

# Role of Age-Specific Lung Function on Survival After CABG in Smokers

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**Abstract :** Coronary artery bypass grafting (CABG) is performed for patients with coronary artery disease (CAD) to improve quality of life and reduce cardiac-related mortality. A coronary artery bypass graft (CABG or CAG) is placed during a surgical procedure to increase blood flow to the myocardium due to coronary stenoses, usually caused by coronary artery disease. Arteries or veins can be grafted during this procedure

**keywords:** cardiac-related mortality , coronary stenoses

## Introduction

Coronary artery bypass grafting (CABG) is performed for patients with coronary artery disease (CAD) to improve quality of life and reduce cardiac-related mortality. A coronary artery bypass graft (CABG or CAG) is placed during a surgical procedure to increase blood flow to the myocardium due to coronary stenoses, usually caused by coronary artery disease. Arteries or veins can be grafted during this procedure <sup>(1)</sup>.

Patients undergoing cardiac surgery are older and more medically complex. Clinical cardiovascular risk factors for major perioperative adverse cardiovascular events include reduced functional status (<4 metabolic equivalent of task), age >60 years, smoking, arterial and pulmonary hypertension, heart failure (HF), acute coronary syndrome (ACS), ischemic heart disease, cardiomyopathy, severe valvular heart disease, significant arrhythmias, peripheral vascular disease, thoracic aortic atheroma, diabetes mellitus requiring insulin, renal insufficiency, chronic pulmonary disease, neurological disease, anemia, previous cardiac surgery, previous mediastinal radiation therapy, and body mass index (BMI) >35 kg/m<sup>2</sup> or <20 kg/m<sup>2</sup> <sup>(2)</sup>.

Although most people are aware of the association between smoking and heart disease, cigarette smoking is still the most preventable cause of death <sup>(3)</sup>.

Cigarette smoking is one of the known major risk factors of coronary artery disease and chronic smoking may cause postoperative alveolar collapse because of damage to the ciliary epithelium; however, the cessation of smoking results in significant improvement in small airway function <sup>(4)</sup>.

Patients undergoing CABG often develop atelectasis and severe reductions in lung volumes and oxygenation in the early postoperative period. The reason for the pulmonary impairment is multifactorial and may be due to effects of anaesthesia, intra-operative events, mechanical alterations, diaphragmatic dysfunction, medication and the patients' postoperative hemodynamic status <sup>(5)</sup>.

Respiratory failure after a successful coronary artery bypass grafting (CABG) operation continues to have an influence on the immediate recovery of a patient. Life-threatening pulmonary complications after CABG are more likely to occur in patients with chronic obstructive pulmonary disease (COPD), which has largely been regarded as a risk factor for early mortality. In fact, reduced forced expiratory volume in 1 second (FEV1) has been shown to be an independent risk factor for early mortality <sup>(6,7)</sup>.

The following pulmonary function tests (PFTs) were measured: vital capacity (VC), forced vital capacity (FVC), vital capacity as a percent of predicted (%VC), forced expiratory volume in the first second (FEV1.0), ratio between FEV1.0 and FVC (FEV1.0%), and percent predicted FEV1.0 (%FEV1.0). Although recent

guidelines for the diagnosis of lung disease have utilized PFTs to diagnose and classify the severity of pulmonary function, preoperative spirometry assessments have revealed differential diagnoses<sup>(8,9)</sup>.

Sex and Age are among the most important non-modifiable risk factors, for example, coronary artery disease (CAD) develops in women later in life comparing to men for an unknown reason. Late-onset of CAD in women results in underestimation of cardiovascular risk by healthcare providers and patients and leads to a higher burden of CAD in women, especially at a young age<sup>(10)</sup>.

Currently, there is no clear consensus in the literature on the impact of age specific Lung function on CABG patient outcomes.

Consequently, we conducted our present study which aimed to: assess early changes in lung volumes by pulmonary function tests before and following CABG in smoking adults and to identify how age might influence these changes by comparing above 60 with below 60 years.

### Material and Methods

200 consecutive patients undergoing elective coronary artery bypass surgery were included in this prospective controlled study. Emergency patients and those who underwent a valve operation in addition to CABG operation were not included in the study.

Informed written consent was obtained from each patient to be included in this study.

Patient and procedure information was collected prospectively for all patients. Patient data included age (we compared above 60 with below 60 years), sex, comorbid conditions (diabetes, hypertension, preoperative dialysis-dependent RF, chronic obstructive pulmonary disease [COPD], congestive heart failure, cancers, and liver disease), current cardiac condition (recent [ $<7$  days] myocardial infarction, current congestive heart failure), and previous cardiac surgery.

HTN was defined by at least two office blood pressure (BP) measurements exceeding 140 over 90 mmHg. Blood pressure was measured using a manual mercury sphygmomanometer in all cases. Trained nurses measured blood pressure in both hands in a sitting position after resting for 5 min. The higher BP was registered in a pre-specified datasheet. This protocol was repeated after 3 min. In case of difference (more than 10 mmHg in systolic blood pressure or 5 mmHg in diastolic blood pressure), the measurement was repeated for the third time and the two measurements closer together were used. The mean systolic and diastolic blood pressure of the two measurements was calculated. Participants with high blood pressure were defined as follows: mean systolic blood pressure  $\geq 140$  mmHg or mean diastolic blood pressure of  $\geq 90$  mmHg or who were taking blood pressure medications. DM was defined by measurements of fasting plasma glucose  $\geq 126$  mg/dL or glycated hemoglobin A1C (HbA1C)  $\geq 6.5\%$  in the presence of confirmatory testing. Patients on antidiabetic medications were also included as diabetic in the study.

Patients were defined as smokers if they had smoked cigarettes within one month of surgery. Patients who were not classified as current smokers but had a history confirming any form of tobacco use in the past were classified as previous smokers.

### Pulmonary Function Tests

Lung volumes (IVC and FEV<sub>1</sub>) were measured by spirometry (Vicatest P2a<sup>\*</sup>). Spirometry was standardized according to American Thoracic Society recommendations and was performed with the patient in a sitting position. The value recorded was the best (the highest IVC, FEV<sub>1</sub>, and forced vital capacity [FVC] measurement) of 3 consecutive attempts. Predicted values for pulmonary functions were calculated from regression equations according to age, height, and sex<sup>(11)</sup>.

### Operation technique

All patients were operated electively. By performing a median sternotomy, arterial cannulation from the ascending aorta and venous cannulation from the right atrium with a two-stage venous cannula was connected to a cardiopulmonary bypass (CPB) device. Moderate hypothermia (28°C) was achieved, cardiac arrest was

achieved with 10 to 15 mL/kg cold blood cardioplegia or 5 mL/kg cold crystalloid cardioplegia (St. Thomas II) after insertion of the aortic cross-clamp. After the surgical procedure, reperfusion was achieved with 5 mL/kg warm blood cardioplegia before the cross-clamp was removed. A roller head pump and hollow fiber membrane oxygenator were used in the CPB device. Left internal mammary artery (LIMA) and saphenous vein were used as the graft in all patients. During the operation, systemic antibiotic prophylaxis, decompression of the left ventricle, and loading excessive fluid were avoided. The patients were extubated as soon as possible (after achieving predetermined extubation criteria). Criteria for the extubation were: 1) resolution of the disease state or condition, 2) hemodynamic stability, 3) adequate oxygenation status on a decreased FiO<sub>2</sub> and decreased PEEP/CPAP; and 4) adequate ventilatory status and PaCO<sub>2</sub>. On the 4th postoperative day and 4 months postoperatively, the patients were asked to quantify their sternotomy wound pain at rest, while taking a deep breath, while coughing and at the performance of the pulmonary function test. A continuous unmarked visual analogue scale (VAS) from 0 (no pain) to 10 (worst imaginable pain) was used. Patients were also asked to state the level of thorax pain (severe, moderate, little or no pain) over the 4 months after surgery and their subjective experience of breathing (improved, unaltered, impaired) compared to the preoperative status. The following outcomes were analyzed: death from any hospital origin and other postoperative complications occurred during the same hospitalization after CABG, or within the first 30 days postoperatively. The following postoperative complications were analyzed: stroke (cerebrovascular accident/CVA) characterized as any transient or permanent neurological abnormality proven by CT or MRI of the brain, reoperation for hemostasis review, circulatory shock requiring intraaortic balloon pump (IAB), respiratory complications characterized by the use of mechanical ventilation > 24 h, or pulmonary infection requiring postoperative unit stay, acute kidney injury (AKI) requiring dialysis process, mediastinitis, sepsis from any source, atrial fibrillation (AF), and complete atrioventricular block (CAVB) requiring temporary or permanent pacemaker.

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

### The used tests were

1. **Student t-test (t):** For normally distributed quantitative variables, to compare between two different groups.
2. **Chi-square test:** For categorical variables, to compare different groups.

### Results

This study was a prospective controlled study that was performed over 200 consecutive patients undergoing elective coronary artery bypass surgery.

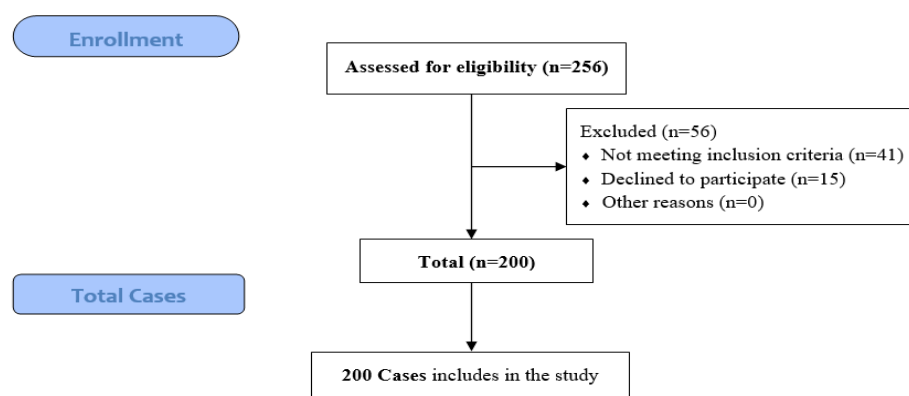


Figure 1: Flowchart of the study

256 patients were admitted in our study, 56 of them were excluded (41 didn't meet our inclusion criteria and 15 declined to participate), so we were left with 200 cases included in the study.

**Table 1: Distribution of the studied cases according to history data**

	<b>Subjects</b> <b>(n = 200)</b>	
<b>Age</b>		
Range.	44 – 70	
Mean $\pm$ SD.	57.07 $\pm$ 7.99	
<b>Sex</b>	No.	%
Female	42	21.0
Male	158	79.0
<b>Residence</b>	No.	%
Rural	65	32.5
Urban	135	67.5
<b>BMI</b>		
Range.	22.1 – 31.9	
Mean $\pm$ SD.	26.82 $\pm$ 2.78	
	No.	%
<b>Airflow obstruction</b>	28	14.0
<b>Diabetes</b>	32	16.0

Data are presented as frequency (%) unless otherwise mentioned, SD: **Standard deviation**

The mean age of the studied cases was 57.07 ( $\pm 7.99$  SD) with range (44-70), among the studied cases there were 42 (21%) females and 158 (79%) males, there were 65 (32.5%) rural residents and 135 (67.5%) urban residents, the mean BMI was 26.82 ( $\pm 2.78$  SD) with range (22.1-31.9), among the studied cases there were 28 (14%) with airflow obstruction and 32 (16%) with diabetes as shown in Table 1.

**Table 2: Distribution of the studied cases according to operation data**

	<b>Subjects</b> <b>(n = 200)</b>
<b>Cardiopulmonary bypass time (min)</b>	
Range.	59 – 141
Mean $\pm$ SD.	98.89 $\pm$ 25.14
<b>Cardiac ischemic time (min)</b>	
Range.	25 – 127
Mean $\pm$ SD.	67.8 $\pm$ 26.6

<b>Time in the ICU (hrs.)</b>		
Range.	4 – 102	
Mean $\pm$ SD.	53.54 $\pm$ 27.98	
<b>Cardioplegia</b>	No.	%
Cold	13	6.5
Warm	187	93.5
<b>Topical cooling</b>	No.	%
Ice slush	13	6.5
Non	187	93.5

Data are presented as frequency (%) unless otherwise mentioned, SD: **Standard deviation**

According to operation data, the cardiopulmonary bypass time was 98.89 ( $\pm 25.14$  SD) with range (59-141) minutes, the mean cardiac ischemic time was 67.8 ( $\pm 26.6$  SD) with range (25-127) minutes, the mean time in the ICU time was 53.54 ( $\pm 27.98$  SD) with range (4-102) hours, according to cardioplegia there were 13 (6.5%) cold and the rest were warm and according to topical cooling there were 13 (6.5%) with ice slush as shown in Table 2.

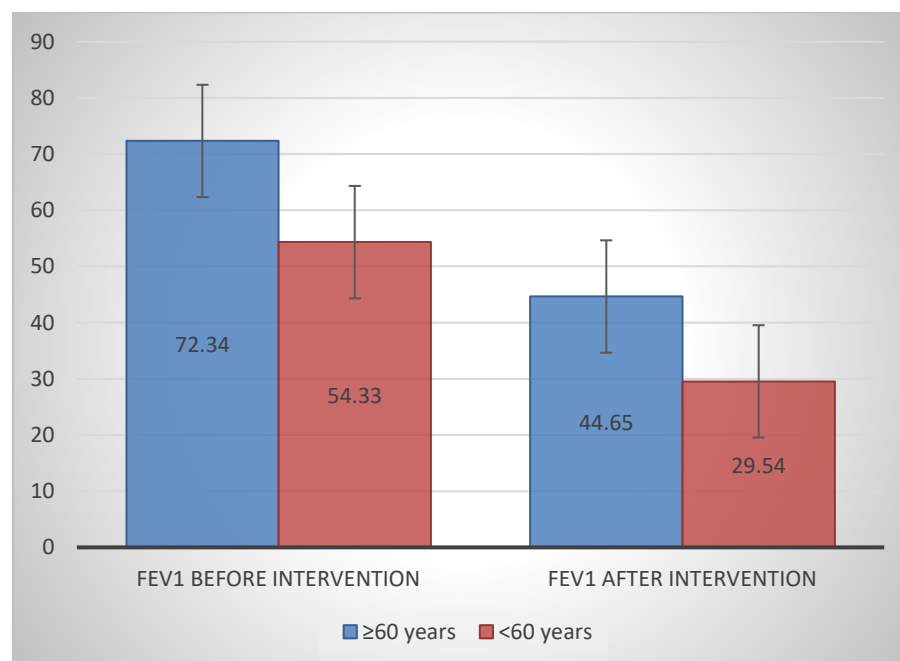
**Table 3: Comparison between age groups according to pulmonary function tests before and after operation**

		Subjects		t	p-value
		$\geq 60$ years (n = 83)	<60 years (n = 117)		
Before intervention	<b>VC</b>				
	Range.	40.1 – 73.6	40.3 – 74.1	0.351	0.726
	Mean $\pm$ SD.	57.47 $\pm$ 10.22	56.95 $\pm$ 10.16		
	<b>FVC</b>				
	Range.	41.6 – 73.9	35.9 – 73.9	11.702	<0.001*
	Mean $\pm$ SD.	62.46 $\pm$ 7.04	48.39 $\pm$ 9.2		
	<b>FEV1</b>				
	Range.	41.8 – 92.4	37.6 – 92.1	12.456	<0.001*
	Mean $\pm$ SD.	72.34 $\pm$ 9.47	54.33 $\pm$ 10.48		
	<b>FEV1/FVC</b>				
	Range.	99.8 – 129.5	98.2 – 129.2	2.542	0.012*
	Mean $\pm$ SD.	115.82 $\pm$ 8.17	112.6 $\pm$ 9.29		
	<b>MVV</b>				
	Range.	18.7 – 56.1	17.7 – 58	0.499	0.619

	Mean $\pm$ SD.	38.31 $\pm$ 10.75	37.5 $\pm$ 11.76		
After intervention	<b>VC</b>				
	Range.	19.1 – 57.7	19 – 60.5	0.416	0.680
	Mean $\pm$ SD.	34.85 $\pm$ 11.76	34.16 $\pm$ 11.29		
	<b>FVC</b>				
	Range.	20.2 – 63.3	19.2 – 53.6	8.367	<0.001*
	Mean $\pm$ SD.	39.32 $\pm$ 10.21	28.08 $\pm$ 8.71		
	<b>FEV1</b>				
	Range.	20.6 – 76.1	18 – 75.9	8.255	<0.001*
	Mean $\pm$ SD.	44.65 $\pm$ 12.67	29.54 $\pm$ 12.81		
	<b>FEV1/FVC</b>				
	Range.	53.1 – 247.3	48.3 – 209.6	2.192	0.030*
	Mean $\pm$ SD.	119.35 $\pm$ 41.03	107.35 $\pm$ 35.97		
	<b>MVV</b>				
	Range.	11.8 – 51.1	11.2 – 50.8	0.520	0.604
	Mean $\pm$ SD.	29.78 $\pm$ 11.06	28.91 $\pm$ 11.92		

Data are presented as frequency (%) unless otherwise mentioned, SD: **Standard deviation**

This table shows that there was statistically significant difference between age groups as regard FVC, FEV1 and FEV1/FVC before and after intervention as shown in Table 3.



**Figure 2: Comparison between age groups according to Pre and Post operative FEV1 before operation**

Table 4: Comparison between age groups according to mortality outcome

	Subjects				$\chi^2$	p-value
	$\geq 60$ years (n = 83)		<60 years (n = 117)			
Mortality	No.	%	No.	%		
No	70	84.3	112	95.7	7.690	0.006*
Yes	13	15.7	5	4.3		

Data are presented as frequency (%) unless otherwise mentioned, SD: **Standard deviation**

This table shows that there was statistically significant difference between age groups as regard mortality outcome as shown in Table 4.

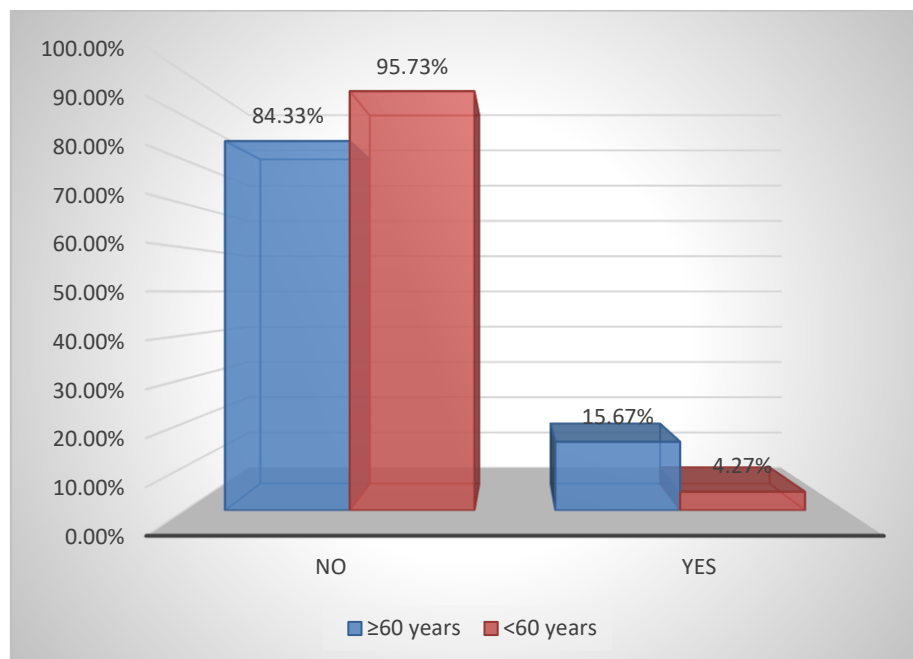


Figure 3: Comparison between age groups according to mortality outcome

## Discussion

Coronary artery disease (CAD) has been known as the leading cause of death worldwide. According to the World Health Organization (WHO), CAD-induced mortality is on the top of the death list, with 7.4 million deaths each year in the world. It is estimated that 16.7 million deaths from heart disease in 2002 would reach 23.3 million in 2030. According to the WHO (2016), 45% of deaths in Iran are due to cardiovascular disease <sup>(12)</sup>.

In patients undergoing CABG, age is independent risk factors for morbidity and mortality. However, some studies have argued that preoperative risk factors and treatment methods are responsible for the perceived effects of age and others have reported no significant differences attributable to these factors <sup>(13)</sup>.

Patients undergoing CABG often develop atelectasis and severe reductions in lung volumes and oxygenation in the early postoperative period. The reason for the pulmonary impairment is multifactorial and may be due to effects of anaesthesia, intra-operative events, mechanical alterations, diaphragmatic dysfunction, medication and the patients' postoperative hemodynamic status <sup>(14)</sup>.

Currently, there is no clear consensus in the literature on the impact of age specific Lung function on CABG patient outcomes. Hence, we conducted our present study which aimed to assess early changes in lung volumes by pulmonary function tests before and following CABG in smoking adults and to identify how age might influence these changes by comparing above 60 with below 60 years.

This study was a prospective controlled study that was performed over 200 consecutive patients undergoing elective coronary artery bypass surgery.

In this study we found the mean age of the studied cases was 57.07 ( $\pm 7.99$  SD) with range (44-70), among the studied cases there were 42 (21%) females and 158 (79%) males, there were 65 (32.5%) rural residents and 135 (67.5%) urban residents, the mean BMI was 26.82 ( $\pm 2.78$  SD) with range (22.1-31.9), among the studied cases there were 28 (14%) with airflow obstruction and 32 (16%) with diabetes

In the same context, **Assmann et al.**<sup>(15)</sup>, conducted a study on 3,237 patients to investigate the impact of socio-demographic factors on CABG outcome. They found among the studied cases 2,684 (82.9%) were males. Regarding age, 746 (23.0%) were <60 years, 1,823 (56.3%) were 60-74 years and 668 (20.6%) were  $\geq 75$  years. the mean BMI was  $28.2 \pm 0.08(\text{kg}\cdot\text{m}^{-2})$  and 368 (11.4%) of patients had COPD.

Also, **Oshvandi et al.**<sup>(12)</sup>, reported that most participants were males (76.5%), under 60 years old (82.35%), urban residents (81.2%), non-smokers (60%), overweight (42.4%), and diabetic (28.2).

The final analysis by **Pakrad et al.**<sup>(16)</sup>, included 2863 patients. The mean age of the patients was  $62.9 \pm 9.4$  years, and the majority of the patients were in the 60–69 years old age group (40.17%, N = 1150). Men accounted for 73.38% (N = 2101) of the surgical cases. Most of the patients resided in urban areas (76.39%, N = 2187).

Characteristics of the patient population in **Canver et al.**<sup>(17)</sup>, study. In group 1 (less than 70 years old; n=710), there were 705 men and 5 women, and in group 2 (more than 70 years old; n = 229), there were 228 men and 1 woman.

According to our operation data, the cardiopulmonary bypass time was 98.89 ( $\pm 25.14$  SD) with range (59-141) minutes, the mean cardiac ischemic time was 67.8 ( $\pm 26.6$  SD) with range (25-127) minutes, the mean time in the ICU time was 53.54 ( $\pm 27.98$  SD) with range (4-102) hours, according to cardioplegia there were 13 (6.5%) cold and the rest were warm and according to topical cooling there were 13 (6.5%) with ice slush

Of the 272 patients in the study of **Brown et al.**<sup>(18)</sup>, low left ventricular ejection fraction patients undergoing isolated CABG, 181 were in the conventional cardioplegia group and 91 in the del Nido group. Mean cardiopulmonary bypass time was  $122.43 \pm 34.3$  and mean cardiac ischemic time was  $94.55 \pm 36.43$  and mean ICU LOS  $3.7 \pm 2.3$ .

According to **Zarrizi et al.**<sup>(19)</sup>, The mean time of cardiopulmonary bypass and aorta clamp were  $59.96 \pm 15.95$  and  $36.59 \pm 10.86$  minutes, respectively. About the postoperative factors, the most common respiratory complication was atelectasis. Research findings indicated that the mean ICU length of stay (LOS) was  $55.27 \pm 17.33$  hours (minimum and maximum of 33 and 192.6 hours, respectively). The LOS of 26.2% of patients was more than the mean ICU LOS.

**Modolo et al.**<sup>(20)</sup>, searched the outcomes following coronary artery bypass graft surgery for left main disease. Total mean procedure duration was  $195.8 \pm 64.50$ . Bypass duration was  $85.8 \pm 48.8$ . Cross clamp duration was  $54.9 \pm 26.5$ . Temperature of cardioplegic solution Warm,  $>35^{\circ}\text{C}$  was 23.1 (89/385) and Cold  $< 35^{\circ}\text{C}$  was 76.9 (296/385).

Our data shows that there was statistically significant difference between age groups as regard FVC, FEV1 and FEV1/FVC before and after intervention.

In similar, **Canver et al.**<sup>(17)</sup>, proved that there was statistically significant difference between age groups as regard pulmonary function before and after intervention. Furthermore, they found Preoperative low FEV1 significantly affected the duration of care both in the ICU and in the hospital in patients less than 70 years old

( $p = 0.0001$  and  $p = 0.0001$ , respectively). Moreover, they found The five-year survival after CABG was significantly influenced by the level of preoperative FEV1 in patients less than 70 years old ( $p = 0.0002$ ) and in patients 70 years old or older ( $p = 0.0431$ ).

In the study of **Moreno et al.** <sup>(21)</sup>, Forty-two volunteers with an average age of  $63 \pm 2$  years were included and separated into three groups: healthy volunteers ( $n = 09$ ), patients with CAD ( $n = 9$ ) and patients who underwent CABG ( $n = 20$ ). At the first evaluation, there were no significant differences in FVC, Maximum inspiratory pressure MIP or maximum expiratory pressure MEP among the groups ( $p > 0.05$ ). In the CABG group, there was a statistically significant decrease in the FVC ( $p < 0.05$ ) on postoperative days 3 and 5. The biggest decrease was on postoperative day 3, and lung function returned to the preoperative level by postoperative day 15.

Pain due to thoracotomy is a limiting factor for mobility and breathing. A high level of postoperative pain is common because of the cutting of the skin, muscles and pleura as well as the retraction of muscles and ligaments, pleural and septal nerve irritation from thoracic drains and occasional rib fractures. Pain may also contribute to decreased cough efficiency, which is the main mechanism for the elimination of secretions from the tracheobronchial tree due to the immobility of the thoracic wall. This immobility causes superficial breathing, which may result in atelectasis, inadequate ventilation-perfusion ratio and pneumonia. These complications lead to increased morbidity <sup>(21)</sup>.

In our study, there was statistically significant difference between age groups as regard mortality outcome.

In agreement with our results, **Canver et al.** <sup>(17)</sup>, found statistically significant difference between age groups as regard mortality outcome as they found early mortality for young patients was 1.1% (8/710); it was 3.0% (7/229) for elderly patients ( $p = 0.0500$ ).

Also, the study findings of **Lemaire et al.** <sup>(13)</sup>, demonstrates that advanced age impacts surgical outcomes after CABG with octogenarians having worse postoperative outcomes including higher complications and mortality than septuagenarians.

Nevertheless, **Nicolini et al.** <sup>(22)</sup>, investigated early and late outcomes in patients aged above 80 years and undergoing CABG, advocating that advanced age should not be a deterrent for CABG in carefully selected patients. They showed that candidate selection based on evaluation of systemic comorbidities offered the greatest benefit to successful revascularization. These findings, although different from our study results, highlight the fact that careful patient selection, regardless of age, is critical in surgical outcomes.

Also, **Smith et al.** <sup>(23)</sup>, reported that CABG in Octogenarians is as safe as and no costlier than in Septuagenarians. However, the relatively small number of Octogenarians ( $n = 71$ ) compared to young ( $n = 579$ ) and old ( $n = 384$ ) Septuagenarians limit the impact of this study.

#### Weaknesses of the study

- This is single center study with small sample size the results further need to be confirmed by multicenter clinical studies.
- Since our study is a prospective study, and they are not efficient for outcomes with long latency. Also, Losses to follow up can bias the measure of association.
- In this study, only patients who underwent coronary artery bypass grafting were assessed. It is suggested that in future studies, patients be examined after a variety of cardiac surgeries, including heart valve surgery.

#### Strengthens of the study

- Since our study is a prospective study, this can provide better quality of data on the primary exposure and on confounding variables.
- Our study was short – term. Thus, further studies with long time follow up to investigate latent outcomes maybe needed.

- The relevance of the study is not limited by the fact that spirometry was measured after surgery, which wasn't addressed in other previous research.

### Conclusions

Based on our results, we conclude that age may affect pulmonary function before and after intervention and mortality outcome since we found that there was statistically significant difference between age groups as regard pulmonary function before and after intervention and a statistically significant difference between age groups as regard mortality outcome.

Nevertheless, the small sample size of our study may limit drawing any firm conclusions. Thus, further studies are needed to emphasize our findings.

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