DOI: 10.7860/JCDR/2022/57305.16624

Original Article

Anaesthesia Section

Incidence of Postoperative Delirium and its Association with Intraoperative Blood Pressure Fluctuation in Elderly undergoing Oncosurgery: A Prospective Cohort Study

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ABSTRACT

Introduction: Postoperative Delirium (POD) is one of the most common complications in geriatric surgical patients. The POD has immense implication because it can initiate a cascade of deleterious events leading to functional decline, reduced cognitive function, prolonged hospitalisation, and death. The risk factors for POD include increased age, cognitive, visual or sensory impairment, functional dependence, infection, and electrolyte abnormalities. Published literature on POD in patients aged >60 years undergoing oncosurgeries are few. According to the American Geriatric Society, evidence for recommendation of intraoperative risk factors is lacking. The relation between intraoperative haemodynamics and postoperative pain with POD is controversial, as studies provide differences in evidence. Hence this relation needs to be studied further.

Aim: To find the incidence of POD in patients >60 years of age undergoing oncosurgery, and its association with intraoperative hypotension and blood pressure fluctuations. The secondary objective was to assess the relation of POD with postoperative pain.

Materials and Methods: The present study was prospective cohort study which was carried on 50 patients aged >60 years undergoing cancer surgery. Intraoperative hypotension and blood pressure fluctuations were measured based on predefined criteria. Postoperative pain and total opioid consumption were also noted. Delirium was assessed with the short Confusion Assessment Method (short CAM), on the first three postoperative days. The association between hypotension and intraoperative blood pressure fluctuations with POD were analysed with Fisher exact test and Mann-Whitney U test. Association of pain scores and total dose of opioid with POD was performed using Student's t-test and Mann-Whitney U test.

Results: The mean age of the study population was 69.5±2.8 years. The mean preoperative Addenbrook's Cognitive Examination (ACE) score was 83.78. The incidence of POD was 22%. There was a significant association between intraoperative blood pressure fluctuation and POD. The mean BP variance ranged from 126.89 to 111.13 mmHg. Increased age and more co-morbidities ≥3 (present in 58%) showed an association with POD.

Conclusion: The incidence of POD was high (22%) among the elderly requiring oncosurgery. Intraoperative blood pressure fluctuation as well as hypotension was associated with increased risk of POD. Hence in elderly patients, tight blood pressure control is advisable during surgery.

Keywords: Haemodynamic, Hypotension, Observational, Surgery, Variance

INTRODUCTION

The POD is one of the most common complication in geriatric surgical population [1]. The incidence of delirium in older hospitalised patients and those in the Intensive Care Unit (ICU) is 10-60% and 11-89%, respectively [2-4]. The overall prevalence of delirium in the elderly patients following surgery ranges from 11-65% [5-7]. According to the American geriatric society, the incidence of POD range from 5% (in low-risk patients undergoing low-risk operations) to 50% (in high-risk patients undergoing high-risk operations) in elderly surgical population [8]. The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) definition of delirium describes an acute and fluctuating disturbance of consciousness with reduced ability to focus, maintain, or shift attention, accompanied by change in cognition and perceptual disturbances secondary to a general medical condition and cannot be accounted for by a pre-existing or evolving dementia [9].

The POD is a form of delirium that manifests in patients after surgical procedures and anaesthesia, usually peaking between one and four days after the surgery often following a lucid interval [10,11]. An episode of delirium leads to a cascade of deleterious events, including major postoperative complications, prolonged hospitalisation, higher healthcare costs, reduced cognitive function, poor functional outcome, increased physical dependence and institutionalisation, increased morbidity and higher likelihood of mortality within six months and increased long-term mortality as well [12,13]. The aetiology of delirium is not yet fully understood and is multifactorial [10]. Delirium risk model by Inouye SK suggests inter-relationship between predisposing factors and precipitating factors in the development of delirium [14]. Established patient-specific risk factors for the development of delirium following surgery include older age, pre-existing dementia, functional impairment, multiple co-morbidities, and history of delirium [15].

The relationship between anaesthesia and delirium is complex, and not yet fully elucidated. One possible focus area to prevent POD is intraoperative blood pressure management. However, the relationship between intraoperative blood pressure and POD is ambiguous. The harmful effect of intraoperative hypotension on the brain can be one of the possible mechanisms of POD and is controversially discussed in different studies [1,12]. Inadequate cerebral perfusion as a result of intraoperative hypotension is one of the possible mechanisms of POD. The oxidative stress hypothesis on the pathophysiology of POD proposes that brain hypoperfusion induces local ischaemia which triggers a chain of events leading to acute brain failure. Another important precipitating

yet modifiable factor contributing to POD is postoperative pain and its management [16]. Admission to ICU, prolonged intubation/ mechanical ventilation, poor pain management, and disrupted sleep patterns are other postoperative factors associated with the development of POD [17].

The aim of the study was to detect the incidence rate of POD in elderly patients undergoing oncosurgeries. The study also determined the association of intraoperative hypotension and blood pressure fluctuations with POD. The secondary objectives were to assess the influence of perioperative risk factors on POD and to study the association of postoperative pain and POD.

MATERIALS AND METHODS

This prospective cohort study was done during the period of June 2016 to May 2017, at a tertiary cancer centre in southern India. The study was done after obtaining Institutional Review Board (IRB) (IRB No: 10/2015/09) and Human Ethics Committee (HEC) clearance (HEC No. 13/2015). Sample size was estimated to be 50 based on an earlier study assuming 80% power and 5% confidence level [18]. This was based on difference in proportion of delirium of 15% in patients with and without intraoperative haemodynamic variability.

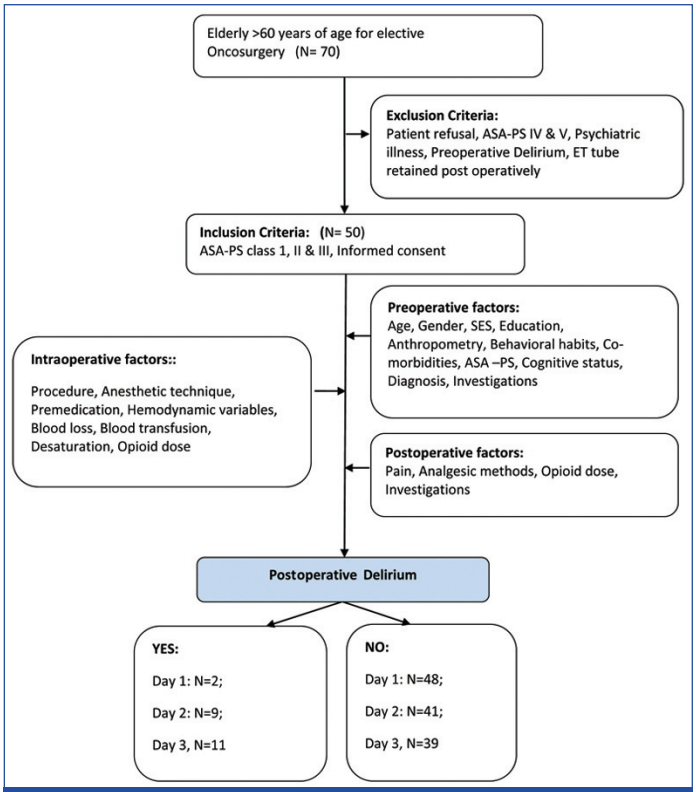
Inclusion criteria: Consenting patients, aged >60 years, undergoing cancer surgery, belonging to American Society of Anaesthesiologists (ASA) class I-III.

Exclusion criteria: Patients with known psychiatric illness and on regular psychiatric medication, patients having endo-tracheal tube retained during postoperative period, deafness, blindness, severe hand deformity or dysfunction, psychosis and other conditions that would affect cognitive testing performance, patients who have evidence of delirium preoperatively based on short CAM [19]. Patients with a Malayalam version of Addenbrooke's Cognitive Examination (M-ACE) score <80 were also excluded from the study.

Study Procedure

The study flowchart is given as [Table/Fig-1]. Preoperative baseline characteristics, co-morbidities, baseline haematological and biochemical values were noted during admission. The socio-economic status (SES) was determined based on per capita income of the family. Families with an annual income less than 24,200 rupees were classified as Below Poverty Line (BPL) and those with more than one lakh per annum as Above Poverty Line (APL). Preoperatively, the baseline cognitive status of the patient was determined using ACE-III questionnaire in Malayalam, on the day of admission to the ward [20]. ACE-III is a cognitive assessment tool, a free to use tool available in the public domain. The five cognitive domains tested by ACE are attention, orientation, memory, language, verbal fluency, and visuospatial skills. The total score is 100, and a higher score denotes better cognitive function. It takes 15-20 min to administer and score. The cut-off for cognitive dysfunction is taken as 80-88/100. The M-ACE has been developed by Mathuranath PS et al., and is validated as a reliable and sensitive screening tool to diagnose cognitive dysfunction [20].

Preoperative pain status was evaluated using Numerical Pain Rating Scale (NRS-11) [21]. It is a patient self-reported scale with 11 points. It assesses pain in a continuum of 0-10, where 0 is no pain and 10 is the worst pain imaginable, 1-3 mild, 4-7 moderate and 8-10 severe pain. Anaesthetic technique was either general anaesthesia alone or with epidural block or combined epidural and spinal anaesthesia. Baseline blood pressure and heart rate was measured. Intraoperative blood pressure, heart rate, type and duration of surgery, type of anaesthesia, total blood loss, transfusion and any events of desaturation (SpO_2 <90%), total dose of opioid used intraoperatively were also noted.



[Table/Fig-1]: Flow chart showing patient selection and follow-up.
ASA-PS: American Society of Anaesthesiologists physical status; SES: Socio-economic status; ET: Endotracheal tube

Intraoperative hypotension was defined as relative intraoperative hypotension- 20 or 40% decrease below the patient's preoperative baseline for either Systolic Blood Pressure (SBP) or Mean Arterial Pressure (MAP). It can also be defined as absolute hypotension-blood pressure decrease below MAP of 60 mmHg. The duration of absolute hypotension was noted. Blood pressure fluctuation was calculated as variance. The patients were followed prospectively on postoperative days 1, 2, and 3 by study personnel and daily interviews with the patient were conducted. A structured interview using the (short-CAM) for the first three postoperative days twice daily (9 am and 6 pm) determined the presence of delirium [19]. Consistency of evaluation was ensured by conducting all three interviews by the same investigator. A second investigator validated all cases of incident delirium.

Postoperative pain was assessed daily which included pain at rest, dynamic pain, maximal pain over the previous 24 hours (h), method of postoperative analgesia, and a 24-hours cumulative dose of opioid converted to fentanyl equivalents. Severity of pain was measured using NRS. The pain experienced by the patient at rest while lying on bed at rest was defined as pain at rest. Pain the patient experienced while ambulating or moving in bed was defined as dynamic pain. Maximal pain was defined as the maximal pain the patient experienced over the previous 24 hours.

STATISTICAL ANALYSIS

From the collected data incidence of POD was analysed. For demographic, and perioperative measures, frequency distribution and summary measures (mean and standard deviation) were studied. For data in proportions Chi-square test and Fisher exact test was used. For analysis of association of POD and intraoperative hypotension and blood pressure fluctuation Fisher exact test and Mann-Whitney U test were used. Comparisons for continuous variables, including pain scores and total dose of opioid (in fentanyl equivalents), was performed using Student's t-test. The Statistical Package for the Social Sciences (SPSS) software version 17.0 (SPSS Inc., Chicago, IL, USA) was utilised for data analysis. Results were considered statistically significant when p-value of <0.05 was obtained.

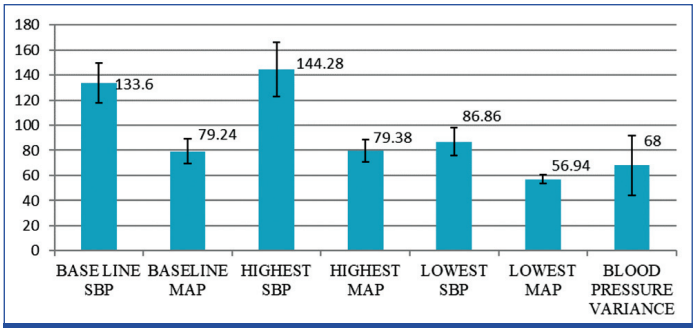
RESULTS

A total of 50 patients undergoing elective cancer surgery were enrolled in the study. Demographic features of the study population are given in [Table/Fig-2]. About 56% of the study population were males and 50% were APL. About 48% had some sort of formal education and 34 persons out of the 50 people studied had either smoking or alcohol habits. Overall 86% of the sample population underwent the surgery under combined general and epidural anaesthesia. Surgery duration was two h for 62% and 3-5 h for 38%.

Type of variable	Frequency n (%)
Age (years)	
60-65	13 (26)
66-70	23 (46)
>70	14 (28)
Mean ± SD	69.5±2.8
Gender	
Male	28 (56)
Female	22 (44)
SE status	
APL	25 (50)
BPL	25 (50)
Educational status	
Illiterate	26 (52)
Literate	24 (48)
Body mass index (kg/m^2)	
Max	33
Min	16
Mean±SD	23.58±3.902
Habits	
Smoking	20 (40)
Alcohol	14 (28)
Clinical diagnosis	
Abdominal mass	1 (2)
Cancer bladder	2 (4)
Cancer cervix	1 (2)
Cancer colon	5 (10)
Cancer endometrium	4 (8)
Cancer oesophagus	2 (4)
Cancer gall bladder	2 (4)
Cancer lung	2 (4)
Cancer ovary	2 (4)
Cancer rectum	21 (42)
Cancer stomach	7 (14)
Retroperitoneal mass	1 (2)
Type of surgery	
Anterior resection	12 (24)
Anteroposterior resection	6 (12)
Anterior resection+hysterectomy	1 (2)
Cholecystectomy	1 (2)
Distal radical gastrectomy	7 (14)
Exploratory laparotomy	2 (4)
Hemicolectomy	1 (2)
Interval cytoreduction	1 (2)
Mc Keown oesophagectomy	1 (2)
Pelvic exenteration	1 (2)
Right lower lobectomy	2 (4)
Radical cholecystectomy	1 (2)
Radical cystectomy	2 (4)
Sigmoid colectomy	4 (8)
Staging laparotomy	6 (12)
Stoma closure	1 (2)
Trans hiatal oesophagectomy	1 (2)
Co-morbidities	
Diabetes mellitus	42 (84)
Hypertension	26 (52)
Thyroid disease	11 (22)
Total number of co-morbidities	
<3	21 (42)
≥3	29 (58)
ASA physical status	
II	48 (96)
III	2 (4)
ACE score	
Minimum	80
Maximum	90
Mean±SD	83.78±3.90
Baseline Hb%	
Minimum	9
Maximum	15
Mean±SD	11.12±1.54
BUN/S.Cr ratio <18	50
Mean fasting blood glucose (mg%)	156.62±6.82
Serum electrolytes (meq/L)	
S. Na+ (mean±SD)	138.2±2.8
S K+ (mean±SD)	3.8±0.4
Anaesthetic technique	
GA	1 (2)
Regional	6 (12)
GA+Epidural	43 (86)
Duration of surgery (hrs)	
2	31 (62)
3	5 (10)
4	8 (16)
5	6 (12)
Mean±SD	2.92±0.7
Intraoperative blood loss >1 litre	Nil
Blood transfusions	Nil

[Table/Fig-2]: Demographic and baseline characteristics.
SD: Standard deviation; DM: Diabetes mellitus; HTN: Hypertension; ASA: American society of anesthesiologists; GA: General anaesthesia; hrs.: Hours; BUN/S Cr: Blood urea nitrogen by serum creatinine ratio; FBS: Fasting blood sugar; S. Na+: Serum sodium; S.K+: Serum potassium, mg%: Milligrams percentage; meq/l: Mill equivalents per litre; APL: Above poverty line; BPL: Below poverty line; SES: Socio-economic status; BMI: Body mass index

In the study population, cognitive status as assessed by ACE score showed that the mean ACE score of the sample was 83.78±3.90. A score of <80 denotes poor cognitive function and hence excluded from the study. None of the patients in the study had a history of POD. The baseline investigations of the patients showed that the mean preoperative haemoglobin of the sample was 11.2±1.54. There was a single incidence of significant desaturation (SpO_2 <90%). None of the study population had intraoperative blood loss of more than one litre or need of any blood transfusion. The mean baseline SBP was 133.60±15.91 mmHg and the mean MAP was 79.24±9.67 mmHg. The average duration of MAP <60 mmHg during surgery was 3.68±2.78 minutes. The intraoperative blood pressure distribution is given in [Table/Fig-3].



[Table/Fig-3]: Intraoperative blood pressure distribution (mm Hg±1 standard deviation).

Postoperatively, patients were followed-up for the first three days monitoring their pain, analgesics and investigations. Pain was assessed using NRS and the maximum pain was observed on day 1 (48% - moderate pain at rest and 78%- moderate pain with movement). The pain scores progressively reduced over time. The mean total opioid consumption in the intraoperative period was 112.20±33.22 mcg in fentanyl equivalents. Average fentanyl consumption was 50.7, 89.8, 84, 46.5 mcg on postoperative day 0, 1, 2 and 3, respectively.

The incidence of delirium was found to be 4% on day 1 following surgery, 18% on the second and 22% on the third postoperative day. On statistical analysis with Mann-Whitney U test, it was observed that the incidence of POD was more in patients with higher age consistently on all the three postoperative days. But this association was not statistically significant (p-value=0.759). The number of co-morbidities ≥3 showed statistically significant association with POD (p=0.042) studied using Fisher exact test. The association of POD and perioperative risk factors is given in [Table/Fig-4]. The POD did not have an association with the type of surgery, duration of the procedure, premedication with midazolam or the type of anaesthesia.

The relation of intraoperative haemodynamic variables and POD is given in [Table/Fig-5]. The association of intraoperative blood pressure with POD was studied using variance of the entire MAP recorded during surgery and tested using Mann-Whitney U test. The blood pressure variance was found to have an association with POD on all the three postoperative days. Intraoperative hypotension (decrease of MAP or SBP >20% from baseline and a MAP or SBP decrease of >40% from baseline) was tested for association with POD using Fisher exact test. The results did not show any statistically significant association. But at the same time, the intraoperative (>40% decrease from baseline MAP as well as SBP) showed statistically significant association with POD both on day 2 and 3.

The patients were followed-up on three postoperative days with pain assessed twice daily. Fischer's exact test was used for testing the association of POD with pain at rest, on movement and maximum pain over 24 hours. But the study could not bring out an association between pain and delirium. The maximum pain over 24 hours on the postoperative days 1 to 3 also did not have an association with POD [Table/Fig-6]. The total opioids consumed postoperatively for three days was not found to be associated

Factor		No Delirium Day 1 (n=48)	Delirium Day 1 (n=2)	p-value Day 1	No Delirium Day 2 (n=41)	Delirium Day 2 (n=9)	p-value Day 2	No Delirium Day 3 (n=39)	Delirium Day 3 (n=11)	p-value Day 3
Age (yrs) Mean±SD		69.44±6.348	71.00±1.414	0.252	68.63 (4.964)	73.44±9.645	0.253	68.90±4.914	71.64±9.584	0.759
Gender	Male n (%)	26 (54.2)	2 (100)	0.497	23 (56.1)	5 (55.6)	1.00	21(53.8)	7 (63.6)	0.734
	Female n (%)	22 (45.8)	0		18 (43.9)	4 (44.4)		18 (46.2)	4 (36.4)	
Education	Illiterate n (%)	26 (54.2)	0	0.225	21 (51.2)	5 (55.6)	1.00	20 (51.3)	6 (54.5)	1.00
	Literate n (%)	22 (45.8)	2 (100)		20 (48.8)	4 (44.4)		19 (48.7)	5 (45.5)	
SES	APL n (%)	23 (47.9)	2 (100)	0.490	19 (46.3)	6 (66.7)	0.463	18 (46.2)	7 (63.6)	0.496
	BPL n (%)	25 (52.1)	0		22 (53.7)	3 (33.3)		21 (53.8)	4 (36.4)	
BMI (kg/m^2)	≤22 n (%)	17 (39.6)	1 (50)	1.00	13 (31.7)	5 (55.6)	0.454	13 (35.9)	5 (54.5)	0.395
	>22 n (%)	31 (60.4)	1 (50)		28 (63.4)	4 (44.4)		26 (64.1)	6 (45.5)	
Behavioral habits	Smoking n (%)	19 (39.6)	1 (50)	1.00	17 (41.5)	3 (33.3)	0.72	15 (38.5)	5 (45.5)	0.676
	Alcohol n (%)	13 (27.1)	1 (50)	1.00	11 (26.8)	3 (33.3)	1.00	10 (25.6)	4 (36.4)	0.476
ASA-PS	Grade 2 n (%)	46 (95.8)	2 (100)	1.00	40 (97.6)	8 (88.9)	0.33	38 (97.4)	10 (90.9)	0.39
	Grade 3 n (%)	2 (4.2)	0		1 (2.4)	1 (11.1)		1 (2.6)	1 (9.1)	
Co-morbidities	Hypertension n (%)	40 (83.3)	2 (100)	1.00	34 (82.9)	8 (88.9)	1	32 (82.1)	10 (90.9)	0.66
	Diabetes mellitus n (%)	25 (52.1)	1 (50.0)	1.00	23 (58.5)	3 (22.2)	0.06	24 (59)	4 (27.3)	0.091
	Thyroid n (%)	11 (22.9)	0	1.00	9 (19.5)	2 (33.3)	0.475	9 (20.5)	2 (27.3)	0.745
	No. of co-morbidities <3 n (%)	21 (43.8)	0	0.503	19 (46.3)	2 (22.2)	0.271	19 (48.7)	2 (18.2)	**0.042**
	No. of co-morbidities ≥3 n (%)	27 (56.2)	2 (100)		22 (53.7)	7 (77.8)		20 (51.3)	9 (81.8)	
ACE score	80-89 n (%)	43 (89.6)	2 (100)	1.00	36 (87.8)	9 (100)	0.570	35 (89.7)	10 (90.9)	1.00
	≥90 n (%)	5 (10.4)	0		5 (12.2)	0		4 (10.3)	1 (9.1)	
Anaesthetic technique	General n (%)	1 (2.1)	0	1.00	1 (2.4)	0	0.428	1 (2.6)	0	0.692
	Regional n (%)	5 (12.5)	0		2 (4.87)	3 (33.3)		2 (5.12)	3 (27.27)	
	General+Regional n (%)	42 (85.4)	2 (100)		37 (90.2)	6 (77.8)		36 (87.2)	8 (81.8)	
Duration of surgery	<3 n (%)	30 (62.5)	1 (50)	1.00	26 (65.9)	5 (44.4)	0.273	25 (66.6)	6 (45.5)	0.293
	≥3 n (%)	18 (37.5)	1 (50)		15 (34.1)	4 (55.6)		14 (33.4)	5 (54.5)	

[Table/Fig-4]: Association between postoperative delirium and perioperative risk factors under study.
APL: Above poverty line; BPL: Below poverty line; SES: Socio-economic status; BMI: Body mass index; HTN: Hypertension; DM: Diabetes mellitus; ASA: PS: American society of anesthesiologists physical status; ACE: Addenbrook's cognitive examination; SD: Standard deviation; N: Number of study subjects

Haemodynamic variable	No Delirium Day 1 (n=48)	Delirium Day 1 (n=2)		No Delirium Day 2 (n=41)	Delirium Day 2 (n=9)		No Delirium Day 3 (n=39)	Delirium Day 3 (n=11)	
	Mean±SD	Mean±SD	p-value	Mean±SD	Mean±SD	p-value	Mean±SD	Mean±SD	p-value
Baseline SBP	133.75±16.23	130±0	0.748	134.37±16.26	130.11±14.58	0.473	134.33±16.65	131±13.38	0.545
Baseline MAP	79.21±9.65	80±14.14	0.911	79.68±9.20	77.22±12.02	0.495	79.54±9.25	78.18±11.47	0.685
Baseline heart rate	71.56±9.56	67±4.24	0.508	70.80±7.54	74±15.82	0.362	71.10±7.53	72.36±14.78	0.699
Max. SBP	144.04±21.92	150±14.14	0.706	141.78±19.36	155.67±28.36	0.05	140.85±19.4	156.45±25.42	0.033
Min. SBP	87.35±10.775	75±21.21	0.129	89.27±10.05	75.89±10.27	0.001	89.59±10.07	77.18±2.65	0.001
Max. MAP	78.65±8.24	97±4.24	0.003	77.46±7.51	88.11±9.78	0.001	76.77±6.70	88.64±9.70	0.001
Min. MAP	57.10±3.43	53±4.24	0.106	57.80±2.84	53±3.71	0.0001	58.05±2.65	53±3.44	0.001
BP variance	45.85±42.19	126.89±39.93	0.042	35.43±33.86	111.36±34.43	0.0001	31.61±28.13	111.13±36.81	0.0001

[Table/Fig-5]: Association of postoperative delirium with intraoperative haemodynamic variables.
SBP: Systolic blood pressure; MAP: Mean blood pressure; SD: Standard deviation, All blood pressure readings in mmHg, all heart rate in beats per minute. N: Number of study subjects

Perioperative period		No Delirium Day 1 (n=48)	Delirium Day 1 (n=2)		No Delirium Day 2 (n=41)	Delirium Day 2 (n=9)		No Delirium Day 3 (n=39)	Delirium Day 3 (n=11)	
		Mean±SD (µg)	Mean±SD (µg)	p-value	Mean±SD (µg)	Mean±SD (µg)	p-value	Mean±SD (µg)	Mean±SD (µg)	p-value
Intraoperative		111.67±33.41	125±35.35	0.583	113.66±32.71	105.56±36.78	0.513	112.56±32.17	110.91±38.33	0.886
Postoperative	Day 0	50.73±19.68	50±40.43	0.961	51.83±20.67	45.56±18.11	0.404	51.92±21.20	46.36±16.30	0.426
	Day 1	90.42±38.53	75±35.35	0.581	91.46±39.98	82.22±29.49	0.517	90.51±39.132	87.27±36.36	0.807
	Day 2	84.79±31.69	65±21.21	0.39	85.37±32.64	77.78±25.87	0.517	83.64±34.72	49.10±20.70	0.966
	Day 3	47.20±19.97	30±14.14	0.23	48.66±20.77	36.67±12.24	0.103	49.10±20.70	37.27±14.21	0.082
Overall opioid consumption		89.8			84			46.5		
Maximum pain over 24 hrs (NRS)	0 n (%)	-	-	0.125	-	-	0.293	-	-	1.00
	1-3 n (%)	15 (31.25)	-		32 (78.05)	4 (44.44)		36 (92.31)	11 (100)	
	4-7 n (%)	33 (68.75)	2 (100)		9 (21.95)	5 (55.56)		3 (7.69)	-	
	8-10 n (%)	-	-		-	-		-	-	

[Table/Fig-6]: Total opioid consumption during perioperative period and postoperative delirium.
SD: Standard deviation; µg: Microgram; Mean: Mean opioid consumption in fentanyl equivalents; NRS: Numerical rating scale

with delirium, as assessed by Student's t-test [Table/Fig-6]. The study could not find any association between POD and serial haemoglobin values.

DISCUSSION

The study aimed at finding out the effect of intraoperative hypotension and blood pressure fluctuations on the incidence of POD in elderly patients undergoing oncosurgery. Specific perioperative precipitating factors for POD include type of surgery and its duration, greater intraoperative blood loss, more postoperative transfusions and postoperative haematocrit of <30%, the use of physical restraints, malnutrition, addition of more than three medications 24-48 h before the onset of delirium, the use of an indwelling urinary bladder catheter, and electrolyte and fluid abnormalities. The present study found a statistically significant association of POD with intraoperative blood pressure variance, a fall in MAP >40% from baseline and co-morbidities ≥3. In a study by Wang N-Y et al., it was seen that in elderly patients, both very high and very low levels of MAP were associated with significantly increased risk of POD [22]. Severe acute pain regardless of the method of analgesia is also associated with POD [23].

In the present study, the incidence of POD was found to be 22%. The incidence increased progressively for 3 postoperative days. This observation was in conformance with metanalyses that reported incidence of 11.5 to 36.11%, 13.2 to 17.9%, and 8.2 to 54.4% [24-26]. Although Dasgupta M and Dumbrell AC; Pinho C et al., showed increased age as an independent risk factor for POD [5,27], the present study could not find a statistical association, even-though it was observed to be more in higher age groups. Gender, educational status, SES, smoking, alcohol intake, BMI, hypertension, thyroid disease and diabetes mellitus were not found to have any association with POD. These observations are consistent with other studies which showed no correlation between POD and these demographic factors [18,28].

In this study, 58% sample had co-morbidities ≥3 and 81.8% of patients who developed delirium by third post operative day had preoperative co-morbidities ≥3, which was statistically significant. Studies by Lee HB et al., and Sanders RD et al., also reported more occurrence of POD with increasing number of comorbidities [29,30]. None of the patients in the study population had a history of POD. Poor preoperative cognitive status has been shown to be a risk factor for POD by many authors [31,32]. As the study excluded patients with cognitive score of <80 we could not find the association between poor cognitive status and POD. Several studies have shown that preoperative anaemia (Hb<7.5 gm%) is associated with POD [33,34]. Inouye SK et al., also suggests BUN/Cr ratio of ≥18, as a predisposing factor for delirium [35]. The present study could not find such a relation as the population studied had BUN/Cr ratio <18.

The lowest SBP and MAP intraoperatively had influence on the occurrence of POD. Similarly, the highest SBP and MAP also showed an association with POD on all three postoperative days. These results are in accordance with the study by Wang NY et al., and several others [22,36,37]. The results of this study showed association of blood pressure variance with POD, similar to the study by Hirsch J et al., also [18]. This suggests that tight control of blood pressure during the intraoperative period is an important preventive measure to avoid POD.

In the current study, none of the patients reported severe pain. There was no statistically significant association between mild

and moderate pain with occurrence of POD. Several studies earlier showed that the use of opioids especially meperidine increases the risk of POD [38,39]. Fong HK et al., in a systematic review showed that meperidine was consistently associated with an increased risk of delirium in elderly surgical patients, but there was no significant difference in POD or cognitive decline among other more frequently used opioids like morphine, fentanyl, or hydromorphone [40]. In the present study, there was no association between opioid dose and POD. This might be due to adequate pain management using multimodal analgesia employing epidural and intravenous routes. In the systematic review by Fong HK et al., of the five studies included, three compared epidural with iv analgesia but all of them used epidural opioids also, and hence they found no significant difference in occurrence of delirium between the groups [40].

Limitation(s)

Depression has been identified as an independent risk factor for POD in some studies. Patients were not screened preoperatively for psychiatric disease and this was one limitation. Medications and perioperative pain therapy was not included as possible predictor for delirium in this study. Incident cases could have been missed as assessment of delirium was not done by a psychiatry specialist and was checked only twice daily. No assessment was done of POD severity, its duration and of delirium subtypes. The study must have missed clinical subtypes like hypoactive delirium in assessment and this could have resulted in under reporting of the incidence in the study.

CONCLUSION(S)

The POD as well as postoperative cognitive dysfunction is a cause for morbidity in elderly surgical patients affecting their quality of life. Hence this is currently a matter of great concern in the field of perioperative medicine. Steps to decrease the incidence are necessary which could be possible only if causes are well understood. According to this study, there was a high incidence of POD about 22% among elderly cancer patients. Detecting the predisposing factors of POD in elderly helps the treating physician to plan management strategies tailored to the patient to reduce morbidities. One of the important precipitating as well as modifiable risk factor for POD was intraoperative blood pressure changes. The study proves that both intraoperative hypotension and hypertension precipitate POD. Adequate blood pressure control during intraoperative period will be an important preventive measure for POD, especially in the elderly.

REFERENCES

[1] Inouye SK, Robinson T, Blaum C, Busby-Whitehead J, Boustani M, Chalian A, et al. Postoperative delirium in older adults: Best practice statement from the American Geriatrics Society. J Am Coll Surg. 2015;220(2):136-48.
[2] Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: Validity and reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). JAMA. 2001;286(21):2703-10.
[3] McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the Intensive Care Unit: Occurrence and clinical course in older patients. J Am Geriatr Soc. 2003;51(5):591-98.
[4] Tilouche N, Hassen MF, Ali HBS, Jaoued O, Gharbi R, Atrous SSE. Delirium in the Intensive Care Unit: Incidence, risk factors, and impact on outcome. Indian J Crit Care Med. 2018;22(3):144-49.
[5] Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: A systematic review. J Am Geriatr Soc. 2006;54(10):1578-89.
[6] Mahanna-Gabrielli E, Schenning KJ, Eriksson LI, Browndyke JN, Wright CB, Culley DJ, et al. State of the clinical science of perioperative brain health: Report from the American Society of Anesthesiologists Brain Health Initiative Summit 2018. Br J Anaesth. 2019;123(4):464-78.
[7] Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. Lancet. 2014;383(9920):911-22.
[8] American Geriatrics Society Abstracted Clinical Practice Guideline for Postoperative Delirium in Older Adults. J Am Geriatr Soc. 2015;63(1):142-50.
[9] DSM-5 Basics | Diagnostic and Statistical Manual of Mental Disorders [Internet]. [cited 2017 Nov 24]. Available from: https://dsm.psychiatryonline.org/doi/full/10.5555/appi.books. 9780890425596. Section1.
[10] Whitlock EL, Vannucci A, Avidan MS. Postoperative delirium. Minerva Anestesiol. 2011;77(4):448-56.
[11] Vijayakumar B, Elango P, Ganessan R. Post-operative delirium in elderly patients. Indian J Anaesth. 2014;58(3):251-56.
[12] Rudolph JL, Inouye SK, Jones RN, Yang FM, Fong TG, Levkoff SE, et al. Delirium: An independent predictor of functional decline after cardiac surgery. J Am Geriatr Soc. 2010;58(4):643-49.
[13] Saczynski JS, Marcantonio ER, Quach L, Fong TG, Gross A, Inouye SK, et al. Cognitive trajectories after postoperative delirium. N Engl J Med. 2012;367(1):30-39.
[14] Inouye SK. Delirium in older persons. N Engl J Med. 2006;354(11):1157-65.
[15] Robinson TN, Eiseman B. Postoperative delirium in the elderly: Diagnosis and management. Clin Interv Aging. 2008;3(2):351-55.
[16] Vaurio LE, Sands LP, Wang Y, Mullen EA, Leung JM. Postoperative delirium: The importance of pain and pain management. Anesth Analg. 2006;102(4):1267.
[17] Schenning KJ, Deiner SG. Postoperative delirium in the geriatric patient. Anesthesiol Clin. 2015; 33(3):505-16.
[18] Hirsch J, DePalma G, Tsai TT, Sands LP, Leung JM. Impact of intraoperative hypotension and blood pressure fluctuations on early postoperative delirium after non-cardiac surgery. BJA. 2015;115(3):418-26.
[19] Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: The confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113(12):941-48.
[20] Mathuranath PS, Hodges JR, Mathew R, Cherian PJ, George A, Bak TH. Adaptation of the ACE for a Malayalam speaking population in Southern India. Int J Geriatr Psychiatry. 2004;19(12):1188-94.
[21] Wayback Machine [Internet]. 2011 [cited 2022 Jul 14]. Available from: https://web.archive.org/web/20111215212528/http://painconsortium.nih.gov/pain_scales/NumericRatingScale.pdf.
[22] Wang NY, Hirao A, Sieber F. Association between intraoperative blood pressure and postoperative delirium in elderly hip fracture patients. Plos one. 2015;10(4):e0123892.
[23] Alvarez-Bastidas L, Morales-Vera E, Valle-Leal JG, Marroquín-González J. Delirium in the elderly patient after anesthesia: Associated factors. Colombian Journal of Anesthesiology. 2018;46(4):273-78.
[24] Zhu Y, Wang G, Liu S, Zhou S, Lian Y, Zhang C, et al. Risk factors for postoperative delirium in patients undergoing major head and neck cancer surgery: A meta-analysis. Jpn J Clin Oncol. 2017;47(6):505-11.
[25] Ansaloni L, Catena F, Chattat R, Fortuna D, Franceschi C, Mascitti P, et al. Risk factors and incidence of postoperative delirium in elderly patients after elective and emergency surgery. Br J Surg. 2010;97(2):273-80.
[26] Scholz AFM, Oldroyd C, McCarthy K, Quinn TJ, Hewitt J. Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. Br J Surg. 2016;103(2):21-28.
[27] Pinho C, Cruz S, Santos A, Abelha FJ. Postoperative delirium: Age and low functional reserve as independent risk factors. J Clin Anesth. 2016;33:507-13.
[28] DeCrane SK, Sands L, Ashland M, Lim E, Tsai TL, Paul S, et al. Factors associated with recovery from early postoperative delirium. J Am Soc Peri Anesthesia Nurses. 2011;26(4):231-41.
[29] Lee HB, Mears SC, Rosenberg PB, Leoutsakos JMS, Gottschalk A, Sieber FE. Predisposing factors for post-operative delirium after hip fracture repair among patients with and without dementia. J Am Geriatr Soc. 2011;59(12):2306-13.
[30] Sanders RD, Coburn M, Cunningham C, Pandharipande P. Risk factors for postoperative delirium. Lancet Psychiatry. 2014;1(6):404-06.
[31] Sprung J, Roberts RO, Weingarten TN, Nunes Cavalcante A, Knopman DS, Petersen RC, et al. Postoperative delirium in elderly patients is associated with subsequent cognitive impairment. Br J Anaesth. 2017;119(2):316-23.
[32] Needham MJ, Webb CE, Bryden DC. Postoperative cognitive dysfunction and dementia: What we need to know and do. Br J Anaesth. 2017;119(suppl_1):i115-25.
[33] Oh ST, Park JY. Postoperative delirium. Korean J Anesthesiol. 2019;72(1):04-12.
[34] Bilotta F, Lauretta MP, Borozdina A, Mizikov VM, Rosa G. Postoperative delirium: Risk factors, diagnosis and perioperative care. Minerva Anestesiol. 2013;79(9):1066-76.
[35] Inouye SK, Bogardus STJ, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999;340(9):669-76.
[36] Radinovic K, Markovic Denic L, Milan Z, Cirkovic A, Baralic M, Bumbasirevic V. Impact of intraoperative blood pressure, blood pressure fluctuation, and pulse pressure on postoperative delirium in elderly patients with hip fracture: A prospective cohort study. Injury. 2019;50(9):1558-64.
[37] Hori D, Brown C, Ono M, Rappold T, Sieber F, Gottschalk A, et al. Arterial pressure above the upper cerebral autoregulation limit during cardiopulmonary bypass is associated with postoperative delirium. Br J Anaesth. 2014;113(6):1009-17.
[38] Adunsky A, Levy R, Heim M, Mizrahi E, Arad M. Meperidine analgesia and delirium in aged hip fracture patients. Archives of Gerontology and Geriatrics. 2002;35(3):253-59.

[39] Morrison RS, Magaziner J, Gilbert M, Koval KJ, McLaughlin MA, Orosz G, et al. Relationship between pain and opioid analgesics on the development of delirium following hip fracture. The Journals of Gerontology. 2003;58(1):M76-81.

[40] Fong HK, Sands LP, Leung JM. The role of postoperative analgesia in delirium and cognitive decline in elderly patients: A systematic review. Anesth Analg. 2006;102(4):1255-66.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 03, 2022
- Manual Googling: Jun 06, 2022
- iThenticate Software: Jun 28, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 25, 2022**
Date of Peer Review: **May 26, 2022**
Date of Acceptance: **Jun 13, 2022**
Date of Publishing: **Jul 01, 2022**