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Transoesophageal Echocardiography of Coronary Artery Ectasia Patients and Intravenous Nitroglycerin Effects

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Abstract

Background: The cause, physiological changes, predictive value, and associated health problems of coronary artery ectasia (CAE) is still not agreed upon by experts.

Objectives: The aim of our study was to evaluate the baseline coronary flow in individuals with coronary artery ectasia and investigate the impact of intravenous nitroglycerin on coronary flow through the use of transesophageal echocardiography (TEE).

Methodology: A total of forty participants were sequentially enrolled in the trial, and all of them underwent elective coronary angiography. The subjects were categorized into two groups based on the findings of elective coronary angiography. Group I consisted of 30 patients with confirmed coronary artery ectasia (CAE) but no stenosis in the left anterior descending coronary artery (LAD). Group II comprised of 10 individuals with normal coronary arteries, serving as the control group. Each participant performed transesophageal echocardiography (TEE) utilizing pulsed wave Doppler to quantify peak systolic and diastolic velocities (m/sec), systolic, diastolic, and total velocity time integrals (cm), as well as systolic, diastolic, and total coronary blood flow (cm/min). Following intravenous administration of 0.3 mg (300µgm) of nitroglycerin (NTG), all participants were reassessed for the previously measured parameters.

Findings: Individuals diagnosed with CAE were of a younger age, with a higher proportion of males. Furthermore, there was a notably lower occurrence of diabetes mellitus within this group. There was no statistically significant difference observed between the two study groups in terms of the initial systolic, diastolic, and total velocity time integrals. Group I exhibited significantly higher systolic, diastolic, and total basal coronary blood flow compared to group II (46.09 ±34.33 versus 23.05±8.21, 123.98±73.33 versus 68.06±21.6, 170.07±97.88 versus 91.10± 26.82, respectively, p value <0.05). Group I participants saw a statistically significant reduction in peak diastolic velocity, systolic velocity, diastolic velocity, and total velocity time integrals following intravenous injection of NTG. Additionally, there was a statistically significant decrease in diastolic coronary blood flow and total coronary blood flow. Meanwhile, in group II, the administration of NTG through intravenous injection resulted in a statistically significant augmentation of overall coronary blood flow. Group II had a greater percentage increase in cross-sectional area following NTG.

Conclusion: Coronary Artery Ectasia is frequently found in young individuals and are rarely linked to diabetes. Normal arteries have a lower basal coronary flow in comparison to these arteries. The intravenous administration of nitroglycerin leads to a substantial decrease in flow characteristics in dilated coronary arteries, while it increases flow in normal coronary arteries.

Key Words: Coronary artery ectasia – Coronary flow – Vasodilators – Transoesophageal echo – Diabetes.

Introduction

Coronary artery ectasia (CAE) is a well-known but uncommon anomaly of the structure of the coronary arteries. Since its discovery forty years ago, there have been multiple investigations that have focused on its general occurrence, underlying mechanisms, and clinical importance [1].

Although there is a continued focus in developing a treatment and a prognosis profile for patients with ectasia, there are still some aspects that are uncertain and undefined. There is a lack of agreement regarding the cause, predictive importance, and associated health issues related to this pathological condition. The current disagreement on the proper care and treatment of patients with CAE is based on this lack of certainty [2].

Patients and Methods

The study comprised a total of forty patients who underwent elective coronary angiography at Ain Shams University Hospital between February 2006 and February 2008.

Selection of patients:

The patients were categorized into two groups:

- Group I consisted of 30 patients who had angiographically confirmed pure ectasia in the left anterior descending coronary artery (LAD) without any stenosis. Ectasia was defined as the expansion of the coronary artery lumen to a size 1.5 times larger than the neighboring normal segment as seen on angiography. If there was no normal segment, the diameter of the equivalent coronary artery in the control group was used as a reference [1].
- Group II consisted of 10 participants who had normal coronary arteries as confirmed by angiography. This group was used as a control group.

Criteria for exclusion:

1- TEE is contraindicated in cases of esophageal or pharyngeal obstruction, esophageal varices or diverticulae, suspected or confirmed perforated viscus, gastrointestinal bleeding, oro-pharyngeal distortion, instability of cervical vertebrae, cervical arthritis, bleeding diathesis, or excessive anticoagulation (defined as INR >5 or PTT >100 sec, platelets <50,000/mm3). TEE should also not be performed on uncooperative patients.
2- Inadequate visualization of the left anterior descending artery (LAD) by transesophageal echocardiography (TEE).
3- Patients exhibiting stenosis in the coronary artery under examination.

Methods:

All patients included in the study underwent the following procedures:

1- Conduct a comprehensive patient interview focusing on the distribution of risk factors for coronary artery disease, such as age, gender, smoking, hypertension, diabetes mellitus, dyslipidemia, family history, as well as symptoms indicative of ischemic heart disease and any contraindications for transesophageal echocardiography (TEE).

2- Thorough clinical examination.
3- Twelve-lead surface electrocardiogram (ECG).
4- Transesophageal echocardiography (TEE):

An echocardiographic investigation was conducted utilizing a Vivid Five system, a cardiac ultrasound machine manufactured by Vingmed Technology in the USA. A 5MHz multi-plane phased-array probe was utilized to acquire 2D images and Doppler measurements. The probe was inserted until it reached a distance of approximately 30 cm from the incisor teeth, at which point the aortic cusps became visible. This was observed using a basal short axis view at the level of the aortic valve. The withdrawal was performed gradually until the opening of the left major coronary artery became plainly visible. Precise modifications involving rotation and flexion were performed to achieve an excellent visualization of the left anterior descending coronary artery. The left major coronary artery was seen at the 2 o'clock location of the aortic ring. The division of the left main coronary artery typically takes the form of a Y shape, where the left circumflex artery extends from the left main coronary artery, and the left anterior descending coronary artery is positioned almost perpendicular to the planes of the left main and left circumflex coronary arteries.

The diameter of the artery under examination was measured using 2D imaging, expressed in centimeters.
* The pulsed wave sample volume was positioned across the proximal segment of the left anterior descending artery (LAD) with the sample volume aligned as closely parallel to the LAD as feasible. Subsequently, the flow velocity was recorded spectrally and the following parameters were computed:

1- Maximum velocity of blood flow during systole (m/sec).
2- Peak diastolic velocity (m/sec).
3- Systolic velocity time integral measured in centimeters.
4- Diastolic velocity time integral measured in centimeters.
5- Cumulative integral of velocity over time (cm).

* The formula provided was used to determine the coronary blood flow, which includes measurements for systolic, diastolic, and total flow. The product of the cross-sectional area of the coronary artery, the velocity-time integral, and the heart rate is represented in Figure 1.
* A 0.3 mg bolus of nitroglycerin (NTG) was administered intravenously with a large diameter cannula. Heart rate, blood pressure, and all previously stated parameters were reevaluated within 5 minutes following the administration of NTG (Fig. 2).
* After the procedure, the probe was examined for any marks, cleaned with flowing water, and then submerged in Cidex® for a duration of 20 minutes. It was thereafter rinsed again with running water. The

patient underwent a 30-minute follow-up period to observe and track blood pressure and heart rate prior to being transferred to the ward or discharged.

Statistical analysis:

Collected data underwent verification and revision. Categorical variables were represented by their absolute and relative frequencies (expressed as a percentage), whereas continuous variables were displayed as mean values with their corresponding standard deviation. The t-test was used to compare continuous variables between the two groups, while the chi-square test and Pearson correlation coefficient were used to compare categorical variables.

The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 12. Statistical significance was determined at a p-value threshold of <0.05, while high significance was determined at a p-value threshold of <0.001.

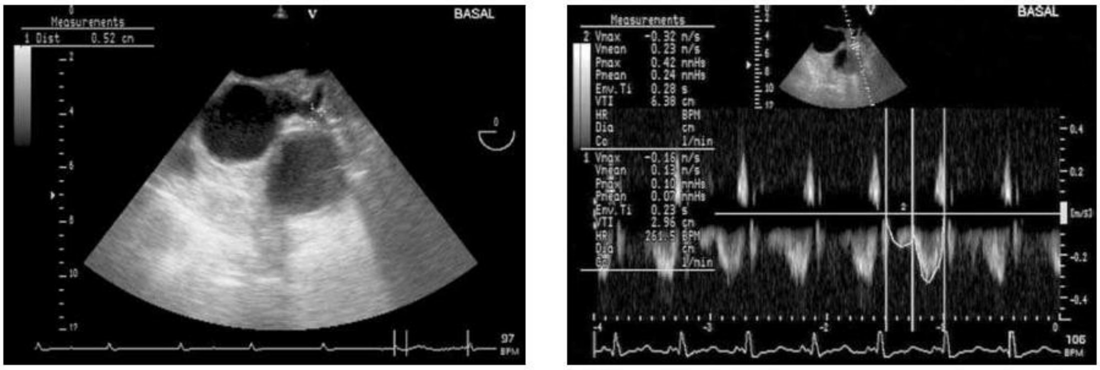

Figure 1: Case number 7 Left coronary system by TEE (2D) and basal Doppler parameters.

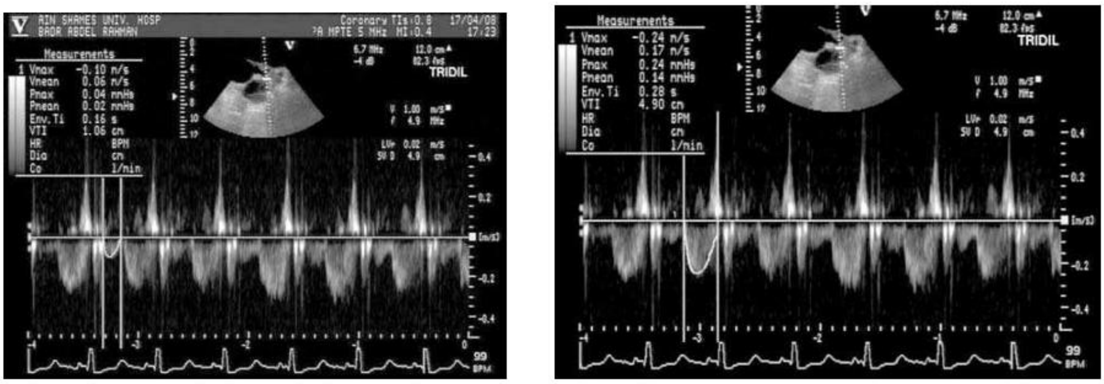

Figure 2: Case number 7; Doppler parameters after nitroglycerin.

The mean age of the study group was 48.55± 7.95 years. Out of the total number of patients, 39 were males, accounting for 97.5% of the group. Out of the total number of patients, 22 (55%) had hypertension, 9 (22.5%) had diabetes, and 27 (67.5%) were smokers. Out of the total number of patients, 10 individuals (25%) were found to have dyslipidemia, and six individuals (15%) had a confirmed family history of early coronary artery disease.

The fundamental characteristics of the entire cohort and the two study groups are displayed in Table (1). The two study groups were similar in terms of age, sex, and risk factors for coronary artery disease, with no statistically significant distinction between them.

Table 1: Basic characteristics of the whole cohort and the two study groups.

Variable	Total cohort N=40	Group I N=30	Group II N=10	*p* value
Age (y)	48.55±7.95	48.97±8.04	47.30±7.94	>0.05
Males (n, %)	39 (97.5)	30 (100)	9 (90)	>0.05
Hypertension (n, %)	22 (55)	16 (53.3)	6 (60)	>0.05
Diabetes mellitus (n, %)	9 (22.5)	6 (20)	3 (30)	>0.05
Smoking (n, %)	27 (67.5)	19 (63.3)	8 (80)	>0.05
Dyslipidemia (n, %)	10 (25)	8 (26.7)	2 (20)	>0.05
Family history (n, %)	6 (15)	4 (13.3)	2 (20)	>0.05

When comparing the two groups in terms of heart rate (measured in beats per minute) and blood pressure, both before and after the injection of nitroglycerin, no statistically significant difference was seen. This is indicated in Table (2).

Table 2: Comparison of vital signs of the two groups before and after nitroglycerin injection.

Variable	Group I Number=30	Group II Number=10	*p* value
BP before NG:			
Systolic	122±20.72	119±16.63	>0.05
Diastolic	77.33±10.48	73.62±9.49	
HR before NG (bpm)	87.07±19. 33	93.90±18.86	>0.05
BP after NG:			
Systolic	124±22.72	120±16.63	>0.05
Diastolic	78.45±10.48	75.22±9.49	
HR after NG (bpm)	90.67±16.71	96.10±20.72	>0.05

Table (3) displays the initial Doppler flow velocity data that was acquired for the 2 groups being studied. There was no statistically significant distinction observed between the two groups in terms of peak systolic and diastolic velocities, as well as systolic, diastolic, and total velocity time integrals.

Table 3: Comparison between the two study groups as regards Doppler parameters.

Variable	Group I Number=30	Group II Number=10	*p* value
Peak systolic velocity (m/sec)	0.22±0.11	0.22±0.09	>0.05
Peak diastolic velocity (m/sec)	0.39±0.15	0.47±0.14	>0.05
Systolic velocity time integral (cm)	3.01±1.89	2.79±1.20	>0.05
Diastolic velocity time integral (cm)	8.24±4.31	8.56±4.75	>0.05
Total velocity time integral (cm)	11.26±5.54	11.37±5.69	>0.05
Systolic coronary blood flow (cm^3/min)	46.09±34.33	23.05±8.21	<0.05
Diastolic coronary blood flow (cm^3/min)	123.98±73.33	68.06±21.6	<0.05
Total coronary blood flow (cm^3/min)	170.07±97.88	91.10±26.82	<0.05

Group I exhibited significantly higher systolic, diastolic, and total coronary blood flow compared to group II (46.09±34.33 versus 23.05±8.21, 123.98±73.33 versus 68.06±21.6, 170.07±97.88 versus 91.10±26.82, respectively, p value <0.05).

The administration of nitroglycerin via intravenous injection in the group I resulted in a substantial statistical reduction in peak diastolic velocity, systolic velocity, diastolic velocity, total velocity time integrals, as well as diastolic and total coronary blood flow. These findings are presented in Table 4 and Figure 3.

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Table 4: Comparison of Doppler parameters in group I before and after nitroglycerin injection.

Variable	Group I Basal	Group I after nitroglycerin	*p* value
Peak systolic velocity (m/sec)	0.22±0.11	0.20±0.10	>0.05
Peak diastolic velocity (m/sec)	0.39±0.15	0.29±0.14	<0.05
Systolic velocity time integral (cm)	3.01±1.89	2.45±1.52	<0.05
Diastolic velocity time integral (cm)	8.24±4.31	5.88±3.83	<0.05
Total velocity time integral (cm)	11.26±5.54	8.33±4.74	<0.05
Systolic coronary blood flow (cm^3/min)	46.09±34.33	43.19±30.55	>0.05
Diastolic coronary blood flow (cm^3/min)	123.98±73.33	105.58±78.02	<0.05
Total coronary blood flow (cm^3/min)	170.07±97.88	148.81±98.05	<0.05

In group II, the intravenous injection of nitroglycerin resulted in a considerable increase in total coronary blood flow. However, the changes in other parameters did not reach statistical significance, as shown in Table 5 and Figure 4.

Table 5: Comparison of Doppler parameters in group II before and after nitroglycerin injection.

Variable	Group II Basal	Group II nitroglycerin	*p* value
Peak systolic velocity (m/sec)	0.22±0.09	0.21±.06	>0.05
Peak diastolic velocity (m/sec)	0.47±0.14	0.40±0.19	>0.05
Systolic velocity time integral (cm)	2.79±1.20	2.468±.77	>0.05
Diastolic velocity time integral (cm)	8.56±4.75	8.05±5.22	>0.05
Total velocity time integral (cm)	11.37±5.69	10.52±5.39	>0.05
Systolic coronary blood flow (cm^3/min)	23.05±8.21	27.43±8.16	>0.05
Diastolic coronary blood flow (cm^3/min)	68.06±21.60	87.86±45.93	>0.05
Total coronary blood flow (cm^3/min)	91.10±26.82	115.30±46.75	<0.05

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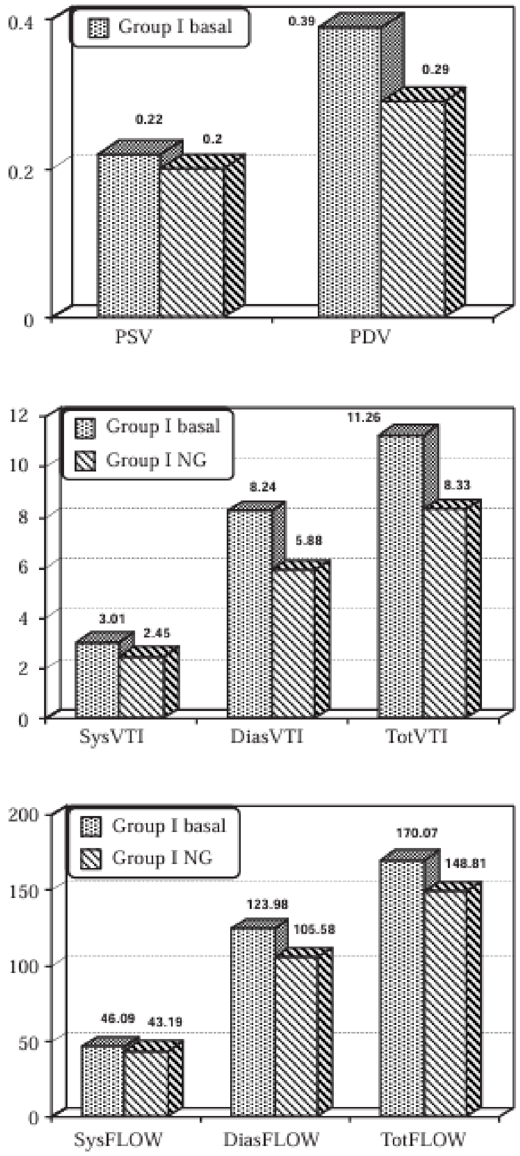
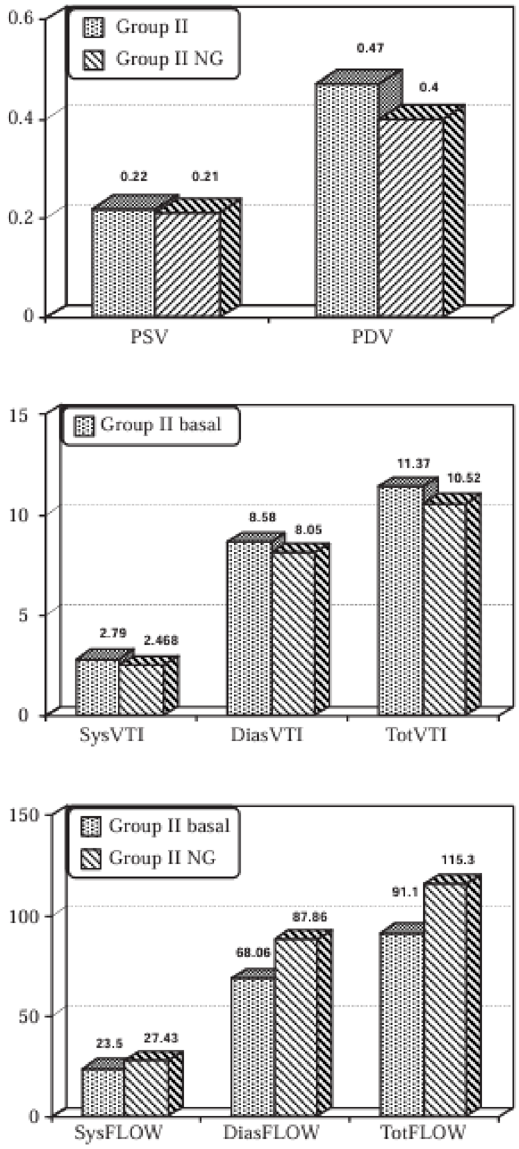


PSV = Peak systolic velocity.
PDV = Peak diastolic velocity.
SysVTI = Systolic velocity time integral.
DiasVTI = Diastolic velocity time integral.
TotVTI = Total velocity time integral.
SysFLOW = Systolic flow.
DiasFlow = Diastolic flow.
TotFLOW = Total flow.

Figure 3: Comparison of Doppler parameters in the coronary artery ectasia group before and after nitroglycerin injection



PSV = Peak systolic velocity.
PDV = Peak diastolic velocity.
SysVTI = Systolic velocity time integral.
DiasVTI = Diastolic velocity time integral.
TotVTI = Total velocity time integral.
SysFLOW = Systolic flow.
DiasFlow = Diastolic flow.
TotFLOW = Total flow.

Figure 4: Comparison of Doppler parameters in group II (angiographically normal coronaries) before and after nitroglycerin injection.

Discussion

The primary angiographic features of CAE are delayed antegrade coronary dye filling, segmental backflow phenomena (milking phenomenon), and stasis with localized deposition of dye in dilated coronary segments [3]. Multiple studies have assessed the conventional profile of cardiovascular risk factors in patients with coronary artery ectasia (CAE). All patients included in this study were male and of a reasonably young age. This result aligns with the findings of Giannoglu et al (2006), who observed a prevalence of males among patients with CAE [4].

Previously, it was claimed that there is a gender difference in the occurrence of CAD, with women having a lower incidence. However, the exact relationship between CAE and CAD is not completely recognized. Furthermore, the increased probability of males experiencing CAE in comparison to females is generally in line with a study conducted in Spain, which found that being male was an independent factor that raised the risk of CAE [7].

Research has demonstrated that age is a crucial factor that is negatively correlated with the existence of CAE [4]. Previously, it was shown that individuals with CAE were significantly younger compared to those without the condition [7,8]. The study conducted by Markis et al (1976) contradicts this finding, as they showed similar sex and average age among patients with CAE and patients with stenotic CAD [9].

In this study, nineteen patients were identified as smokers, sixteen patients were diagnosed with hypertension, and eight patients were diagnosed with dyslipidemia. This evidence is consistent with the findings of Gardiner and Lindop (1989), who concluded that hypertension and dyslipidemia play a role in the development of CAE [10]. In their study, Bermudez et al. (2003) found that the prevalence of smoking was higher among individuals with coronary artery ectasia (CAE) compared to those with stenotic coronary artery disease (CAD) [7]. Diabetes mellitus is a widely recognized risk factor that is strongly linked to coronary atherosclerosis and its consequences [11,12].

Diabetes mellitus was present in 20% of participants with coronary artery disease (CAE) in the research. This aligns with the research conducted by Bermudez et al. (2003) and Androulakis et al. (2004), which found a notable and opposite correlation between CAE and diabetes mellitus [7,13]. Providing evidence for this opposite relationship, research have presented demographic data that demonstrate a low occurrence of diabetes in individuals with CAE [14]. The inverse connection between diabetes mellitus and CAE can be expected due to the recognized effects of diabetes mellitus on promoting negative remodeling in the arterial wall and impairing compensatory arterial expansion throughout the atherosclerotic process [15].

In the current investigation, no statistically significant difference was found at the beginning between both groups in terms of peak systolic and diastolic velocities. The observations presented here align with the findings of Akyurek et al. (2003), who observed that the peak velocities of coronary blood flow at baseline were comparable in both ectatic and normal vessels. However, patients with isolated coronary artery ectasia (CAE) had reduced resting blood flow velocity [1].

Nevertheless, our findings contradict those of Mavrogeni et al. (2005), as they observed that the control group exhibited notably higher peak flow velocity and lower TIMI frame count in both the right coronary artery (RCA) and left anterior descending artery (LAD) compared to individuals with coronary artery ectasia (CAE). The variation can be attributed to the utilization of diverse techniques for evaluating the flow of coronary arteries [16].

The current study found a notably elevated resting coronary blood flow (including systolic, diastolic, and total) in ectatic arteries. This result aligns with the study conducted by Akyurek et al, which demonstrated that the volume of blood flow in the coronary arteries was notably greater in the group with coronary artery ectasia (CAE) compared to their control group [1].

The presence of ischemia in patients with coronary artery ectasia (CAE) despite having increased resting coronary blood flow can be attributed to various potential pathophysiologic processes.

1- The increased diameter of the blood vessel leads to a change from smooth and regular blood flow to chaotic and irregular blood flow in the widened sections [17].
2- Blood flow velocity reduces in accordance with Hagen-Poiseuille's law, which states that as the diameter of the blood artery increases, the velocity of blood flow decreases. Nevertheless, this particular law holds true solely when there is a smooth flow of a uniform fluid [18].
3- Elevated viscosity; blood exhibits distinct flow characteristics (according to Reynold's law); this implies that when blood flow velocity falls below a certain threshold, viscosity rises, resulting in the aggregation of red blood cells and/or the activation of platelets and the coagulation system, potentially causing microembolization in distant areas [19].
4- Decreased coronary flow reserve, potentially caused by decreased nitric oxide (NO) generation. The study showed that when papaverine, a strong hyperemic stimulus, was administered directly into the coronary artery, the coronary flow reserve was measured to be 1.51 in patients with coronary artery ectasia (CAE), while it was 2.67 in patients with normal arteries. This suggests that the reason of myocardial ischemia in CAE may be due to malfunction in the endothelial cells and/or microvasculature [1].

The administration of nitroglycerin via intravenous injection in patients with coronary artery ectasia resulted in significant reductions in peak diastolic velocity, velocity time integrals (systolic, diastolic, and total), as well as diastolic and total coronary blood flow. However, there was no statistically significant decrease observed in peak systolic velocity and systolic coronary blood flow. These findings align with the research conducted by Kruger et al. (1999), which concluded that nitroglycerin worsens exercise-induced coronary ischemia and does not provide any therapeutic advantages [3]. This conclusion contradicts the results of Kim et al. (2006), who observed that the administration of nitrates did not decrease the value of Fractional Flow Reserve (FFR) in individuals with coronary artery ectasia (CAE). Nevertheless, their investigation was carried out on an only 10 individuals [21].

The notable reduction in diastolic and overall blood flow, despite an increase in the measured cross-sectional area (CSA), can be attributed to the substantially greater percentage increase of CSA in patients with typical coronary arteries. In a prior study by Dunker et al. (1995), it was found that the extent of arterial dilatation is negatively associated with the initial diameter [22]. Aksoy et al. (2006) postulated that poor generation or reaction to nitric oxide, as well as the degradation of the arterial media, could be potential processes contributing to impaired arterial responsiveness in patients with CAE [23].

Conclusion

This study demonstrates that there is a higher prevalence of coronary artery ectasia (CAE) in young individuals, whereas it is less frequently observed in patients with diabetes, when compared to stenotic coronary arteries. The intravenous administration of nitroglycerin leads to a notable decrease in flow characteristics in dilated coronary arteries, while it increases flow in normal coronary arteries. Ectatic coronary arteries exhibit a larger baseline coronary flow compared to normal arteries, but have a diminished ability to increase blood flow when needed. Therefore, it is advisable to refrain from using nitroglycerin regularly in individuals with coronary artery disease (CAE) because it has the potential to worsen the blood flow to the heart muscle.

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