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Deep Hypothermic Circulatory Arrest in Patients With High Cognitive Needs: Full Preservation of Cognitive Abilities

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Background. **Owing to controversy regarding the efficacy and safety of deep hypothermic circulatory arrest (DHCA) during thoracic aortic surgery, we conducted a psychometric study in which high-cognitive patients and their informants were interviewed to determine whether DHCA had any adverse effect on their daily activities or work performance.**

Methods. **A total of 29 patients (18 males, 11 females; age, 26 to 75 years; mean 52.6 years) whose jobs require high cognitive capability and who had undergone aortic surgery using DHCA (range, 17 to 54 minutes; mean arrest time, 27.4 minutes) at Yale-New Haven Hospital were retrospectively studied. These 29 patients represented the responders among 45 such patients to whom questionnaires were mailed. A control group of 21 high-cognitive patients (20 males, 1 female; ages, 36 to 77 years; mean, 54.7 years) who underwent aortic surgery without DHCA were surveyed as well. During surgery, DHCA was used as the sole means of cerebral protection. The head was packed in ice, and carbon dioxide flooding of the field was used in all cases. The ascending aorta was resected with an open distal anastomosis and a hemiarch or total arch replacement. A 21-part questionnaire (adapted from A.F. Jorm's Short Form IQCODE and supplemented by our own questions) was distributed postoperatively to subjects and to their informants (generally a spouse). A value of 3 on the questionnaire indicated "not much change" from preoperative status (1 indicated much worse and 5 indicated much improved).**

Results. **There were no statistically significant differences in any functional outcomes by study group (by patient: DHCA 3.01, control 3.09; by informant: DHCA 3.00, control 3.03; $p > 0.05$). Mean values of the outcomes for study groups and control subjects were essentially identical and quite close to 3 (the value assigned to "not much change") for overall score, for occupational score, and for memory-related score.**

Conclusions. **These data indicate that high-cognitive patients experienced very little cognitive change as a result of undergoing DHCA. Our assessment strongly supports the adequacy of straight DHCA as a cerebral protectant strategy during short- to moderate-duration circulatory arrest. We found excellent preservation of functional state and no difference from patients undergoing aortic surgery without DHCA.**

(Ann Thorac Surg 2009;87:117–23)

At the Yale Center for Thoracic Aortic Disease, we noted clinically that many of our deep hypothermic circulatory arrest (DHCA) patients were able to return successfully to highly demanding professions after extensive aortic surgery. Deep hypothermic circulatory arrest has become an accepted cerebral protection strategy for complex aortic surgery by virtue of reducing cerebral metabolic rate, free radical release in neuronal tissue, and postischemic cerebral edema [1, 2]. Deep hypothermic circulatory arrest allows the surgeon to work in a bloodless, uncluttered operative field. Furthermore, the aortic arch can be replaced without direct cannulation of the carotid arteries [3]. Despite these advantages of DHCA, several studies have reported increased perioperative morbidity, including increased blood loss, postoperative renal dysfunction, and neuronal apoptosis [4, 5]. Immediate and late neurologic morbidities of DHCA have become an issue of concern among cardiothoracic surgeons, not only in adult but also in pediatric patients [6]. One study has shown that DHCA duration greater than 20 minutes adversely affects quality of life in patients undergoing surgery of the thoracic aorta [7]. We recently published a retrospective study supporting the safety and efficacy of straight DHCA as a sole means of cerebral protection in 394 consecutive patients [8]. Although our study showed that cognitive function, by gross clinical assessment, was excellent, there are numerous important studies that report detrimental neurologic issues associated with DHCA [3, 9–11].

This study takes a closer look at 29 patients of the 394 of our recent report whose professions required high

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cognitive levels (patients mentioned briefly in Table 3 of our 2007 paper [8]). The high cognitive variable was selected because the central nervous system is quite sensitive to ischemia, and much research has been centered on neurologic outcome after DHCA. High-cognitive professions were loosely defined, but were essentially limited to physicians, lawyers, doctorates, clergymen, artists, musicians, accountants, and managers. Our goal was to determine whether these professionals noted any difference in their cognitive ability at home or at work after aortic surgery with straight DHCA. We were especially interested in individuals with high cognitive requirements at work, as we anticipated that any substantive adverse effects of DHCA would be less able to "hide" in such individuals than in those with less cognitively demanding occupations. Also, we saw an opportunity to compare functional status with a group of patients undergoing ascending aortic replacement without DHCA. Patients were interviewed and completed a questionnaire. Spouses or relatives were used as additional informants to control for self-reporting bias. Patients and their informants, and a 21-patient control group, were given a 21-part questionnaire to determine whether DHCA had adversely affected their cognitive function. We looked at a variety of questions, including the following: Are the patients able to perform their jobs at the same high cognitive level as before surgery? Have people been pointing out abnormalities in patients' function that have started since surgery? Can the patients not perform tasks now that they could before? We believe that specific neuropsychiatric assessment using validated metrics will extend our understanding of any potential detrimental effects of DHCA beyond nonspecific clinical assessment during and after hospitalization.

Table 1. Summary of Various Professions of Study Subjects (Highly Cognitive Assignments)

DHCA	Non-DHCA
Accountant	Artist/illustrator
Administrator, hospital	Business consultant
Administrator, insurance company	Casino manager
Artist/painter	CEO, financial analyst company
Businessman	Cell biologist/researcher
Construction manager	Chairman and CEO, plastics business
Dentist (n = 2)	Computer programmer
Firefighter, supervisor	Corporate accountant
Graphic artist	Dean, medical school
IBM technician	Defense technology specialist
Investment advisor	Director of library services
Manager, computer systems design	MD, child psychiatrist
Manager, research technology	Naval engineer
Manager, supermarket	Priest
MD, ophthalmologist	Research scientist
MD, orthopedic surgeon	Sales manager, beer manufacturer
MD, pathologist	State police union president
Naval acoustics researcher	Teacher, special education
Office manager, phone company	Telecommunications specialist
Physician's assistant	Vice president, investment company
President and CEO, business	Vice president, research company
Priest	
Registered nurse (n = 2)	
Speech pathologist	
Superintendent, school system	
Teacher	
Town clerk	

CEO = chief executive officer; DHCA = deep hypothermic circulatory arrest; IBM = International Business Machines.

Patients and Methods

This study was approved by the Yale University School of Medicine Human Investigative Committee (number 0609001813).

Patients

Forty-five high-cognitive patients in the above-specified categories, undergoing thoracic aortic surgery requiring circulatory arrest at Yale-New Haven Hospital, were identified among the 394 total patients who underwent DHCA, predominantly during a 5-year period. Twenty-nine patients (64% yield) and their informants responded, and are included in this study. Patients were operated on from 1993 to May 2006. There were 18 male and 11 female patients. Ages ranged from 25 to 75 years with a mean age of 52.6 years. The professions of patients were varied, but required high cognition to function (Table 1). With the exception of 1 patient who was treated for acute type A aortic dissection, all patients were treated for ascending or aortic arch aneurysm, or both. Of the 29 total patients in the DHCA group, 17 had root-sparing procedures (10 with aortic valve replacement, 7 without aortic valve replacement), 11 had root replacement procedures, and 1 had a valve-sparing procedure. For the distal anastomoses, 26 patients had hemiarch replacements and 3 had total arch replacements. The range of DHCA duration was 17 to 54 minutes, and mean DHCA duration was 27.4 $\pm$ 10 minutes. Clinical assessment of patients after surgery revealed that 2 patients had a seizure, and none experienced a clinical stroke. Ten patients had postoperative atrial fibrillation, and all patients were alive at the time of contact. The interviews were administered at a mean of 48 months from operation (range, 11 to 168 months).

Questionnaires were mailed to 34 control high-cognitive patients who underwent ascending aortic replacement without the use of DHCA. This group underwent the same neuropsychiatric assessment as the DHCA patients. This group of control patients was operated on at this institution from April 2004 to June 2006. Twenty-one patients (62% yield) and their informants responded, and were included as the control cohort. Of the 21 patients in the control group, 4 patients had root-sparing procedures (3 with aortic valve replacement, 1 without aortic valve replacement), 13 had root replacement procedures, and 4 had valve-sparing procedures. Among these patients, 2 patients underwent additional surgery of the descending aorta, and 1 patient underwent thoracoabdominal aortic replacement. The control patients did not need DHCA because of a lesser distal extent of their aneurysms, permitting resection with the

Table 2. Patient Demographics Between the Deep Hypothermic Circulatory Arrest Group and the Non–Deep Hypothermic Circulatory Arrest Group

Variable	DHCA Group	Non-DHCA Group
Total	29	21
Sex		
Male	18	20
Female	11	1
Age (y)		
Average	52.6	55.6
25–50	14	6
51–75	15	15
Duration DHCA (min), average	27.4	0
DHCA temperature (°C)	18.8	NA
Proximal anastomosis		
Root-sparing	17	4
With valve	10	3
No valve	7	1
Root replacement	11	13
Valve-sparing	1	4
Distal anastomosis		
Hemiarch	26	0
Total arch	3	0
Duration CPB (min), average	150.2	127.8
Duration cross-clamp (min), average	85.3	96.8
Stroke		
Preoperatively	0	0
Postoperatively	0	0
Seizure		
Preoperatively	0	1
Postoperatively	2	0

CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest.

distal aortic clamp in place, without need for an open distal anastomosis under DHCA. In a sense, the disease severity in the control group and the complexity of their operations were less than the DHCA group (Table 2).

Neuropsychiatric Assessment

A 21-part questionnaire was mailed to study patients and their informants, as well as to the control group and their informants. The questionnaire was adapted from A.F. Jorm's Short Form IQCODE (Informant Questionnaire on Cognitive Decline in The Elderly), a 16-question self-administered questionnaire, developed specifically to measure cognitive change. Important questions pertain to memory and intellectual functioning. Responses require patients to rate their function on a five-point scale ranging from "1 = much worse," to "5 = much improved" with respect to their preoperative to postoperative conditions [12]. In this rating system, a value of 3 connotes "not much change."

Importantly, the test does not discriminate based on years of education, and thus does not favorably bias our study cohort. Our test included Jorm's questions as well as 5 additional questions we compiled pertaining to the patients' behavior in their workplace. These additional questions required the patient and informant to comment on the patient's ability to communicate with others at work; to accomplish work at a normal speed; to accomplish work with a normal degree of efficiency; to produce quality work; and to generate creative ideas in the work environment. A key feature of the questionnaire asks the patient and informant to evaluate subjectively the patient's prospective memory as well (eg, going to store, getting in car and forgetting what they originally set out to do). In most cases, informants were the spouses of patients, but could be chosen at the discretion of the patient. Informants were an important part of the study as patients who are cognitively impaired may fail to evaluate correctly their own cognitive deficiencies [13]. Informants were used to provide a second opinion on the current cognitive functioning of the patient. Informants were asked to fill out a separate copy of the same questionnaire as the patients, answering the questions as they pertained to the patient from the informant's point of view.

Deep Hypothermic Circulatory Arrest Management

The head was packed in ice. No barbiturate coma was used during the operation. No electroencephalogram, sensory evoked potential, or jugular venous bulb oxygen saturation monitoring were used. No special glucose management techniques were applied. Deep hypothermic circulatory arrest management was by the Alpha-stat method. Aprotinin was our antifibrinolytic of choice at the time that these patients were operated on. The femoral artery was our cannulation site of choice; in the minority of patients with descending atheroma seen on intraoperative transesophageal echocardiography (performed routinely), we used the axillary artery. The mean core temperature (bladder) during DHCA was 19.0°C (range, 17.5° to 22°C). The maximum temperature gradient between perfusate and body temperature during rewarming was kept less than 10°C. Rewarming was taken to a temperature of 34° to 36°C. Patient body mass index ranged from 17.4 to 45 kg/m^2 (mean, 27.5 kg/m^2). The duration of DHCA is shown in the histogram in Figure 1. (Responders and nonresponders both had a preponderance of patients in the 25- to 29-minute DHCA category.) Neither duration of DCHA nor patient age was predictive of subsequent scores in neuropsychiatric testing. The non-DHCA patients were cooled to 26°C.

Surgical Techniques

Deep hypothermic circulatory arrest was used as the sole means of cerebral protection during this time period. Carbon dioxide flooding of the field was used in all cases. Extent of aortic resection was determined by the extent of disease, with the goal of excising all severely dilated aortic segments.

Postoperative Follow-Up

All discharged patients were reevaluated in the office within 8 weeks postoperatively and screened for any

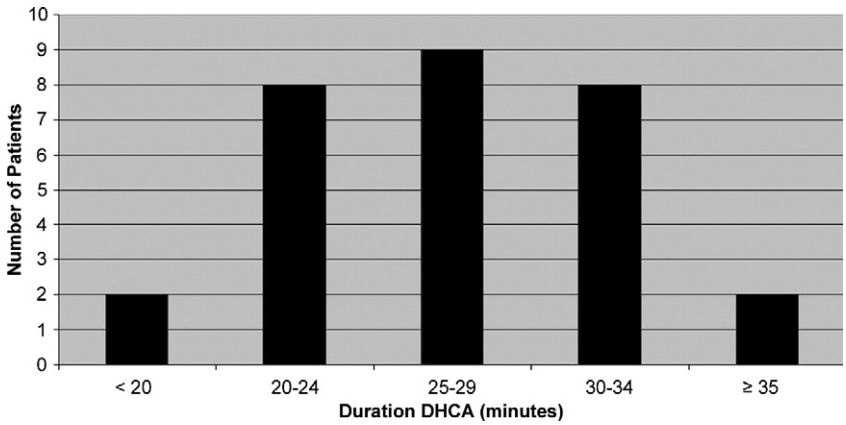

Fig 1. Histogram of deep hypothermic circulatory arrest (DHCA) duration in all 29 high-cognitive responders. Nonresponders had similar distribution.

gross neurologic sequelae or impaired mental or physical functioning.

Statistical Analysis

In addition to determining means of desired groups, Fisher's exact test was used to statistically compare DHCA versus non-DHCA and patients versus informants among a variety of cognitive outcomes. Probability values greater than 0.05 were considered to be statistically insignificant.

Results

The DHCA and the control groups were similar in their demographic and other variables (Table 2) except for the expected greater complexity of the operation in the DHCA group, with more extensive disease, reflected in longer bypass and total cross-clamp and DHCA times.

The questionnaire results are summarized in Figure 2. The mean value of the questionnaire grade for the DHCA group was 3, indicating "not much change" from the preoperative functional class. This was very similar to the value obtained for the control group, operated on without DHCA. Mean values of the outcomes for both study and control groups were very similar and quite close to 3 ("not much change"; Table 3). Three primary categories were analyzed: total responses to all questions, responses to the occupational or work-related questions, and responses to the memory-related questions. For both the total and occupational questions, responses were all greater than 3 ("not much change"). The memory-related questions produced responses that were slightly less than 3, with patient values at 2.96 ± 0.43 for those with DHCA and at 2.99 ± 0.25 for those without DHCA (not significantly different). It is interesting to note (see mean column in Table 3) that some patients, both DHCA and non-DHCA, reported better cognitive function (values greater than 3) after surgery than before. Multiple DHCA patients have spontaneously reported better cognitive function during their clinic visits compared with preoperatively.

Fisher's exact test results showed no statistically significant differences between any of the outcomes by

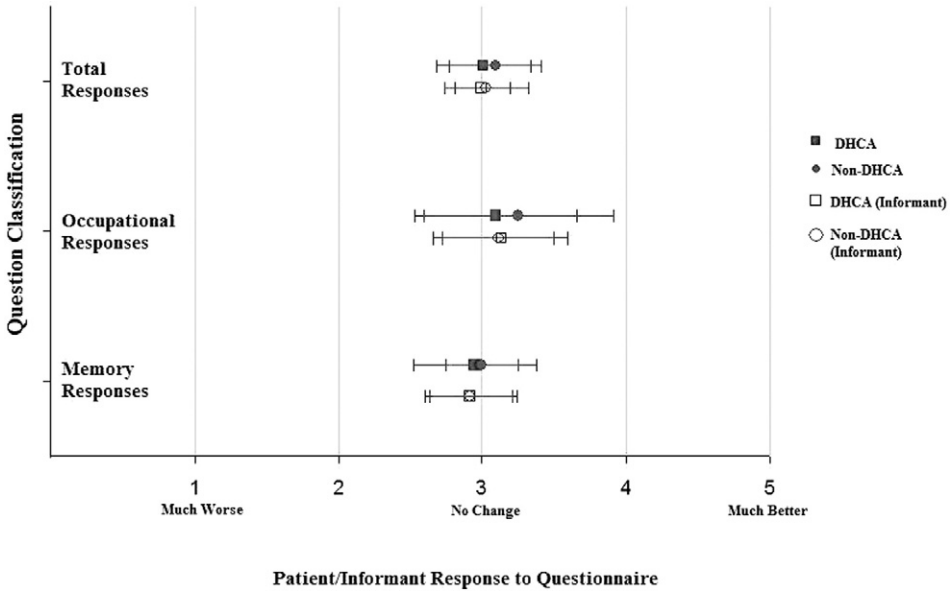

Fig 2. Depiction of questionnaire results (see text). Note near identity of response grades for deep hypothermic circulatory arrest (DHCA) and non-DHCA groups, both according to patient and according to informant.

Table 3. Mean Scores for Full Sample, Deep Hypothermic Circulatory Arrest Group, and Non–Deep Hypothermic Circulatory Arrest Group[a]

Group	N	Mean	SD	Minimum	Maximum
Patient/informant responses					
Full sample	46/40	3.05/3.02	0.32/0.24	2.43/2.57	3.86/4.05
DHCA	25/23	3.01/3.00	0.33/0.19	2.43/2.57	3.86/3.43
Non-DHCA	21/17	3.09/3.03	0.32/0.29	2.57/2.76	3.81/4.05
Difference between DHCA and non-DHCA	4/6	0.08/0.03	0.01/0.10	0.14/0.19	0.05/0.62
Patient/informant occupational responses					
Full sample	47/42	3.16/3.12	0.61/0.43	2.00/2.60	5.00/4.80
DHCA	26/23	3.09/3.13	0.56/0.47	2.00/2.60	4.80/4.80
Non-DHCA	21/19	3.25/3.11	0.66/0.39	2.40/2.60	5.00/4.00
Difference between DHCA and non-DHCA	5/4	0.16/0.02	0.10/0.08	0.40/0.00	0.20/0.80
Patient/informant memory-related questions					
Full sample	49/45	2.97/2.92	0.36/0.30	2.29/2.00	4.43/3.86
DHCA	28/27	2.95/2.92	0.43/0.32	2.29/2.00	4.43/3.71
Non-DHCA	21/18	3.00/2.92	0.25/0.29	2.57/2.57	3.71/3.86
Difference between DHCA and non-DHCA	7/9	0.05/0.00	0.18/0.03	0.28/0.57	0.72/0.15

[a] Responses based on a 1–5 scale where 1 = Much worse since surgery, 3 = Not much change since surgery, and 5 = Much better since surgery. Responses separated into total responses, occupational responses, and memory responses. As indicated in the table, the first number is the patient score and the number after the slash is the informant's score for the patient.

DHCA = deep hypothermic circulatory arrest; SD = standard deviation.

study group (DHCA versus non-DHCA), sex, age, or DHCA duration (Table 4).

Because of the human error associated with this type of study, some patients failed to include an informant response, and some (very few) failed to complete various sections of the questionnaire. The n breakdown by category is included in Table 3.

To examine the possibility of bias in responding, all 16 nonresponders in the DHCA group were contacted in person or by phone. There were no deleterious new job changes (retirement, termination, and so forth). A non-English primary language was the reason for noncompletion in multiple patients.

Comment

This study presents relatively strong evidence that patients with high cognitive needs who underwent aortic surgery using DHCA experienced no perceptible cognitive change as a consequence of this procedure. This study, using a self-administered questionnaire, supplemented by a familial informant, provides direct subjective feedback by patients who underwent DHCA and their families. Our study found excellent preservation of cognitive function after surgery, according to both patient and informant responses. Although subtle deficits after DHCA might hide in individuals with less intellectually demanding professions, it is unlikely that substantive deficits could remain undetected in our high-cognitive needs group.

Although some studies have investigated the clinical outcomes of DHCA, very few have studied the patients on a subjective level with quantitative techniques. Immer and colleagues [7] investigated quality of life after interventions on the thoracic aorta with DHCA by using the Short Form 36 Health Survey questionnaire. They concluded that quality of life in such patients is "fairly good" and "comparable to an age-matched standard popula-

Table 4. Probability Values of the Fisher's Exact Test Comparing Deep Hypothermic Circulatory Arrest Group Versus Non–Deep Hypothermic Circulatory Arrest Group Between Patients and Informants Among a Variety of Criteria[a]

Variable	Patients	Informants
Sum of all questions	0.5561	0.3314
Occupational	0.5501	0.8774
Memory	0.7941	0.5322
Age group >70 y		
Sum of all questions	1.0000	. . .[b]
Occupational	1.0000	0.2500
Memory	1.0000	0.4000
Age group ≤70 y		
Sum of all questions	0.4979	0.3396
Occupational	0.2016	0.9622
Memory	0.9335	0.7883
Male sex		
Sum of all questions	0.6203	0.1649
Occupational	0.6591	0.1767
Memory	0.5160	0.1076
Female sex		
Sum of all questions	1.0000	1.0000
Occupational	1.0000	1.0000
Memory	1.0000	1.0000

[a] The lack of values less than 0.05 indicates that there were no significant differences between any groups. [b] No test statistic was calculated because there were no subjects in the non–deep hypothermic circulatory arrest group matching these criteria.

tion." Their favorable findings are fully consistent with the excellent function confirmed in our study. Our study may have been more sensitive to subtle neurologic deficits because we included a large number of questions gauging cognitive performance and we looked at high-cognitive professionals. Even in this group with demanding cognitive needs, functional preservation was excellent. Moreover, we compared the study group with a non-DHCA cohort undergoing less technically demanding operations. Again, even compared with this group with milder disease, no deficiencies attributable to DHCA were identified. Furthermore, in Immer's study, the Short Form 36 questionnaire does not as rigorously ask patients to compare their preoperative to postoperative status. Of the 36 questions in the Short Form questionnaire, only one asks patients to compare their current general health now to that of 1 year prior. Because all of our questions asked patients to specifically compare their preoperative to postoperative status, we gained more in-depth information about their perceptions of the overall surgical experience and quality of life before and after surgery.

Our results indicate that there was no significant difference in quality of work generated after surgery between patients who had DHCA and those without. This validates the initial motivation of this study, based on our clinical impression that DHCA did not seem to affect or bias patients' postoperative performance in their work field. It is interesting that the cognition scores in both groups were greater than 3, the value assigned "not much change" (ie, better function than preoperatively). It is also interesting that multiple responses of individual patients showed a score that indicated better cognition postoperatively than preoperatively (maximum column in Table 3).

Memory is often the main physiologic detriment anticipated in DHCA patients [14, 15], but our study found that memory (questions 6 through 12 on the questionnaire) was not significantly different in DHCA patients than in patients without DHCA. Memory scores were essentially identical between the DHCA and the control groups (Table 3) and reflected memory status essentially identical to the preoperative state. Like the other variables, memory scores did not significantly differ between patient or informant responses, or by age groups, sex, or DHCA duration.

Limitations

HIGH COGNITIVE DESIGNATION. Our study has limitations. The assignment to a highly cognitive group (Table 1) is clearly somewhat arbitrary; on the other hand, most would agree that the patients assigned to this category cannot perform their work without excellent cognitive abilities.

CONTROL GROUP. Although there is no universally acknowledged control group for DCHA, we were pleased with our selection of a control population: patients who underwent ascending aortic surgery without DHCA. These patients were on bypass, and they had a graft placed. In other words, they had a similar operation, but without DHCA. The fact that their operations were shorter and simpler should bias against the relative safety of DHCA in this comparison. So, the equivalency in neuropsychologic outcome is strengthened by the choice of a control group who had a less extensive operation.

RETROSPECTIVE NATURE OF STUDY. Another important issue is that the retrospective nature of this study precluded us from examining preoperative variables measuring patients' neuropsychological states. Weaknesses of Jorm's questionnaire, or of any informant-based scale, are that they can be biased by the current state of the informant and by the relationship between the informant and the patient. Jorm [12] reports that cognitive decline is perceived to be greater when the informant is anxious or depressed or when there is a poor relationship. This factor could lead to false exaggeration of any cognitive deficit. Despite this potential adverse bias, we still found excellent cognitive preservation.

Along the same lines, one could argue that this study is not as effective as a series of objective tests, rather, that it is based only on the subjective findings of two individuals, patient and informant. Although this is generally true, a study investigating the validity of Jorm's test was performed in which his questionnaire was compared with the findings of a battery of neuropsychological and psychological tests, clinical diagnosis of dementia, computed tomographic scan findings, and psychological characteristics of the individuals who acted as informants [16]. The study confirmed that both the IQCODE and the MMSE (Mini-Mental State Examination) act as similar indicators of cognitive impairment. However, the study noted that the IQCODE (on which our study is based) is advantageous over the MMSE because it is not affected by education or premorbid ability. On the other hand, the IQCODE may be contaminated by the fact that it is influenced by the affective state and personality of the subject, the affective state of the informant, and the quality of the relationship between the subject and the informant. Therefore, the study concludes, it is desirable to use both types of cognitive assessments [16]. In fact, there are inherent advantages to using the IQCODE over objective tests like the MMSE. Specifically, unlike the MMSE, the IQCODE is unaffected by premorbid ability and education [17].

LIMITATIONS OF JORM'S QUESTIONNAIRE. We chose the Jorm test because of its extensive testing and validation in the field as well as its demonstrated immunity to educational bias. The questions are appropriate for postoperative cognitive decline. We thought that developing our own specific test would open our study to potential criticism about prior validation.

NONRESPONDERS. Additionally, not all patients in either the DHCA or non-DHCA groups responded to our questionnaire. Our protocol allowed us to telephone patients who did not promptly mail back their responses. More than one telephone call to encourage questionnaire completion was not permitted, however, so as not to limit the patients' ability to opt out of the study. Some patients, on speaking to them by telephone, explained that they felt

no different after surgery, but simply did not want to be part of the study. Four DHCA patients indicated they were fine but preferred not to take time for the questionnaire, and the remainder were alive and clinically well when seen in clinic, without obvious or expressed deficit or concern. All nonresponders were eventually contacted in person or by phone in the course of this study, permitting us to rule out any deleterious job changes in all the nonresponders. For 6 nonresponders, having a language other than English as their native tongue contributed to their nonresponse.

SPOUSAL INFORMANTS. It is important to recognize as well that, although spousal informants are usually aware of work-related issues, they are not often present directly in the workplace, so that their assessment of the patient's work capacity is indirect.

SHORT DURATION OF DEEP HYPOTHERMIC CIRCULATORY ARREST IN MOST PATIENTS. Finally, all patients in this study underwent efficient aortic replacement, with a mean arrest time of 27.4 minutes and no arrest time exceeding 54 minutes. The positive findings of this study should not be construed as validating DHCA as a means of brain preservation in complex or prolonged aortic replacements requiring extremely prolonged circulatory arrest time.

Conclusions

In conclusion, our detailed neuropsychiatric questionnaire assessment strongly supports the adequacy of straight DHCA as a cerebral protectant strategy. We found excellent preservation of functional state and no difference from patients undergoing aortic surgery without DHCA. This study was not intended to compare straight DHCA with other forms of cerebral protection in aortic surgery (specifically, antegrade or retrograde cerebral perfusion). This study does, however, find favorable results in the reported high-cognitive patients with DHCA as a sole means of brain preservation for short to moderate duration circulatory arrest in thoracic aortic surgery.

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