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Original Research Article

# Predictors of Postoperative Cognitive Dysfunction in adult patients undergoing elective Cardiac surgery

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**Abstract:** Despite improvements in surgical techniques and the implementation of effective brain protection strategies, the incidence of cerebral injury after cardiac surgery has remained relatively constant. Cognitive dysfunction is the most common clinical manifestation of brain injury after cardiac surgery constituting approximately 30 -40%. It can affect different cognitive domains such as attention, memory, learning, visual spatial, motor skills, and executive function. 111 patients aged over 30 years undergoing elective cardiac surgery at our institution between September 2013 and July 2015 were included and tested with addenbrooke score before and 7 days after surgery. Transfusion of stored homologous blood which contains micro particulates (MP) (size <1 micron, leading to embolisation that causes cerebral injury and even alcohol has a toxic effect on the central nervous system. After testing various variables and factors we conclude that POCD is a known entity as a complication after manipulation of aorta during cross clamping, but less emphasised but important factors are blood and it's product transfusion and alcohol intake.
**Keywords:** postoperative, cognitive dysfunction, addenbrook score, alcohol induced injury, blood transfusion, microparticles, aortic cross clamp.

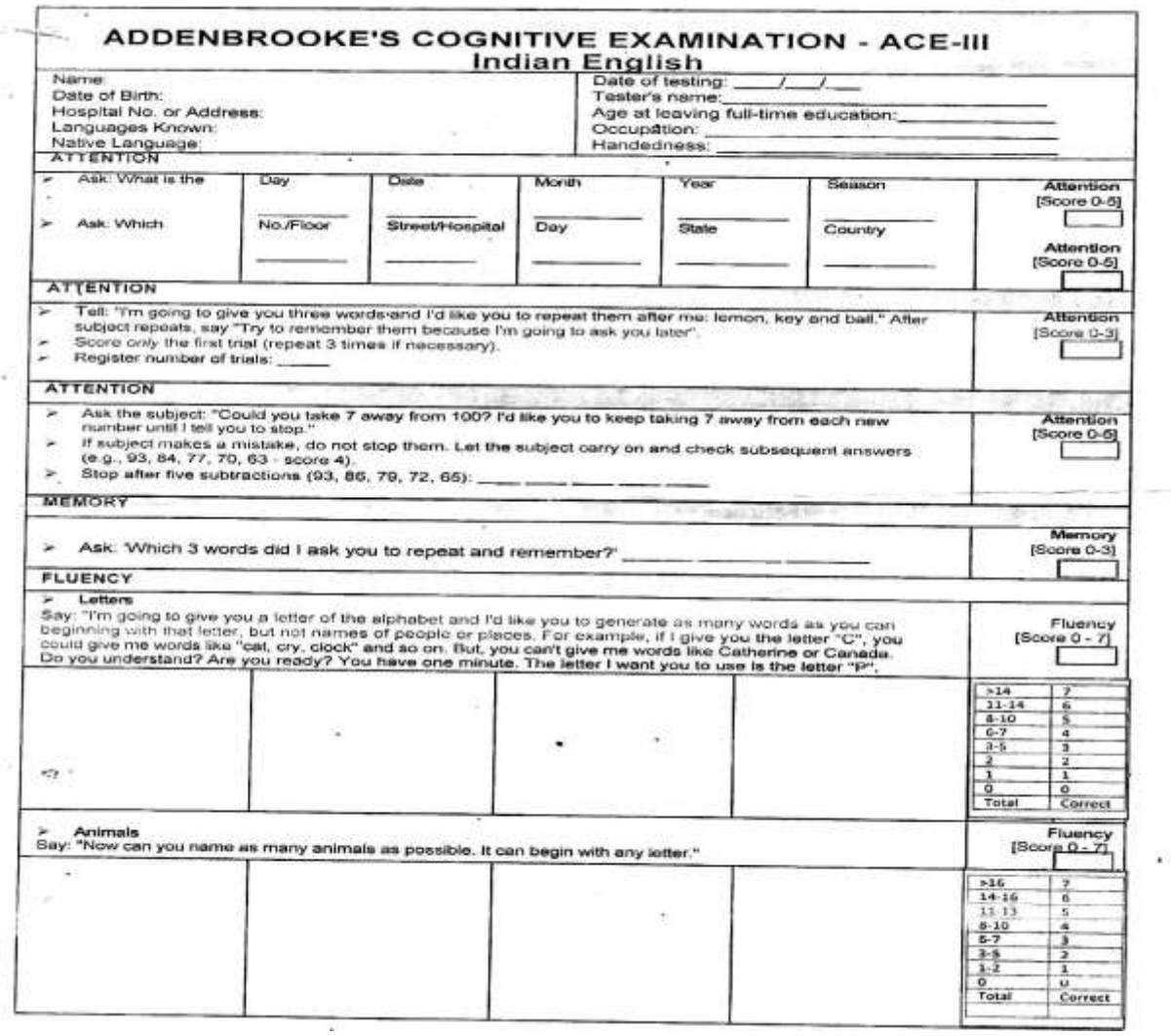
## INTRODUCTION

Every year, about 1,000,000 patients are undergoing open heart surgery worldwide. There is progressive decrease in mortality in cardiac surgery since the 1980.The incidence of postoperative neurologic complications has remained unchanged and has significant impact on quality of life[1]. Neurological dysfunctions can range from neuro cognitive deficit to stroke. They have been classified by The American College of Cardiology and the American Heart Association into Types 1 and 2. Type 1 neurological injury is attributable to brain death, non-fatal stroke, and new transient ischemic attack, whereas delirium and postoperative cognitive dysfunction (POCD) are classified as Type 2 neurological injuries. The two most significant clinical neurological abnormalities after cardiac surgery are stroke and POCD.Studies have reported variedly about incidence and risk factors for POCD following cardiac surgery[2]. POCD can still occur in the absence of the high risk factors. Despite improvements in surgical techniques and the implementation of effective brain protection strategies, the incidence of brain injury after cardiac surgery has remained relatively constant. Cognitive dysfunction is the most common clinical manifestation of brain injury after cardiac surgery constituting approximately 30 -40%. It can affect different cognitive domains such as attention, memory, learning, visual spatial, motor skills, and executive function. It may also be accompanied by behavioural change. A clinical suspicion of POCD may be confirmed with neuropsychological testing completed several weeks after surgery and compared with baseline tests performed preoperatively. Though there are various tests like MMSE (mini mental state examination), auditory memory span test etc., there is no international agreement on what test batteries should be used for the diagnosis of POCD.

## MATERIAL AND METHODS

This Prospective observational study was designed evaluates the risk factors for the development of POCD in adult patients undergoing elective cardiac surgery. Patients aged over 30 years undergoing elective cardiac surgery at our institution between September 2013 and July 2015 were included in the study. Patients with history of Previous cardiothoracic surgery, high BP [>180/110 mm of Hg] at the time of admission, Preoperative active hepatic disease ,Severely impaired left ventricular function (LVEF <30%), Patients with preoperative ADDEN BROOKE SCORE <84, those who were intubated preoperatively ,

concomitant surgery like surgery on great vessels, Preoperative Atrial Fibrillation ,Emergency surgeries, Patients who remained intubated for >24 hr, had cardiac arrest pre or post CPB, who died within 7 days postoperatively were excluded from this study. The study protocol was approved by the IEC and all patients gave written informed consent. Hundred and eleven patients aged 30 years or older completed neuropsychological tests using ADDENBROOKE'S cognitive examination - Ace-R final revised version a (2005, INDIAN VERSION) which consists of scoring for 5 components-sub scores like attention, memory, fluency, language and visuospatial before surgery and at the end of 7th postoperative day. Anaesthetic management standardized for all patients Blood was added to venous reservoir during CPB when Hb was<7 gm/dl. After weaning from CPB Hb was maintained >10 gm/dl by transfusing blood. Intraoperative blood sugars maintained 140-180 mg/dl in all patients.All the components like cardiopulmonary bypass time aortic cross clamp time, blood and its products transfusion, renal dysfunction ,h/o moderate alcohol intake, low preoperative hb%,preop unstable angina which may contribute to POCD were also considered for analysis.



**ADDENBROOKE'S COGNITIVE EXAMINATION - ACE-III**
**Indian English**

Name:
Date of Birth:
Hospital No. or Address:
Languages Known:
Native Language:

Date of testing: ___/___/___
Tester's name:
Age at leaving full-time education:
Occupation:
Handedness:

**ATTENTION**

- Ask: What is the — Day | Date | Month | Year | Season — **Attention** [Score 0-5]
- Ask: Which — No./Floor | Street/Hospital | Day | State | Country — **Attention** [Score 0-5]

**ATTENTION**

- Tell: "I'm going to give you three words and I'd like you to repeat them after me: lemon, key and ball." After subject repeats, say "Try to remember them because I'm going to ask you later".
- Score only the first trial (repeat 3 times if necessary).
- Register number of trials: _____

**Attention** [Score 0-3]

**ATTENTION**

- Ask the subject: "Could you take 7 away from 100? I'd like you to keep taking 7 away from each new number until I tell you to stop."
- If subject makes a mistake, do not stop them. Let the subject carry on and check subsequent answers (e.g., 93, 84, 77, 70, 63 - score 4).
- Stop after five subtractions (93, 86, 79, 72, 65): _____

**Attention** [Score 0-6]

**MEMORY**

- Ask: 'Which 3 words did I ask you to repeat and remember?' _____

**Memory** [Score 0-3]

**FLUENCY**

- **Letters**

Say: "I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. For example, if I give you the letter "C", you could give me words like "cat, cry, clock" and so on. But, you can't give me words like Catherine or Canada. Do you understand? Are you ready? You have one minute. The letter I want you to use is the letter "P".

**Fluency** [Score 0 - 7]

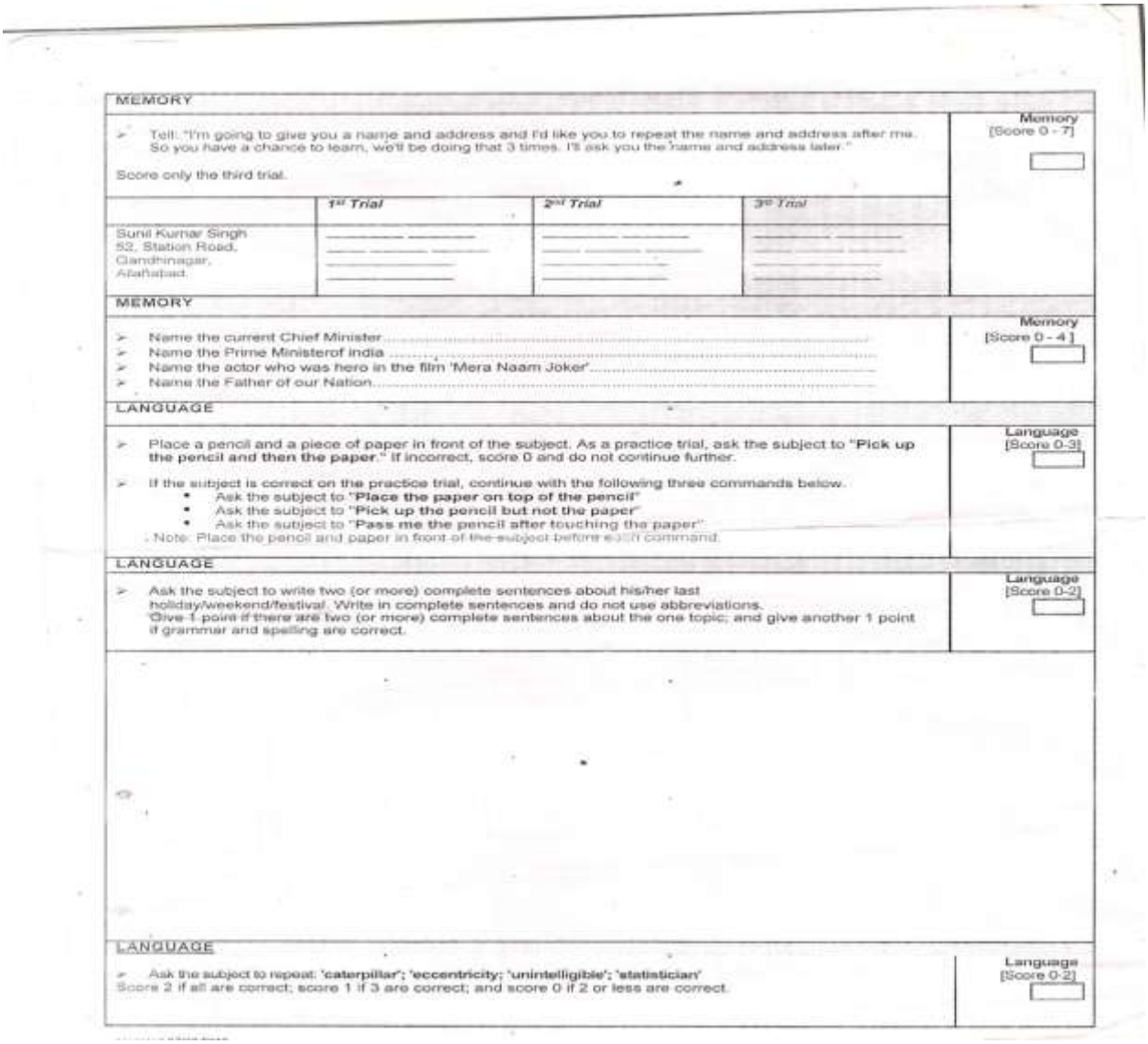
| | |
|---|---|
| >14 | 7 |
| 11-14 | 6 |
| 8-10 | 5 |
| 6-7 | 4 |
| 3-5 | 3 |
| 2 | 2 |
| 1 | 1 |
| 0 | 0 |
| Total | Correct |

- **Animals**

Say: "Now can you name as many animals as possible. It can begin with any letter."

**Fluency** [Score 0 - 7]

| | |
|---|---|
| >16 | 7 |
| 14-16 | 6 |
| 11-13 | 5 |
| 8-10 | 4 |
| 5-7 | 3 |
| 3-5 | 2 |
| 1-2 | 1 |
| 0 | 0 |
| Total | Correct |



MEMORY

- Tell: "I'm going to give you a name and address and I'd like you to repeat the name and address after me. So you have a chance to learn, we'll be doing that 3 times. I'll ask you the name and address later."

Score only the third trial.

Memory [Score 0 - 7]

| | 1st Trial | 2nd Trial | 3rd Trial |
|---|---|---|---|
| Sunil Kumar Singh<br>52, Station Road,<br>Gandhinagar,<br>Allahabad. | | | |

MEMORY

- Name the current Chief Minister.....
- Name the Prime Ministerof india .....
- Name the actor who was hero in the film 'Mera Naam Joker'.....
- Name the Father of our Nation.....

Memory [Score 0 - 4]

LANGUAGE

- Place a pencil and a piece of paper in front of the subject. As a practice trial, ask the subject to **"Pick up the pencil and then the paper."** If incorrect, score 0 and do not continue further.
- If the subject is correct on the practice trial, continue with the following three commands below.
  - Ask the subject to **"Place the paper on top of the pencil"**
  - Ask the subject to **"Pick up the pencil but not the paper"**
  - Ask the subject to **"Pass me the pencil after touching the paper"**

Note: Place the pencil and paper in front of the subject before each command.

Language [Score 0-3]

LANGUAGE

- Ask the subject to write two (or more) complete sentences about his/her last holiday/weekend/festival. Write in complete sentences and do not use abbreviations. Give 1 point if there are two (or more) complete sentences about the one topic; and give another 1 point if grammar and spelling are correct.

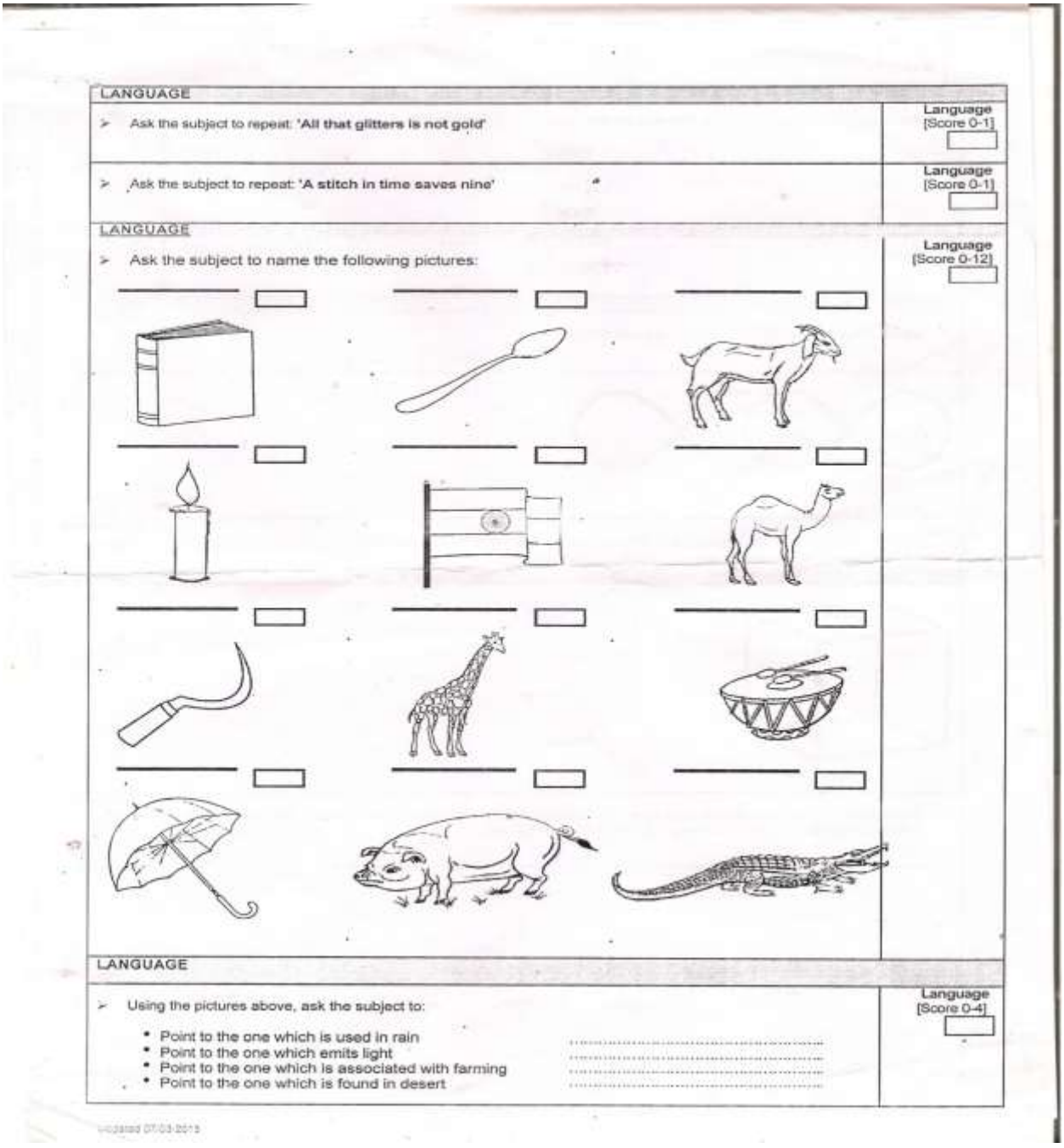
Language [Score 0-2]

LANGUAGE

- Ask the subject to repeat: **'caterpillar'; 'eccentricity; 'unintelligible'; 'statistician'**

Score 2 if all are correct; score 1 if 3 are correct; and score 0 if 2 or less are correct.

Language [Score 0-2]



LANGUAGE

- Ask the subject to repeat: **'All that glitters is not gold'**

Language [Score 0-1]

- Ask the subject to repeat: **'A stitch in time saves nine'**

Language [Score 0-1]

LANGUAGE

- Ask the subject to name the following pictures:

Language [Score 0-12]

LANGUAGE

- Using the pictures above, ask the subject to:
  - Point to the one which is used in rain .....
  - Point to the one which emits light .....
  - Point to the one which is associated with farming .....
  - Point to the one which is found in desert .....

Language [Score 0-4]

Updated 07/03/2013

LANGUAGE

- Ask the subject to read aloud the following words: (Score 1 only if all correct)

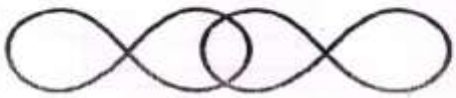
Language [Score 0-1]

sew
pint
soot
dough
height

VISUOSPATIAL ABILITIES

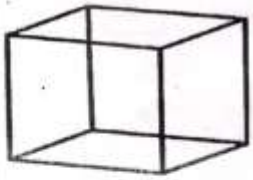
- Infinity Diagram: Ask the subject to copy this diagram.

Visuospatial [Score 0-1]



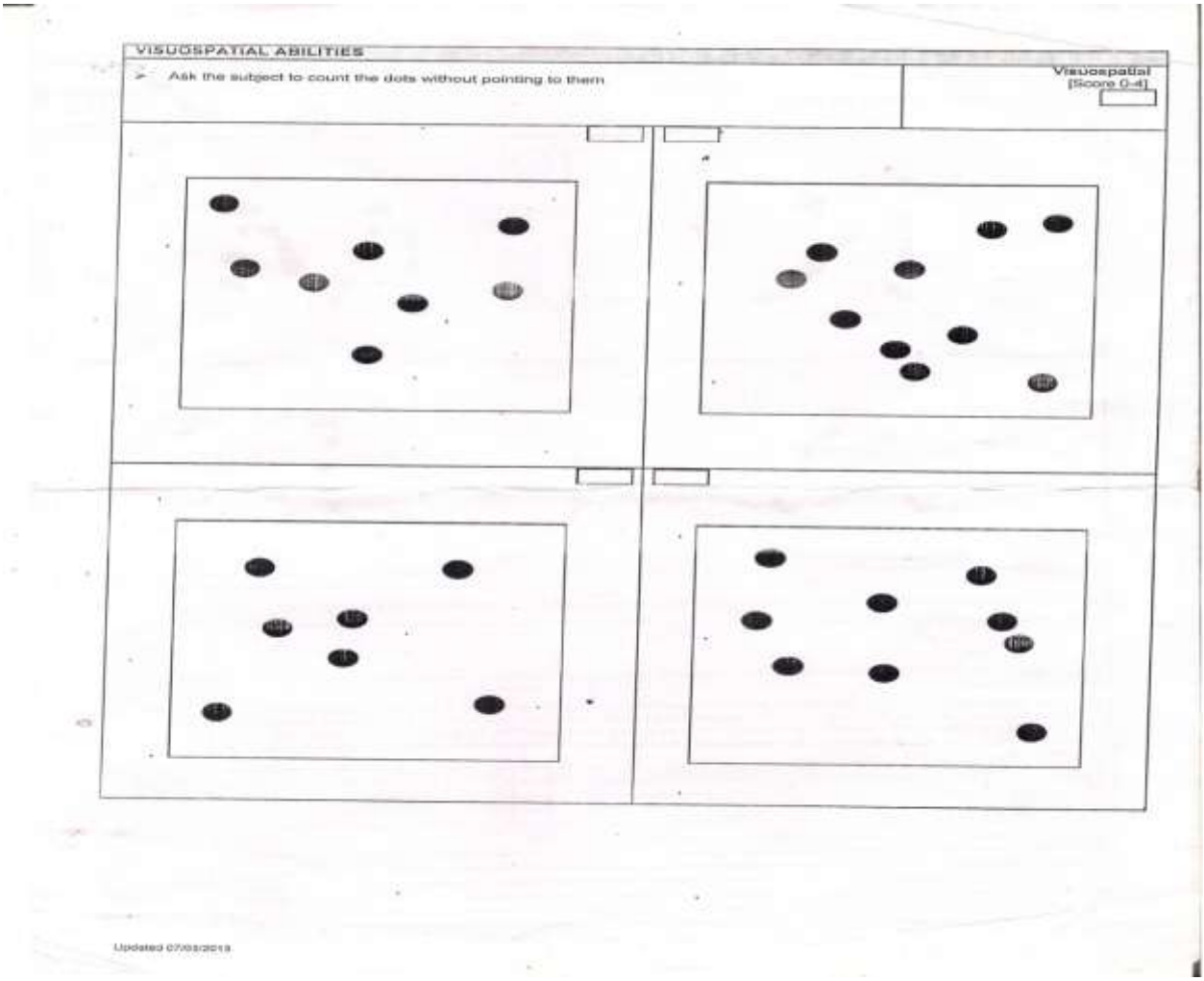
- Wire cube: Ask the subject to copy this drawing (for scoring, see instructions guide).

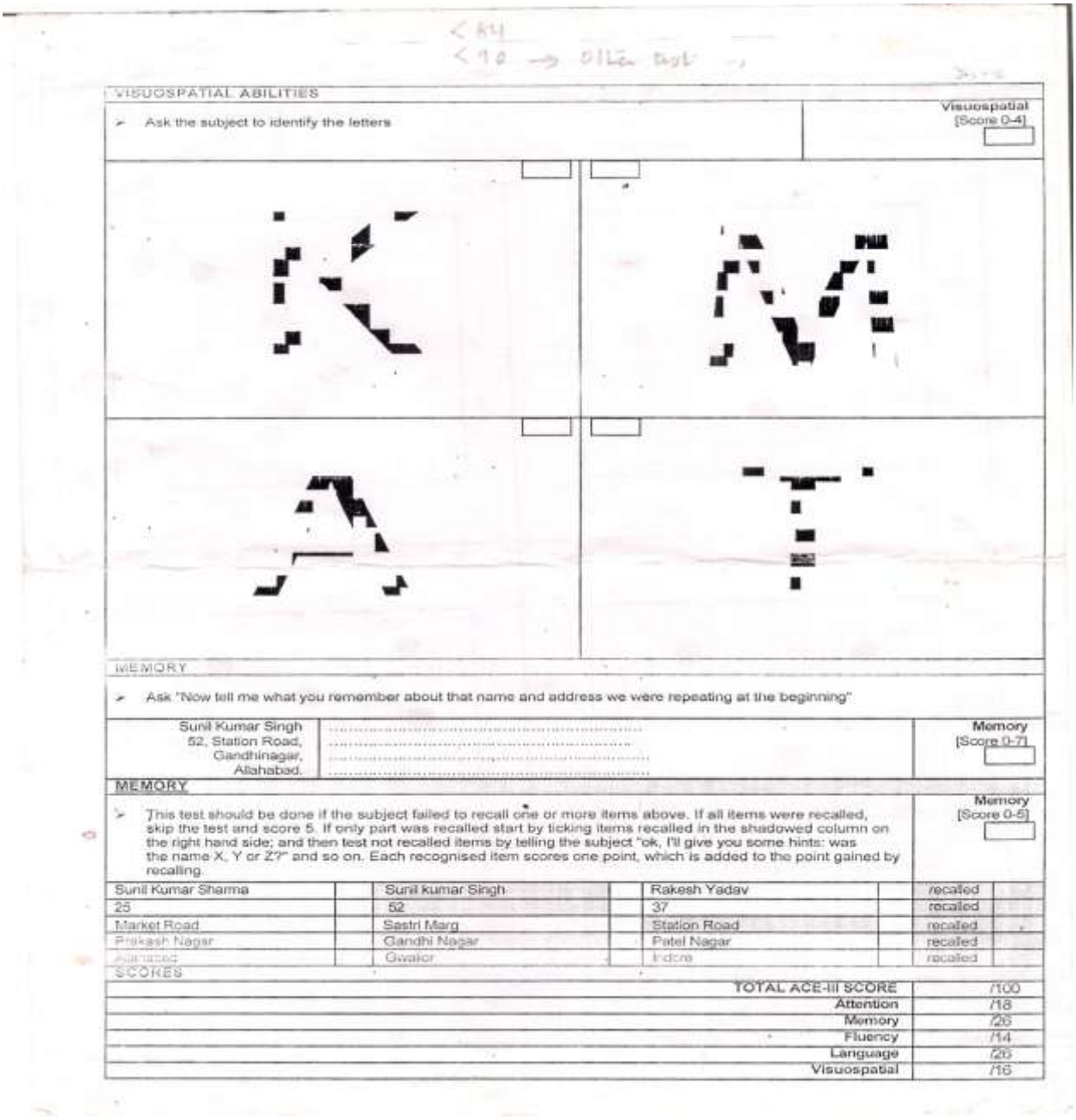
Visuospatial [Score 0-2]



- Clock: Ask the subject to draw a clock face with numbers and the hands at **"ten past five"**. (For scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct).

Visuospatial [Score 0-5]


VISUOSPATIAL ABILITIES
Ask the subject to count the dots without pointing to them
Visuospatial
[Score 0-4]
Updated 07/03/2013



VISUOSPATIAL ABILITIES

- Ask the subject to identify the letters

Visuospatial [Score 0-4]

MEMORY

- Ask "Now tell me what you remember about that name and address we were repeating at the beginning"

Sunil Kumar Singh
52, Station Road,
Gandhinagar,
Allahabad.

Memory [Score 0-7]

MEMORY

- This test should be done if the subject failed to recall one or more items above. If all items were recalled, skip the test and score 5. If only part was recalled start by ticking items recalled in the shadowed column on the right hand side; and then test not recalled items by telling the subject "ok, I'll give you some hints: was the name X, Y or Z?" and so on. Each recognised item scores one point, which is added to the point gained by recalling.

Memory [Score 0-5]

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Sunil Kumar Sharma | | Sunil kumar Singh | | Rakesh Yadav | | recalled | |
| 25 | | 52 | | 37 | | recalled | |
| Market Road | | Sastri Marg | | Station Road | | recalled | |
| Prakash Nagar | | Gandhi Nagar | | Patel Nagar | | recalled | |
| Allahabad | | Gwalior | | Indore | | recalled | |

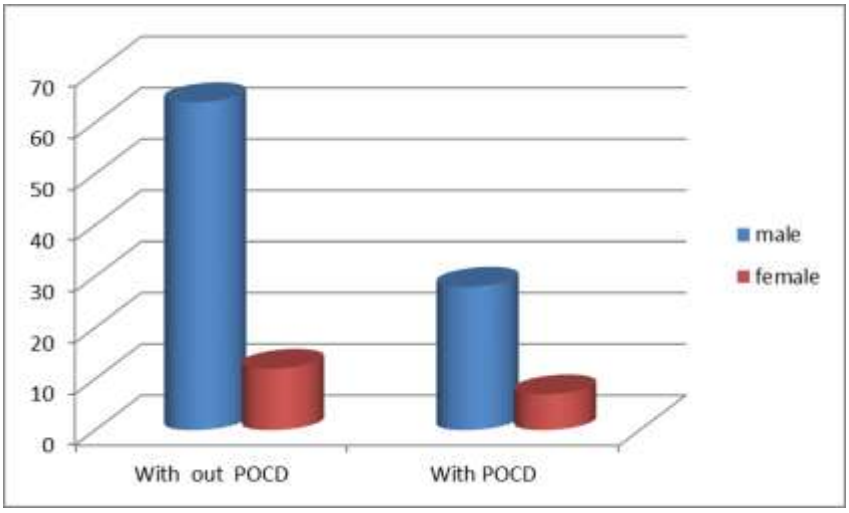
SCORES

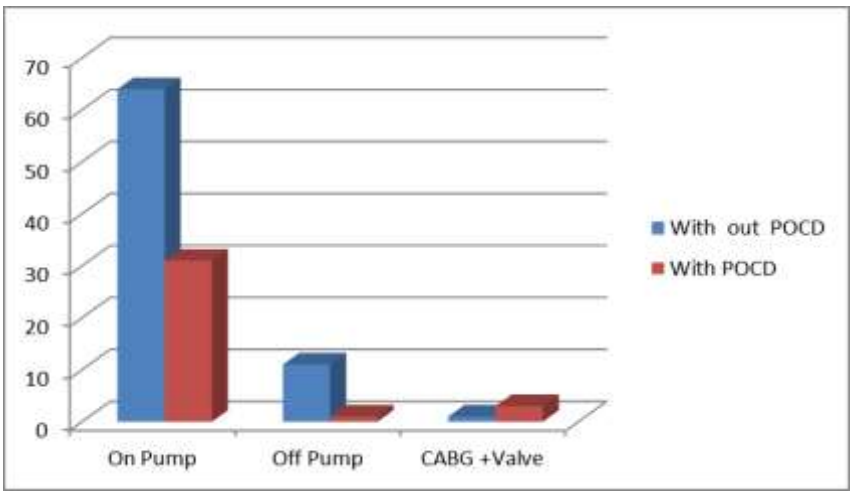
| | |
|---|---|
| TOTAL ACE-III SCORE | /100 |
| Attention | /18 |
| Memory | /26 |
| Fluency | /14 |
| Language | /26 |
| Visuospatial | /16 |

**Statistical analysis**

Cognitive dysfunction is defined as a decrease in score falling below some predetermined threshold, such as decrease in postoperative score of magnitude of one standard deviation or more derived from the preoperative performance of the study as a whole. Statistical analysis was performed with SPSS version 17(SPSS, Chicago, IL). Data is expressed as mean ± SD for continuous variables and frequency of occurrence with percentages for categorical variables. Univariate analyses were performed by comparing patients with and without POCD (ACER VARIABLES, LANGUAGE, ATTENTION ORIENTATION, VISUOSPATIAL, FLUENCY, MEMORY) on 7$^{th}$ POD using $X^2$ test or Fisher exact test when applicable for categorical variables. The Student t test for continuous variables. A 'p' value of <0.05 was considered significant for all tests. Multivariate analyses were performed by forward stepwise logistic regression using the variables that were found to be significant on univariate analysis to identify independent predictors for POCD.

**RESULTS AND DISCUSSION**




In some studies extreme haemodilution (decrease in haematocrit of 12% from baseline) during cardiac surgery had adverse neurocognitive outcomes especially in the elderly but in this study when other factors are analysed ,statistical significance in patients without POCD and with POCD is found with patients with history of alcoholism,smoking,intra aortic balloon pump use, blood and blood product transfusion, aortic cross clamp and lowest hemoglobulin only. Age, pre operative haemoglobin percentage, cardiopulmonary bypass time, history of diabetes mellitus, hypertension, unstable angina, renal dysfunction, drug history with ecosprin, clopidogrel, heparin, statins, steroids, betablockers and ACEI, antioxidants and mannitol had no significant difference between the groups. ultrafiltration, post op glucose management has no difference. The most important risk factor associated is age; numerous studies have proved there is a strong relationship between increasing age and POCD. Greater incidence in the elderly could be attributable to changes in their vasculature and auto regulation of cerebral blood flow. Age is also linked to the risk factors for cerebrovascular disease, which contributes to POCD, such as diabetes, atherosclerosis, and hypercholesterolemia. All these risk factors can contribute to priming of the immune system, so that patients are already in a pro-inflammatory state when subjected to cardiac surgery, leading to amplification of systemic and neuronal inflammation. This precipitates widespread neuronal dysfunction contributing to POCD but in this study age had no statistical significant effect on POCD. Initial preoperative low-baseline scores during neuropsychological testing are associated with age, hypertension, and low education levels, indicating mild cognitive decline: this may increase the risk of POCD. In this study pre operative low addenbrook scores were excluded to identify other factors contributing to POCD. The aetiology of CNS injury may be 1) Cerebral micro emboli (gaseous and particulate) 2) Global cerebral hypo perfusion 3) inflammation and 4)genetic susceptibility aortic cross clamp time and intermittent clamping of aorta, are well known contributors of POCD. Lowest Hb% recorded and blood and its product transfusion were also found to have contributed to POCD[3,5]. Transfusion of stored homologous blood which contains micro particulates (MP) (size <1 micron, leading to embolisation that causes cerebral injury. MP's numbers increase with time of storage. Alcohol has a toxic effect on the central nervous system. ARBI-(alcohol related brain injury)-alcohol impairs absorption of thiamine It can cause dehydration which may lead to wastage of brain cells

associated with changes in cognition (memory and thinking abilities), difficulties with balance and coordination .Frontal Lobe Dysfunction-results in changes in thinking patterns, behaviour and personality[4]. These findings were also observed in our study .Though few studies support the role of alcohol in early post operative cognitive dysfunction in non cardiac surgery we observed its role in cardiac surgery also along with other factors.Limitations of this study are small sample size, cognitive function assessed only in the immediate postoperative period. Longer periods of follow up are required to understand the course of POCD. Further large multicentre studies required to confirm the findings of this study. POCD is a serious complication of cardiac surgery associated with significant long-term morbidity and a decrease in the patient's quality of life, resulting in adverse social, and economic consequences. Pathophysiology is multi-factorial and it can be associated with a wide range of surgical, anaesthetic, and patient factors[6]. As there is no evidence that POCD can be treated successfully, emphasis should be on Prevention. POCD is a known entity as a complication after manipulation of aorta during cross clamping, but less emphasised but important factors are blood and it's product transfusion and alcohol intake[6].

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