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INTRODUCTION

The recognition of neurological complications associated with cardiac surgery has been reported since the dawn of the specialty. Neurological dysfunction includes a spectrum which ranges from neurocognitive dysfunction to cerebrovascular accidents. Cognition is defined as process of perception, memory and information processing which allows the individual to acquire knowledge, solve problems & plan for future. Cognitive dysfunction is thus impairment of these processes.

Post-operative cognitive dysfunction (POCD) has been documented after major surgeries both cardiac and non-cardiac. With improvement in surgical & anaesthesia techniques survival after major surgeries-cardiac as well as non-cardiac has improved & thus post-operative comorbidities have gained major attention which includes POCD, which may affect quality of life of patients after surgery. Incidence of POCD after cardiac surgeries worldwide as indicated by previous studies ranges from 5 to 40 percent within first post-operative week. Indian population data is not accurately available for POCD.

Over time, the demographic characteristics of patients undergoing cardiac surgery have shifted to include a higher proportion of elderly patients, undergoing increasingly complex procedures. The average age of cardiac surgery patients has increased from ~64 years in 2001 to ~67 years in 2010. The number of patients with neurological disease prior to surgery has nearly doubled from 1.4% in 2001 to ~2.8% in 2010. Cardiac surgery procedures have also become more complex, with the number of patients undergoing isolated valvular heart surgery, decreasing by almost 20% from 2001 to 2010. Despite higher patient risk profiles,

the mortality rate has fallen slightly from 4.0% in 2001/2002 to 3.1% in 2010/2011 (National Cardiac Surgery Audit, UCL, 2012).

POCD may range from short term cognitive changes affecting memory & visuospatial functions to post-operative delirium & dementia. But the most common complaint in the

first few weeks following valvular heart surgery relates to memory. The recognition of such cognitive changes by patients, families, and physicians led to a series of studies in which different areas of cognitive performance were tested before and at varying times after valvular heart surgery. Verbal, visual & tactile perceptions, intellectual performance like calculation & retention, speaking etc. forms constellation of features in early post-operative period while affection of thought processes like insight may be affected in long term. Pre-operative co-morbidities like diabetes, hypertension, and history of stroke are associated with an increased risk of POCD as documented by previous studies. Patients with impaired cognition pre-operatively or those having neurological diseases are at increased risk of POCD. An early assessment of cognitive function, after the surgical stress & effect of anaesthesia wean off, may be useful in early diagnosis of any cognitive changes if present. If there are any changes which may affect the cognitive functions of the patient timely remedial measures may be instituted.

It is therefore of paramount importance, to determine the etiology and the extent of brain injury leading to complications which may vary from subtle cognitive impairment to catastrophic stroke events.

The present study is an attempt to assess the cognitive function of patient undergoing valvular heart surgery using cardio-pulmonary bypass before and after the surgery.

The Hindi mini mental scale has been used for the assessment of POCD in the study. It is a rapid screening battery, to explore different cognitive domains: attention/orientation, memory, fluency, language and visuospatial Hindi mini mental scale. is considered useful in discriminating cognitively normal subjects from patients with mild dementia.

AIM & OBJECTIVES

Aim: -

To test occurrence of early post-operative cognitive dysfunction after valvular heart surgery using bypass machine in patients having normal cognitive function pre-operatively.

Objectives: -

1. To assess the cognitive function of patient undergoing valvular heart surgery using cardio-pulmonary bypass one day prior to surgery.

2. Reassessment of patient's cognitive functions 72 hours post-operatively.

3. To compare the patient's pre-operative assessment of cognitive function before surgery with their post-operative assessment.

PATHOPHYSOLOGY

The exact pathophysiology of POCD remains undefined. Previous studies on POCD have focused on investigating the risk factors associated with early POCD. Table 1 describes the variables that have been shown to be associated with early/intermediate POCD. In terms of patient-related baseline factors, or sometimes called predisposing factors, increasing age and lower levels of education have been identified as the main ones in the early study by the International Study on Postoperative Dysfunction (ISPOCD) [33] In a subsequent study by Johnson et al [34] that included only a subset of the population reported in the initial study, alcohol intake was determined to be a predisposing factor for POCD. Preoperative impaired cognitive status also has been shown to be associated with POCD [35]

Whether patients have a genetic predisposition for development of POCD is not well understood because findings from studies to date are conflicting.

Methodological differences between delirium and cognitive assessments, difference in the timing of assessments, and potential differences in patient populations among different studies may result in differences in the findings. Following factors are implicated in the development of POCD

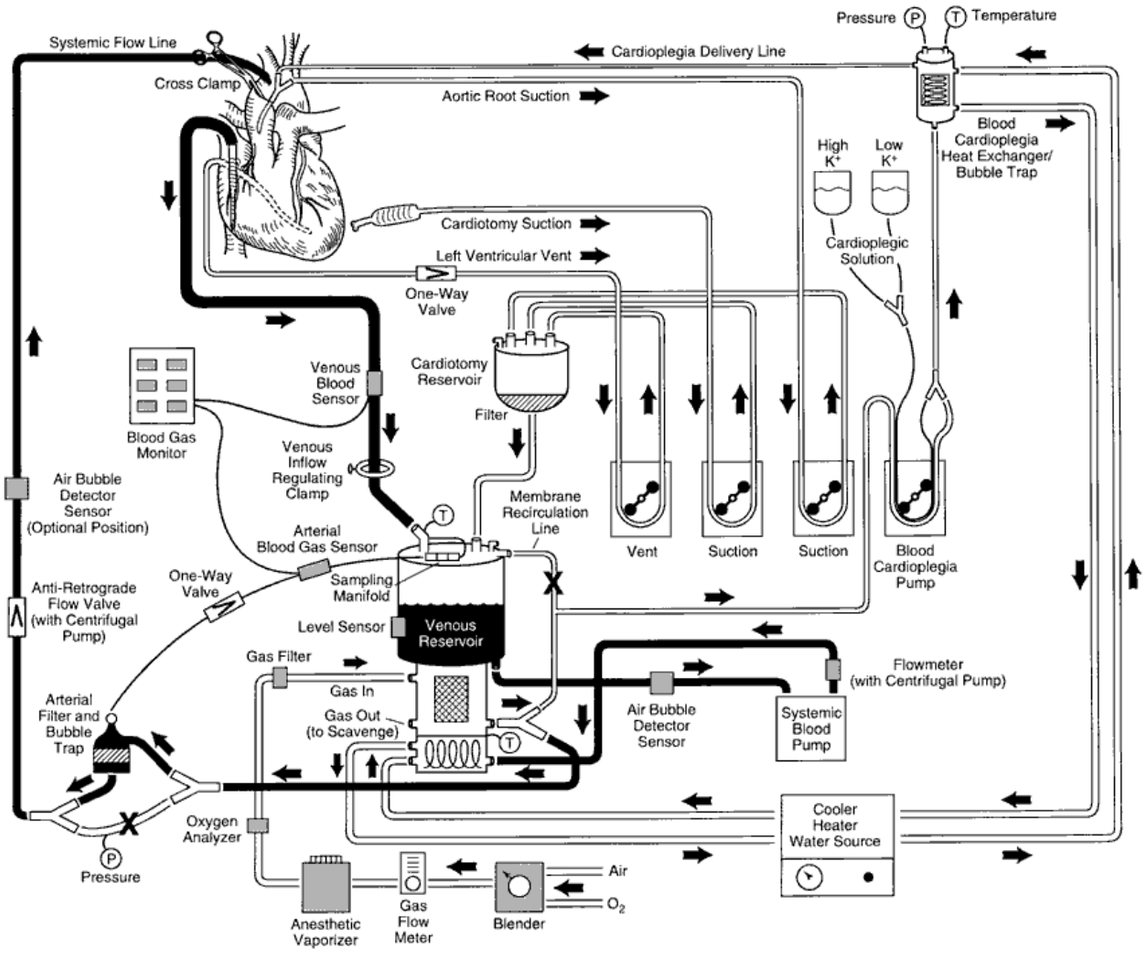


TABLE 2

Risk factors for postoperative cognitive dysfunction (POCD)

	Risk factors
Patient	advanced age; pre-existing cerebral, cardiac, or vascular disease; preoperative mild cognitive impairment (MCI); low educational level; history of alcohol abuse
Operation	extensive surgical procedure, intra- or postoperative complications, secondary surgery
Anesthesia	long-acting anesthetic, marked disturbance of homeostasis, organ ischemia due to hypoxia and hypoperfusion, intra- or postoperative anesthesiological complications

VALVULAR HEART SURGERY AND POCD

2 Most frequently described mechanism of brain injury in valvular heart surgery is based on the recognition that micro emboli are generated by the surgeon manipulating the heart and aorta, through cardiotomy suctioning, and by the cardiopulmonary bypass

Circuit itself. Micro emboli can be detected intraoperatively as high-intensity transient. signals by trans cranial Doppler sonography. They have the potential to lodge in cerebral microvasculature, impairing blood supply to the brain and thus cerebral oxygenation. Several phases during cardiac surgery have been associated with increased risk of embolic showers. Aortic cannulation and clamping (during application of cardiopulmonary bypass) increase the high-intensity transient signal rate, particularly if there is extensive atheroma in the ascending aorta.[61] It is not surprising, therefore, that most (81%) micro emboli are generated at the point of aortic cross-clamp release.[62] Retaining the shed mediastinal blood with cardiotomy suckers provides an additional source of lipid emboli and other fragments,[63] which can be returned into the circuit and onto the brain. Furthermore, a variety of particulate matter and air emboli are generated within the cardiopulmonary bypass circuit itself. These can be filtered before blood is returned to the patient with the assumption that fewer micro emboli then travel to the brain. The use of cell salvage techniques by which red blood cells are filtered and washed before being returned to the circulation may help, but this has shown no specific neurological benefit or reduction in POCD, and, indeed, that it may disrupt coagulation [63]. Whatever the mechanism, there is apparently no straightforward association between the number of micro emboli released and postoperative pathological changes found on brain imaging or incidence of POCD.[64,65] In addition to

Studies targeting the identification of risk factors of POCD, recent investigations have focused on identifying the pathophysiology for POCD

VALVULAR HEART SURGERY is a major surgery which results in a complex systemic response, which includes neuro inflammation. [52] Both systemic and neural inflammation, which occurs because of surgery, may directly affect patient outcome. For example, blood loss and tissue injury might affect the immune system to produce an inflammatory response.[53] Data from preclinical studies support the concept that inflammation is a possible pathogenic mechanism for POCD, and cytokines such as interluekin-1β have been implicated.[54,55,56]. However, the clinical relevance of these experimental findings remains to be determined. Future studies using translational and multidisciplinary approaches are indicated to determine the role of inflammation as a possible causative factor in the pathophysiology of POCD...Numerous studies over the

past decade have reported an acute change in cognitive status in adult patients after major surgery. Most evidence suggests that these early cognitive changes are transitory and do not persist in the long term. However, the prognostic significance of POCD remains a hotly debated topic, especially considering recent data showing that patients with early POCD were at higher risk of morbidity after discharge. Furthermore, whether patients with early POCD have preexisting mild cognitive impairment and experience a steeper downward cognitive trajectory independent of the effect of anesthesia and surgery is another question that warrants further investigation. It is anticipated that future studies will elucidate better the pathophysiology of POCD using large sample sizes and longitudinally collected patient data in both the early and late postoperative period. Thus, to conclude many risk factors for development of POCD have been identified but exact pathophysiology is yet to be established

MATERIALS AND METHODS

Study Design:

It is a cross sectional study.

Ethics:

The study initiated after obtaining necessary permission from the institutional ethics committee. It is done only after obtaining informed consent from the study participants who fulfill the inclusion criteria for the study.

Study Population:

The study population consisted 110 patients of age group 25-65 years who underwent Valvular Heart Surgery using cardiopulmonary bypass machine who fulfilled the criteria for the participation in the study.

Place of Study:

Cardiovascular & thoracic surgery ward & recovery room in a tertiary care hospital in the Metropolitan city in Maharashtra.

Duration of Study:-Study was conducted over a period of one year.

Details of study procedure:

- The study was conducted after approval of Institutional ethics committee.

- Each patient was visited one day prior to surgery in the wards.

- The procedure to be done was explained to the patient in their understandable language and a written informed consent obtained for participation in the study.

- A structured questionnaire that is Hindi Mini Mental Scale was used to know pre-operative cognitive function of the patient.

- Same questionnaire was used 72 hours after operation and results compared to assess the cognitive dysfunction in study subjects in the postoperative period.

- Training to apply and interpret Hindi Mini Mental Scale was taken from Neuro-psychologist.

A. Sampling method:

Study population selected by non-probability convenience sampling method.

B. Inclusion criteria:

• Patients undergoing Valvular Heart Surgery with use of bypass machine intra-operatively.

• Patients in whom anaesthesia is reversed & patients extubated at or before 24 hours of surgery.

• Age: 25 – 65 years

• Sex: Male and Female

• On pump time, less than two hours

• Patients years of education more than 4 years and able to comprehend the test

C. Exclusion criteria:

• Refusal by the patient

• Patients having significant neurological deficit pre-operatively

• Patients with known psychological illness or those with cognitive dysfunction at baseline assessment.

• Patients having any difficulty in talking or affected speech.

• Patients on any sedation at or after 24 hours of surgery.

D. Sample size calculation

Sample size was calculated by using the Formula[64]

$$\text{Sample size (n)} = Z2\,(1-\alpha/2) \times \frac{P * Q}{d^2}$$

Considering variations in POCD prevalence in different studies for early cognitive dysfunction, prevalence of POCD (P) was considered as 7% as observed in the study [67]

P= 7%

Q=100-P = 93%

Z is the value of Z score at 95% confidence interval = 1.96

d= Absolute precision required on either side of the proportion (in percentage points) = 5 percentage points

Calculated sample size: N=99.99= 100

Therefore N= 100, so sample size is taken as 110 considering drop outs (10%).

Tool for study:

5

- Hindi Mini Mental Scale is a rapid screening battery, including five subscales to explore different cognitive domains: attention/ orientation, memory, fluency, language and visuospatial ability.

- HMMS is considered useful in discriminating cognitively normal subjects from patients with mild dementia.

- HMMS was used one day prior to surgery and only those patients were included in study who had normal HMMS score that is less than -1.5 standard deviation for years of education.

- The repeat assessment was done on 72 hours of surgery and value less than -1.5 standard deviation for years of education is taken as normal while value more than -1.5 standard deviation is indicative of POCD

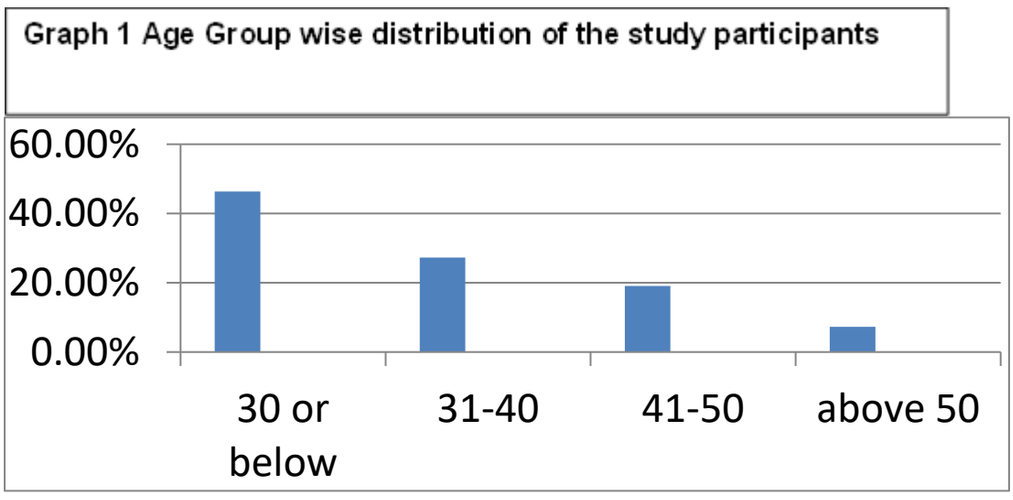
- Post-surgery score was compared with the baseline score & any significant difference if present was noted.

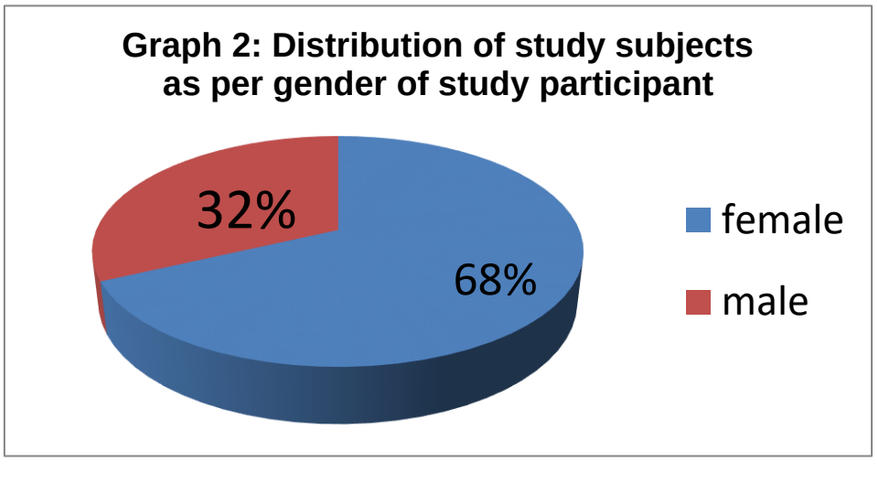
Results and Observations

14 **Table 1 Age Group wise distribution of the study participants**

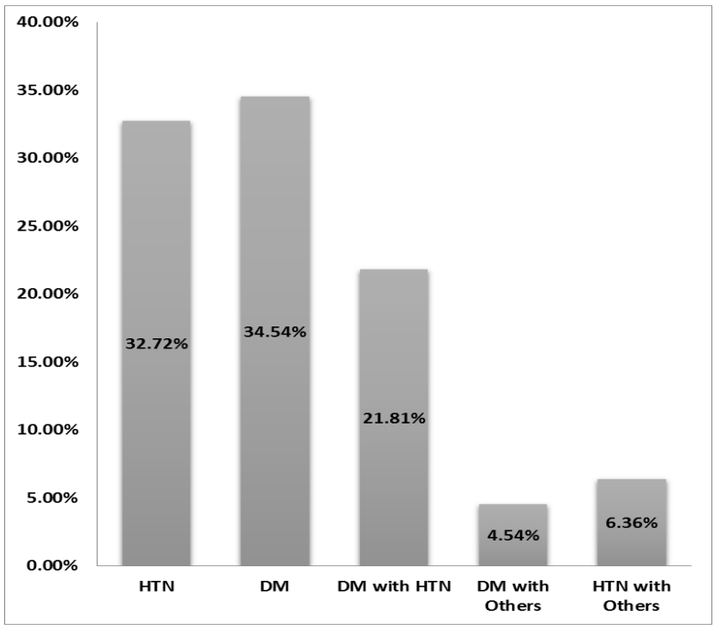
Sr. no	Age group (years)	No. of study participant
1	30 year or below	51 (46.36%)
2	31-40	30 (27.27%)
3	41-50	21 (19.09%)
4	Above 50	8 (7.27%)
TOTAL		110

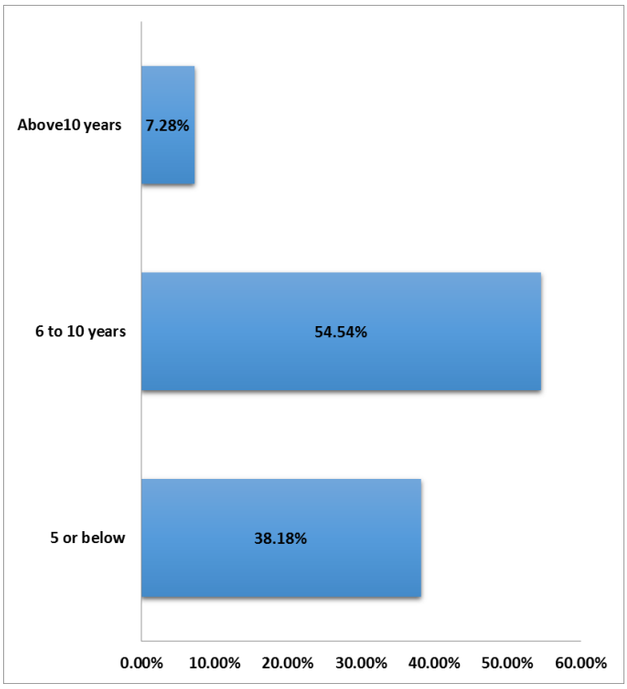
The above table shows the age wise distribution of study subjects. Total 110 cases were studied out of which 51 were below 30 years of age comprising 46.36% of study subjects, 30 were between 31 to 40 years of age comprising 27.27% of the study group.21 subjects that is 19.09% of study group population was of 41 to 50 years and 8 (7.27%) were above 50.





GRAPH 3: Distribution of study subjects as per Associated Co-morbidities





GRAPH 4- Distribution of study subject as per duration of associated co- morbidities

Table 2: Distribution of study subjects as per presence of POCD

Sr. No.	Presence of POCD	No. of Study Participants
1	Yes	02(1.82%)
2	No	108(98.18%)
Total		**110**

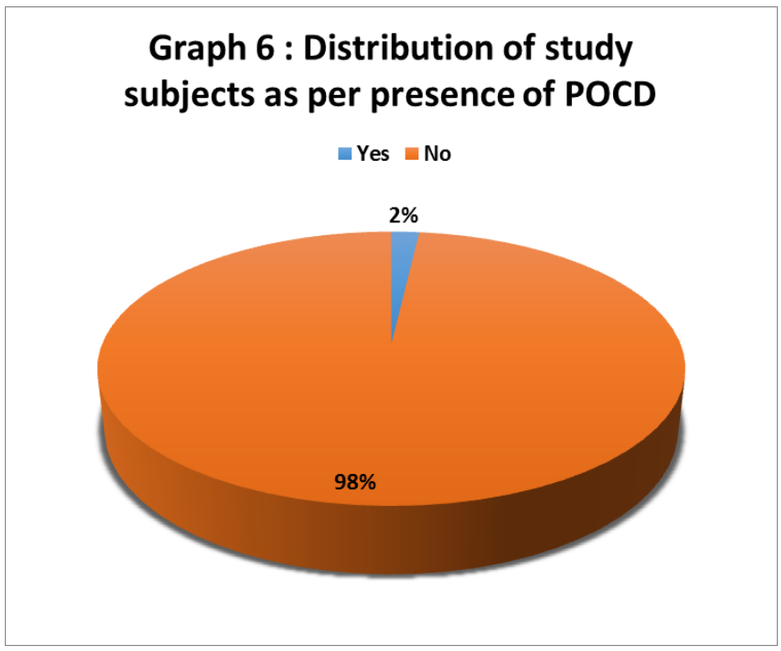


Table 3: Sex wise distribution of study subjects as per presence of POCD

Sr. No.	Sex	Presence of POCD		Total
		Yes (%)	No (%)	
1	Female	01(1.34)	74(98.66)	**75**
2	Male	01(2.86)	34(97.14)	**35**
	Total	02(1.85)	108(98.15)	**110**

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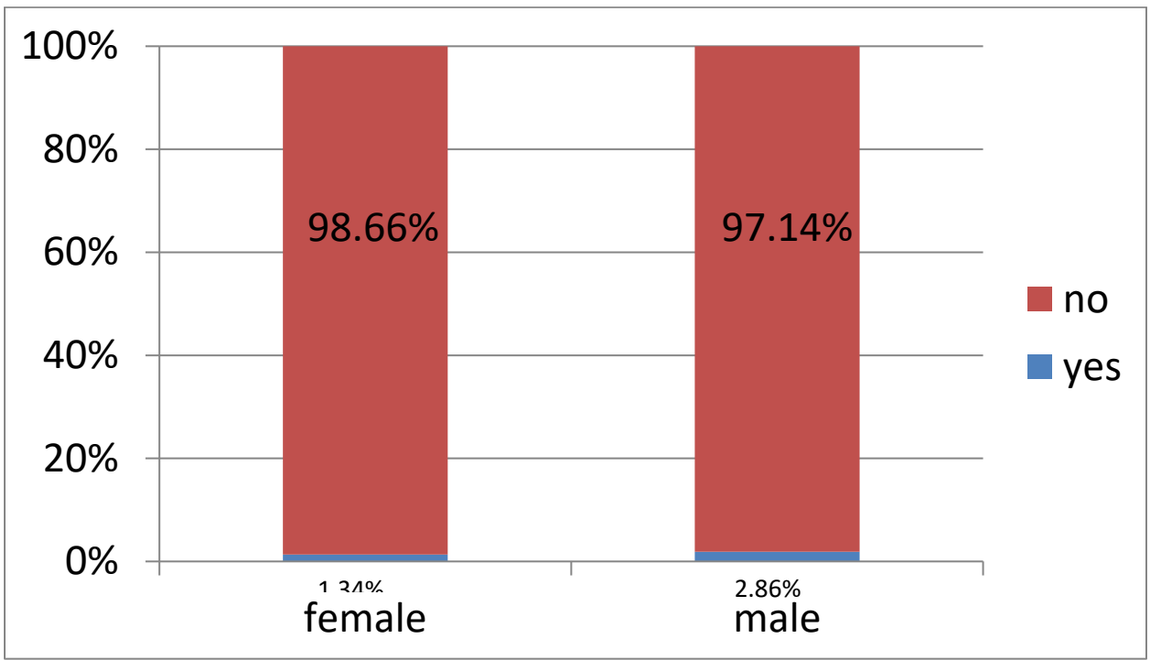
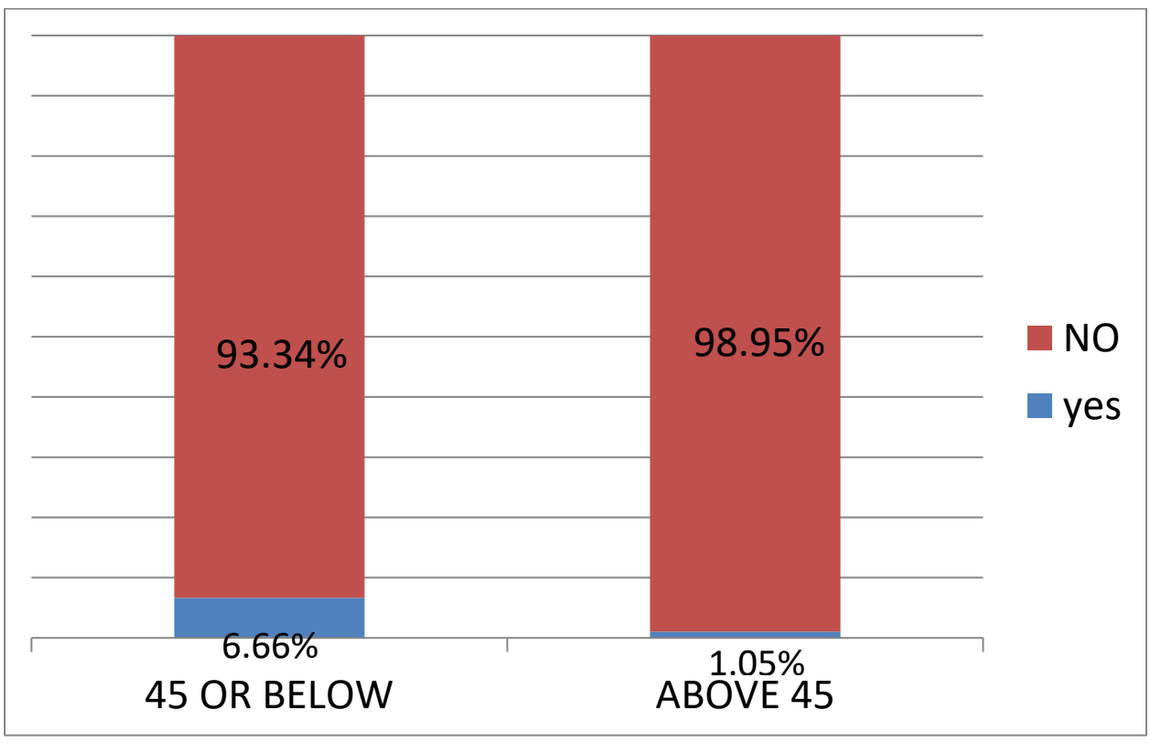
GRAPH 7: Sex wise distribution of study subjects as per Presence of POCD



GRAPH 8: Distribution of study subjects as per presence of POCD and age Group



Discussion

Post-operative cognitive dysfunction (POCD) has been documented after major surgeries both cardiac and non-cardiac. With improvement in surgical & anaesthesia techniques survival after major cardiac surgeries has improved & thus post-operative comorbidities have gained major attention including POCD, which may affect quality of life of patients after surgery. Incidence of POCD after cardiac surgeries worldwide as indicated by previous studies range from 5 to 40 percent within first post-operative week. Preoperative cognitive impairment has been implicated as one of the reason for development of POCD hence our study focused on comparing the preoperative cognitive function of the study subjects with their postoperative one.

Although the pathogenesis of adverse neurologic events after Valvular heart surgery is multifactorial, there is growing evidence that patient-related risk factors, such as the extent of pre-existing cerebrovascular diseases and cognitive impairment have a greater effect on both short- and long-term neurologic sequelae. The most commonly used method of assessing patients for cognitive decline after cardiac surgery is neuropsychological testing. This typically involves administering a battery of tests, before and after surgery, that examines several cognitive domains, including memory, attention, language, executive functions, and motor speed. Although such testing allows for detection of even subtle changes in cognitive performance, it is now increasingly apparent that the incidence of both short- and long-term cognitive decline after Valvular heart surgery has been greatly overestimated, owing to the lack of a uniform definition of what constitutes cognitive decline.

In our study emphasis was on accessing the pre-operative cognitive function of the study subjects using Hindi mini mental scale which is validated as a screening test for cognitive impairment. Total 110 study subjects were studied, Hindi mini mental scale was used 24 hours prior to surgery to know the pre-operative cognitive function of the subject and only those with normal cognitive function were included in the study. Hindi mini mental scale was applied again post-operatively after 72 hours to find out POCD. Hindi mini mental scale score of -1.5 Standard deviation from baseline was considered

as POCD. Thus, a uniform criterion was used with a valid test to define POCD in study group.

Total 110 cases were studied out of which 8 were above 50 years were comprising 7.27% of study subjects, 21 were between 41 to 50 years of age comprising 19.06% of the study group. 30(27.27%) were between 31 to 40 years of age. 51 subjects that is 46.36% of study group population was in the range of 30 year 0r below., thus major proportion of subjects were in the range of 30 or below years of age. This age distribution of study subjects is attributed to incidence of cardiovascular disease and need for Valvular heart surgery for that population. Age group of 25 to 65 was only studied as age more than 65 is an independent risk factor affecting the cognitive function of the patient.

Out of 110 study participants 75(68.18%) were Female and 35(31.82%) were male. This is because of a higher proportion of valvular heart disease in females and a resultant

Graph 3 shows the distribution of co-morbidities in study subjects, 36(32.72%) subjects had isolated hypertension and 38(34.54%) had isolated diabetes while 24 (21.81%) of them had both diabetes and hypertension. Five (4.54%) study subjects had diabetes with other co-morbidity like bronchial asthma or hypothyroidism while 7(6.36%) of them had hypertension with other co-morbidities. Thus, in summary diabetes was the most commonly associated co-morbidity followed by hypertension and hypertension-diabetes combined.

Subjects having history of stroke or cerebrovascular accidents, psychiatric illness, documented memory problems like dementia, speech problems were not included in study to avoid confounding results.

Table 2 here depicts the distribution of study subjects as per presence of POCD, 108 (98.18) subjects did not show the post-operative cognitive dysfunction while only two that is 1.82% showed the POCD.

Hindi Mini Mental scale was the test used to define cognitive impairment in our study which is easy to apply and is in form of a questionnaire which gives a 31-point score which is again easy to compare. Hindi Mini Mental Scale is a valid test for defining cognitive function. Battery of five tests was used by Newman et al and mean of each

test was calculated, finally scores of all five tests were combined to yield a composite cognitive index and its mean score was then used to define cognitive function of the individual. Variation of results is attributed to use of different tests to define subject's cognition and its impairment.

Table 3 shows the gender wise distribution of subjects as per presence of POCD, out of 75 Female patients only one patient developed POCD which is 1.34% of total Female patients, while 74(98.66%) had normal cognitive function post-operatively. One male patient out of 35 developed POCD which is 2.86% of total male subjects studied while rest 34(97.14%) had normal cognitive function post-operatively.

10 Chi square test was applied which yielded a value of 0.310 and p value of 0.5774 as p value is more than 0.05 this is statistically not significant and thus occurrence of POCD is not related to gender of the patients.

Graph 8 shows the distribution of study subjects as per presence of POCD and Age Group, of the two patients who developed POCD one is below 45 years of age and other is having age more than 45 years. Study groups were thus divided above and below 45 years of age to see whether POCD has any relation to age of the patient.

Out of 15 patients of age of above 45 years one patient developed POCD which is 6.66% and 14 patients had normal post-operative cognitive function. In 45 years and below' age group one patient that is 1.05% showed POCD while 94 had normal post-operative cognitive function.

10 Chi square test was applied to these observations which yielded a value of 0.223 and p value of 0.6365, p value is more than 0.05 and hence it is statistically not significant. Thus, distribution of POCD in study subjects is not related to the age of the patients.

Reassessment was scheduled at 72 hours post-operative as it is the period required for weaning of anesthetic effect and surgery related stress. Also, it is the desired earliest interval at which any dysfunction if present can be screened with much accuracy. 72 hours post-operative day is the usual time of discharge from CVTS Recovery to ward in uneventful cases of Valvular Heart Surgery thus an assessment now will help the patient to seek any medical advice if needed.

The two patients who developed POCD had both diabetes mellitus and hypertension over long duration. Becoz of this comorbidity there are chances of developing calcification of valve and microemboli.also age of the patient was above 55 years that is also a independent risk factor for POCD.Cardiopulmonary bypass time intraoperatively for these patient was more than other patients who didn't develop POCD.

Other patient who didn't develop POCD have existing comorbidity of less duration, most of the patient were of age less than 55 years, less cardiopulmonary bypass time, and also inspite of use of new generation oxygenator in all patients undergoing valvular heart surgery using cardiopulmonary bypass circuit, chances of emboli decreases as compare to past.

Results of our study indicate that incidence of POCD is not related to gender of the study subject, existing comorbidities and their duration. These results are comparable with those by Newman et al. However, our study did not show a significant association between POCD and age of the patient, all previous studies including one by Newman et al have shown that old age is an independent risk factor for developing POCD. It is related to the inclusion criteria applied in our study as per which age group of 25-65 years was studied, excluding subjects above 65 years of age. Previous studies included the old age subjects, Newman et al studied a sample of 261 in which age of the patients was 61+10.6 including a higher number of patients above 65 years of age. Our study did not show any relation between POCD and number of years of education. Contrary finding in our study can also be attributed to small sample size studied which is 110 compared with 261 in previous study. Large sample size can provide more comparable results.

To conclude low incidence of POCD in our study is attributed to inclusion criteria for study subjects as per it only subjects with normal cognition were included in study, Age group studied was 25 to 65 years and patients with any history of stroke or psychiatric illness were excluded. Screening test used was Hindi Mini Mental Scale which is a valid test and POCD defined at -1.5 SD below pre-operative level. All this may be responsible for a low incidence of POCD 1.82% at 72 hours of surgery.

SUMMARY

This cross sectional comparative study was conducted to study the POCD in patients undergoing valular heart surgery using CPB having normal preoperative cognitive function, conducted in a tertiary care hospital. A total of 110 study subjects fulfilling the eligibility criteria were included in the study after taking the written informed consent from the participants. Permission from the institutional ethics committee was obtained.

- 110 subjects with normal preoperative cognition were studied of which two developed POCD that is incidence of POCD 1.82% on 72 hours post-operatively.
- One male and one female patient developed POCD showing an incidence of 1.34% among Females and 2.86% in males, chi-square test applied showed no significance between gender of the patient and POCD.
- Forty-five years or less age group had one patient who developed POCD with an incidence of 1.05% while incidence was 6.6% in above 45 years' age group. Relationship between age of the study subjects and occurrence of POCD was not significant.
- Incidence of POCD was 2.38% in study subjects having comorbidities for five years or less, those who had coexisting diseases for more than 5 years had incidence of 1.47%. There was no significant relationship between duration of comorbidities and POCD.
- Both study subjects who developed POCD had 8 years of education and hence no test of significance was applied.
- Incidence of POCD was found lower that is 1.82% in patients having normal cognitive function preoperatively.

CONCLUSION

POCD is one of the important morbidity in patients undergoing Valvular Heart Surgery; it can limit neurological function of the subject significantly affecting memory, reasoning, thought process and mathematical calculations. Neuropsychological tests to determine preoperative cognitive function should be included in the preoperative examination of the patients undergoing Valvular Heart Surgery to screen those with impaired cognition, as they are at an increased risk of developing POCD.

As Per our study POCD prevalence is not significant in subjects having normal cognitive function preoperatively.

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