCUSSION

Our meta-analysis examined individual variables that were thought to be predictive of CPR outcome. Azotemia, cancer, and age more than 60 years were strong significant predictors of a negative outcome, while sepsis and CVA were slightly weaker predictors, although still significant. In contrast, the presence of an AMI was a relatively strong predictor of survival. These findings support the original application of CPR to patients with electrical cardiac disturbances. In other words, patients suffering AMIs theoretically represent a highly appropriate group for CPR. In contrast, CPR is not therapy for underlying systemic disease and hence is less effective in such cases, especially when the systemic disorder is chronic and not readily reversible.

Although many of the patient variables examined in our meta-analysis were significant predictors of outcome, the issue of how to properly combine them is within the realm of the PAM index. Confirming prior research,[30,31] the present findings suggest that the PAM index was a statistically significant discriminator between patients who survived to hospital discharge and those who did not. However, the results of the meta-analysis suggest ways in which the PAM index might be improved. One shortcoming of this index is that it weights all morbidities as negative predictors of survival. This is probably not valid, especially in the case of AMI. Also, our meta-analysis suggests that pneumonia may be a predictor of survival, although weaker than AMI. Since pneumonia is a potentially reversible, acute illness in many instances, extraordinary measures might be warranted. However, the results for pneumonia must be viewed in the context of the low combined r and the very low failsafe. For patients with multiple morbidities, the presence of positive predictors must be weighted in relation to negative predictors. For example, CPR may be more appropriate for a 70-year-old patient with renal failure and AMI than for the same patient without AMI. If the patient with AMI is to suffer an arrest, it is possibly due to an acute, reversible (i.e., electrical) disturbance. Conversely, if the same patient without an AMI suffers an arrest, it is much more likely due to chronic, irreversible disease. Future research with larger, better-controlled samples should thus develop more sophisticated scoring rules in an attempt to increase classification accuracy.

How can an index such as PAM be used most effectively? It could help equip the physician with concrete, quantitative information regarding a patient's chances of surviving CPR. This could aid in the decision-making process for physicians, patients, and family members in contemplating whether to withhold CPR. The most useful application of this index may be for those patients with very high PAM scores. Since no patient with a PAM score higher than 8 survived to hospital discharge (higher than 7 in the original study), it may be appropriate for physicians and families to withhold CPR in such cases. From the data presented here, an estimated 15–20% of patients receiving CPR in our hospital had a negligible chance of survival, as judged by their PAM scores. Because our selection of patients purposely oversampled survivors, all of whom had PAM scores of 8 or lower the actual percentage of patients with a negligible chance of survival is undoubtedly higher. Thus, use of an index such as PAM to determine when a patient's risk of surviving CPR is extremely low could significantly decrease the inappropriate use of CPR.

It should be stressed that PAM is a great deal more accurate in predicting death than survival. Patients with low PAM scores can, and often do, still die. Also, no single number can replace clinical acumen. There are always exceptions and mitigating circumstances for each individual patient. Neither the PAM index nor any other single variable could or should dictate complex patient management decisions for a physician, but the PAM rather can be used as a powerful adjunct tool in the decision-making process.

There are several limitations to this study. Concerning the meta-analysis, the difficulties of combining disparate studies with differing methodologies, conducted over a span of more than 25 years, was formidable. We utilized only raw data, where available, and attempted to use only those patient morbidities that were adequately defined. Still, many differences in patient populations, resuscitation techniques, and patient classifications remain, threatening the validity of our meta-analysis. However, several strong trends emerged that we believe are valid in the face of these limitations. The factors most predictive of death or survival (e.g., renal failure, malignancy, and AMI) are unlikely to be spurious. Also, our findings were replicated when only the studies of moderate or high quality were considered.

The primary limitations of the PAM validity study were that our validation sample was a relatively small retrospective study and that our methods of retrieval did not involve prospective identification of all patients undergoing resuscitation in a given time period. Because it is often difficult to identify adequate numbers of survivors based on previous studies, our method of retrieving from computerized records patients who both had resuscitation charges and survived to discharge allowed us to readily identify survivors of in-hospital CPR. However, the sensitivity of our retrieval process in relation to the total number of patients receiving CPR during this period is unknown.

Future research could be directed toward prospective studies that carefully examine a series of sequential cardiac arrests and attempt to develop a potentially more accurate PAM index. Direct questioning of physicians about the decision-making process regarding patient status could be explored in relation to the PAM index. Is the performance of CPR on patients who cannot be expected to benefit the result of physicians' reluctance to withhold CPR, patients' or families' insistence on doing "everything possible," or some other factors? Finally, future research could quantify the among of medical resources expended during and after attempts to resuscitate patients who are unlikely to benefit from this intervention.

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REFLECTIONS

Continuing Medical Education

It takes decades to learn the value of Kleenex,
several degrees and board examinations, years, a few
tears of your own to know that truth,
not part of the standard curriculum, not even an elective.
Anatomy lab, a fellowship in cardiology, staying up late
are not enough, graduating AOA, an occasional meeting
in Orlando are not enough to teach you this.

I have lived enough to know—rifled morphine
at that beast angina, cocked the defibrillator
for a second shot at pectorals sizzling over sinus rhythm,
aimed at veins bigger than a .30-.30
with Silastic water guns blazing, watched the crater
of blood spray faces leaning into the abdomen's hole,
clipped small threads short.

Wounded organs have been teachers to remember,
professors of medicine emeriti, yet no more silver,
no more distinguished in the wards of learning
than this man outside his wife's death room,
with a tissue concealed behind his back, not knowing
how to cry, but knowing how to care, knowing how
to make me listen, teaching me to be a doctor.

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