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A note on survival after anoxic brain injury in adolescents and young adults

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Abstract.
BACKGROUND: Much is known about survival after traumatic brain injury (TBI), yet relatively little about survival after anoxic brain injury (ABI).
OBJECTIVE: To determine whether long-term survival after ABI is comparable to that after TBI.
METHODS: We identified 237 patients with ABI and 1,620 with TBI in California who were aged 15 to 35, survived at least 1 year post injury, and were injured in 1986 or later. We analyzed the long-term follow-up data using the Cox Proportional Hazards Regression Model, controlling for age, sex, and severity of disability.
RESULTS: After adjustment for risk factors, no significant differences in long-term survival between ABI and TBI were found (hazard ratio = 0.97; 95% c.i. 0.57–1.65).
CONCLUSIONS: In adolescents and young adults, long-term survival after ABI appears to be similar to that after TBI.

Keywords: Survival, traumatic brain injury, life expectancy

1. Introduction

There is considerable literature on life expectancy after traumatic brain injury (TBI), the most common acquired brain injury in young adults (Baguley et al., 2012; Brooks et al., 2013; Shah et al., 2007). Conversely, little is known about the long-term survival prognosis after anoxic or hypoxic brain injury (ABI). For otherwise similar persons, functional recovery after ABI is known to be similar to, or perhaps worse than, recovery after TBI (Cullen et al., 2008, 2009; Cullen & Weisz, 2011; Estraneo et al., 2010, 2014; Gray and Burnham, 2000; Groswasser et al., 1989; Heindl & Laub, 1996; Hopkins et al., 2005; Jennett, 2002; Katz et al., 2009; Kwasnica et al., 2008; Multi-Society Task Force on the Persistent Vegetative State, 1994; Schmidt et al., 1997; Shah et al., 2004; Shavelle et al., 2007; Whyte et al., 2009). It may that the prognosis for long-term survival is similarly related. We investigate this issue here.

2. Methods

Subjects were selected from a computerized database of 357,629 persons with long-term disabilities who received any services from the California Department of Developmental Services between January 1980 and December 2010. Services include medical treatment, occupational or physical therapy, and board and care. All subjects are evaluated approximately annually, using the Client Development Evaluation Report (CDER) (California Department of Developmental Services, 1978). This instrument contains several hundred measurements, including psychological, medical, functional, behavioral, and cognitive items. The reliability of the functional items has been assessed previously and judged satisfactory (Arias et al., 1983; Citygate Associates, 1998; Harris et al., 1982; Widaman et al., 1985;

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Widaman, 1984). This database has been the subject of many prior publications on life expectancy and disability (Brooks et al., 2013, 2014; Shavelle et al., 2007; Strauss et al., 1999).

From this database we selected the subset of 1,857 persons who met the following criteria:

a. Disabilities due to acquired (rather than congenital) brain injury:
   - TBI: Specified on the CDER as being due to either a motor vehicle accident or a cranial injury. The latter was identified by International Classification of Diseases (ICD) codes 800-804, 850-854, 905.0, 907.0, 310.2, 959.01 (9th Revision) or S02, S06-07, F07.81, S09.8 (10th Revision).
   - ABI: Specified on the CDER as being due to either near-drowning or ICD codes 348.81, 427.5, 994.1, 994.7, G93.1, G93.4, G93.9.
b. Injured between ages 15 to 35.
c. Survived at least 1 year from injury.
d. Evaluated in 1986 or later.

Persons with multiple acquired conditions, or any concomitant degenerative condition or cancer, were excluded. The California database also contains information on persons with other acquired brain injuries – including stroke (430–438, I60–I69), infectious diseases (001–139, 324, A00-B99, G06-79, G81-92), and meningitis (013, 047, 139.0, 320–322, G00-05) – and many congenital conditions (such as downs and cerebral palsy). A comparative study of these is outside the scope of the present work.

Condition (b) was imposed because children with acquired brain injury form a distinct group that may deserve separate consideration. One reason is that they are injured before they are fully grown, and this may influence the pattern of survival and recovery. Condition (c) reflects our interest in long-term survival, rather than on the short-term effects during the acute post-injury period.

Because much of the above etiologic information began to be reported in 1985, we chose the study period as the 25-year interval 1986–2010. Specifically, the beginning of the "at risk" period for a given subject was the later of (i) the first CDER after the first anniversary of the injury, and (ii) January 1, 1986.

Mortality information was obtained from annual electronic records from the State of California (State of California), and would not be sensitive to deaths that occurred outside of the state. To minimize the potential bias associated with subjects who may have left California, we defined the end of each person's "at risk" period to be the earliest of (i) the date of death, (ii) the end of the study period (December 31, 2010), and (iii) three years after the date of the subject's last CDER evaluation. Condition (iii) ensures that subjects who may have left the state would be counted as being at risk for only a fairly short period. We used the Cox Proportional Hazards Regression Model to test whether the etiology of acquired brain injury was predictive of long-term survival after adjustment for known predictive factors of age, sex, and severity of disability.

3. Results

There were 1,620 patients with TBI, of whom 110 died over the follow-up period. For ABI the figures were 237 and 16. These groups were similar with respect to age at evaluation. Persons with ABI tended to be slightly more disabled (details not shown), which is why it is important to control for this factor when making survival comparisons between TBI and ABI.

After controlling only for age and sex, we found that persons with ABI had a slightly higher mortality risk (hazard ratio [HR] = 1.12, 95% CI 0.66 – 1.89) than those with TBI, though the difference was not statistically significant ($p = 0.68$). After additionally controlling for the severity of disability, we found the difference to be negligible (HR = 0.97, 95% CI 0.57 – 1.65), and not statistically significant ($p = 0.92$). Results did not appear to vary by sex, age, or severity of disability (test for interactions, $p > 0.20$ in all cases).

4. Discussion

There is evidence on comparative functional recovery after TBI and ABI. A few studies have found the two conditions to have similar outcomes (Gray and Burnham, 2000; Shah et al., 2007; Whyte et al., 2009), and one found that ABI patients do better in some ways (Shah et al., 2004), though a larger number have suggested that ABI patients do worse (Cullen et al., 2008, 2009, 2011; Estraneo et al., 2010; Gray and Burnham, 2000; Groswasser et al., 1989; Heindl & Laub, 1996; Hopkins et al., 2005; Katz et al., 2009; Kwasnica et al., 2008; Multi-Society Task Force on the Persistent Vegetative State, 1994). Notably, Grosswasser et al. and Schmidt et al. found that ABI patients had poorer outcomes, required more care, and needed longer rehabilitation stays. Schmidt et al., summarizing four prior studies, wrote that this differential "may be due to the

continued impairments known to affect the brain with diffuse damage by cerebral anoxia." Similarly, for those in the vegetative state (VS), it has been found that ABI patients improved to a minimally conscious state (or better) at a lower rate than those with TBI, and their mortality appeared to be higher (Estraneo et al., 2010; Jennett, 2002; Kwasnica et al., 2008; Multi-Society Task Force on the Persistent Vegetative State, 1994). The differences were not necessarily statistically significant, however, which is consistent with our findings with respect to long-term survival.

Hopkins et al. investigated neuropsychological outcomes after ABI and TBI. They concluded that "In the absence of localized lesions, the amount of neural tissue loss, rather than etiology, may be the critical factor in neuropsychological outcome." Our research question, on the other hand, was whether, for a given severity of resulting disability ("outcome"), the etiology of acquired brain injury is associated with differential long-term survival. To our knowledge, this is the first study to examine this issue.

After adjustment for age, sex, and severity of disability, we found no significant difference in long-term survival of persons with disabilities due to TBI or ABI. The point estimate (HR = 0.97) suggests that persons with ABI may have slightly better prognosis, but this difference (even if confirmed statistically with studies using larger sample sizes) is unlikely to be of clinical significance. For example, the hazard ratio of 0.97 implies a difference in life expectancy of only a few months in most cases. A notable limitation here is that the sample size for the ABI group (237 persons and 16 deaths) was rather small. There was thus not sufficient power to detect small differences in survival. Future studies are therefore required to corroborate our findings.

Conflict of interest

The authors act as consultants on life expectancy in litigation and other settings.

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