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Comparing Effects of Isoflurane, Sevoflurane and Desflurane, using TEE, on Diastolic Dysfunction of Patients Undergoing CABG

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Abstract

Introduction: Diastolic dysfunction is a cause of morbidity and mortality in patients of coronary artery with normal systolic function. Diastolic dysfunction is highly predictive of adverse events after myocardial infarction. Transesophageal Echocardiography (TEE) is a non-invasive tool to investigate and diagnose perioperative diastolic dysfunction, which may influence the anesthetic management and post-operative outcome. This study was designed to compare the effects of Isoflurane Sevoflurane and desflurane on left ventricular diastolic dysfunction, using TEE in patients posted for CABG. *Materials and Methods:* 90 consenting adult patients, below the age of 70 years with grade 1 diastolic dysfunction posted for elective CABG surgery were included in this randomized cross sectional observational study and randomly divided in 3 groups of 30 patients each using a sealed envelope method. Group I received isoflurane, group S received sevoflurane & group D, desflurane. Ventricular relaxation criteria measured by the TEE were E (early diastolic peak velocity across the mitral valve), A (late diastolic peak velocity across the mitral valve), E/A ratio, S/D ratio, deceleration time (DT), e′ (early mitral annular velocity), E/e′ ratio. Parameters measured by the PA catheter were pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI), pulmonary vascular resistance (PVR). Other hemodynamic parameters recorded were mean arterial blood pressure (MAP), central venous pressure (CVP), heart rate (HR), oxygen saturation (SpO_2). *Statistical analysis and Results:* Descriptive statistics like mean, median and proportions were used to describe the study results. Binary or ordinal data were expressed as number (%) and continuous numeric variables were expressed as Mean±SD. Qualitivedata was analyzed by Pearsons chi square test. Analysis of variance was done for repeated measure of continuous variables by one way ANOVA. A p value of < 0.05 was considered as statistically significant. Significant improvement was seen in all the left ventricular relaxation indices as measured by TEE after using the three inhalational agents in the study. *Conclusion:* Our study establishes the safety of all the three inhalational agents which are currently used in cardiac anesthesia. The pre-existing grade 1 diastolic dysfunction in patients remained the same. It is recommended to study this with larger sample size.

Keywords: Diastolic Dysfunction; CABG; TEE.

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Introduction

Diastolic dysfunction is acause of morbidity and mortality in patients of coronary artery disease and is seen in 50% cases of congestive heart failure (CHF) with preserved systolic function [1].

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Cardiac surgery patients having perioperative diastolic dysfunction have beenassociated with a longer hospital stay, difficult weaning from cardiopulmonary bypass,post-operative CHF and prolonged requirement for inotropes [2,3].

Isoflurane, sevoflurane and desflurane are essential for balanced anaesthesia. However, their effects on left ventricular (LV) diastolic function have not been precisely defined.

Transesophageal Echocardiography (TEE) is a non-invasive tool to diagnose perioperative diastolic dysfunction, which may influence the anesthetic management and post-operative outcome.

This study wasdesigned to compare the effects of Isoflurane sevoflurane and desflurane on left ventricular diastolic dysfunction, using TEE in patients posted for Coronary Artery Bypass Grafting (CABG).

Materials and Methods

After approval of hospital ethics committee, 90 consenting adult patients, below the age of 70 years with grade 1 diastolic dysfunction posted for elective CABG surgery were included in this randomized cross sectional observational study.

The patients were randomly divided into 3 groups of 30 patients each using a sealed envelope method. Group Ireceived isoflurane, group S received sevoflurane & group D, desflurane.

A complete pre-anaesthesia evaluation of allthe patients was done before their allotment in the three groups including a full (pre-induction) 2DECHO. Preoperatively, patients took all prescribed drugs on the morning of operation except ACE-inhibitors.

Patients with an ejection fraction of less than 50%, significant ventricular arrhythmias, atrial fibrillation, hypertrophic obstructive cardiomyopathy, with pericardial disease, valvular heart disease, on inotropes, coexisting severe renal,neurological and respiratory distress were excluded from this study.

All patients were shifted to the operating room with oxygen given by a venturi mask. Intravenous cannulae wereinserted after local anaesthesia under asepsis. Premedication of injection fentanyl 1mcg/kg and midazolam 0.03mg/kg were given intravenously. Arterial line was inserted under local anaesthesia and invasive blood pressure monitoring initiated. Baseline activated clotting time and arterial blood gas analysis (ABG) were done.

Anaesthesia was induced withinj fentanyl 5 mcg/kg,pancuronium 0.1mg/kg, etomidate 0.3 mg/kg in all the three groups. After intubation, patients received an internal jugular vascular sheath.A swan ganz catheter was inserted through the sheath till wedge position.

A TEE ECHO probe was inserted and a second full 2D ECHO (post induction) was done to have baseline diastolic (LV relaxation) data. At the same time second ABG sample was taken.

Randomly, either of the three inhalational agents were started at 1 MAC (as calculated and displayed by the anesthesia machine) and continued for 10 minutes. Transesophageal 2D ECHO evaluation was done 10 minutes after inhalational agent and final (post- inhalational) diastolic data were noted. All hemodynamic and pulmonary artery (PA) catheter data were stored in the server with snapshot values earmarked for use of the study. Surgery was started only after the post–inhalational ECHO and ABG were done.

Ventricular relaxation criteria measured by the TEE were E (early diastolic peak velocity across the mitral valve), A (late diastolic peak velocity across the mitral valve), E/A ratio, S/D ratio, deceleration time (DT), e' (early mitral annular velocity) and E/e' ratio.

Parameters measured with the PA catheter were pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), stroke volume (SV), stroke volume index (SVI), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI), pulmonary vascular resistance (PVR), pulmonary vascular resistance index (PVRI).

Other hemodynamic parameters recorded were mean arterial blood pressure (MAP), central venous pressure (CVP), heart rate (HR), oxygen saturation (SpO_2).

No intravenous anesthetic agent was given for 20 minutes before & 20 minutes after the start of inhalational agent.Cardiac filling pressures (CVP, PCWP, SVRI) were kept as near baseline as possible, i.e. within 20% of baseline values.

No Surgical work wasdone until the end of the final (post-inhalational) TEE readings.

Results and Statistical analysis

Descriptive statistics like mean, median and proportions were used to describe the study results.

Binary or ordinal data were expressed as number (%) and continuous numeric variables were expressed as Mean±SD. Qualitative data was analyzed by Pearsons chi square test. Analysis of variance was done for repeated measure of continuous variables by one-way ANOVA. Software used for analysis was SPSS version 17.0. A p value of <0.05 was considered as statistically significant.

The patients of our study in all the three groups were similar in terms of demographicdata as seen in Table 1.

Statistically significant improvement in the E values were observed post inhalational agent use in all the three groups.

Normal range = 50-90 cm/sec. E values improved significantly in all individual groups All values remained within grade 1 diastolic dysfunction. Comparably similar in all groups

Normal range is > 1-1.5. Grade 1 diastolic dysfunction is ≥ 1 Grade 2 diastolic dysfunction is ≥ 1.5 Significant improvement seen in all the three groups

Statistically significant improvement in the E/A ratio was observed in all the three groups post use of an inhalational agent.

Significant reduction in deceleration time was observed in all the three groups after the inhalational agent was used.

Table 1: Demographic and Anthropometric Characteristics

Group	No. of patients (n)	Gender Distribution		Mean Age (in years)	Height (cm)	Weight (kg)	Body Surface Area
		Male	Female				
Desflurane	30	30	0	59.37	163.57 ± 18.91	67.93 ± 18.11	1.73 ± 0.14
Isoflurane	30	30	0	58.33	166.17 ± 4.28	65.37 ± 10.19	1.74 ± 0.13
Sevoflurane	30	29	1	58.83	167.40 ± 4.07	68.33 ± 9.91	1.78 ± 0.14

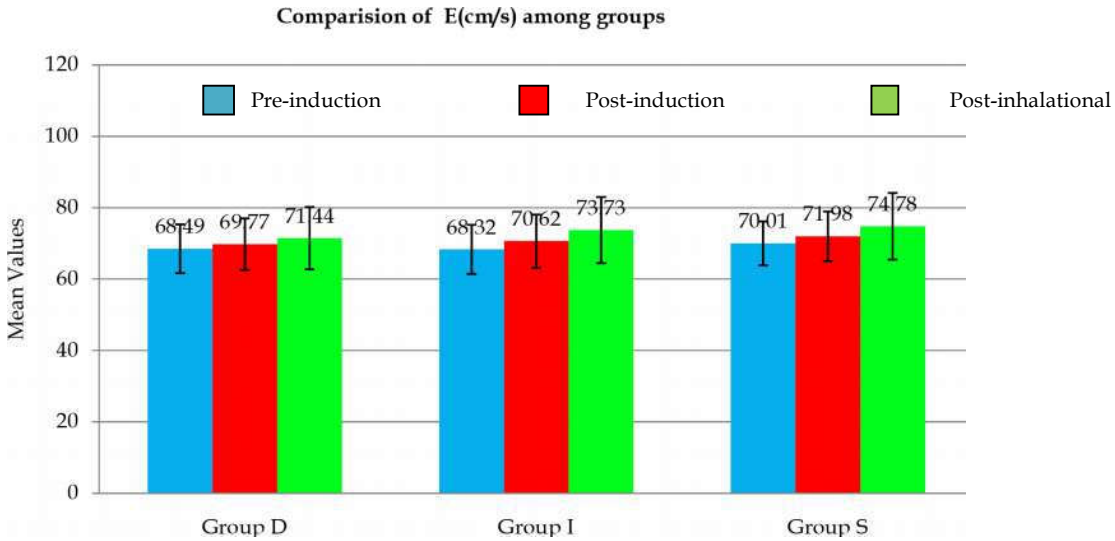

Fig. 1: Pre-induction Post-induction Post-inhalational

Table 2: Comparison of relaxation criteria (E values) in individual groups

E(cm/s)	Group D		Group I		Group S	
	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value
Pre induction	68.49 ± 6.85		68.32 ± 7.20		70.01 ± 8.74	
Post induction	69.77 ± 6.88	0.003	70.62 ± 7.45	<0.001	71.98 ± 9.26	<0.001
Post inhalational	71.44 ± 6.17	<0.001	73.73 ± 6.94	<0.001	74.78 ± 9.33	<0.001

Normal range = 50-90 cm/sec.
E values improved significantly in all individual groups
All values remained within grade 1 diastolic dysfunction.
Comparably similar in all groups

Table 3: Comparison of relaxation criteria (E/A ratio) in individual groups

E/A	Group D		Group I		Group S	
	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value
Pre induction	0.849± 0.044		0.846 ± 0.05		0.85 ± 0.05	
Post induction	0.87 ± 0.04	0.004	0.87 ± 0.04	<0.001	0.87 ± 0.06	0.001
Post inhalational	0.90 ± 0.05	<0.001	0.94 ± 0.09	<0.001	0.93 ± 0.11	<0.001

Normal range is > 1-1.5.
Grade 1 diastolic dysfunction is ≥1
Grade2diastolic dysfunction is ≥1.5
Significant improvement seen in all the three groups

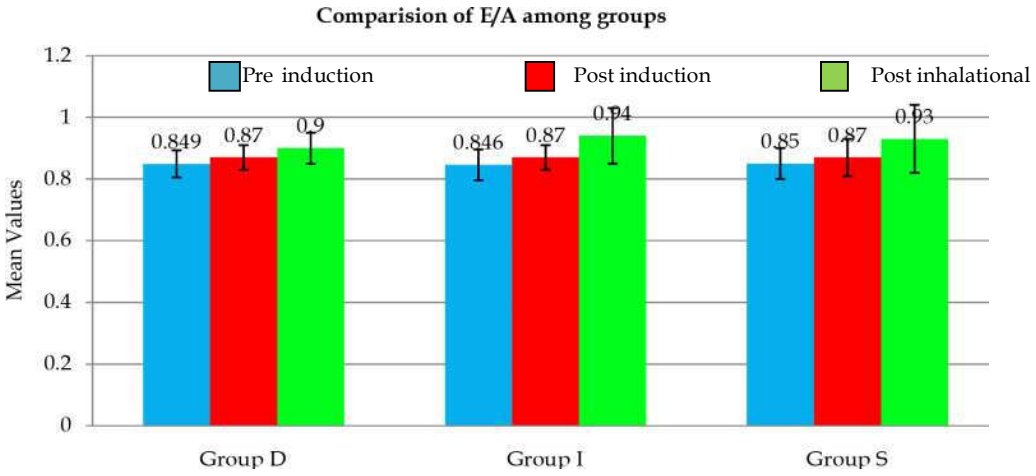

Fig. 2: Pre induction Post induction Post inhalational

Table 4: Comparison of relaxation criteria (e' values) in individual groups

e'(cm/sec)	Group D		Group I		Group S	
	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value
Pre induction	8.48 ± 0.51		8.55 ± 0.50		8.57 ± 0.44	
Post induction	8.48 ± 0.52	0.801	8.58 ± 0.44	0.271	8.55 ± 0.43	0.573
Post inhalational	8.91 ± 0.77	0.001	8.61 ± 0.72	0.706	8.51 ± 0.71	0.645

Normal range = 10-14 cm/sec
Grade 1 diastolic dysfunction = 8-10 cm/sec
Grade 2 diastolic dysfunction ≤ 8 cm/sec
Significant improvement (moving towards normal) in Group D

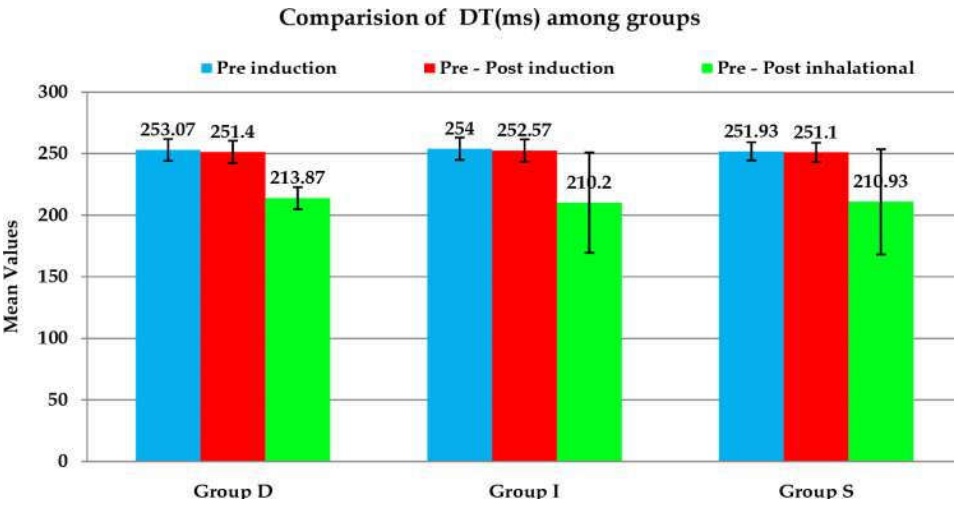

Fig. 3:

Table 5: Comparison of relaxation criteria (E/e' values) between groups

E/e'	Group D Mean ± SD	Group I Mean ± SD	Group S Mean ± SD
Pre induction	8.24 ± 0.65	8.65 ± 1.49	8.79 ± 1.59
Post induction	8.21 ± 0.57	8.23 ± 0.76	8.40 ± 0.95
Post inhalational	8.08 ± 0.62	8.0 ± 0.75	8.16 ± 0.85

Normal range = 5-8 cm/sec
Grade 1 diastolic dysfunction = 8-10 cm/sec
Grade 2 diastolic dysfunction = >15 cm/sec
Results obtained are comparable in all groups.

Discussion

The effect of volatile anesthetic agents on LV diastolic function has been investigated in numerous animal studies and in vitro experiments with myocardial tissue. The human research is limited to a few publications only.

Sarkar S et al. [4], in their review article pertaining to patients ofischemic heart disease with preexisting LV diastolic dysfunction concludedthat isoflurane, sevoflurane and desflurane do not have any detrimental effects on LV diastolic dysfunction and infact improvement was noticed in relaxation criteria. A similar observation was also noted in our study as seen in Fig 1 and Table 2 in which the diastolic dysfunction remained grade 1 in all the three groups. Beneficial effects were noted in E/A ratio, DT in patients of all three groups as seen in Table 3, Fig 2 and Fig 3.

However, the hemodynamic measurements in the former study were noted once the surgery had commenced which contrasts with our study in which all measurements were noted before surgery began and hence the effects of surgical stress have been nullified.

Filipovic M. et al. [5] in theirresearch article studied the effects of sevoflurane and propofol in patients with pre-existing diastolic dysfunction and concluded that during anesthesia and IPPV, there was no difference in e' between the study groups. They also noted that Sevoflurane impaired systolic atrial and ventricular functions. In our study patients depicted a similar effect on e' (early LV filling velocity) as seen in Table 4.

Oxorn et al. [6] reported in their study of healthy patients undergoing peripheral orthopedic surgery that isoflurane at MAC 1 and 1.5 resulted in decreased A velocity, shortening of the deceleration time and at both (MAC 1 and 1.5) doses caused an equal increase in the E/A ratio. No changes in E velocity and S/D ratio were seen.These findings on healthy patients are consistent with our findings on patients of CAD with grade 1 diastolic dysfunction as seen in table 5 and Fig 3.

Neuhauser et al. [7], in their study of patients with diastolic dysfunction, noted that there was an increase in Eleading to a larger E/A ratio and DT decreased with isoflurane. They concluded that changes in loading conditions as well as theinotropic state are more likely to cause the LV to operate on a steeper region of thepressure-volume curve, rather than direct alterations of the intrinsic viscoelasticproperties of the myocardium. These findings on diastolic dysfunction are consistent with our findings on patients of CAD with grade 1 diastolic dysfunction as seen in fig 2 and 3.

Bollinger et al. [8] concluded that desflurane and isoflurane, and most likely sevoflurane, have no clinically relevant negative effect on early diastolic relaxation in young subjects without cardiovascular disease. We also have similar findings in our study pertaining to the inhalational agents but in our study, we evaluated patients of IHD with grade 1 diastolic dysfunction.

Houltz et al. [9] investigated the effects of halothane and isoflurane in controlling the stress response to sternotomy and concluded that both impair the early diastolic relaxation in patients of IHD. This is in contrast to our study where there was a significant improvement in the E values in all the groups.

Hemodynamic viewpoints indicate thatthe three inhalational agents (isoflurane, sevoflurane and desflurane) are statistically safe for patients with coronary artery disease with grade 1 diastolic dysfunction.

Conclusion

Anesthesiologists strive to find an ideal inhalational agent which is cardiostable and does not worsen the already reduced myocardial function of patients with ischemic heart disease.

Our study establishes the safety of all the three inhalational agents which are currently used in cardiac anesthesia. The pre –existing grade 1 diastolic dysfunction in patients remained the same.It is recommended however to do this study in a larger number of patients.

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