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The Effect of General Anesthesia Induction Drugs on Cardiac Output of Patients in Azadi Teaching Hospital/Duhok/Iraq

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Abstract

Background: Cardiac output can be decreased by many factors whose effects may be exaggerated during induction of anesthesia (which is already insulted to have negative effect on cardiac output) till the point of cardiac stand still.

Aims: This study aims to answer the questions that "Is there any effect of general anesthesia induction agents on cardiac output? If there is any, which patient is affected more?".

The Study Design: It is a cross sectional study with convenient sampling procedure. According to the inclusion criteria, it includes patients planning to perform surgical procedure under general anesthesia while it excludes patients who refused to participate in the study or their surgical procedures had been canceled for certain reasons.

Method and Patients: The study targeted a population from Duhok province and its territories; 207 patients, were admitted to Cardiac Center Operation theatres from 12/9/2021 to 30/10/2021 and Azadi Teaching Hospital operation theatres from 2/11/2021 to 15/1/2022. The data were collected pre operatively after taking a verbal consent as age, sex, weight, chronic diseases and duration of chronic diseases. Foreword by using echocardiography machine pre and post general anesthesia induction ejection fraction would be obtained. All this information would put in previously designed excel form. This data had been analyzed by Microsoft Excel Worksheet and transferred to SPSS V. 23(IBM). Descriptive statistics (central tendency) and proportions of uni-variant variables were calculated. Paired t test for sample mean difference and ANOVA test for more than two group means were applied to test the mean differences. A P value of < 0.05 considered statistically significant.

Results: For the age of patients the mean was 40 years with range 77 years, minimum 1 year, maximum 78 year and standard deviation 15.731 years, for weight the mean was 71kg with range 130 kg, minimum 7kg, maximum 137kg, and standard deviation17.210 kg, for pre general anesthesia induction anesthesia the mean was 0.6055 %with range 0.45%, minimum 0.35%, maximum 0.80%, and standard deviation 0.06587%, for post general anesthesia induction the mean was 0.5531% with range 0.54%, minimum 0.24%, maximum 0.78% and standard deviation 0.087485, for duration of chronic diseases out of 41 patients the mean was 1.47 years with range 26 years, maximum 26 years, and standard deviation 3.802 years fortunately 166(80%) of patients were without any chronic diseases. The post induction ejection fraction significantly differs with the pre operation ejection fraction for (207) patients received anesthesia in Duhok hospitals during 2021. The average means difference was of 0.04499 (95% confidence interval, 0.04499, 0.05984.69). This difference is statistically significant at a \leq .05 by the paired τ test (two-tailed). In this study, patients underwent induction of anesthesia had an average of .05242 (standard deviation, .00377) change in ejection fraction.

Key words: induction of general anesthesia, cardiac output.

Introduction

Cardiac output **(**CO) is the volume of blood pumped by the ventricles during one minute; this is the way through which all human body parts gain oxygen and nutrients and get rid of waste products. CO is the product of heart rate (HR) and stroke volume (SV). The heart will respond by modulating one or both of the HR and SV when the demand of body's parts for oxygen increases, as during exercise. This processes under the regulation of a complex cooperation of the autonomic nervous system, endocrine, and paracrine signaling pathways ⁽¹⁾.

So, any cardiovascular dysfunction has the potential to result in significant morbidity and mortality. This functional impairment has a variety of methods to be assessed and in turn guides diagnosis, prognosis, and treatment ^(2,3,4,5,6).

General anesthesia is using anesthetic agents to induce unconsciousness, amnesia, analgesia and the loss of autonomic system reflexes with or without skeletal muscle relaxation ⁽⁷⁾.

concentration of halogenated The agents, including sevoflurane, desflurane, isoflurane, enflurane, and halothane, all decrease the MAP in a dose-dependent manner ^(8,9,10). This effect can be explained systemic by decrease in vascular resistance (SVR) except for halothane which also decreases the MAP but by directly relaxing myocardium which in turn decreases the CO that leads to decreasing MAP in a direct relation with dose ^(9,10,11). Sevoflurane has demonstrated less impact on cardiovascular dynamic parameters than desflurane and isoflurane, leading to reduced morbidity and mortality ^(8,28).

Some intravenous anesthetics may act by increasing the concentration of the inhibitory neurotransmitter γ -aminobutyric acid (GABA) in the central nervous system (CNS), like etomidate, midazolam, propofol and thiopental. Meanwhile, ketamine antagonizes the effect of the excitatory neurotransmitter N-methyl-D-aspartate (NMDA) on N-methyl-D-aspartate (NMDA) receptors, and opioid agonists stimulate opioid receptors. Propofol is highly hydrophobic and distributes rapidly into the CNS and other tissues, which accounts for its rapid onset of action and its wide use ⁽¹²⁾.

The reduction in the cardiac output caused by anesthetic agents can be partially preserved by an increase in HR in healthy individuals while the presence of comorbidities, aging and concurrent medication may inhibit this compensation, unmasking the reduction in cardiac output ^{(13).}

An echocardiography is the use of standard ultrasound or Doppler ultrasound to form a dynamic medical image of the heart ⁽¹⁴⁾. The echocardiogram gives the physicians the privilege to estimate the systolic function by calculating the CO and ejection fraction, as well as the Therefore, diastolic function. it is of following-up potential importance in patients with heart failure and their treatments^(15,16). Using pulsedor continuous-wave Doppler ultrasound and echocardiogram can produce an accurate assessment of the blood flowing through the valves of the heart. The Doppler echocardiography technique can also be used for tissue motion and velocity measurement ⁽¹⁷⁾.

There are several types of echocardiography, transthoracic echocardiography, stress echocardiography and transesophageal chocardiography. Transthoracic echo is the most common type of echocardiogram test as it is painless and noninvasive diagnostic tool that needs minimal training in image acquisition and interpretation to estimate global left ventricular (LV) function with reasonable Bedsides, accuracy. transthoracic echocardiography (TTE) is increasingly

used by intensivists and anesthesiologists for cardiac evaluation of hemodynamically unstable patients ⁽¹⁸⁾.

American college of cardiology (ACC)/ American heart association (AHA) guidelines as well as European society of cardiology (ESC) guidelines document echocardiography as the single most beneficial test for the diagnosis of heart dysfunction since the presence of abnormality, structural dysfunction in systole or diastole, or a combination of these abnormalities have to be documentted to establish a definitive diagnosis in patients present with resting or/and exertional symptoms of heart failure ^(19,20).

Methodology:

This is a cross sectional prospective descriptive study with convenient sampling procedure. The included patients were those who plan to perform surgical procedure under general anesthesia and verbally agree to be examined bv echocardiography while the excluded were those among the above but refused to participate in the study or their surgical procedure had been canceled for any This reason. study targeted Duhok Province and its territories population.

Resources were all at the researcher's except two echocardiography expenses machines: one had been supplied by the Azadi Teaching Hospital/ Coronary Care Unit and the other one by the Cardiac Center in the same hospital. The ejection fraction was calculated by M Mode which is consisting of putting the cardiac prop in left lateral parasternal long axis view and moving this prop to be as much as possible in perpendicular position on the left ventricular image then to freeze the picture to activate the measuring which had measured both end diastolic (EDV) and end systolic (ESV) volumes and finally the ejection fraction would be resulting from the ratio of EDV-ESV/EDV.

In this study, 207 patients had been examined in Azadi Teaching Hospital; they were planned to undergo different operations. The effect of deneral anesthesia induction drugs on the cardiac function was represented by ejection fraction in the duration from 12/9/2021 to 30/10/2021 in cardiac center operation theatres and from 2/11/2021 to 15/1/2022 Azadi teaching hospital operation in theatres. The patients' assessment was conducted in ratio of 3 - 4 operation theatres fumigation days a week including weekends and some occasionally vacant days. The everyday examination included at least four patients in the operation theatre complex and one patient in cardiac center. It procedurally begins checking the operations list first, selecting the patients who best fit in for the study regarding type of anesthesia that expected to be given, the type of surgery and its duration, age, their sequence in the list (preferred not to be the first), and finally examining the patients who are fit by echocardiography. Firstly, the data of the patient would be collected

individually before being examined by echocardiography but after verbal consent. The data include name, age, gender, weight, chronic disease, and the drugs used for these chronic diseases and the duration of chronic diseases. The data would be admitted in excel form at the same examining night. Secondly, the ejection fraction of selected patients will be preoperatively measured in the pre anesthesia room in supine with 30 degree tilting to the left by LV study and M Mode. The resulted ejection fraction would admit also in the above excel form. Thirdly, when patients is taken to operation room to perform the surgical procedure, the ejection fraction would be measured again 3 to 5 minutes after induction of general anesthesia and before starting the surgical procedure in order to exclude the effect of

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the last on ejection fraction. Routinely the patients had been vitally monitored by electrocardiography, pulse oximetry, noninvasive blood pressure, temperature and end-tidal CO2. Meanwhile the drugs of general anesthesia induction would be documented in details and then transferred to the same excel form. The collected data would be analyzed by Microsoft Excel Worksheet and transferred to SPSS V. 23(IBM). Descriptive statistics (central tendency) and proportions of uni-variant variables were calculated. A paired t test, for sample, mean difference and ANOVA test for more than two group means were applied to test the mean differences. A P value of < 0.05 is considered statistically significant.

The data on the general anesthesia induction drugs used by doctor for the patients had been collected. Hence, if the patient had taken specific drug the study would write (Yes) but if s/he hadn't taken the same specific drug the study would write (No). Those general induction drug agents include Propofol, Midazolam, Fentanyl Narcotic meant both and Morphine, Muscle relaxant meant both Rocuronium and Atracurium. Inhalation meant both Isoflurane and sevoflurane. The percentage of these general anesthesia drugs had been listed in Table (2).

The preoperative assessment of ejection fraction was the cause behind the surgical intervention postponement as it was too low to tolerate the negative inotropic effect of general anesthesia induction for three patients, one of them in the Cardiac Center and to in the Azadi Teaching Hospital.

It is worth noting that all the patients were quite cooperative and highly satisfied with assessment. However, the major problem that faced in the study was that there was no echocardiographic machine specially belong to the operation theater; so, it was necessary to bring the one in the Coronary Care Unit in the second floor to the first floor where the operation theater complex existed whenever patients' data had to be collected.

Results:

The study has found the standard deviation, mean, minimum, maximum of age, weight, pre general anesthesia induction ejection fraction and post general anesthesia induction ejection fractions, and duration of chronic diseases for all the patients (n=207) as follows:

- For the age of patients, the mean was 40 years with range 77 years, minimum 1 year, maximum 78 year and standard deviation 15.731 years;
- for weight, the mean was 71kg with range 130 kg, minimum 7kg, maximum 137kg, and standard deviation17.210 kg;
- for pre general anesthesia induction anesthesia the mean was 0.6055 %with range 0.45%, minimum 0.35%, maximum 0.80%, and standard deviation 0.06587%;
- for post general anesthesia induction, the mean was 0.5531% with range 0.54%, minimum 0.24%, maximum 0.78% and standard deviation 0.087485;
- for duration of chronic diseases out of 41 patients the mean was 1.47 years with range 26 years, maximum 26 years, and standard deviation 3.802 years fortunately 166(80%) of patients were without any chronic diseases. (Table 1)

Accordingly, it could be noticed that, with the patients who took morphine and rocuronium, the ejection fraction (CO) of the patients decreased about (0.15) more than with those who took other drugs, after morphine and rocuronium. Yet, the decrease in the ejection fraction was of about **(**0.13) in the patients who took ketamine combination with other drugs like midazolam, atracurium. propofol, isoflurane only in three patients; the combination with propofol, fentanvl. atracurium, sevoflurane in two patients; the combination of ketamine with propofol, midazolam, fentanyl, atracurium, isoflurane in eight patients; and the combination of ketamine with propofol. midazolam, fentanyl, atracurium, and sevoflurane in two patients. Meanwhile combination of ketamine with midazolam, fentanyl, rocuronium and isoflurane had increased the ejection fraction in three patients. With patients who took propofol and midazolam, the ejection fraction was decreasing about (0.10) but fentanyl and isoflurane decreased about (0.09) of the patients ejection fraction. With the patients who took atracurium the ejection fraction was decreased about (0.08) less than the other anesthesia induction general druas. inhalation anesthesia like sevoflurane decreased ejection fraction about (0.11).

Inversely, the combination of propofol, midazolam. fentanyl and sevoflurane increased ejection fraction in only six patients, two of them took rocuroniom in while addition the other two took atracurium instead, in addition, the combination of propofol, midazolam. fentanyl, isoflurane increased CO (ejection fraction) in only the two other patients: one of them had taken atracurium in addition. Finally, no change in ejection fraction had been noticed in two patients who took combination of propofol, midazolam, fentanyl and atracurium in addition to sevoflurane in one of them and isoflurane in the other (Table 2).

It can be seen that the means and standard deviations of the pre-operative ejection fraction and post induction ejection fractions for 207 patients were 0.6055, and 0.06587 and 0.5531 and 0.08748 respectively (Table 3). The study displays the correlation between the two means of pre-operative ejection fraction & post induction ejection fraction of the study patients (n=207) which are indeed correlated positively with correlation coefficient of 0.786 at a p value = .000. (table 4)

The study also shows the average difference between the two values (paired differences mean = 0.05242), the 95% confidence interval around the difference (0.04499, 0.5984), the value of the t-statistic(13.918), computed and the associated actual p-value with the computed statistic (p = .000, or p < .001). (table 5)

This study gave some aside outcomes regarding the effects of using chronic diseases drugs on the changing of ejection fraction after induction of general anesthesia. Among these drugs, betablockers and unexplained antidiabetics owned the highest level of lowering cardiac output, followed by nitroglycerin and diuretics. Unexpectedly calcium channel blocker had the minimal decreasing factor on the cardiac output along with heparin (Table 6).

Hence, the post induction ejection fraction significantly differs from the pre operation ejection fraction for (207) patients who received anesthesia in Duhok hospitals during 2021. The average means difference was of 0.04499 (95% confidence interval, lower is 0.4499, upper is 0.5984.69). This difference is statistically significant at a \leq .05 by the paired T test (two-tailed).

Tab	e 1:Descriptive statistics of	f age, weight	, pre general	anesthesia	induction	ejection	fraction and	post	general
	anesthesia induction eject	tion fractions	, and duratio	n of chronic	diseases	of the stu	udy patients	(n=20	7)

	Ν	Range	Minimum	Maximum	Mean	Std. Error	Std. Deviation
Age of patients(Year)	207	77	1	78	40.00	1.093	15.731
Weight(kg)	207	130	7	137	71.00	1.196	17.210
Pre general anesthesia induction Ejection Fraction	207	.45	.35	.80	.6055	.00458	.06587
Post general anesthesia Induction Ejection Fraction	207	.54	.24	.78	.5531	.00608	.08748
Duration of Chronic Diseases(Year)	41	26	0	26	1.47	.264	3.802
Total	207						

Table 2: Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction EjectionFraction, and Difference between pre and post induction ejection fractions for anesthetic drugs given to the
study patients(n=207)

Anesthetic Drugs	Pre general anesthesia induction Ejection Fraction	Post general anesthesia Induction Ejection Fraction	Difference between pre and post general anesthesia induction ejection fraction
Propofol	.61	.55	.10
Midazolam	.61	.55	.10
Fentanyl	.61	.56	.09
Morphine	.49	.42	.15
Ketamine	.61	.55	.13
Rocuronium	.54	.48	.15
Atracurium	.62	.57	.08
Isoflurane	.61	.56	.09
Sevoflurane	.60	.54	.11
Total	.61	.55	.10

 Table 3: The descriptive statistics of Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction Ejection Fraction, of the study patients(n=207)

Paired Sa	amples Statistics	Mean	Ν	Std. Deviat	tion Std. Error Mean
Pair 1	Pre-Operative Ejection Fraction	.6055	207	.06587	.00458
	Post Induction Ejection Fraction	.5531	207	.08748	.00608

Table 4:Correlation between the Pre general anesthesia induction Ejection Fraction & Post general anesthesia induction Ejection Fraction of the study patients(n=207).

Paired Sar	nples Correlations	Ν	Correlation	Sig.
Pair 1	Pre-Operative Ejection Fraction & Post Induction Ejection Fraction	207	.786	.000

Table 5: The mean difference, and the 95% confidence interval of the Pre general anesthesia induction Ejection

 Fraction & Post general anesthesia Induction Ejection Fraction of the study patients(n=207).

		Paired Di	Т	df	Sig.				
		Mean	SD	Std. Error Mean	95% Confidence Interval of the Difference				(2-tailed)
					Lower	Upper	_		
Pair 1	Pre-Operative Ejection Fraction - Post Induction Ejection Fraction	.05242	.05418	.00377	.04499	.05984	13.918	206	.000

 Table 6: The means Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction

 Ejection Fraction, and Difference between pre and post induction ejection fractions for chronic disease drugs used the study patients(n=207).

		Pre general anesthesia induction Ejection Fraction	Post general anesthesia induction Ejection Fraction	Difference between pre and post general anesthesia induction ejection fraction
Chronic	Angiotensin blocker	.56	.47	.17
Disease Drugs	Nitroglycerin	.48	.38	.21
	Beta blocker	.52	.40	.24
	Diuretic	.47	.38	.20
	Anti-diabetic	.51	.39	.24
	Aspirin	.51	.41	.19
	Heparin	.55	.53	.04
	Anti-uric acid	.50	.44	.13
	Calcium channel blocker	.51	.49	.05
	Thyroxin	.63	.58	.08
	Total	.55	.47	.15

Discussion:

Hua et al., (2017) study conducted at a London teaching hospital between June-November 2014. Patients of American Society of Anesthesiologists grade I-II aged between 18-45 years, had perform elective lower-limb arthroscopic surgeries examined to record HR, MAP, SV, CO, SVR and BIS continuously prior to induction and up to 3-minutes after anesthesia. The result of this study can be said to be the same result of the present study because they said HR, SVR, MAP, SV and CO were decreased by post general anesthesia induction. Their findings highlight the significance of involving cardiovascular assessment in routine perioperative monitoring ⁽²¹⁾.

Hubner et al., (2013) demonstrated that general anesthesia through decreased SVR, decreased myocardial contractility, decreased SV, and increased myocardial irritability, affects arterial and central venous pressures, CO, and varying heart rhythms. Specifically They document that systemic arterial pressure decrease by 20-30% after induction of general anesthesia, but blood pressure will return up about 20-30 mm Hg because of tracheal intubation. Compared with inhaled anesthetics the use of fentanyl, sufentanil, of alfentanil causes less myocardial depression. This depression is by venodilation which results in decreasing preload ⁽²²⁾.

Homi *et al.*, (1972), Filner and Karliner (1976), Dale et al, (1987) and Friesen (1983) show different effects of inhalation agent on CO. The decrease in arterial pressure by halogenated anesthetics results either from a reduction in CO that showed in (enflurane> halothane >> isoflurane) or decrease in SVR that came with use of (isoflurane > enflurane > halothane) ^(23,24,25,26).

Cahalan *et al.*, (1991), and Brioni *et al.*, (2017) stated that the patient's CO is

indirectly related with concentrations of inhaled anesthetics ^(11,8).

Brioni *et al.*, (2017), and Li and Yuan (2015) demonstrated that sevoflurane compared with desflurane and isoflurane, has less morbidity and mortality due to its low impact cardiovascular dynamic parameters ^(8,27).

Aguirre (2016) and Park et al, (2007) displayed that systemic hemodynamics as isoflurane, desflurane, and sevoflurane reduce MAP, (CO), and cardiac index in a dose-dependent fashion ^(28,29).

Alwardt et al, (2005) said that nitrous oxide, halothane, enflurane, isoflurane, sevoflurane desflurane. will decrease blood pressure, SVRs and CO with less effect of halothane on systemic resistance and isoflurane and desflurane on CO while HR will increase in enflorane, isoflurane and desflurane but decreased by halothane, nitrous oxide do not change all of them parameter and sevoflurane and do not change CO. Although isoflurane may result in the greatest decrease in SVR leads to arterial blood pressure decline, CO is preserved as the result of an active carotid baroreceptor reflex and decreased afterload (30).

Lippmann *et al.*, (1986) mentioned that the decrease in CO may be quite correct in high risk patients among those who had taken general anesthesia induction, CO will be decreased more and in a degree higher than healthy individuals. This is completely agree with result of present study which documented that CO decrease more in the patients who had chronic diseases such as cardiovascular and endocrine diseases ⁽³¹⁾.

Anyhow, Green (2015) still thinks that most anesthesiologists continue to regard the decrease in MAP on induction due either to cardiac depression, as Kakazu and Lippmann propose, or to decrease in SVR. Furthermore, Green, believed that the reduction in cardiac contractility has little to do with decrease in CO regarding the effect on preferentially reducing venous rather than arterial tone ⁽³²⁾.

Bentley et al, (1989) and Goodchild and Serrao (1989) stated that venorelaxation and an increase in venous capacitance is the cause of venous return and SV decline resulted in decrease of CO and MAP. This result is similar to the results of the present in that propofol cause decrease of CO ^(33,34).

Petrun and Kamenik (2013) are to be congratulated for pointing out that the driving of decrease in MAP post-induction is the decrease in CO which is more evident with both propofol and etomidate ⁽³⁵⁾.

Pagel and Warltier (1993) and Larsen et al., (1988) stated that propofol causes reduction in arterial blood pressure in proportion to dosage and plasma concentration. They found that this reduction was related to decrease in SVR and CO which already found in the present study (36,37).

Chen and Ashburn (2015) said that most opioids have low direct negative inotropic effect. As opioids are rarely the sole anesthetic agent used, interestingly mentioned that combination of opioid with other drugs especially with benzodiazepines effect on the cardiac function and cause decrease in cardiac function. This study is parallel with the present study. In addition, significant diminishing in cardiovascular parameters can be observed when opioids are administered with inhaled anesthetics (38).

Chen and Ashburn (2015), Benyamin Shirani (2010) et al.. (2008),and Aghadavoudi (2015) summarize numerous studies that have investigated the harmful effects of opioids on the body organs especially the cardiovascular system, especially when applied with benzodiazepines causing by decrease CO.

bradycardia, histamine release, heart electrical disturbance and cardiac arrhythmia ^(38,39,40,41).

The effect of fentanyl, even after large doses, on hemodynamics like HR, MAP and CO is minimal. This is described by Bailey *et al.*, (2000) ⁽⁴²⁾.

Khanderia et al (1987) stated that benzodiazepines have less cardiorespiratory effects which include a slight decrease in CO and blood pressure. These effects are more evident when used in conjunction with narcotics ⁽⁴³⁾.

Mehmet et al., (2014) displayed that haemodynamic variations are of three general anesthesia induction agents (thiopental, propofol, and etomidate) when used in conjunction with fentanyl. The decrease in CO was more marked with than with etomidate propofol or thiopentone. So they concluded that the combination of fentanyl with propofol is less safe than both the groups of fentanyl with etomidate and fentanyl with thiopental in terms of providing haemodynamic stability. Again, the result of the present study demonstrated that the combination of propofol with fentanyl can decrease CO (44)

Khan *et al.*, (2014) said that ketamine could increase arterial pressure, HR and CO as opposed to other intravenous anesthetics due to central stimulation of the sympathetic nervous system ⁽⁴⁵⁾.

Yet, it is said that ketamine has negative inotropic actions but this is to somehow reversed as it has a centrally mediated ability of catecholamine release, which appear as an increasing HR, blood pressure and CO (Traber et al, 1968) ⁽⁴⁶⁾.

<u>Elisha</u> *et al.*, (2022) determinated the cardiovascular effects⁽⁴⁷⁾. Mazzeth *et al.*, (2015) identified that ketamine, unlike other intravenous anesthetics, has a circulatory stimulant charachter, producing increases in systemic blood pressure, HR,

cardiac contractility and output, and central venous pressure ⁽⁴⁸⁾. Yet, Ivankovich *et al.*, (1974) showed SVR responded, differently among patients undergoing cardiac catheterization and angiography, possibly because of patient variability in autonomic tone and disease states. Other studies have failed to show significant effects in SVR but have found evidence of an increase in pulmonary vascular resistance, pulmonary artery pressure, and right ventricular stroke work ⁽⁴⁹⁾.

Kuipers et al., (2001) proposed that models recirculatory can explain accurately first-pass pharmacokinetics and the influence of CO, which is obvious in drugs with a fast onset of effect. This explains what this present study said that rocuronium can decrease CO by 0.15 (15%) because the mean pre general anesthesia induction was 0.54 (54%) and general anesthesia the mean post induction was 0.48 (48%) so, the mean different between pre and post general anesthesia will be $0.15 (15\%)^{(50)}$.

Shiraishi *et al.*, (2018) justified in their study that there was a statistically significant inverse correlation between the onset time of rocuronium and CO mainly in the elderly patients ⁽⁵¹⁾.

Gallo et al., (1988) explained that the cause of a statistically significant decrease in blood pressure at 2 minutes and a statistically significant increase in CO and decrease in SVR at 2, 5, and 10 minutes, was changes in serum histamine levels. Although histamine level did not change after vecuronium, there were no statistically significant differences between the two groups. The result of this study have the opposed result to present study because it state that CO decrease by using atracurium⁽⁵²⁾.

Conclusion: The overall effect of general anesthesia induction agents is negative inotropic with mean decreasing of 10% of

baseline ejection fraction. This is a considerable level in patients of border line CO (heart failure). Anesthesiologist should give special caution when use the drugs of high negative inotropic effect like Morphine and Rocuronium.

Recommendation: it will be very informative if this study extended to individually examine the effect of each general anesthesia induction drugs on the CO or to be comparative study between groups of these drugs.

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