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Assessment of short-term neuropsychologic changes after normothermic versus hypothermic coronary artery bypass grafting

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Summary

Aim: *Coronary artery bypass grafting (CABG) is one of the main methods of treatment of coronary artery disease. Neuropsychological testing is a sensitive method for quantitative assessment of cognitive dysfunctioning following cardiopulmonary bypass. The aim of the present clinical study was to evaluate the neuropsychologic changes in CABG patients, operated with normothermic or hypothermic cardiopulmonary bypass (CPB).*

Method: *Neuropsychological changes were assessed in 33 first-time CABG patients before and 3-10 days after surgery. Patients underwent CABG with hypothermic (H, N=17) or normothermic (N, N=16) CPB with standard anaesthesia. Neuropsychological performance was assessed using a well-established battery of 10 tests. A neuropsychological test battery includes: Digit Span- subtest of WAIS-R (PL), the Trail Making Test, Raven Test, Benton Visual Retention Test, The Bourdon Test, Verbal Fluency - "Supermarket", Verbal Fluency - F-A-S, Turm von Hanoi, Rey Auditory Verbal Learning Test, Digit Symbol- subtest of WAIS-R (PL), Raven's Progressive Matrices. All patients completed the test for: perception, attention, immediate and delayed verbal and visual memory, visual and verbal learning, problem-solving strategies, abstraction, recognition, word fluency, visual- motor co-ordination and psychomotor speed. For comparison, the incidence of decline using the 1,5 standard deviation (at least in 2 tests) was also calculated.*

Results: *Comparing the reliable change and SD methods, statistically significant differences in the incidence of decline were observed in 6 of 10 neuropsychological measures. Patients' scores showed a significant deterioration in concentration of attention, immediate verbal memory, psychomotor speed, visuoconstructive tasks and verbal learning. Neuropsychological deficits were found in 66,7% of patients after surgery. Post-operative deficits were not associated with the method used (normothermy or hypothermy).*

Key words: cognitive function, cardiopulmonary bypass, coronary artery bypass grafting, hypothermy, and normothermy

Introduction

Traditionally coronary artery bypass grafting surgeries (CABG) with extracorporeal circulation Were conducted in hypothermy body temperature lowered to 27-32 ^{0}C. The aim of this condition was to slow down cell metabolism and reduce tissue sensitivity

to possible ischaemia occurring during the surgery. It was important given the fact that CABG was a surgery where the heart was the only organ totally lacking blood perfusion at the very moment of bypassing occluded coronary vessels. Cooling down the myocardium to about 4-10^{0}C proved to be a successful way of preventing it from ischaemia after-effects. Since electro-mechanical cardioplegy with oxidised blood heart perfusion was introduced into clinical practice, hypothermy has become no longer indispensable. Simultaneous technical advances and development of farmacotherapy made extracorporeal circulation quite a safe procedure. Moreover, in the late 1980's hypothermy as a part of routine bypass grafting surgery has been questioned and the issue of severe side effects brought up. Finally in the 1990's, surgery in normothermy (i.e. in 35-37^{0}C) gained much enthusiasm [1].

Postoperative central nerve system (CNS) damage is one of the most serious complications associated with CABG as a method of curing coronary artery disease. The brain is particularly sensitive to ischaemia; its after-effects, may be vast, even in case of injury of a very narrow brain area [1, 2].

Neurological symptoms as well as cognitive deficits and psychiatric disturbances are all clinical manifestations of such damages to CNS that easily escape the physician's attention during general medical examination. They hinder cardiosurgical patients from quick readaptation in the environment and prolong the period of vocational inpairment and the rehabilitation process. According to various authors, the frequency of neuropsychological complications after CABG is over 50% [3, 4, 5, 6, 7, 8, 9, 10, 11, 12].

In the past, prevention of CNS was the major argument for hypothermy during CABG, but nowadays its effectiveness in minimising the possibility of brain ischaemia in extracorporeal circulation is rather controversial. That is why the research for optimal temperature in heart revascularisation surgery with extracorporeal circulation is still being carried out.

The aim of this study was to evaluate the influence of heart revascularisation with extracorporeal circulation on the patient's cognitive functioning. The subjects of research were: the type, the level of neuropsychological changes and their correlation with surgery temperature.

Material and Method

The protocol had been granted the approval of the Committee of Bioethics at Wrocław University of Medicine. All patients had given a written consent to participate in the research. The examined group consisted of 33 patients who had been qualified from September 1998 to July 1999 for the first CABG performed in the Department of Cardiac Surgery Wrocław University of Medicine. Patients were divided into two groups, depending on the temperature during the operation. Group N consisted of 16 normothermic patients and group H consisted of 17 hypothermic patients. The assignment to the two groups was random. The groups of normothermic and hypothermic patients were homogeneous as for demographic features and the general level of

intellectual functioning. Among the operated subjects were 8 females, their mean age being 63.5, and 25 males whose mean age was 58.6. The mean age of the whole group was 58.9, spanning from the age of 43 to 74. In group N there were 3 females and 13 males. In group H there were 5 females and 12 males. The mean age of the group was general: 58.9 (in group N: 58.5 and in group H: 59.3).

The mean general level of intellectual functioning measured by Raven's Progressive Matrices (standard version) and Vocabulary Scale, was 80.75 C (78.12 in group N, and 83.23 C in group H) ($p>0.50$). Differences are not statistically significant.

The methods of premedication, anaesthesia, postoperative care had been uniform with no essential alteration during the operative period under survey. All the patients had been under regular cardiological surveillance and their medication had been adjusted optimally.

All patients have been operated by the same surgeon. Antegrade, blood cardioplegia of the actual perfusate temperature was delivered according to the schema described by Calafiore [13].

The characteristics of patients from both groups and selected clinical data are presented in tables 1 and 2.

In order to compare the ability of preoperative and post operative cognitive functioning two measures had been taken: the first measure within 3 to 10 days before

Table 1

Characteristics of the study population

Variable	General N=33	Group N N=16	Group H N=17	Value
Age (mean)	58,9	58,5	59,3	n.s
Education: Primary Secondary Higher (University)	 7 21 5	 4 10 2	 3 11 3	n.s
Sex: Females Males	 8 25	 3 13	 5 12	n.s
General level of intelligence (I.I.) – Raven's Progressive Matrices	80,75	78,12	83,23	n.s

n.s.– not statistically significant

Table 2

Operative data

Variable	General N=33	Group N N=16	Group H N=17	Value
NYHA: I / II III / IV	24 9	13 3	11 6	n.s
Temperature:		36 C	28 C	
No. of grafts (mean):		2.875	2.8125	n.s.
ECC Duration (min; mean):		81	85	n.s.
Postoperative Intubation Duration (min.):		86.85	90.33	n.s
Cross-clamp time (min, mean):		42.6	45.0	n.s.

n.s. – not statistically significant
NYHA (functional class I-IV) – New York Heart Association;
ECC – extracorporeal circulation

surgery and the second measure within 5 to 10 days after surgery (before hospital discharge).

Standard criteria of time and place of testing were assumed. A trained neuropsychologist administered the tests. The psychologist had not been informed about the operative method (normothermic or hypothermic). Patients were tested individually. The ability of cognitive functions was assessed according to recommended criteria for neuropsychologic dysfunction [5, 6, 13, 14, 15, 16, 17]. In neuropsychologic diagnosis two categories of methods were employed: specific methods (tests and experiments detecting the CNS damage) and non specific methods, by means of which may the characteristic of functions, processes, mechanisms of regulation can be e.g. assessed or such as conversation, interview, observation, tests, experiments. The objective of neuropsychologic examination was the diagnosis of cognitive dysfunctioning which indicate a change in CNS (functional diagnosis) [7, 18]. In the diagnostic process two groups of methods were used. The first group of methods involved experimental standardised methods, among which the psychometric tests offered the opportunity of interindividual comparisons. The other group of methods consisted of the chosen samples of test methods, the scores of which are not interpreted in a standardised way [6, 8, 16, 18]. Because of the clinical condition of cardiosurgical patients, it was necessary to use relatively short neuropsychologic tests [15, 16, 19]. The mean time of conducting the battery of tests examining the ability of cognitive functions was about one hour. All patients were alert, oriented, and medically stable at the time of preoperative examination. The verification of the hypothesis of the CABG postoperative cognitive deficits required the application of a group of methods which take into account the quantity and quality scores of interpretation [18] and which are recommended by The

Statement of Consensus on Assessment of Neurobehavioral Outcomes after Cardiac Surgery [1, 2, 5, 9, 10, 13, 14, 15, 16, 17, 19, 20, 21, 22].

The following tests were administered in the research:

1. The Bourdon Test- (concentration of attention);
2. Rey Auditory Verbal Learning Test- (immediate and delayed recall verbal and visual memory, working memory, recognising);
3. Digit Symbol subtest of the Wechsler Adult Intelligence Scale-Revised [WAIS-R-PL]- (visual perception, psychomotor speed, attention);
4. Turm von Hanoi – (thinking of abstraction, problem-solving strategies, planning tasks, learning, working memory);
5. TMT- Trail Making Test Parts A and B (visuospatial ability, working memory, visual- motor co-ordination, psychomotor speed, planning, abstractions);
6. Benton Visual Retention Test- (visual perception, visual immediate recall, spatial orientation);
7. Digit Span-Forwards, Backwards- subtest of the Wechsler Adult Intelligence Scale-Revised [WAIS-R-PL]), (Immediate memory, working memory);
8. Fluency Test "Supermarket"- (criteria: category verbal fluency);
9. Fluency Test "F-A-S" –(criteria: letter verbal fluency)
10. Raven's Progressive Matrices (standard version) and Vocabulary Scale – general lever of intellectual ability.

Raven's Progressive Matrices (standard version) and Vocabulary Scale were applied in order to assess the general level of intellectual functioning.

Neuropsychological testing was utilised to study short-term effects of cardiac procedures on neuropsychological functioning.

The objective of the neuropsychologic examination was to diagnose brain functioning in its cognitive and affective areas. The neuropsychologic diagnosis enabled to determine spheres and functions affected by dysfunction resulting from the impairment of CNS [7, 8]. Neuropsychologic tests made it possible to examine brain functioning concerning particular cognitive functions [6, 18, 20, 21]. The subject of the examination was:

- perception (visual, verbal);
- attention (concentration, durability, selectivity);
- verbal and visual memory (immediate and delayed recall, working memory, recognition);
- language abilities (fluency: category and letter, naming);
- constructional abilities (visual-motor co-ordination, speed, exactness, visuospatial);
- abstraction (problem-solving strategies, planning tasks);
- learning (visual and verbal);
- psychomotor speed.

Neuropsychologic deficits were determined by calculating mean and standard

deviation for each patient, for the whole study population in measures II and I and for the normothermic and hypothermic groups.

In calculating the difference between preoperative and postoperative test results the following categories were introduced [3, 4, 5, 10, 21]:

1. Lack of change – means that the ability of cognitive functions in measures I and II did not decline and did not improve by more than 1,5 standard deviation, as compared with the preoperative score.
2. Improvement of cognitive functioning – means that cognitive functioning in measure II improved by more than 1,5 standard deviation, as compared with measure I.
3. Decline of cognitive functioning means that cognitive functions in measure II declined by more than 1,5 standard deviation in relation to measure I (preoperative scores).

Neuropsychologic tests allow the detection of brain dysfunction; however, lack of difficulties cannot be the basis for excluding organic brain impairment.

Statistical analyses were performed using the EXCEL 97 and STATISTICA, with a á value of 0.05 considered statistically significant. Quantitative data were compared with one-way analysis of variance (ANOWA) or Mann-Whithney U tests (depending on normality of variable distribution). Categorical data were analysed with the ÷¸ statistic.

Mean value and standard deviation for individual psychological tests in measures I and II (pre- and postoperative scores) were calculated. The differences between the preoperative and postoperative scores were the variables used in the statistical analysis of the data. It has been stated that intraindividual changes in scores from the preoperative test to the postoperative test seem to be the best measure of postoperative mental function. Patients were later classified as showing deterioration in function on a particular test if the postoperative test scores were more than 1,5 standard deviation lower than their preoperative score in at least 2 tests. Change in psychological test scores between measures I and II was verified by means of Student t test.

Mean values for normothermic and hypothermic groups were compared by means of Student t test, and additionally they were verified by non-parametric Mann-Whithney U tests.

The groups of patients with either decline, improvement or lack of change were compared with the ÷¸ statistic.

All factors thought to be related to neuropsychological dysfunction were initially analysed separately through correlation coefficients and one-way analyses of variance. However, in view of the probable interrelationship of many of these factors, the data were reconsidered through multiple regression analyses.

Results

The incidence of deterioration in the ability of cognitive functions (according to the criterion: a decline of 1.5 SD or more in at least two neuropsychologic tests) was observed in 66,7 % of CABG patients.

The mean scores of neuropsychologic tests in measures I and II (pre- and postoperative measures) are presented in table 3.

Table 3

Mean and SD for both groups in measures I and II

Index	Mean N=33		Value p<0.05
	measure I SD	measure II SD	
Bourdon	63.66 17.71	56.66 16.18	0.000019*
Turm von Hanoi	38.63 27.62	40.27 28.88	0.770000
Rey-immediate	40.76 10.35	36.97 12.59	0.005184*
Rey-delay	6.12 1.96	5.84 2.74	0.316868
Rey-recognition	12.06 2.72	11.63 3.11	0.259230
DigitSpan	7.3 2.62	6.39 2.54	0.002730*
TMT	10.78 3.71	10.09 3.66	0.116151
DigitSymbol	8.72 2.12	7.87 1.93	0.002153*
Fluency Supermarket	18.18 6.04	16.33 5.17	0.001135*
Fluency FAS	6.76 2.52	6.17 2.52	0.053173*

$p<0.05$ (* – Statistical significance)

In preoperative measure the results of tests estimating the ability of cognitive functions indicate non-specific, yet permanent deficits in these functions of at least 0.5 SD below the mean standards of a group of reference representative for the certain population. All the results obtained by patients qualified for CABG tended downward. After the operation, the results deteriorated by average 1.5 SD below the original level, and the intensification of cognitive deficit amounted to ca. 1 to 2 SD below the mean score obtained by healthy individuals. The overall level of intellectual functioning measured on the basis of non-verbal material by means of Raven's Progressive Matrices (standard version) was assessed to be average.

The results of examining the cognitive functions in patients after CABG varied profoundly in measure I and II (in Wilcoxon's test and Student t test). On average, the results of all tests declined, which clinically occurred as the deterioration in the ability of cognitive functions. Cognitive deficits occurred mostly in the following functions: concentration of attention, immediate verbal memory, psychomotor speed, visual-motor co-ordination, learning on the basis of verbal material, and verbal fluency.

No statistically significant changes between test scores in pre- and postoperative measures (measures I and II) occurred in delayed recall and the ability to solve problems. The deterioration of neuropsychologic test scores in postoperative examination varied according to a test type. It is presented in table 4.

The incident of deterioration in test scores was most often reported in the following

Table 4

The change in neuropsychologic test scores between measures I and II for the hypothermic (H) and normothermic (N) groups of patients

Index	Number of patients			Sum	%		
	Improvement	Lack of change	Decline		Improvement	Lack of change	Decline
Bourdon	1	26	6	33	3.03	78.79	18.18
Turm von Hanoi	5	25	3	33	15.15	75.76	9.09
Rey-immediate recall	3	19	12	33	8.82	55.88	35.29
Rey-delayed recall	6	11	16	33	18.82	33.33	48.48
Rey-recognise	5	23	5	33	8.82	69.70	15.15
Digit Symbol	2	18	13	33	18.18	54.55	39.39
TMT	3	24	6	33	15.15	72.73	18.18
Benton	1	12	20	33	6.06	36.36	60.61
Digit Span	3	22	8	33	9.09	66.67	24.24
Fluency Superm.	1	18	14	33	3.03	54.55	42.42
Fluency F-A-S	2	23	8	33	6.06	69.70	24.24

tests: Benton Visual Retention Test (60,6%, Rey Auditory Verbal Learning Test- trial: VII (48,5%), Digit Span (39,4%), Rey Auditory Verbal Learning Test (trials: I-V) (35,5%); therefore, the subject to deterioration are most often: immediate memory (visual and verbal), psychomotor speed, visual- motor co-ordination, attention, language abilities.

In table 5, mean scores of a particular test with SD for group hypothermic (H) and normothermic (N) taking into account changes between measures I and II are presented. The changes between the scores in two groups between measures I and II were determined on the basis of Student t test and additionally verified by means of non-parameter Mann-Whithney U tests.

There was a significant change in values obtained in neuropsychologic tests and measure II for both groups. In normothermic group (N), score deterioration occurred in 9 tests, whereas in the hypothermic group (H) it occurred in 10. Improvement was reported in 2 tests in normothermic group (N) (Turm von Hanoi, Rey–recognise), and in 1 test in hypothermic group (H) (Benton Visual Retention Test).

Both groups displayed score deterioration in:

Table 5

Mean and SD for both groups N and H in measures I and II and differences between them [Δ (N), Δ (H)]

TESTS	N and H Patient Groups						
	Normothermic N: [illegible]			Hypothermic N: 11			Value Δ (N)-Δ(H) [illegible]
	Mean and SD		Δ (N)	Mean and SD		Δ (H)	
	I	II		I	II		
1. Bourdon	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2. Hand	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3. Rey-Immediate recall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
4. Rey-deler. recall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
5. Rey recognitive	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
6. Digit Span	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
7. TMT	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
8. Benton: w/+ w/-	[illegible] [illegible]	[illegible] [illegible]	[illegible] [illegible]	[illegible] [illegible]	[illegible] [illegible]	[illegible] [illegible]	[illegible] [illegible]
9. Digit Symbol	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
10. Superm.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
11. F-A-S	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
12. RAVEN	[illegible]			[illegible]			

$p<0.05$ (* – statistic significance)

- concentration of attention (The Bourdon Test, TMT, Digit Span subtest of the Wechsler Adult Intelligence Scale – Revised [WAIS-R-PL]);
- visual perception (Benton Visual Retention Test, Digit Span subtest of the Wechsler Adult Intelligence Scale – Revised [WAIS-R-PL]);
- working memory (TMT – Trail Making Test Part A and B);
- immediate memory (Rey Auditory Verbal Learning Test, TMT);
- verbal learning – number of words recalled on trials 1 through 5 (Rey Auditory Verbal Learning Test – trials: I–V);
- verbal fluency (Fluency Test – criteria: category and letter);
- verbal recall – number of words recalled after 20-minute delay – (Rey Auditory Verbal Learning Test – trial: VII);
- visual-motor speed (Digit Span subtest of the Wechsler Adult Intelligence Scale-Revised [WAIS-R-PL]), TMT – Parts A and B);

Statistically significant differences in normothermic and hypothermic patients were reported only in a case of two variables. The normothermic group, compared with the hypothermic group, displayed improvement in recognition (Rey Auditory Verbal Learning) and strategic thinking (the ability to solve problems, aim directing, comparing, concluding). However, the hypothermic patients obtained slightly better scores in immediate visual memory (Benton Visual Retention Test).

The comparative analysis of scores in both groups (N and H) did not confirm the significant influence of temperature administered during CABG on the decline in the ability of cognitive functions.

Discussion

High rate of decline in cognitive functions in CABG patients noticed in this study is consistent with similar observations made by authors investigating this issue. Blumenthal et al. [3], Stump [5, 10], Newman [7], Weiss [11], McKhann [5] and Mora [6] confirmed that deterioration of cognitive functioning was quite common, and ranged from 20% to 79% of cases. The extent to which cognitive functioning declined after heart surgery did not reduce in spite of improved techniques of heart protection during the operation. Kneebone et al. [21] in the study with a control group noticed deterioration in cognitive functioning in nearly 64% of patients submitted to CABG.

This study shows that the most profound deterioration of cognitive functions concerns: concentration of attention, immediate memory (visual and verbal), psychomotor speed, visual-motor co-ordination and language abilities. The data seem to be concordant with observations made by other authors (Blumenthal et al. [3], Bruggemans [23], Buschbeck's [14], Kneebone et al. [21], Jodzio [16], Newman [7], McKhann [5], Mora [6], Shaw [9], Walzer et al. [24], Weiss [11]). The neuropsychological impairment of a minor extent concerned such functions as the ability to learn, abstract thinking, verbal abilities. The opinions about the impairment of functions following CABG vary. (Blumenthal et al. [3], Buschbeck's [14], Shaw [9] Walzer et al. [24])

There was an interesting observation made in this study that the patient's body temperature during the operation had no significant impact on the characteristics

of determined impairment. The conducted research revealed postoperative changes in the results of all neuropsychological tests. No significant differences in cognitive functioning were recognised between normothermic and hypothermic patients. Similar conclusions were made by Weiss[11] and Taggart [25, 26] .

The above results are not in accordance with the results obtained by Buschbeck [14] , Mc Lean [15], Wong et al. [27]. Patients operated in normothermia scored better in neuropsychological tests immediately after CABG, compared with hypothermic patients. Normothermy had a less serious effect on immediate memory and attention impairment than hypothermy; deterioration in psychomotor speed was quite the same in both groups (Buschbeck [14]).

Different results emerged from work by Regragui et al.[20] , Martin et al.[19] and Mora [6]. These authors reported the improvement of cognitive functioning directly after the surgery in patients put into hypothermy when set against the group of patients in normothermy. Martin et al.[19] had confirmed that the risk of neurobehavioral complications was smaller in hypothermic patients (1,4%) than in normothermic ones (4,5%).

It should be stressed here that the results of studies found in the literature concentrating on this specific issue are highly ambiguous and therefore require further investigation combined with employing a control group of patients. There is no agreement to the frequency, extent and character of observed cognitive dysfunction occurring after heart revascularisation surgery. This is all a result of various methodological problems and difficulties in establishing clear criteria of damage.

CABG carries a risk of neurological, neuropsychological and psychiatric complications. Changes to brain functioning after CABG are an often recognised problem in cardiosurgery nowadays. [1] Advising a patient to undergo CABG, one should not only take into consideration the clinical outcome of the surgery and its direct psychopathologic complications, but all the issues concerning patient's professional and social functioning as well. Scores achieved during assessment of cognitive functioning could be of a prognostic value in evaluating effectiveness of rehabilitation process.

The growing awareness of significance of brain dysfunction as a result of heart surgery encourages the development of new, better techniques of recognition, treatment and prevention.

Conclusions

1. Research results show that CABG has a significant influence on deterioration of the ability of cognitive functions.
2. The incident of decline in of cognitive functions occurred in 66,7 % of the cases (the criterion for a result decline of at least 1.5 SD in at least 2 tests).
3. The research revealed deterioration of most examined functions. The most significant deterioration after CABG concerns concentration of attention, psychomotor speed, visual-motor co-ordination, immediate memory (verbal and visual), learning on verbal material, language abilities.
4. The comparative analysis of results did not confirm a varying influence of the ap-

plied operative method on the dynamics of postoperative changes in the two groups normothermic (N) and hypothermic (H). Statistically significant changes in the results of most neuropsychological tests in the normothermic group, as compared with the hypothermic group, were not found.

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