Post-Anoxic Encephalopathy After an Episode of Aborted Sudden Cardiac Death

Miquel Gómez, Jordi Serra, Antoni Curós, Eduard Claver, Oriol Rodríguez-Leor, Eva Bernal, and Vicente Valle

Servicio de Cardiología, Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona, Spain.

Introduction and objectives. The presence of post-anoxic encephalopathy after an episode of aborted sudden cardiac death is a serious medical and social problem.

Pacientes and method. Of 193 patients admitted to the coronary unit during a 12-year period with aborted sudden cardiac death, 104 died (54%) and 89 survived the episode (46%). We compared the characteristics and 6-month prognosis between survivors according to the presence or absence of post-anoxic encephalopathy.

Results. Of 89 survivors, 38 patients were discharged alive with post-anoxic encephalopathy (42%) and 51 were discharged without neurological disturbances (58%). Patients with post-anoxic encephalopathy were older (65 ± 13.6 vs. 59 ± 12.9 years; p = 0.04). Mean time to care for cardiac arrest was 11.1±4.9 min in the post-anoxic encephalopathy group, versus 3.4±3 min (p < 0.01). The first documented rhythm was VF/VT in 57% and asystolia in 29% in the post-anoxic encephalopathy group, vs. 88% and 3% (p = 0.02). More than half (58%) of the patients in the post-anoxic encephalopathy group had coronary artery disease, vs. 49% (p = NS). Slightly more than half (52%) of the patients in the post-anoxic encephalopathy group had infectious complications, vs. 21% (p = 0.01). After 6 months of follow-up, mortality in patients discharged with post-anoxic encephalopathy was 62%, vs. 10% (p < 0.01); 21% of then showed significant functional improvement and 18% remained neurologically stable.

Conclusions. Most patients admitted to a coronary unit with aborted sudden cardiac death died during hospitalization. Almost half of the survivors had post-anoxic encephalopathy at discharge; of these patients, 62% died within the following 6 months, and functional status improved only in a minority of them.

Key words: *Cardiopulmonary resuscitation. Sudden death. Prognosis. Follow-up studies.*

Full English text available at: www.revespcardiol.org

Encefalopatía postanoxémica tras un episodio de muerte súbita cardíaca recuperada

Introducción y objetivos. La encefalopatía postanoxémica tras un episodio de muerte súbita cardíaca recuperada constituye un problema de gran impacto médico y social.

Pacientes y método. De los 193 pacientes que ingresaron en la unidad coronaria por muerte súbita cardíaca recuperada durante un período de 12 años, 104 fallecieron (54%) y 89 sobrevivieron al episodio (46%). Se comparan las características y el pronóstico a los 6 meses, de los pacientes ingresados por muerte súbita cardíaca recuperada, según la presencia o no de encefalopatía postanoxémica.

Resultados. De los 89 supervivientes, 38 fueron dados de alta con encefalopatía postanoxémica (42%) y 51 sin secuelas neurológicas (58%). Los pacientes con encefalopatía postanoxémica presentaban una mayor edad media (65 ± 13,6 frente a 59 ± 12,9 años; p = 0,04). El tiempo medio de atención al paro en el grupo con encefalopatía postanoxémica fue de 11,1 ± 4,9 frente a 3,4 ± 3 min (p < 0,01). El grupo con encefalopatía postanoxémica presentó: fibrilación ventricular/taquicardia ventricular (FV/TV) como primer ritmo en el 57% y asistolia en el 29%, frente al 88 y al 3%, respectivamente (p = 0,02). El 58% presentó cardiopatía isquémica como sustrato frente al 49% (p = NS). El 52% sufrió complicaciones infecciosas frente al 21% (p = 0,01). A los 6 meses había fallecido el 62% de los pacientes con encefalopatía postanoxémica frente al 10% (p < 0,01); el 21% mejoró funcionalmente y el 18% permaneció estacionario.

Conclusiones. La mayoría de los pacientes ingresados en una unidad coronaria tras una muerte súbita cardíaca recuperada fallece durante la hospitalización, y cerca de la mitad de los supervivientes son dados de alta con encefalopatía postanoxémica. De éstos, más de la mitad habrán fallecido a corto plazo y sólo una minoría mejorará funcionalmente.

Palabras clave: *Resucitación cardiopulmonar. Muerte súbita. Pronóstico. Estudios de seguimiento.*

INTRODUCTION

Epidemiological data from our region indicate that sudden cardiac death accounts for 12% of all deaths

Correspondence: Dr. M. Gómez Pérez.
Servicio de Cardiología. Hospital Universitari Germans Trias i Pujol.
Crta. del Canyet, s/n. 08916 Badalona. Barcelona. España.
E-mail: miquelgomez@comb.es

Received: 5 March 2003.
Accepted for publication: 7 August 2003.

ABBREVIATIONS

PAE: post-anoxic encephalopathy.
GCS: Glasgow Coma Scale.

from natural causes and for 50% of all cardiovascular deaths.[1] In Canada, the Ontario Prehospital Advanced Life Support (OPALS) study revealed that over a 6-year period, only 366 of 5335 patients (7%) seen in emergency services for out-of-hospital cardiac arrest survived and were admitted to the hospital. Of these 366 patients, 187 survived and were discharged, which corresponds to 3% of all patients and 50% of those admitted.[2] Similarly, Escorial et al reported that 30% of the patients admitted for out-of-hospital cardiac arrest were discharged without neurological sequelae, whereas 70% either died or had serious neurological sequelae.[3] There are few reports in the medical literature about the follow-up of patients who survive from a cardiac arrest after being discharged from critical care units. Moreover, data on the prognosis of those who experience post-anoxemic encephalopathy after an episode of aborted sudden cardiac death are even rarer.

Although post-anoxemic encephalopathy is considered to be the most precise term semantically, both anoxic encephalopathy and hypoxic encephalopathy, which is perhaps the most commonly used term, are also used. All three terms are regarded as acceptable for referring to the serious neurological lesions caused by the oxygen and circulatory deficits that result in cessation of the aerobic metabolic processes required to maintain cerebral neuronal functioning.[4]

The aim of this study was to investigate the prognosis of patients admitted after aborted sudden cardiac death according to whether or not they had post-anoxemic encephalopathy (PAE).

PATIENTS AND METHODS

Between January 1990 and January 2002, 193 patients who had recovered from out-of-hospital cardiac arrest were admitted to our coronary unit. These patients accounted for 3% of all admissions to the unit during the study period. The 89 patients who survived were divided into 2 groups: those who were discharged with PAE and those who did not have this complication. Neurological sequelae were evaluated in all patients using the Glasgow Coma Scale (GCS). Post-anoxic encephalopathy is defined as the presence of a depressed level of consciousness (i.e., a GCS score <15) more than 48 hours after admission following recovery from a cardiac arrest in patients who do not have detectable levels of sedatives and who have not undergone orotracheal intubation.

We compared the data in both patient groups and analyzed variables related to demographic factors, treatment of cardiac arrest, complications occurring during admission, and prognosis in the 6 months after discharge. Prognosis was evaluated in terms of both mortality and neurological function. The delay before treatment of cardiac arrest was defined as the time between loss of consciousness, as observed by a witness, and the time when appropriate basic cardiopulmonary resuscitation was initiated. In 49 cases, reliable data on resuscitation were recorded by emergency medical service personnel. The first documented heart rhythm was defined as that recorded electrocardiographically when the patient was first monitored by emergency medical personnel. Appropriate recordings were made in 52 cases.

In order to determine the prognosis, in terms of mortality and neurological function, in patients who were still alive 6 months after discharge from the coronary care unit, we examined the clinical records of those who remained in the hospital in other departments. For those who were fully discharged, we telephoned either the center at which the patient was receiving care during convalescence or the patient's relatives. Neurological function was assessed 6 months after discharge with the GCS. These examinations were done by the doctor who regularly treated the patient.

Statistical analysis

Quantitative variables, which are expressed in terms of mean±standard deviation (SD), were compared with Student's *t* test. Categorical variables, which are expressed as percentages, were compared with the chi-squared test. *P* values <.05 were considered statistically significant. The statistical analysis was done with SPSS 10.0 statistical software (Chicago, Illinois, USA).

RESULTS

Of the 193 patients admitted, 143 were men and 50 were women (male/female ratio, 3:1). Mean age was 63 years, with a range of 17 to 78 years. In all, 89 of the 193 patients (46%) survived cardiac arrest. Figure 1 shows the Kaplan-Meier survival curve for all patients who were admitted to the coronary care unit because of aborted sudden cardiac death. Of the 89 patients who were discharged from the unit, 38 (42%) had PAE and 51 (58%) had no neurological sequelae. Table 1 compares the demographic factors, cardiac arrest treatment given, and complications occurring during admission in the two groups.

Mean age of the patients with PAE was higher than that of patients without PAE, at 65±13.6 years versus 59±12.9 years (*P*=.04). There were no significant dif-

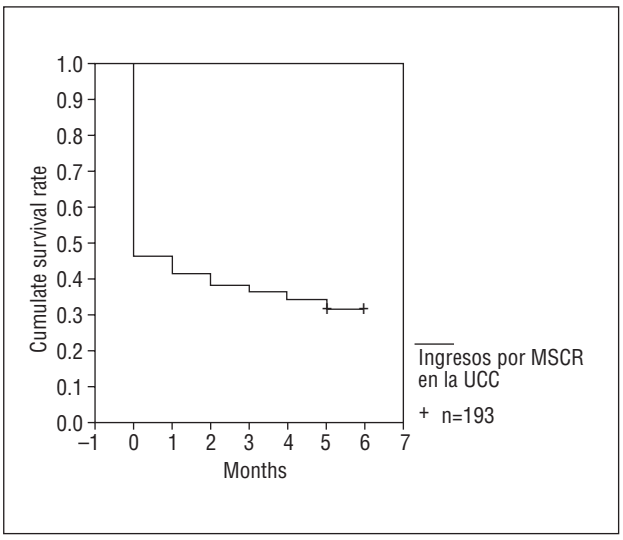

Fig. 1. Kaplan-Meier survival curve for patients admitted to the coronary care unit after an episode of aborted sudden cardiac death.

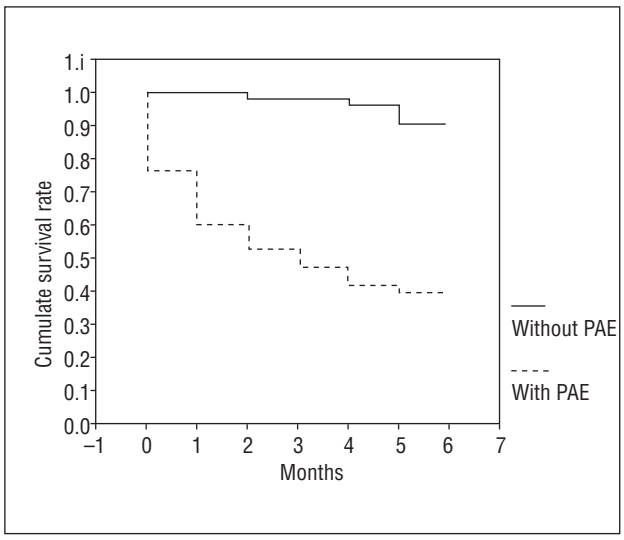

Fig. 2. Kaplan-Meier survival curves for patients discharged from the coronary care unit after an episode of aborted sudden cardiac death, with and without post-anoxic encephalopathy (PAE).

ferences in the sex ratio (male/female ratio 3:1). Patients with encephalopathy were more likely, though not significantly so, to have a history of previous heart disease (58% vs 49%, *P*=NS). The mean time to primary treatment was much shorter in the group of patients without PAE (3.4 minutes vs 11.1 minutes, *P*<.01). The first documented heart rhythm was either ventricular fibrillation or ventricular tachycardia in 88% of the patients without PAE. The proportion of patients with PAE in whom these were the first rhythms (57%) was significantly lower (*P*<.02). In this latter group, the first documented heart rhythm was asystole in a substantial proportion (29%) of patients.

TABLE 1. **Clinical characteristics of patients with and without post-anoxic encephalopathy (PAE), care received after cardiac arrest, and clinical course in the coronary care unit**

	No. patients	Without PAE (n=51)	With PAE (n=38)	*P*
Age, years (mean±SD)	89	59±15	65±14	.04
Sex	89			
Women	22	13 (25%)	9 (24%)	NS
Men	67	38 (75%)	29 (76%)	
History of ischemic heart disease	89	25 (49%)	22 (58%)	NS
First documented heart rhythm	52			
Ventricular tachycardia/fibrillation	38	26 (88%)	12 (57%)	.02
Asystole	7	1 (3%)	6 (29%)	
Other	7	3 (9%)	4 (14%)	
Time to treatment, min (mean±SD)	49	3.4±3.0	11.1±4.9	<.01
Complicated by infection	89	10 (21%)	20 (52%)	.01
New cardiac arrest	89	5 (10%)	8 (22%)	NS
Required intubation	89	30 (59%)	35 (91%)	<.01
Required tracheostomy	89	14 (27%)	24 (63%)	.01
Length of stay in coronary care unit, days (mean ± SD)	89	7±4.4	20±7	<.01

SD indicates standard deviation; NS, not significant.

On admission, the infection rate was much higher in the group of patients with PAE (52% vs 21% in those without PAE, *P*=.01). In addition, mean stay in the coronary care unit was longer in patients with PAE (mean 20 days) than in patients without PAE (7 days, *P*<.01). Tracheostomies were required in 63% of the patients in the former group, compared to 27% in the group without PAE (*P*=.01).

After discharge from the coronary care unit, most patients were transferred to another unit within the same hospital: 46% were sent to the cardiology department, and 24% went to other departments such as neurology, internal medicine or rehabilitation. In addition, 15% were referred to local hospitals, 5% went to their family home, and 10% went to specialized rehabilitation centers. The mean level of consciousness in patients with PAE at the time of discharge was 7.2, as assessed with the GCS.

Prognosis for mortality and neurological function at 6 months

At 6-month follow-up after discharge from the coronary care unit, the mortality rate was 62% (i.e., 23 patients died) for patients discharged with PAE and 10% (i.e., 5 patients died) for those without PAE (*P*<.01). Figure 2 illustrates the Kaplan-Meier survival curves for patients with and without PAE. Most patients with

PAE died within the first 2 months after discharge from the coronary care unit. In patients with encephalopathy, the causes of death at 6 months were infectious disease (n=13), sudden death (n=5), and other non-cardiac disease (n=5). In patients without neurological sequelae, the most frequent causes were sudden death (n=1), heart failure (n=2), and non-cardiac disease (n=2).

With regard to neurological status, of the 15 patients with encephalopathy who were still alive at 6-month follow-up, eight (i.e., 21% of those discharged) had significantly improved function, and seven (i.e., 18% of those discharged) were unchanged. The 8 patients who improved functionally all had a GCS score greater than eight (mean, 11) at discharge, and all subsequently followed a rehabilitation program. In these patients, the mean GCS score at 6-month follow-up was 13.5 and improvements in function occurred steadily, especially during the first 3 months. No patient with PAE had achieved a GCS score of 15 by the end of follow-up. All patients who either died during the 6-month follow-up period or who failed to show significant improvement in their vegetative state had GCS scores less than eight at discharge.

DISCUSSION

Of our series of 193 patients who were admitted to the coronary care unit for out-of-hospital cardiac arrest, 46% survived and were discharged, 20% had PAE at discharge, and 25% had no neurological sequelae. Escorial et al studied patients admitted to an intensive care unit for the same reason. They found that the survival rate in patients who did not have moderately severe sequelae was 30%, although the overall survival rate was somewhat less.[3]

Earlier studies[5–7] have shown that the clinical factors associated with non recovery free from neurological sequelae after an out-of-hospital cardiac arrest are age, asystole as the first documented heart rhythm, and time to the start of resuscitation in the «chain of survival.» In our experience, the presence of certain combinations of these factors may justify withholding resuscitation because it would be ineffective. This is especially so when more than 10 minutes have elapsed since cardiac arrest, because the likelihood of recovery without serious sequelae is zero.[5-11]

We know that in general, between 21% and 35% of the patients who survive an episode of aborted sudden cardiac death will die in the short term. In 16%–20%, death will result from a further episode of sudden cardiac death.[12,13] In our series, the 6-month mortality rate in patients who survived cardiac arrest was 31%. When mortality is analyzed in terms of whether or not the patient had neurological sequelae, it becomes clear that most of those who die had serious neurological sequelae. In patients thus affected, the mortality rate was 62%, whereas in those without encephalopathy it was 10%. In other words, 82% of the patients who died within 6 months of discharge from the hospital had encephalopathy, whereas 18% did not have serious neurological sequelae.

The predominance of patients with encephalopathy among those who died may not have been due solely to the high rate of complications observed, but may also have resulted from a less aggressive diagnostic and therapeutic approach in these patients because of their severe neurological impairment. In patients who survived cardiac arrest and had PAE, both initial symptoms and late neurological sequelae depend on the intensity and duration of hypoxemia. If coma ensued in a patient who experienced a short period of hypoxemia, its duration was usually less than 12 hours.[14–20]

When should diagnostic and therapeutic cardiological techniques be used in patients with post-anoxemic encephalopathy?

The results of the present study and registry data[21,22] indicate that patients whose cognitive status and level of consciousness have been seriously affected, such that they score less than eight on the GCS, will probably not benefit from the diagnostic and therapeutic techniques used in a tertiary cardiological care setting (e.g., coronary arteriography, revascularization and implantable defibrillators) because short-term mortality is high.[21] Other researchers have used the cerebral performance category (CPC) scale to correlate level of consciousness at discharge with prognosis for mortality and function at one-year follow-up. Their findings indicate that a score greater than or equal to 2 on this scale is associated with high mortality in the year following hospital discharge.[13]

In our series, all patients with PAE who were still alive at 6-month follow-up and who showed functional improvement after rehabilitation had low or moderate grade neurological impairment after the hypoxemic episode, with a GCS score greater than eight. Hence, the decision on whether or not to carry out invasive studies or treatment should be based on the patient's neurological status after rehabilitation and on the views of the patient's nearest relatives.[22,23] Studies on the effects of rehabilitation programs specifically designed for this group of patients show that the level of dependency for carrying out normal daily activities is minimal in 10%, moderate in 35%, and significant in 55%.[23] In addition, there are serious consequences for the patient´s family, especially financially and emotionally, since psychosomatic problems occur in more than 60% of these patients.[24]

Limitations of the study

The limitations of this study include those characteristic of any retrospective study, in that it was not possible to obtain all the data in every case. Therefore our conclusions regarding the problem posed by recovery from a post-anoxemic state after receiving care for an out-of-hospital cardiac arrest must be viewed as tentative. In addition, it was not possible to control changes in therapy and general care in patients with out-of-hospital cardiac arrest in our healthcare region during the 12-year period of analysis. Moreover, we do not know how many patients received care for this condition from emergency medical services. This last limitation prevents us from offering a general assessment of the prognosis for the condition we analyzed. Nevertheless, our results are very similar to those published previously.[3,13,15] We felt that it would be of interest to communicate our findings at a time when cardiologists around the world are advocating the widespread adoption of a more intensive approach to the treatment of patients who have suffered out-of-hospital cardiac arrest.[25–28]

CONCLUSIONS

In our experience, 46% of the patients admitted to the coronary care unit after treatment for and recovery from out-of-hospital cardiac arrest will be discharged. However, 42% of these discharged patients will have post-anoxic encephalopathy. Follow-up in this patient group reveals that 62% will die within 6 months and that 21% will have achieved significant functional improvement.

REFERENCES

1. Marrugat J, Elosua R, Gil M. Epidemiología de la muerte súbita cardíaca en España. Rev Esp Cardiol 1999;52:717-25.
2. Stiell I, Wells G, Demaio V, Spaite D, Field B, Munkley D, et al. Modifiable factors associated with improved cardiac arrest survival in a multicenter basic life support/defibrillation system: OPALS study phase I results. Ann Emerg Med 1999;33:44-50.
3. Escorial V, Meizoso T, Alday E. Pronóstico de los pacientes ingresados en la unidad coronaria o de cuidados intensivos tras un episodio de muerte súbita extrahospitalaria. Rev Esp Cardiol 2001;54:832-7.
4. Schneck S. Cerebral anoxia. En: Joynt R, editor. Clinical neurology. New York: Lippincott Williams & Wilkins, 1998; p. 1-7.
5. Eisenberg M, Mengert T. Cardiac resuscitation. N Engl J Med 2001;344:1304-8.
6. Herlitz J, Bang A, Gunnarson J, Engahl J. Factors associated with survival to hospital discharge among patients hospitalised alive after out of hospital cardiac arrest: change in outcome over 20 years in the community of Goteborg. Sweden. Heart 2003;89:25-30.
7. Laurent I, Monchi M, Chiche JD, Joly LM. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. J Am Coll Cardiol 2002;40:2110-6.
8. Marín-Huerta E, Peinado R, Asso A, Loma A, Villacastín JP, Muñiz J, et al. Muerte súbita cardíaca extrahospitalaria y desfibrilación precoz. Rev Esp Cardiol 2000;53:851-65.
9. Curós Abadal A. Parada cardíaca extrahospitalaria, nuestra asignatura pendiente. Rev Esp Cardiol 2001;54:827-30.
10. Curtis J, Park D, Krone M, Pearlman R. Use of the medical futility rationale in Do-Not-Attempt-Resuscitation orders. JAMA 1995;273:124-8.
11. Hillis M, Sinclair D, Butler G, Cain E. Prehospital cardiac arrest survival an neurologic recovery. J Emerg Med 1993;11:245-52.
12. Granja C, Cabral G, Pinto AT, Costa-Pereira A. Quality of life 6-months after cardiac arrest. Resuscitation 2002;55;37-44.
13. Graves JR, Herlitz J, Bang A. Survivors of out of hospital cardiac arrest: their prognosis, longevity and functional status. Resuscitation 1997;35:117-21.
14. Eisenburger P, List M, Schorkhuber W. Long-term cardiac arrest survivors of the Vienna emergency medical service. Resuscitation 1998;38:137-43.
15. Rien de Vos RN, Hanneke CJM, de Haes MS. Quality of survival after cardiopulmonary resuscitation. Arch Intern Med 1999;159: 249-54.
16. García-Guasch R, Castillo J. Parada cardiorrespiratoria, ¿y después qué? Med Clin (Barc) 1999;113:132-6.
17. Urbano-Márquez A, Rosich A, Estruch R. Enfermedades metabólicas del sistema nervioso central. En: Farreras-Rozman, editores. Medicina Interna. 13.ª ed. Madrid: Mosby/Doyma, 1995; p. 509-10.
18. The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (part one). N Engl J Med 1994;330: 1499-508.
19. The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (part two). N Engl J Med 1994;330: 1572-9.
20. Nakabayaskhi M, Kurokawa A, Yamamoto Y. Immediate prediction of recovery of consciousness after cardiac arrest. Intensive Care Med 2001;27:1210-4.
21. Zandbergen E, de Haan R, Stoutenbeek C. Systematic review of early prediction of poor outcome in anoxic-ischaemic coma. Lancet 1998;352:1808-12.
22. Berkhoff M, Donati F, Bassetti C. Postanoxic theta coma: a reappraisal of its prognostic significance. Clin Neurophysiol 2000; 111:297-304.
23. Fertl E, Vass K, Sterz F, Gabriel H, Auff E. Neurological rehabilitation of severely disabled cardiac arrest survivors. Part I. Resuscitation 2000;47:231-9.
24. Pusswald G, Fertl E, Falta M, Auff E. Neurological rehabilitation of severely disabled cardiac arrest survivors. Part II. Resuscitation 2000;47:241-8.
25. Caffrey S, Willoughby P, Pepe P, Becker L. Public use of automated external defibrillators. N Engl J Med 2002;347:1242-5.
26. Weaver W, Peberdy MA. Defibrillators in public places: one step closer to home. N Engl J Med 2002;347:1223-9.
27. Nichol G, Hallstrom AP, Ortato JP. Potential cost-effectiveness of public access defibrillation in the United States. Circulation 1998;97:1315-20.
28. Bunch T, White R, Gersh B, Meverden R, Hodge D, Ballman K, et al. Long-term outcomes of out-of-hospital cardiac arrest after successful early defibrillation. N Engl J Med 2003;348:2626-33.