

Coronary artery ectasia: Pattern and distribution in different coronary arteries segments-retrospective analysis

Abstract

Coronary Artery Ectasia (CAE), reported in 0.3%-5.3% of coronary angiograms, has been defined as the dilatation of an arterial segment to a diameter of at least 1.5 times that of the adjacent normal coronary artery. The purpose of this research was to study the pattern and distribution of CAE in relation to other associated diseases and risk factors in patients subjected to coronary angiography in Mansoura University, cardiology department. Among major coronary vessels, CAE was more prevalent in Left Anterior Descending (LAD) (67.1%), then RCA (66.7%), Left Circumflex (LCX) (57.9%), and LM (22.6%). Among minor (Branch) coronary vessels, CAE was more prevalent in PDA and OM2 (2.5%), then D1 and OM1 (2%), OM3 (1.5%), PL (1%), and D2 and RVB (0.5%). Among all ectatic coronary arteries, combined ectasia was more prevalent (85.1%) than isolated CAE (15.3%). Among minor (Branch) ectatic coronary arteries, combined ectasia was more prevalent (92.0%) than isolated CAE (8.0%). Mild ectasia is the most common form, detected in 90.5% of coronary arteries. Moderate ectasia was detected in 6.5% of coronary arteries. Severe ectasia was detected in only 1.6% of cases, while aneurysmal dilatation of coronaries was the least detected in 1.4% of cases. CAE is more common in LAD. Proximal segments are commonly affected. Mild ectasia is the most common form. Additionally, there is an increased prevalence of wall atherosclerosis among ectatic vessels.

Keywords: Pattern • Distribution • Coronary artery ectasia • Coronary artery segments

Abbreviations: CAE: Coronary Artery Ectasia; RF: Risk Factors; LAD: Left Anterior Descending; LCX: Left Circumflex; MI: Myocardial Infarction; CAD: Coronary Artery Disease; STEMI: ST-Elevation Myocardial Infarction; ECG: Electrocardiogram; IHD: Ischemic Heart Disease; HTN: Hypertension; DM: Diabetes Mellitus; HCV: Hepatitis C Virus; RWM: Regional Wall Motion; LV: Left Ventricular; RCA: Right Coronary Artery; LMCA: Left Main Coronary Artery

Introduction

Coronary Artery Ectasia (CAE) is characterized by an abnormal dilatation of the coronary arteries. As Morgagni initially characterized its cause, clinical consequences, and treatment, it is thought that 50% of CAE is attributable to atherosclerosis, and 20% to 30% of cases may be attributable to congenital abnormalities [1,2].

A coronary angiogram is the high-standard diagnostic tool in detecting coronary aneurysms. Moreover, it provides detailed information about their shape, size, extent, and associated Coronary Artery Diseases (CAD) [3]. The shape of the CAE and the degree of coronary artery involvement are two factors frequently used to categorize it

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[4].

Most patients with CAE are men, which appears to be because of coronary atherosclerosis [5].

The assessment and characterization of coronary aneurysms and ectasia represent a significant diagnostic task with clinical and therapeutic consequences because aneurysms and ectasia are linked to a wide range of diseases [6]. The underlying etiology is varied, encompassing degenerative, congenital, inflammatory, infectious, toxic, and traumatic origins. Ectasia, as opposed to aneurysms, is more often associated with atherosclerosis or acts as a protective mechanism when the opposite coronary artery has proximal stenosis; ectasia is also observed in some coronary artery anomalies, such as those with an abnormal pulmonary artery origin or those with high flow state, such as coronary artery fistulas [7].

The four kinds of CAE identified by Markis are type 1 (diffuse ectasia involving two or three vessels); type 2 (diffuse ectasia involving one vessel and discrete ectasia in another); type 3 (diffuse ectasia in just one vessel); type 4 (localized or segmental ectasia in only one vessel) [8]. Exercise-induced ischemia may result from CAE, particularly when it takes a diffuse form. Patients with sluggish blood flow are thought to have CAE [4]. Since the usual smooth laminar flow is disrupted and there is a chance of thrombus formation, it is typically not benign. CAE is characterized by diffuse or localized improper dilatation of coronary arteries and is frequently linked with sluggish coronary blood flow in hypertrophic cardiomyopathy [9].

This study was designed to study the pattern and distribution of CAE in relation to other associated diseases and risk factors in patients subjected to coronary angiography over the year 2019 at Mansoura University Hospital, cardiology department.

Materials and Methods

This single-center, retrospective study reviewed coronary angiography reports of all patients who underwent coronary angiography at Mansoura university hospital, cardiovascular medicine department from “January 2019 to December 2019”.

The purpose of this study was to ascertain the prevalence and pattern of CAE among the patients subjected to a diagnostic coronary angiogram. The study comprised 2929 diagnostic coronary angiographic reports. They were selected from 4030 coronary angiographic reports performed at the same setting mentioned above. The included reports comprised 195 reports denoting the presence of CAE and 2734 reports without CAE.

Exclusion criteria were reports with failed access (5), reports with incomplete diagnostic procedures (8), reports of PCI procedures (1053), and reports denoting patients with previous CABG surgery (35).

Methods for report selection and analysis

First step: Was reviewing soft copies of all angiographic reports (4030) from January 2019 to December 2019. All report data items were copied and pasted into a specific prepared Excel sheet designed by the principal supervisor.

This Excel sheet was prepared to fulfill the following items: Date of coronary angiography, patient ID, demographic data (age, sex), indication for coronary Angiogram (Chest pain/Angina/Angina equivalent (effort dyspnea/fatigue), unstable angina, acute myocardial infarction (STEMI/Non-STEMI), remote myocardial infarction (recent and old), assessment of coronaries in DCM or unexplained HF, assessment of coronaries after PCI and CABG, assessment of coronaries before prosthetic valve surgery, correction of congenital anomaly, excision of LA myxoma and non-cardiac major surgery). Risk Factors were hypertension, diabetes mellitus, dyslipidemia, smoking, and family history of CAD.

Coronary angiography data; approach site, femoral, radial, angiographic description of each vessel (LM, Ramus if present, LAD, D1, D2, D3, LCX, OM1, OM2, OM3, RCA, PDA, PL, RVB), dominance of circulation (right, left or balanced), angiographic reports, either normal coronary angiography, atherosclerotic CAD, non-obstructed CAD, obstructed CAD, ectasia (either isolated or combined with another lesion).

Second step: Was revising the main angiographic indication and procedure. Accordingly, the following 1101 reports were excluded from the study: Failure to vascular access (5 reports), incomplete diagnostic procedure (8 reports) due to failure to cannulate left coronary (3 reports) or failure to cannulate right coronary (5 reports), PCI procedures (1053 reports) (Ad hoc PCI (595 reports), Non-Ad hoc PCI (410 reports) and primary PCI (48 reports)), and previous CABG surgery (35 reports).

Third step: The remaining 2929 reports were included in the study. They were refined, coded, and prepared for initial analysis. The main reports were categorized as normal coronary angiography, atherosclerotic CAD without angiographic lesions, non-obstructed CAD, any lumen stenosis either (obstructed CAD, spontaneous dissection and previously deployed stent (patent stent or ISR)), presence of associated ectatic lesions. The initial included reports were categorized according to the presence of ectasia in the angiography report into two main groups: The non-ectasia group (2707), and the CAE group (222).

Fourth step: The angiographic videos of all 222 reports with CAE were reviewed by two observers, unaware of the initial angiography report. Reports classified as CAE reports were those that one or two observers determined to have ectasia (195 reports). Reports that two observers determined to have no ectasia were included in the study as non-CAE reports (22 reports). The final included

angiography reports were the non-ectasia group (2734) and the CAE group (195).

Fifth step: More detailed Excel items (variables) were added to the prepared sheet to fulfill the following: a detailed global analysis of the angiographic appearance of each coronary artery segment and branches that cover the following items: Wall (normal/atherosclerotic), flow (normal/slow flow), lumen (normal caliber/lumen stenosis/dilated or ectatic segments), and presence of any previously deployed stent (patent stent or ISR). Specific detailed angiographic analysis was done for ectasia vessels regarding the distribution of ectasia in each vessel (LM, Ramus if present, LAD, D1, D2, D3, LCX, OM1, OM2, OM3, RCA, PDA, PL, RVB), sites of ectasia in each vessel (proximal, mid, or distal or combined segments), degree of ectasia dilatation (mild/ moderate/ severe/ aneurysmal), number of ectasia segments and extent of dilatation (isolated segment or diffuse ectasia), any associated stenotic lesion and its relation to ectatic segment (either proximal or distal to the ectatic segment), and ectasia type (classification) according to Markis, et al., [10-12].

Statistical analysis

Version 21 of the Statistical Package for Social Sciences (SPSS) was used for data analysis. Means, standard deviations, and ranges were used to represent the numerical data. Numbers and percentages were used to represent the categorical data. The t-test compared the two groups concerning normally distributed numerical variables. Differences between categorical variables were analyzed using X² (chi-square) tests and, when necessary, Fisher’s exact tests. All p-values are two-sided. P-values<0.05 were considered significant.

Results

All sociodemographic data are shown in Table 1. Among major coronary vessels, CAE was more prevalent in LAD (67.1%), then RCA (66.7%), LCX (57.9%), and LM (22.6%). Among minor coronary vessels, CAE was more prevalent in PDA and OM2 (2.5%), then D1 and OM1 (2%), OM3 (1.5%), and PL (1%). It was the least in D2 and RVB (0.5%). No ectasia was observed in D3 (Table 2).

Table 1: Analysis of demographic of the studied cases.

Gender	
Male	1824
Female	1105
Age	
(Mean age)	(56.2 ± 9.18)
Smoking	540
HTN	1331
DM	891
IHD	99
Dyslipidemia	1

Note: Data were expressed as number, mean ± Standard Deviation(SD), HTN: Hypertension, DM: Diabetes Mellitus, IHD: Ischemic Heart Disease

Table 2: Frequency of each coronary vessel ectasia among the analyzed 195 CAE cases.

Name of coronary vessel	Ectasia frequency	
	No	Percent
Major vessels		
LM	44	22.5%
Ramus*	1	0.51%
LAD	131	67.1%
LCX	113	57.9%
RCA	130	66.6%
Minor vessels		
D1	4	2.05%
D2	1	0.51%
D3	0	0.0%
OM1	4	2.05%
OM2	5	2.56%
OM3	3	1.54%
PDA	5	2.56%
PL	2	1.02%
1.02%	1	0.51%

Among All ectatic coronary arteries, combined ectasia was more prevalent (85.1%) than isolated CAE (15.3%). Among minor ectatic coronary arteries, combined ectasia was more prevalent (92.0%) than isolated CAE (8.0%) (Table 3).

Table 3: Frequency of isolated and combined ectasia among each ectatic coronary vessel.

Ectatic vessel	Total number	Combined ectasia (with one or more vessel)	Isolated ectasia (one vessel only)
Major vessel			
LM	44	44(100 %)	0(0.0%)
Ramus	1	1(100 %)	0(0.0%)
LAD	131	109(83.2%)	22(16.2%)
LCX	113	102(90.3%)	11(9.7%)
RCA	130	100(76.9%)	30(23.1%)
Minor vessel			
D1	4	3(75%)	1(25.0%)
D2	1	1(100 %)	0(0.0%)
D3	0	0(0.0%)	0(0.0%)
OM1	4	4(100 %)	0(0.0%)
OM2	5	5(100 %)	0(0.0%)
OM3	3	3(100 %)	0(0.0%)
PDA	5	5(100 %)	0(0.0%)
PL	2	2(100 %)	0(0.0%)
RVB	1	1(100 %)	0(0.0%)
All vessels	444	376(84.6%)	64(15.4%)
Major vessel	419	356(84.9%)	63(15.1%)
Minor vessel	25	24(96.0%)	1(4.0%)

Wall Atherosclerosis was the most prevalent angiographic lesion

among all ectatic vessels (87.4%), followed by all major ectatic vessels (87.11%) and all minor ectatic vessels (92.0%). The stenotic lesion was found in 11.03% of all ectatic vessels, 11.22% of major ectatic vessels, and 8.0% of minor ectatic vessels. The normal vessel was observed in 1.57% of all ectatic vessels and 8.0% of major ectatic vessels, while it was absent in minor ectatic vessels (0%) (Table 4).

Table 4: Detailed analysis angiographic lesions of all ectatic vessels.

Ectatic vessels	No	Normal	Atherosclerosis	Lumen stenosi
Major vessel				
LM	44	1(2.27%)	41(93.2%)	2(4.5%)
Ramus	1	0(0%)	1(100%)	0(0%)
LAD	131	2(1.53%)	104(79.4%)	25(19.1%)
LCX	113	2(1.77%)	109(96.5%)	2(1.77%)
RCA	130	2(1.53%)	110(84.6%)	18(13.85%)
Minor vessel				
D1	4	0(0%)	3(75%)	1(25%)
D2	1	0(0%)	0	0(0%)
D3	0	0(0%)	0(%)	0(0%)
OM1	4	0(0%)	4(100%)	0(0%)
OM2	5	0(0%)	5(100%)	0(0%)
OM3	3	0(0%)	3(100%)	0(0%)
PDA	5	0(0%)	4(80%)	1(20%)
PL	2	0(0%)	2(100%)	0(0%)
RVB	1	0(0%)	1(100%)	0(0%)
Total vessels	444	7(1.57%)	388(87.4%)	49(11.03%)
Major ectatic vessels	419	7(1.67%)	365(87.11%)	47(11.22%)
Minor ectatic vessels	25	0(0%)	23(92.0%)	2(8.0%)

Mild ectasia is the most common form detected in 90.5% of coronary arteries. Moderate ectasia was detected in 6.5% of coronary arteries. Severe ectasia was detected in only 1.6% of cases, while aneurysmal dilatation of coronaries was detected in 1.4% of cases (Table 5).

Table 5: Morphologic appearances (degree of segment dilatation) of all analyzed 444 ectatic coronary arteries.

Ectatic coronary arteries(n)	Grades of CA ectasia (degree of ectasia segment dilatation)			
	Mild ectasia N (%)	Moderate ectasia N (%)	Severe ectasia N (%)	Aneurysm N (%)
LM(44)	37(18.9%)	5(2.6%)	1(0.5%)	1(0.5%)
RAMUS(1)	1(0.5%)	0(0%)	0(0%)	0(0%)
LAD(131)	121(62%)	4(2.05%)	2(1.02%)	4(2.05%)
LCX(113)	104(53.3%)	6(3.07%)	1(0.5%)	0(0%)
RCA(130)	114(58.46%)	14(7.17%)	1(0.5%)	1(0.5%)
D1(4)	3(1.5%)	0(0%)	1(0.5%)	0(0.0%)
D2(1)	1(0.5%)	0(0%)	0(0%)	0(0%)

D3(0)	0(0%)	0(0%)	0(0%)	0(0%)
OM1(4)	5(2.56%)	0(0%)	0(0%)	0(0%)
OM2(5)	6(3.07%)	0(0%)	0(0%)	0(0%)
OM3(3)	3(1.5%)	0(0%)	0(0%)	0(0%)
PDA(5)	4(2.05%)	0(0%)	1(0.5%)	0(0%)
PL(2)	2(1.02%)	0(0%)	0	0(0%)
RVB(1)	1(0.5%)	0(0%)	0	0(0%)
Total	0(0%)	0(0%)	0(0%)	0(0%)
(444)	402(90.5%)	29(6.5%)	7(1.6%)	6(1.4%)

The main sites of ectasia location were the proximal segments (55.4%), followed by all three segments (30%), combined both proximal and mid segments (10.1%), mid-segment (2.95%), distal segments (0.9%), and combined both mid and distal segments (0.67%) (Table 6).

Table 6: Sites (location or distributions) of ectasia segment in all analyzed 444 ectatic coronary arteries.

Ectatic coronary arteries	Sites of ectasia segment					
	Proximal segment	Mid segment	Distal segment	Proximal and mid	Mid and distal	All 3 segment
LM(44)	42	2	0	0	0	0
RAMUS(1)	1	0	0	0	0	0
LAD(131)	90	0	0	14	0	27
LCX(113)	50	4	0	15	2	42
RCA(130)	43	4	1	16	2	64
D1(4)	2	2	0	0	0	0
D2(1)	1	0	0	0	0	0
D3(0)	0	0	0	0	0	0
OM1(4)	4	0	0	0	0	0
OM2(5)	5	0	0	0	0	0
OM3(3)	2	1	0	0	0	0
PDA(5)	3	0	2	0	0	0
PL(2)	2	0	0	0	0	0
RVB(1)	2	0	0	0	0	0
Total(444)	246(55.4%)	13(2.95%)	3(0.67%)	45(10.1%)	4(0.90%)	133(30.0%)

Discussion

CAE is a well-recognized coronary anatomical anomaly. It is described as dilation of more than 1.5 times normal neighboring vessel segments, which can be localized or diffuse [13].

In our study, CAE was present in 195 cases among 2929 diagnostic coronary angiography (6.65%). The prevalence was more among males than females. Many published CAE studies showed a rise in the prevalence of CAE among males than females. In agreement with our study, Wang, et al., [14], conducted a prospective study on (4788) patients. They revealed that CAE was present in (174) patients (3.6%). They also reported that CAE comprised more males (81.6%) than females (18.4%). Also, Qin, et al., [15], in their study, reported a rise in the prevalence of CAE among males (70%) than females (30%).

The current work showed a significant increase in the prevalence of CAE among smokers (11.1%) than non-smokers (5.65%). A retrospective study conducted by Rashid, et al., [16], supported our findings. They found that patients with ectasia had a significantly higher smoking rate than those without CAE (56.8% vs. 43.9%, respectively, $P < 0.001$).

Regarding the angiographic findings of CAE cases, a retrospective study was conducted by Singh et al. [17], on 447 patients who underwent coronary angiography. They found that CAE was most prevalent in LAD (83.3%), followed by RCA (66.7%) and LM (16.7%). Çetin, et al., [18], found that the LAD was the most frequently implicated vessel. Moreover, Malviya, et al., [8], discovered that the LAD was the vessel most frequently implicated, followed by the RCA, LCX, and left main coronary artery. Although this higher predisposition of the LAD to develop CAE has been previously observed compared to the other coronary arteries, the underlying pathophysiology is still unknown [19].

However, Wang, et al., [14], reported that among their studied 174 CAE patients, CAE was more prevalent in RCA (79.3%) than LAD (66.1%), LCX (51.7%), and LM (31.6%). In addition, Rashid, et al., [16], stated that RCA was the vessel most frequently affected by ectasia in 57 cases (70.4%), LAD in 43 cases (54.3%), and left circumflex was involved in 30 (38.3%) of patients. Hgwapl, et al., [20], reported that among their studied 107 CAE patients, CAE was more prevalent in RCA (60.75%) than LAD (47.66%) then LCX (42.99%) and least LM (9.35%).

Most of the literature reported CAE on major vessels only and did not report any minor vessel ectasia [8,16,21]. Only Wang, et al., [14], reported CAE in minor vessels in their prospective study. They reported CAE in diagonal branches in 15 cases (8.6%), obtuse marginal in 35 cases (20.1%), and posterior descending artery in 64 cases (36.8%). The differences in the prevalence of minor vessel ectasia between our study and Wang, et al., [14], could be related to the fact that all their included ectasia patients had acute coronary syndrome. In contrast, a minority of our patients had acute coronary syndrome (5.64%).

Regarding the topographic appearance of CAE, most of the literature revealed information on sites of dilated artery segments. Only Salah reported that among his studied 145 CAE patients, the ectatic segments were more prevalent in the proximal segments (72.5%) of the coronary tree than the mid and distal ones (27.5%).

The current study found that combined ectasia was more prevalent among all ectatic coronary arteries (85.1%) than isolated CAE (15.3%). Among minor (Branch) ectatic coronary arteries, combined ectasia was more prevalent (92.0%) than isolated CAE (8.0%). In the same line, Willner, et al., [21], found that combined ectasia was present in 75.2% of patients, while 24.8% had isolated CAE. Also, Malviya, et al., [8], found that of 4950 angiograms

analyzed, isolated CAE was found in 52 patients, with a prevalence of 1.05%.

There are three well-known classifications for ectasia; Markis, et al., [10-12]. In Markis classification, type I refers to diffuse ectasia in 2 or 3 coronary vessels. Type II refers to diffuse ectasia in one vessel and localized CAE in another. Type III refers to diffuse ectasia in only one vessel. Type IV refers to localized or segmental ectasia in only one vessel. Harikrishnan's classification was similar to Markis's classification but with more details (sub-types) to include cases not involved in Markis, et al., [10], classification. Type I refers to diffuse ectasia in one or more vessels (IA, IB, IC), Type II refers to diffuse ectasia and discreet in combinations (IIA, IIB), and Type IV refers to localized or segmental ectasia in 1 or more vessels (IVA, IVB, IVC).

In Nyamus and his associate's 2003 classification [12], Type 1 refers to diffuse ectasia in 1 or more vessels (A and B), type 2 refers to diffuse ectasia and discreet in combinations (A, B, and C), type 3 refers to isolated discreet ectasia in 1 or more vessels (A and B) and Type 4 refers to involvement of LMCA. However, by applying each of these classifications to our studied CAE cases, many cases could not be categorized by any of these classifications.

According to Markis, et al., [10], classification, 19 of our cases were categorized as type I (9.7%), 40 were categorized as type II (20.5%), 24 were categorized as type III (12.3%), 39 were categorized as type IV (20%), and 73 cases could not be categorized by any type (37.4%). The 73 cases who were not categorized by Markis, et al., [10], comprised 17 cases with two vessel ectasia (each with 1 Segment) (8.7%), 16 cases with three vessels ectasia (each with 1 Segment) (8.2%), 11 cases with three vessels ectasia (1 with one Segment and two diffuse) (5.6%), 16 cases with four major vessel ectasia (8.21%), 12 cases with major and minor ectasia (6.15%), and one case with minor vessel ectasia (0.02%). Also, in a retrospective study conducted on 81 CAE cases, Markis classification was non-applicable in 38.3% of their cases [16].

According to Harikrishnan, et al., [11], classification, 30 of our cases were categorized as type I (15.4%), 40 were categorized as type II (20.5%), 24 were categorized as type III (12.3%), and 72 were categorized as type IV (36.9%), and 29 cases could not be categorized by any type (14.9%). The 29 cases who were not categorized by Harikrishnan, et al., [11], comprised 16 cases with four major vessel ectasia 16 (8.21%), 12 cases with major and minor ectasia (6.15%), and one case with minor vessel ectasia (0.02%).

According to Nyamus et al. [12], classification, 44 of our cases were categorized as type I (22.1%), 51 were categorized as type II (26.2%), 50 were categorized as type III (25.6%), 38 were categorized as type IV (19.5%), and 13 cases could not be categorized by any type (6.7%). The 13 cases who were not

categorized by Nyamus, et al., [12], comprised 12 cases with major and minor ectasia (6.15%) and one case with minor vessel ectasia (0.02%).

All 3-ectasia classifications [10-12], did not include minor ectasia or four major vessel ectasia in their description. In the current study, we reported 12 cases with combined major and minor vessel ectasia cases and one isolated minor vessel ectasia case, which could not fulfill the anatomical description of the three classification systems. Also, both Markis, et al. [10,11], classification did not include four major vessel ectasia in their description. In the current study, we recorded 16 with four major vessel ectasia cases, which could not fulfill the anatomical description of both classification systems.

Markis, et al., [10,11], classifications categorize the disease extension in a reverse way, with type I for the more extensive disease and type IV for the less extensive disease. This typing is against logic, as most diseases (hypertension grading, Angina grading, Dyspnea grading, Liver cirrhosis grading) are categorized from mild to severe (or grade I to IV) according to severity.

Therefore, it is advisable to identify a new CAE classification (grading) system that could include all ectatic vessel morphology in logic ectasia burden from mild to severe patterns according to the number and extent of affected coronaries.

There are a few limitations to our study. First, relying solely on reports could result in underestimating the true distribution and pattern of CAE. Second, we do not have any healthy controls to compare to CAE patients. However, given the uncommon frequency of CAE, a retrospective analysis is still appropriate. Stronger evidence of a possible relationship between CAE in events would be provided by additional research using cohort matching on sex, age, and traditional risk variables.

Conclusion

We can conclude that CAE, is predominant disease in males and smokers' patients with CAD. Its pattern and distribution more common in LAD and proximal coronary segments. Mild ectasia is the most common form. Additionally, there is an increased prevalence of wall Atherosclerosis among ectatic vessels. However, many unanswered questions remain concerning their etiology, pathology, association with other vascular risk factors, prognosis, and treatment modalities. Therefore, further prospective multicenter studies with long-term follow-up are essential to elaborate on this particular subset of patients with CAE.

Declarations

Ethics approval and consent to participate

The study was approved from the institutional ethical committee, Mansoura University. The study did not require any consent form

the patients as it was a retrospective study which was done on previously taken data.

Consent for publication

All authors give their consent for publication; they all have agreed to publish this work.

Availability for data and materials

The data is available upon reasonable request from the authors.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by AH, IY and AE. The first draft of the manuscript was written by EE and AE, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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