

Course and outcome of patients in vegetative state of nontraumatic aetiology

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Abstract

A follow up study is reported of 100 consecutive unconscious patients admitted to an intensive care coma facility with a history of 30 days or more of unconsciousness of nontraumatic cause. Twenty recovered consciousness, all within 5 months of injury. 31 of the remaining patients died within 6 months following injury, while 49 continued unconscious until death. The mean life expectancy of these 49 was 26-34 months from that time. All 20 patients who recovered awareness continued to suffer from major disability. The prognosis for life or death and for recovery or not of consciousness was not significantly correlated with age or aetiology of the vegetative state. Among those who recovered consciousness, the younger patients showed somewhat better results in three parameters of function: locomotion, ADL and day-placement, but not in cognition, behaviour or speech accuracy and fluency. The overall results for these nontraumatic patients with postcomatose unawareness are clearly worse than those for patients with a similar period of unconsciousness following craniocerebral trauma.

(*J Neurol Neurosurg Psychiatry* 1993;56:407-409)

The development of medical facilities for prolonged intensive care of the unconscious patient has resulted in the growth of a previously negligible medical problem, namely the patient who remains unconscious but alive. This problem includes two major pathogenetic subtypes, traumatic and non-traumatic, which differ greatly in their course and prognosis. Over the past decade numerous series have been published dealing with the prognosis of patients with persistent vegetative state or "Post-coma unawareness" (PCU)¹ patients. However, these studies have mostly dealt either with post-traumatic unconsciousness²⁻⁵ or with patients whose prolonged duration of post-anoxic unconsciousness is defined as 24 hours or more.⁶⁻⁹ The specific problem of the patient who remains unaware for weeks following non-traumatic coma has not yet been addressed.

We have followed 100 consecutive patients admitted to our unit with post-anoxic unconsciousness of at least 30 days duration.

Materials and methods

The study group includes the first 100 patients with PCU state lasting at least 30 days following anoxia who were admitted to our intensive care coma unit during 1974-87. They included 63 males and 37 females. The age range was 2-80 years, with a mean of 38. Sixteen patients were aged 2-16, 47 were aged 17-45, and 37 were aged 46 years or more. The aetiology of post-coma unawareness (PCU) was cardiac arrest or respiratory failure in 34 cases, complications of anaesthesia and/or neurosurgery in 34, stroke in 15, encephalitis in 8 and various other causes in 9.

Twenty of the patients recovered consciousness, as defined by establishment of meaningful verbal or visual-motor communicative contact with their environment. They were discharged after a median period of 328 days of inpatient rehabilitation (range 55-1254 days). Their function was assessed in a number of areas. Locomotor function, independence in activities of daily living (ADL), cognition, communication and behaviour were assessed semi-quantitatively by a multidisciplinary team at discharge. The patients' overall occupational placement was assessed at outpatient follow up which was performed at least a year after discharge. This was classified in three categories: normal employment or school setting, sheltered day-placement, or round-the-clock nursing care.

The remaining 80 patients failed to recover consciousness, and 68 of them died before the final follow up, which was at least 72 months after onset of unconsciousness. During this period five living unconscious patients were lost to follow up following their transfer to other medical facilities. Seven patients remain in hospital in our centre in a state of post coma unawareness.

Most of the statistical analyses performed were those suited to ordered outcome categories. These included the Mann-Whitney test when two groups were compared, and the Spearman rank correlation when three or more ordered groups were compared.

Results

Table 1 presents the outcomes of each of the various aetiologies of PCU. When the outcome was classified as conscious, unconscious or dead, there was no significant difference among them in outcome. Similarly, there was no significant association between outcome and age (table 2).

All 20 patients in this series who recovered consciousness did so within five months of

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Received 8 April 1992
and in final revised form
23 July 1992.

Accepted 31 July 1992.

Table 1 Aetiology and late outcome in 100 cases of prolonged (≥ 1 month) nontraumatic PCU

Outcome	Conscious	Unconscious	Dead	Total
Aetiology:				
Cardiorespiratory Disease:	5	5	24	34
Stroke:	7	1	26	34
Aneesthesia:	4	2	9	15
Encephalitis:	1	2	5	8
Other:	3	2	4	9
Total:	20	12	68	100

$\chi^2 = 7.61$ DF = 8 $p \geq 0.1$.

Table 2 Age and late outcome in 100 cases of prolonged (≥ 1 month) nontraumatic PCU

Age/Outcome	Conscious	Unconscious	Dead	Total
2-16	2	3	11	16
17-45	11	6	30	47
>45	7	3	27	37
Total	20	12	68	100

$r_{\text{SPEARMAN}} = -0.04$ $t = 0.41$ DF = 98 $p \geq 0.1$.

losing it. As seen in table 3, by six months after onset a further 31 had died, while 49 remained unconscious for the remainder of their lives. Since there was no recovery after the first six months, we calculated life expectancy for these 49 patients from that point in time. Life table methods gave a median life expectancy of 12 months and a mean of at least 26 months after the loss of all hope for recovery. As it is rare in our experience for an unconscious patient to survive more than 10 years, we may assume that this will be the upper limit of survival of our seven patients who are still alive; on this assumption, the upper bound of estimate for mean life expectancy in this group would be 34 months, and the most probable estimate for mean life expectancy would be the midpoint between the upper and lower bounds of estimate, that is, 30 months after loss of hope for recovery.

All of the 20 patients who recovered consciousness after being unconscious for at least a month remained with major disability. Seventeen of them showed tetraparesis, 19 of them had significant cognitive deficits, 15 were dysphasic, and 13 had behaviour problems. Of the 18 for whom follow up data were available regarding occupational placement, only one was gainfully employed, while three were in sheltered day-placement conditions and 14 were in round-the-clock nursing care.

Among those patients who recovered consciousness, age at injury was significantly associated with some but not all of the outcome parameters. The younger patients achieved more independence in ambulation than the older ones. Six of the seven patients over the age of 45 remained bedridden, while

the seventh was restricted to a wheelchair; 6 of the 11 patients aged 17-45 were bedridden, 4 were wheelchair-bound and one achieved assisted walking. By contrast both of the children attained at least partially independent walking ($p \ll 0.01$).

The younger patients also attained a greater degree of independence in activities of daily living. The two children attained complete independence in this area, compared with one of 11 young adults and none of the 7 older patients ($p < 0.02$). Similarly, the late occupational placement of the younger patients was significantly better (although not good).

All of the seven older patients remained in nursing care, compared with none of the patients aged ≤ 16 and seven of the nine young adults for whom placement data were available ($p \geq 0.01$).

Despite their relative advantage, even the younger patients remained quite handicapped, although less so than the older ones. By contrast, no significant association was seen between age and dysphasia, cognitive deficits or neurological findings.

Among the 20 patients who recovered awareness, the duration of unconsciousness was not significantly associated with the eventual functional level. Among the five who were unconscious less than 60 days, two could be discharged home and three were transferred to nursing units, while among the 15 who were unconsciousness 61-150 days 4 were sent home ($p \geq 0.1$).

Discussion

Our salient findings in patients with nontraumatic PCU of over 30 days duration were: 1) By 6 months after onset 20% had recovered consciousness and another 31% were dead. The other 49% remained permanently unconscious. 2) The cause of PCU and the age at injury showed no significant correlation with the above prognosis. 3) No patient regained awareness after unconsciousness of more than 5 months duration. 4) Among those patients who remained unconscious after 6 months, mean additional life expectancy was estimated as 26-34 months, and median additional life expectancy was 12 months. 5) Among those who regained consciousness, several parameters of quality of survival were significantly correlated with age at injury. Younger patients showed somewhat better locomotor status, independence in ADL and day placement. Age was not correlated significantly with cognitive status, dysarthria or behaviour disturbances. 6) There was no significant difference in functional outcome between patients who recovered awareness after 30-60 days of unconsciousness and those who recovered after 61-150 days.

As no comparable series of patients with post-anoxic unconsciousness of over a month's duration has been previously published, it is difficult to compare our findings 1, 2 and 4 with other studies. Our third finding can, however, be taken as a rule to which there are already published exceptions, since

Table 3 Late outcome in 100 cases of prolonged (≥ 1 month) nontraumatic PCU, by duration of follow up since onset

Follow up in months:	1	3	6	9	12	18	24	30	36	48	72
Conscious	0	12	20	20	20	20	20	20	20	20	20
Unconscious	100	73	49	38	33	23	20	20	18	12	7
Dead	0	15	31	41	46	56	59	59	60	64	68
Untraced	0	0	0	1	1	1	1	1	2	4	5

These statistics are cumulative. All patients who once recovered consciousness are tabulated from then on as conscious, regardless of the time of follow up. One of these conscious patients died from sepsis after recovering consciousness, but is not included among the deaths in the table.

single cases have been reported of recovery of consciousness after 6–18 months.^{10,11} These exceptions would indicate that our data may be taken as a basis for statistical expectations, but not as an absolute denial of the possibility of later recovery of awareness. It should be added, however, that the few published cases of very late recovery after nontraumatic PCU remained very severely disabled.

The influence of age on prognosis of nontraumatic PCU has been a subject of controversy. A previous series from this institution found that 13 patients aged ≥ 25 had a better functional prognosis than did 19 patients aged >25 .¹² However, only nine of these patients were unconscious for more than 4 weeks. Two other series^{13,14} failed to find a correlation between age and functional prognosis, but these also included mainly patients with shorter periods of unconsciousness than those of our study. A similar controversy exists as to whether age is correlated with outcome in post-traumatic coma,^{15–23} but mostly the published studies of traumatic as well as nontraumatic injury have dealt with considerably shorter periods of unconsciousness than those of the present series. Our findings support an intermediate view of the effect of age on prognosis, given the fact of prolonged post-anoxic unconsciousness. Under these circumstances, age seems to have no association with likelihood of death or recovery of consciousness; among those who recover consciousness, the functional status of the younger patients is significantly, but not dramatically, less bad.

Our finding that duration of unconsciousness is not correlated with functional outcome may seem paradoxical at first glance, especially when contrasted to the findings of other studies.^{3,6} However, the paradox is more apparent than real. Given the fact of at least 30 days of unconsciousness, all these patients had suffered an extremely severe degree of brain damage, which rendered relatively negligible any further differences in duration of unconsciousness. It is obvious that if the full range of possible durations of unconsciousness had been included, this parameter would have been correlated with outcome.

Our data show that the prognosis of nontraumatic PCU is much worse than that of the same duration of unconsciousness following trauma. The overall results are inferior to those reported by us for trauma,^{2,15,16} and the period during which recovery of consciousness is likely is shorter.¹² This difference in prognosis between trauma and anoxia parallels that reported for shorter periods of unconsciousness.^{12,17,24} These differences in outcome may be related to differences in pathology. Ischaemia and anoxia cause cortical damage, cortical disconnection, laminar necrosis and/or diffuse demyelination,^{3,9,15} while trauma tends to cause diffuse axonal injury due to shearing forces, and microhaemorrhages in the border zone between white and grey matter, with relative sparing of the cerebral cortex.²⁵

The surprisingly long (26–34 months) additional life expectancy of patients who

have already been unconscious for 6 months, and who have essentially no hope of ever recovering consciousness, indicates that this is a significantly large new category of need for medical and nursing care. We have followed 49 such patients over a 14 year period, out of a total Israeli population of 4–5 million. This implies an incidence of approximately 0.75 per million population per year. Since many additional such patients are in hospital in other facilities, the real extent of this problem is considerably greater. The mean economic cost of each of these patients is that of almost 1000 days of hospital stay in an intensive care facility. The human cost to their families and caretakers is incalculable, but no less important.

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