Early outcome predictors of post cardiac arrest patients

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Abstract: When pulse and blood pressure return after cardiopulmonary resuscitation (CPR), the brain may have already been critically injured. When severe, a post resuscitation anoxic-ischemic encephalopathy leaves patients comatose. Awakening generally takes place within 3 days after CPR, and neurological impairment is expected if a patient fails to do so. These patients are often left in a severely cognitively disabled and fully dependent state; some remain in a minimally conscious or vegetative state, and very few awaken neurologically. The aim of this research was to evaluate the efficacy of some clinical, radiological, electrophysiological and laboratory tests as early predictors of the outcome in post arrest patients. This study was carried out on 54 patients- in critical care department of Alexandria university main hospital in Egypt- who survived after successful cardiopulmonary resuscitation for at least 12 hours after the event. All patients were subjected to the routine ICU care with emphasis on neurological examination and investigations in the form of CT brain, SomatoSensory Evoked Potential and serial serum creatinine measurement. Outcome evaluation was done using Glasgow- Pittsburgh Cerebral Performance Categories (GP-CPC). Patients were categorized into two groups: group 1 (favourable outcome) including GP-CPC1and 2; group 2 (unfavourable outcome) included GP-CPC 3,4 and 5. Regarding the neurological assessment of patients , it was found that 4 out of 24 patients (16.7%) developed myoclonus in group I versus 7 patients out of 30 (23%) in group II with no significant difference between the 2 groups. The (SEP) results were significantly better in group I compared to group II (p= 0.0001*). Significant higher creatinine level was recorded in day 2 in group II being 1.6±1.1 versus 1.31± 0.78 in group I (P =0.045*). No significant statistical difference was found between the 2 groups regarding the CT results. As a conclusion from this study, the duration of cardiac arrest, the SSEP and the changes in serum creatinine are the parameters which carry the highest ability to differentiate between patients with good prognosis from those with bad prognosis. No gold standard single test can be used to predict the prognosis in post cardiac arrest patients.

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1. Introduction

With the advent of emergency medicine and improvements in the provision of emergency medical services, the number of patients who survive a cardiorespiratory arrest has increased. However, many of these survivors never regain consciousness(1) and progress to a persistent vegetative state.(2) Even when patients are resuscitated in the hospital, fewer than one in five patients survive to discharge.(3)

Considerable research has been carried out to identify those comatose patients who will recover sufficiently to live a meaningful life.(4) An accurate prediction of neurological outcome not only has ethical and legal implications but is also in the interest of the patient and his or her family. The ability to predict very poor outcome would relieve pressure on the finite resources of intensive care. At present, such outcome predictions are based on clinical history and physical examination, electrophysiological findings, neuro-imaging tests and levels of biochemical markers in the serum and cerebrospinal fluid (CSF). (5)

2. Material and Methods

this study was carried out- in critical care department of Alexandria university main hospital in Egypt- on 54 patients who survived after successful cardiopulmonary resuscitation for at least 12 hours after the event and for whom informed consents were obtained from the next of kin in the critical care department in the main hospital of Alexandria University . Approval of local ethical committee was also obtained.

Exclusion criteria:

1- Patients with significant neurological insult before the cardiac arrest.
2- Patients with significant renal insufficiency before the cardiac arrest.
3- Patients under the age of 16.

The aim of this research was to evaluate the efficacy of some clinical, radiological,

electrophysiological and laboratory tests as early predictors of the outcome in post arrest patients.

All patients in the study were subjected to the following:

I. Thorough history taking and complete physical examination with emphasis on the periarrest factors and neurological examination.

.II. Investigations:

1- Arterial blood gases after cardiac arrest and as needed.

2- Somatosensory evoked potential (SSEP) 24 to 48 hours post cardiac arrest. (6)

3- Computerized Tomographic Scan (CT) of the brain 24 to 48 hours post cardiac arrest.(7)

4- Laboratory investigations:

A. complete blood count, liver function tests, serum electrolytes and coagulation tests.

B. Serum creatinine at time of cardiac arrest, 24 hours and 48 hours after. (8)

Outcome of the patients was assessed at 28 days using Glasgow- Pittsburgh Cerebral Performance Categories (GP-CPC) using five points scale: (9)

GP-CPC 1: conscious, alert, and oriented with normal cognitive functions

GP-CPC 2: conscious and alert with moderate cerebral disability

GP-CPC 3: conscious with severe disability

GP-CPC 4: comatose or in persistent vegetative state

GP-CPC 5: certified brain death or dead by traditional criteria.

Patients were categorized into two groups: group 1 (favourable outcome) including GP-CPC1and 2; group 2 (unfavourable outcome) included GP-CPC 3,4 and 5. The Mann–Whitney *U* test, Student's *t* test and Chi square test were used to compare the 2 groups.

3. Results

The age distribution (table1) in group I was ranging from 26 to 80 years with a mean of 60.88 ± 13.65 while in group II it was ranging from 37 to 76 years with a mean of 59.93 ± 10.68. There was no statistical significant difference between the 2 groups regarding the age distribution.

There was 15 male patients and 9 female patients in group I versus 18 male and 12 female in group II with no statistical significant difference between the 2 groups regarding the Sex. (Table 1)

Multiple diagnoses were there in both groups ranging from type I and Type II respiratory failure, cardiogenic shock, septic shock and metabolic disorders as acute poisoning and hepatic cell failure. (Table1)

The duration of cardiac arrest(table 2) in group I was ranging from 4 to 18 minutes with a mean of 9.67 ± 3.55 which was significantly shorter than the duration of arrest in group II Which was ranging from 3 to 24 minutes with a mean of 12.23 ± 5.88 (P=0.0328*).

The cardiac arrest rhythm(table 2) in group I was asystole in 8 patients, pulseless electrical activity in 11 patients and ventricular fibrillation in 5 patients while in group II it was asystole in 12 patients, pulseless electrical activity in 12 patients and ventricular fibrillation in 6 patients with no statistical significant difference between the 2 groups regarding rhythm in arrested patients.

The number of DC shock among the patients with ventricular fibrillation patients (5 patients in group I & 6 patients in group II) was significantly less in group I ranging from 1 to 3 shock with a mean of 2 ± 0.71 versus 2 to 5 shock with a mean of 3.33 ± 1.37 (P= 0.04*)(table2)

Regarding the neurological assessment of patients (table3), it was found that 4 out of 24 patients (16.7%) developed myoclonus in group I versus 7 patients out of 30 (23%) in group II with no significant difference between the 2 groups.

GCS was ranging from 4 to 11 with a mean of 7.63 ± 2.24 in group I versus 3 to 11 with a mean of 7.50 ± 2.42 in group II with no significant difference between the 2 groups.

Pupillary light reflex was present in 13 out of 24 patients (54.2%) in group I versus 12 out of 30 patients (40%) in group II with no significant difference between the 2 groups.

Somatosensory Evoked Potential (SEP) results were significantly different between the 2 groups (table 4). In the patients with favorable outcome 20 out of 24 patients (83.3%) showed normal response, 4 out of 24 patients (16.7%) showed delayed response while no patient in this group showed poor response while in the other group with unfavorable outcome only 6 patients out of 30 (20%) showed normal response, 12 patients out of 30 (40%) showed delayed response and poor response was recorded in the remaining 12 patients (40%). The (SEP) results were significantly better in group I compared to group II (p= 0.0001*)

CT brain (table 5) in group I was unremarkable in 15/24 patients (62.5%), global ischemia was detected in 5/24 patients (20.8%) while the remaining 4/24 patients showed signs of focal ischemia (16.7%). In group II 16/30 patients (53.3%) had unremarkable CT, 8/30 patients (26.7%) had a CT findings matched with global ischemia and 6/30 patients (20%) showed CT findings of focal ischemia. No significant statistical difference was found between the 2 groups regarding the CT results.

Regarding serum creatinine level (Table 6) & (Figure 1), there was no significant difference in the level between both groups in day 0 and day 1 after

cardiac arrest as it was in day 0, 1.26± 0.54 in group I versus 1.33±0.46 in group II while in day 1 it was 1.28±0.55 in group I versus 1.41±0.75. Significant higher creatinine level was recorded in day 2 in group II being 1.6±1.1 versus 1.31±0.78 in group I (P =0.045*).

Table (1): Comparison between the two studied groups regarding demographic data and diagnoses

	Favorable outcome "n=24"	**Unfavorable outcome "n=30"**	p
Age			
Range	26 - 80	37 - 76	
Mean	60.88	59.93	0.388
S.D.	13.65	10.68	
Sex			
Male	15 (62.5%)	18 (60.0%)	
Female	9 (37.5%)	12 (40.0%)	0.412
Diagnosis			
ARDS	2	3	
Respiratory failure	6	4	
Bronchial asthma	0	2	
Cardiogenic shock	2	1	
Hepatic failure	0	3	
Sepsis (Septic shock)	4	7	
MI	3	4	
Pancreatitis	0	1	
Polytrauma	3	4	
Pulmonary embolism	2	2	
Poisoning	2	0	

Table (2): Comparison between the two studied groups regarding circumstances of cardiac arrest (duration, rhythm, number of DC shock)

	Favorable outcome "n=24"	**Unfavorable outcome "n=30"**	p
Duration of arrest			
Range	4 - 18	3 - 24	
Mean	9.67	12.23	
S.D.	3.55	5.88	0.0328*
Rhythm			
Asystole	8 (33.3%)	12 (40.0%)	
PEA	11 (45.8%)	12 (40.0%)	0.87
VF	5 (20.8%)	6 (20.0%)	
Number of DC Shock			
Range	1 - 3	2 - 5	
Mean	2.00	3.33	0.04*
S.D.	0.71	1.37	

Table (3) Comparison between the two studied groups regarding clinical Data (neurological signs): *myoclonus, Glasgow Coma Scale (GCS) & pupillary light reflex (PLR)*

	Favorable outcome "n=24"	**Unfavorable outcome "n=30"**	p
Myoclonus			
Yes	4 (16.7%)	7 (23.3%)	0.7911
No	20 (83.3%)	23 (76.7%)	
GCS			
Range	4 - 11	3 - 11	0.4231
Mean	7.63	7.50	
S.D.	2.24	2.42	
PLR			
Yes	13 (54.2%)	12 (40.0%)	
No	11 (45.8%)	18 (60.0%)	0.299

Table (4) Comparison between the two studied groups regarding electrophysiological parameter *(SSEP)*

	Favorable outcome "n=24"	**Unfavorable outcome "n=30"**	p
SSEP			
Poor	0 (0.0)	12 (40.0%)	
Delayed	4 (16.7%)	12 (40.0%)	0.0001*
Normal	20 (83.3%)	6 (20.0%)	

Table (5): Comparison between the two studied groups regarding radiological parameter (CT brain)

	Favorable outcome "n=24"	**Unfavorable outcome "n=30"**	p
CT brain			
Focal ischaemia	4 (16.7%)	6 (20.0%)	
Global ischaemia	5 (20.8%)	8 (26.7%)	0.793
Unremarkable	15 (62.5)	16 (53.3%)	

Table (6) Comparison between the two studied groups regarding the creatinine level at different period of follow up.

Days	**Favorable outcome "n=24"**	**Unfavorable outcome "n=30"**	p
0	**1.26+0.54**	**1.33+0.46**	0.215
1	**1.28+0.55**	**1.41+0.75**	0.155
2	**1.31+0.78**	**1.6+1.1**	0.045*

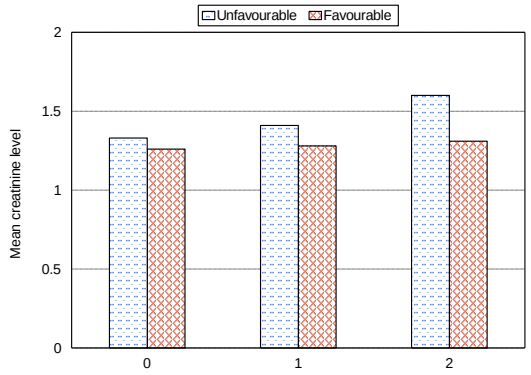

Figure 1. Level of ceratinine at different period of follow up.

4. Discussion

The age distribution in this study does not reflect any significant correlation with the outcome as in group I the mean was 60.88 ± 13.65 while in group II it was 59.93 ± 10.68. This result was in agreement with Berger and Kelley including 255 in hospital cardiopulmonary arrests in non-critical patients demonstrated age was not an independent predictor of survival (10).

In contrast to Schultz *et al* study which reviewed 75 post-arrest patients and showed a significant difference in survival between patients under the age of 60 years and those over the age of 80 years (15% *v* 4%, respectively)(11) .

The mean duration of cardiac arrest (table 2) in group I was 9.67 ± 3.55 which was significantly shorter than group II Which was 12.23 ± 5.88 (P=0.0328*). Schultz *et al* concluded that the duration of the cardiorespiratory arrest was related to outcome as they reported survival rates of 48% for less than 10 minutes duration and 2% for longer than 10 minutes (11) .

Saklaven et al confirmed a shorter duration of arrest was associated with a better outcome and that this correlated with a witnessed arrest or resuscitation by a health professional indicating earlier effective intervention (12) .

The cardiac arrest rhythm did not show any significant correlation with the outcome in our study .In contrast to our study was Andreasson *et al* as They showed a survival rate of 64% from VT/VF arrest, 24% from asystole, and 10% from a PEA arrest. Monitored patients had a survival rate of 52% while unmonitored patients had a survival rate of 27%.(13) This difference may be attributed to the different outcome end point used in both studies as Andreasson et al used the mortality as the end point outcome while in our study GP-CPC 3, 4 and 5 were included in the poor outcome group.

The number of DC shock among the patients with ventricular fibrillation patients (5 patients in group I & 6 patients in group II) was significantly less in group I with a mean of 2 ± 0.71versus 3.33 ± 1.37 (P= 0.04*). This result was in agreement with Denton and Thomas study who also correlated the number of DC shocks with poor outcome(14) .

Inspite literature showed that myoclonus is a very ominous sign for very poor prognosis and death, In our study, it was found that 4 out of 24 patients (16.7%) developed myoclonus in group I versus 7 patients out of 30 (23%) in group II with no significant difference between the 2 groups. Myoclonus in comatosed patients following ROSC was reported to be an agonal sign by Wijdicks *et al* as all patients with myoclonus died(15). However, since that report this finding has been contradicted in a number of case reports. Morris *et al* reported three survivors with mild disability and in a litereature review found five similar cases(16). In a prospective study done by Zandbergen EG etal involving 407 patients, myoclonic status epilepticus at 24 hours after arrest was associated with no false positives (95% CI) (17)

GCS mean was 7.63 ± 2.24 in group I versus 7.50 ± 2.42 in group II with no significant difference between the 2 groups. These results are in agreement

with Zandbergen *et al* systematic review which showed that GCS of 5 or less in the first 24 hours was not helpful in predicting outcome(18) .

In view of the brainstem reflex activity which has been examined as a predictor of individual outcome. The simplest clinical examination is the pupillary response to light. Numerous studies have raised doubts about the specificity of pupillary responsivity due to small numbers of patients who make a good recovery despite no response to light. In the present study, Pupillary light reflex was present in 13 out of 24 patients (54.2%) in group I versus 12 out of 30 patients (40%) in group II with no significant difference between the 2 groups. The discrepancy of results of different studies regarding the predictive outcome of pupillary light reflex is mainly raised from the different timing in performing the examination post cardiac arrest.

In our study, Significant different between the 2 groups were recorded regarding the somatosensory evoked potential. In the patients with favorable outcome (83.3%) showed normal response, (16.7%) showed delayed response while no patient in this group showed poor response while in the other group with unfavorable outcome only (20%) showed normal response, (40%) showed delayed response and poor response was recorded in (40%) of patients .most of the studies showed similar results to what be reached as Madel et al study published in 1993, of 66 patients investigated with SSEP between 4 and 48 hours after ROSC. In 17 patients with "favourable outcome" a normal response was demonstrated whereas in 49 with a "poor outcome" the evoked response was delayed or absent. However, further studies have qualified these initial findings. A study of SEP in 62 patients demonstrated an abnormal SEP was associated with a "poor prognosis" but a normal SEP did not predict recovery(1).

Nakabayashi *et al*, Chen *et al*, and Sandroni et a*l* demonstrated a 100% negative predictive value for a good outcome (persistent disability after awakening or complete recovery) with delayed or absent SEPs but a poor positive predictive value for normal SEPs. Nakabayashi demonstrated that of 12 patients with normal cortical response on SSEP, eight recovered consciousness. Chen demonstrated that bilaterally absent or low amplitude SSEP predicted brain death or persistent unconsciousness while with a normal SSEP the rate of complete recovery was only 44% (19,20,21) .

Madl C et al suggested that a recording of the N70 peak is more accurate in predicting individual outcome than physician review of clinical data. However, SSEP is difficult to record reliably in an intensive care environment. The anaesthetic and sedative agents used **in** patient management can themselves depress or extinguish the evoked potentials, and status epilepticus will interfere with SSEP recording(22).

No significant statistical difference was found between the 2 groups regarding the CT results in the current study. Few studies have tried to use neuroimaging to predict outcome in comatose patients. Torbey *et al* carried out a retrospective review of 25 patients who had CT of the brain. They showed that loss of distinction between grey and white matter on CT predicted poor outcome especially at the basal ganglia level and produced a qualitative analysis that suggested a cut-off for loss of distinction and guaranteed poor outcome. This was based on a small sample and has yet to be validated(7). It appears that [magnetic resonance imaging] MRI can certainly identify the most severely affected patients fairly easily, but whether it's going to be predictive in a prospective data set would need to be validated.

Regarding serum creatinine level , there was no significant difference in the level between both groups in day 0 and day 1 after cardiac arrest while Significant higher creatinine level was recorded in day 2 in group II being 1.6±1.1 versus 1.31± 0.78 in group I (P =0.045*). These findings are partially different from Dietrich Hasper et al study which showed that changes in serum creatinine may contribute to the prediction of outcome in patients with cardiac arrest. Whereas a decline in serum creatinine (> 0.2 mg/dL) in the first 24 hours after cardiac arrest indicates good prognosis, the risk of unfavourable outcome is markedly elevated in patients with constant or increasing serum creatinine(8).

As a conclusion from this study, the duration of cardiac arrest, the SSEP and the changes in serum creatinine are the parameters which carry the highest ability to differentiate between patients with good prognosis from those with bad prognosis. No gold standard single test can be used to predict the prognosis in post cardiac arrest patients. More accurate prognostication can potentially be achieved by using several methods to investigate neurological injury. I believe that in the near future we will see more studies using incorporated indices using multiple neurological, laboratory and radiological tools to increase the sensitivity and specificity in prediction of neurological outcome.

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References

1. Madl C, Grimm G, Kramer L, et al (1993). Early prediction of individual outcome after cardiopulmonary resuscitation. Lancet 341:855–8.
2. Saltuari L, Marosi M (1994). Coma after cardiac arrest: Will he recover all right? Lancet 343: 1052–3.
3. Peberdy MA, Kaye W, Ornato JP (2003). Cardiopulmonary resuscitation of adults in the hospital: a report of 14,720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. Resuscitation 58:297–308.
4. Berek K, Jeschow M, Aichner F (1997). The prognostication of cerebral hypoxia after outof- hospital cardiac arrest in adults. EurNeurol 37: 135.
5. Goh W.C, Heath P., Ellis S.J, et al (2002). Neurological outcome prediction in a cardiorespiratory arrest survivor .Br J Anaesth 88: 719–22.
6. Ahmed I (1988). Use of somatosensory evoked responses in the prediction of outcome from coma. Clin Electroencephalogr 19:78–86.
7. Torbey MT, Selim M, Knorr J, et al (2000). Quantitative analysis of the loss of distinction between gray and white matter in comatose patients after cardiac arrest. Stroke. 31: 2163–7.
8. Dietrich H, Stephan von H, Christian S, et al (2009). Changes in serum creatinine in the first 24 hours after cardiac arrest indicate prognosis: an observational cohort study. Critical Care 13:1186.
9. Cummins RO, Chamberlain DA, Abramson NS et al: Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style. Task Force ofthe American Heart Association, the European Resuscitation Council, the Heart and StrokeFoundation of Canada, and the Australian Resuscitation Council.
10. Berger R, Kelley M (1994). Survival after in-hospital cardiopulmonary arrest of noncritically ill patients. A prospective study. Chest106:872–79.
11. Schultz SC, Cullinane DC, Pasquale MD, et al (1996). Predicting in-hospital mortality during cardiopulmonary resuscitation. Resuscitation 33:13–17.
12. Saklayen M, Liss H, Markert R (1995). In-hospital cardiopulmonary resuscitation. Survival in 1 hospital and literature review. Medicine74:163–75.
13. Andreasson AC, Herlitz J, Bang A, et al (1998). Characteristics and outcome among patients with a suspected in-hospital cardiac arrest. Resuscitation 39:23–30.
14. Denton R, Thomas AN (1997). Cardiopulmonary arrest: a retrospective review. Anaesthesia 52:137–40.
15. Wijdicks EF, Parisi JE, Sharbrough FW (1994). Prognostic value of myoclonus status in comatose survivors of cardiac arrest. Ann Neurol 35:239–43.
16. Morris HR, Howard RS, Brown P (1998). Early myoclonic status and outcome after cardiorespiratory arrest. J Neurol Neurosurg Psychiatry 64:267–8.
17. Zandbergen EG, Hijdra A, Koelman JH, et al (2006). Prediction of poor outcome within the first 3 days of postanoxic coma. Neurology 66:62-68.
18. Zandbergen EG, de Haan RJ, Stoutenbeek CP, et al (1998). Systematic review of early prediction of poor outcome in anoxic-ischaemic coma. Lancet 352:1808–13.
19. Nakabayashi M, Kurokawa A, Yamamoto Y, et al (2001). Immediate prediction of recovery of consciousness after cardiac arrest. Intensive Care Med 27:1210–14.
20. Chen R, Bolton CF, Young B (1996). Prediction of outcome in patients with anoxic coma: a clinical and electrophysiologic study. Crit Care Med 24:672–78.
21. Sandroni C, Barelli A, Piazza O, et al (1995). What is the best test to predict outcome after prolonged cardiac arrest? Eur J Emerg Med 2:33–7.
22. Madl C, Kramer L, Domanovits H, et al (2000). Improved outcome prediction in unconscious cardiac arrest survivors with sensory evoked potentials compared with clinical assessment. Crit Care Med 28:721–6.

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