

## Long-Term Observational Study of the Isolated Ostial Diagonal Stenosis in Patients with Chronic Coronary Syndrome

### Kronik Koroner Sendromlu Hastalarda İzole Osteal Diyagonal Stenozun Uzun Süreli Gözlemsel Çalışması

#### ABSTRACT

**Objective:** Isolated ostial diagonal stenoses are very rare lesions in which percutaneous intervention could cause significant vessel compromise, and the long-term results have been reported in a few studies. This study sought the characteristics and long-term follow-up of the patients with isolated osteal diagonal stenosis regarding percutaneous coronary intervention and presence of angina.

**Methods:** The study was an observational retrospective study conducted between January 2014 and December 2020. A total of 9769 patients who underwent coronary angiography were analyzed, and 87 patients had isolated diagonal stenosis. The patients were evaluated according to treatment modality and angina severity in long-term pattern.

**Results:** Median follow-up time was 36 months. A total of 54 (83.1%) patients were followed up with only medical treatment, and 11 (16.9%) patients underwent revascularization in addition to medical treatment. The degree of stenosis of the diagonal artery was significantly higher in the percutaneous coronary intervention group than medical group ( $P=0.002$ ) and the patients with wider reference diameter of diagonal artery complaint of more angina ( $P=0.007$ ). Class I angina was significantly higher in percutaneous coronary intervention group than medical and the patients with no angina were significantly higher in medical group than percutaneous coronary intervention group.

**Conclusion:** Percutaneous coronary intervention was mainly performed for diagonal arteries with a higher degree of stenosis; however, the patients who underwent percutaneous coronary intervention had angina more than 50% rates. Furthermore, the patients with ongoing angina had a larger diameter of the diagonal artery regardless of the type of treatment.

**Keywords:** Angina, isolated diagonal artery, coronary artery disease, osteal lesion, percutaneous coronary intervention

#### ÖZET

**Amaç:** İzole osteal diyagonal lezyonları çeşitli komplikasyonlara neden olabilecek tedavi seçeneğinde ikileme yol açabilecek çok nadir lezyonlardır ve uzun vadeli sonuçları birkaç çalışmada bildirilmiştir. Bu çalışmada izole osteal diyagonal stenozu olan hastaların PKG ve anjina varlığı açısından özellikleri ve uzun dönem takibi araştırıldı.

**Yöntem:** Çalışma, Ocak 2014-Aralık 2020 tarihleri arasında yapılan gözlemsel retrospektif bir çalışmadır. Koroner anjiyografi yapılan toplam 9769 hasta incelendi ve seksen yedi hastada izole diyagonal stenoz saptandı. Hastalar uzun dönem takiplerinde tedavi şekli ve angina şiddetine göre değerlendirildi.

**Bulgular:** Ortanca takip süresi otuz altı aydı. Toplam 54 (%83,1) hasta sadece medikal tedavi ile izlendi ve 11 (%16,9) hastaya medikal tedaviye ek olarak revaskülarizasyon uygulandı. Diyagonal arter darlık derecesi PKG grubunda medikal gruba göre anlamlı derecede yüksekti ( $P=0,002$ ) ve diyagonal arter referans çapı daha geniş olan hastalarda daha fazla anjina şikayeti vardı ( $P=0,007$ ). PKG grubunda sınıf 1 anjina medikal tedavi grubuna göre daha yüksekti ve anjinası olmayan hastalar medikal tedavi grubunda belirgin şekilde daha yüksekti.

**Sonuç:** PKG esas olarak yüksek derecede darlığı olan diyagonal arterlere uygulandı; ancak PKG uygulanan hastalarda yüzde elliden fazla oranda anjina vardı. Ayrıca, devam eden anjinası olan hastalarda, tedavi türünden bağımsız olarak, diyagonal arterin çapı daha büyüktü.

**Anahtar Kelimeler:** Anjina, izole diyagonal arter, koroner arter hastalığı, osteal lezyon, perkütan koroner giriş

#### ORIGINAL ARTICLE KLİNİK ÇALIŞMA

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Received: February 16, 2023

Accepted: March 8, 2023

**Cite this article as:** Torun A, Acar B, Kahraman G, et al. Long-term observational study of the isolated osteal diagonal stenosis in patients with chronic coronary syndrome. *Türk Kardiyol Dern Ars.* 2023;51(5):314-321.

DOI:10.5543/tkda.2023.74422



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Isolated ostial diagonal stenoses are relatively rare lesions in which selection of the treatment modality is difficult due to their anatomical features. The ideal treatment approach in coronary artery disease should aim not only to good prognosis but also to reduce intra-operative and post-operative risks.<sup>1</sup> A recent study showed that major adverse cardiac and cerebrovascular events rates were found to be 14.6% and 5.9% in coronary artery side branch disease, respectively.<sup>2</sup> Due to the critical relationship between diagonals and the left anterior descending artery, the intervention of ostial diagonal stenosis might cause leading vessel injury. In the literature, there are very few studies about the isolated diagonal lesions.<sup>3,4</sup> They mostly revealed that percutaneous coronary intervention (PCI) was not superior to medical treatment. In this study, we investigated PCI and medical therapy on angina treatment in isolated ostial diagonal lesion in long-term follow-up time, and we also sought the associated factors to affect performing PCI.

## Materials and Methods

### Study Population

This retrospective observational study was conducted between January 2014 and December 2020 and included 7 years of angiographic data. The angiographic data of 9769 patients were screened and 87 patients of them had isolated diagonal ostial lesions. Only patients with ostial diagonal artery disease as a culprit lesion were included in the study. Those with more than 50% stenosis in other segments of left anterior descending (LAD), circumflex (CX), and right coronary artery (RCA) were excluded from the study. The patients with acute coronary syndrome, who died during follow-up, and the patients who had undergone coronary angiography despite no angina were excluded from the study.

A total of 65 patients were included in the final analysis, and a complete follow-up of all remaining patients was ensured. First, the patients were divided into PCI plus medical therapy (PCI group) and medical therapy alone (medical group). Secondly, the patients were also evaluated according to presence of angina during follow-up.

Additional information such as frequency of angina and recurrent angiography, treatments before and after coronary angiography were obtained from the patients by telephone or face-to-face outpatient examination. Ten patients underwent

stent implantation which were mostly made maximum in 3 months and 1 patient underwent only balloon angioplasty without the use of a stent. Available exercise electrocardiography (ECG), myocardial perfusion scintigraphy (MPS), and fractional flow reserve (FFR) results were obtained.

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and was approved by the Local Ethics Committee.

### Coronary Angiography

All patients had at least Canadian Cardiovascular Society (CCS) class I angina and 50% or more stenosis of the diagonal artery ostium.<sup>5</sup> Images of all angiographic records of patients with isolated ostial diagonal stenosis were viewed. Two experienced cardiologists performed angiographic evaluations, and the degree and length of the stenosis were evaluated visually. Additionally, support was obtained from the software of the angiography device when necessary (Siemens Axiom Artis Software). The operator decided to treat the patients with medical or percutaneous intervention.

Coronary angiography was performed using standard techniques in all patients. Femoral or radial arteries were chosen as the arterial intervention site. 5Fr, 6Fr, or 7Fr sheaths were used in patients. At least 4 images were obtained from the left coronary system and 2 from the right coronary system in all patients.

Standard 70–100 U/kg intravenous heparin was administered in addition to dual anti-aggregant in patients who underwent angioplasty. The procedure technique was chosen according to the patient's coronary anatomy. The flush ostial method was used for stent replacement. Drawback technique was used in only one patient. The absence of significant stenosis in the diagonal artery ostium or left descending artery trunk at the end was considered a successful procedure.

### Definitions

Index angiography was defined as the procedure in which the patient was diagnosed with isolated diagonal coronary artery disease. Examples of patients with isolated ostial stenosis followed by medical or PCI are shown in Figures 1 and 2.

Lesions with a stenosis of 50% or more in the diagonal ostium were accepted as side branch disease, and the first 3–5 mm of the diagonal artery with diameter of<sup>3</sup> 1.5 mm after branching from the LAD main trunk was taken as the ostial segment. The concept of isolation is the absence of significant coronary artery stenosis (50% or more) in other coronary arteries. Diagonal artery lesions in which the ostial segment is not affected were not included in this study. All patients were O01 lesions according to the Medina classification.<sup>6</sup>

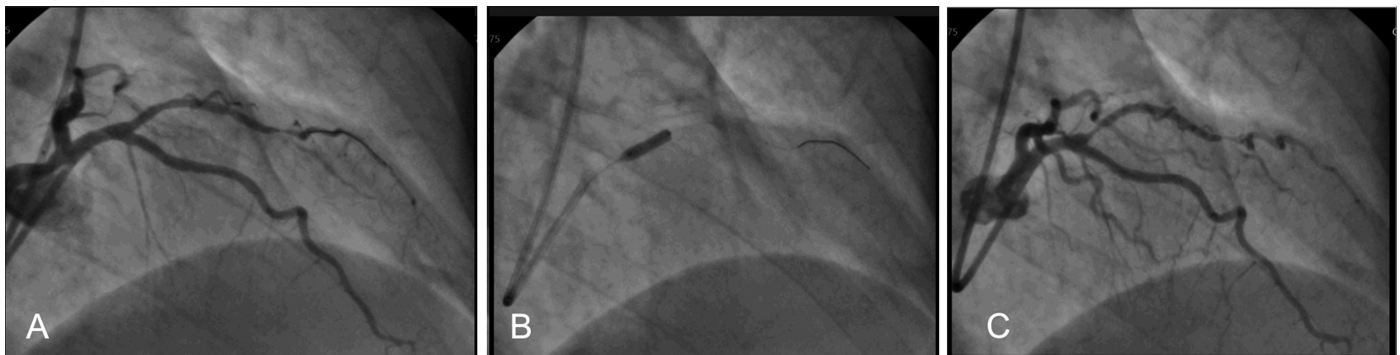
Dyslipidemia was defined according to the latest guidelines or history of using statins. Family history of coronary artery disease (CAD) was defined as the diagnosis of CAD before age 60 for a first-degree female relative and before 55 years for a first-degree male relative.<sup>7</sup> Diabetes mellitus was defined as the patient being treated with insulin or oral antidiabetics or having a fasting plasma glucose above 126 mg/dL or a HbA1c value of 6.5 and above.<sup>7</sup> Chronic kidney disease was defined as glomerular filtration rate (GFR) below 60 mg/dL or when the patient was on a routine

## ABBREVIATIONS

ACEIs	Angiotensin converting enzyme inhibitors
ARB	Angiotensin receptor blockers
BMI	Body mass index
CAD	Coronary artery disease
CCS	Canadian Cardiovascular Society
CX	Circumflex
ECG	Electrocardiography
FFR	Fractional flow reserve
GFR	Glomerular filtration rate
IQR	Interquartile range
LAD	Left anterior descending
MPS	Myocardial perfusion scintigraphy
PCI	Percutaneous coronary intervention
RCA	Right coronary artery



**Figure 1. Coronary angiography in antero-posterior cranial view (A), in right cranial oblique view (B), and left anterior oblique caudal view (C) showing severe ostial diagonal lesions.**



**Figure 2. Coronary angiography showing severe ostial stenosis diagonal artery with angle of approximately 90° (A). Percutaneous coronary intervention with stenting (B) and angiography after stenting (C).**

hemodialysis program. Cigarette exposure was determined as all patients who are current smokers and have quit before. Smoking levels were questioned in terms of pack/patient-year. Hypertension was defined as documented systolic blood pressure of  $\geq 140$  mmHg and/or diastolic blood pressure of  $\geq 90$  mmHg in at least 2 measurements or active use of any antihypertensive agent. Patients' weight and height were recorded, and body mass index (BMI) was calculated as weight in kg divided by the square of height in meters.

#### Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences software version 20.0 (SPSS Inc., Chicago, Ill, USA). Mean  $\pm$  standard deviation was used for normally distributed continuous variables, and median and interquartile range were used for non-normally distributed data. Kolmogorov-Smirnov test was performed to test normality. If continuous variables were normally distributed, Student's *t*-test was used, while non-normally distributed and ordinal variables were evaluated using the Mann-Whitney *U* test. Categorical data were expressed as numbers and percentages and assessed with a chi-square test. Post hoc analysis was made by z-test (Bonferroni method). A *P*-value of 0.05 was considered statistically significant.

#### Results

Three patients who underwent diagonal artery intervention due to acute coronary syndrome, 3 patients with acute coronary syndrome during follow-up period, 5 patients without angina

who underwent coronary angiography for any reason, 6 patients who died in their follow-ups (only 1 patient died due to acute coronary syndrome), and 5 patients whose information could not be reached were excluded from the study.

#### Basal Characteristics of the Patients According to Treatment Groups

A total of 65 patients (mean age  $61.5 \pm 11$  years, 65% male) were included in the final analysis of this study. The median follow-up time was 36 months. A total of 54 (83.1%) patients were followed up with only drug therapy, and 11 (16.9%) patients underwent revascularization in addition to medical treatment (Table 1).

There was no significant difference between the 2 groups regarding age, gender, BMI, smoking, hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, family history, and peripheral arterial disease (Table 1). There was a significant difference between the 2 groups in terms of angina scoring ( $P=0.002$ ). While class I angina was more common in the medical treatment group (27.2% vs. 74%), class II angina was more common in the PCI group (20.3% vs. 45.4%). There was also no significant difference among the groups regarding positive exercise ECG test, MPS, or FFR values.

#### Index Angiographic Findings of the Patients According to Treatment Groups

After index angiography, 54 patients were followed up only with medical treatment, and 11 patients underwent PCI in addition to

**Table 1. Basal Characteristics of the Patients During the Index Coronary Angiography**

Variable	All Patients	Medical Group	PCI Group	P
Patients, number	65	54	11	
Male, n (%)	42 (64.6)	36 (66.7)	6 (54.5)	0.443
Age, years (mean ± SD)	61.5 ± 11	61 ± 11.5	65 ± 7.6	0.611
Body mass index, kg/m <sup>2</sup> (mean ± SD)	27.3 ± 10.5	26.7 ± 11.4	29.8 ± 3.7	0.387
Hypertension, n (%)	37 (56.9)	31 (57.4)	6 (54.5)	0.861
Diabetes mellitus, n (%)	27 (41.5)	23 (42.6)	4 (36.4)	0.702
Hyperlipidemia, n (%)	26 (40)	22 (40.7)	4 (36.4)	0.787
Smoking, n (%)				0.918
Current	10 (15.4)	8 (14.8)	2 (18.2)	
Former	27 (41.5)	23 (42.6)	4 (36.4)	
Never	28 (43.1)	23 (42.6)	5 (45.5)	
Family history, n (%)	22 (33.8)	18 (33.3)	4 (36.4)	0.846
Peripheral artery disease, n (%)	11 (16.9)	11 (20.4)	0	-
Chronic renal failure, n (%)	4 (6.2)	4 (7.4)	0	-
Canada angina classification, n (%)**				<b>0.0002</b>
I		40 (74.0) <sup>a</sup>	3 (27.2) <sup>b</sup>	
II		11 (20.3) <sup>a</sup>	5 (45.4) <sup>a</sup>	
III		3 (5.5) <sup>a</sup>	3 (27.2) <sup>b</sup>	
IV		0	0	
Medical treatment on admission, n (%)				
Acetylsalicylic acid	16 (24.6)	14 (25.9)	2 (18.2)	0.587
P <sub>2</sub> Y <sub>12</sub> receptor blocker	1 (1.5)	1 (1.9)	0	0.649
Anticoagulants	3 (4.6)	2 (3.7)	1 (9.1)	0.438
Statin	4 (6.2)	3 (5.6)	1 (1.5)	0.657
ACEI/ARB	15 (23.1)	13 (24.1)	2 (18.2)	0.672
Beta blocker	10 (15.4)	8 (14.8)	2 (18.2)	0.778
Nitrate	0			
Ivabradine	0			
Ranolazine	0			
Trimetazidine	0			
Calcium channel blocker	6 (9.2)	5 (9.3)	1 (9.1)	0.986
Positive exercise ECG	25/34 (73%)	20 / 27 (74.1%)	5/7 (71.4%)	0.887
Ischemia in myocardial perfusion scintigraphy, n (%)	21/30 (70%)	17/24 (70.8%)	4/6 (66.7%)	0.842
FFR value < 0.80	2 (3.0)	0/2 (0%)	-	-
Follow-up time (median, IQR)	36 (35)			
Follow-up with only medical therapy, n (%)	54 (83.1)			
Follow-up with Medical plus PCI, n (%)	11 (16.9)			

\*\*Post-hoc analysis was made Bonferroni method. a-b, there was difference when different letter in each line.

P < 0.05

ACE, angiotensin receptor blocker; ARB, angiotensin receptor blocker; IQR, interquartile range; PCI, percutaneous coronary intervention; SD, standard deviation.

**Table 2. Index Angiographic Findings of the Patients According to Treatment Groups**

Variable	Medical Group (n = 54)	PCI Group (n = 11)	Pe
Diagonal artery diameter, mm (median, IQR)	2.25 (0.50)	2.25 (0.25)	0.082
Percent stenosis, % (median, IQR)	60 (45)	80 (20)	<b>0.002</b>
Diagonal artery branches, n (%)			0.654
First branch	32 (59)	7 (63)	
Second branch	16 (30)	3 (29)	
Both branches	6 (11)	1 (9)	

Mann-Whitney *U*-test was performed; IQR, interquartile range.

medical treatment (Table 2). Affected diagonal artery diameter was not different between the groups [(median, IQR) 2.25 (0.25) for PCI group vs. 2.25 (0.50) for medical group,  $P=0.082$ ]. The degree of stenosis of the diagonal artery was significantly higher in the PCI group than medical group [(median, IQR), 80 (20) versus 60 (45),  $P=0.002$ ].

**Table 3. Comparison of Patients' Follow-Up Data and Medical Treatment among the Groups**

Variable	Medical (n = 54)	PCI (n = 11)	P
Acetylsalicylic acid, n (%)	41 (75.9)	8 (72.7)	0.822
P <sub>2</sub> Y <sub>12</sub> receptor inhibitors, n (%)	7 (13.0)	3 (27.3)	0.231
Anticoagulants, n (%)	4 (7.4)	2 (18.2)	0.260
ACEI /ARB, n (%)	30 (55.6)	10 (90.9)	<b>0.028</b>
Beta blocker, n (%)	26 (48.1)	10 (90.9)	<b>0.009</b>
Lipid lowering drugs, n (%)	25 (46.3)	7 (63.6)	0.294
Nitrate, n (%)	5 (9.3)	2 (18.2)	0.384
Ivabradine, n (%)	0	0	
Ranolazine, n (%)	9 (16.7)	1 (9.1)	0.526
Trimetazidine, n (%)	9 (16.7)	2 (18.2)	0.903
Calcium channel blockers, n (%)	6 (11.1)	1 (9.1)	0.844
Follow-up time, months (median, IQR) **	33.5 (36)	40 (28)	0.134
Recurrent angiography, n (%)	19 (35.2)	5 (45.5)	0.520
Angina class (CCS), n (%)***			0.106
0	33 (61.1) <sup>a</sup>	3 (27.3) <sup>b</sup>	
I	17 (31.5) <sup>a</sup>	7 (63.6) <sup>b</sup>	
II	4 (7.4) <sup>a</sup>	1 (9.1) <sup>a</sup>	
III-IV	0	0	

\*\*Mann-Whitney *U* test was performed.

\*\*\*Post-hoc analysis was made using Bonferroni method. <sup>a-b</sup>Different letter in each line indicate difference.

ACEIs, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCS, angina according to the Canadian Heart Association classification; IQR, interquartile range; SD, standard deviation.

Thirty-nine patients had a first diagonal lesion (32 patients were medical, 7 patients were from the PCI group), 19 patients had a second diagonal lesion (16 patients were medical, 3 patients were from the PCI group), and 7 patients had stenosis in both diagonals (6 patients were medical, 1 patient was from the PCI group).

### Comparison of Patients' Follow-Up Data According to Treatment Groups

The median follow-up period for the medical treatment group was 33.5 (36) months, and 40 (28) months for the PCI group (Table 3). The medical treatments used by the patients in the follow-up were examined comparatively, and there was no significant difference between the groups' use of acetylsalicylic acid, P2Y12 inhibitor, anticoagulant, lipid-lowering drugs, calcium channel blockers, and other antianginals including nitrates, ivabradine, and ranolazine. The number of patients using beta-blockers (90.9% vs. 28.1%,  $P=0.009$ ) and angiotensin-converting enzyme inhibitor or angiotensin receptor blockers (90.9% vs. 55.6%,  $P=0.028$ ) was significantly higher in the PCI group than the medical group. There was no significant difference between the 2 groups in terms of angina severity in chi-square test. After post hoc analysis, class I angina was significantly higher in PCI group than medical group (63.6% vs. 31.5%, respectively). The patients with no angina were significantly higher in medical group than PCI group (61.1% vs. 27.3%, respectively).

### Comparison of the Patients According to the Presence of Angina during Follow-Up

Twenty-nine patients had at least class I angina during the follow-up (Table 4). There was no statistically significant difference between groups with and without angina in terms of the male gender, BMI, age, hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, peripheral artery disease, and family history. Medical treatment was also not statistically different between the groups. Diagonal vessel diameter was significantly wider in patients with angina [(median, IQR), 2.25 (0.25) vs. 2.00 (0.50),  $P=0.007$ ].

### Discussion

The critical findings of our study included the following: The severity of angina and degree of stenosis of the diagonal artery were higher in patients who would undergo PCI. Also, the patients with angina at follow-up had a wider diagonal artery with or without PCI. The patients with no angina were higher in medical group and the patients who underwent PCI had higher rates of class I angina during follow-up.

**Table 4. Assessment of the Patients according to Angina Presence during Follow-Up**

Variable	Patients With Angina (n=29)	Patients Without Angina (n=36)	P
Age, year (mean ± SD)	61 ± 9.4	61.8 ± 12.2	0.864
BMI, kg/m <sup>2</sup>	27 ± 9.2	27.4 ± 11.6	0.858
Male gender, n (%)	19 (65.5)	23 (63.9)	0.891
Follow up, months (mean ± SD)	33.8 ± 22.7	33.9 ± 24.9	0.858
Hypertension, n (%)	14 (48.3)	23 (63.9)	0.206
Diabetes mellitus, n (%)	9 (31)	18 (50)	0.123
Hyperlipidemia, n (%)	12 (41.4)	14 (38.9)	0.839
Smoking, n (%)			0.879
Current	4 (13.8)	6 (16.7)	
Quit	13 (44.8)	14 (38.9)	
Never	12 (41.4)	16 (46.7)	
Family history, n (%)	11 (37.9)	11 (30.6)	0.532
Peripheral artery disease, n (%)	4 (13.8)	7 (19.4)	0.546
Chronic kidney disease, n (%)	1 (3.4)	3 (8.3)	0.415
Medical treatment, n (%)			
Acetylsalicylic acid	21 (72.4)	28 (77.8)	0.618
P <sub>2</sub> Y <sub>12</sub> inhibitor	5 (17.2)	5 (13.9)	0.710
Anticoagulants	4 (13.8)	2 (5.6)	0.254
Lipid lowering drugs	16 (55.2)	16 (44.4)	0.390
ACEI/ARB	17 (58.6)	23 (63.9)	0.664
Beta blocker	19 (65.5)	17 (47.2)	0.140
Nitrate	2 (6.9)	5 (13.9)	0.366
Ivabradine	0	0	-
Ranolazine	4 (13.8)	6 (16.7)	0.750
Trimetazidine	4 (13.8)	7 (19.4)	0.546
Calcium channel blocker	3 (10.3)	4 (11.1)	0.921
Re-catheterization, n (%)	12 (41.4)	12 (33.3)	0.504
Diagonal diameter, (median, IQR)**	2.25 (0.25)	2.00 (0.50)	<b>0.007</b>
Percentage of diagonal stenosis, (median, IQR)**	70 (20)	70 (25)	0.462

\*\*Mann-Whitney U-test was performed.

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; IQR, interquartile range; SD, standard deviation.

Bifurcation lesions compose approximately 21% of all PCI procedures and are associated with major cardiac events.<sup>8</sup> Isolated ostial lesions are encountered less than 5% in invasive coronary angiography and they are also defined as Medina 001 lesion.<sup>8</sup> In the current practice, medical treatment is the mainstay of stable coronary artery disease. Percutaneous treatments are mostly reserved for refractory angina pectoris despite the optimal drug therapy or acute coronary syndrome. Latest trials, including COURAGE,<sup>10</sup> the ISCHEMIA,<sup>11</sup> and the ORBITA,<sup>12</sup> have shown that PCI affects angina, but it has a limited role in eliminating major cardiac events. In the present study, major cardiac events were not assessed; however, more than 50% of the patients with PCI have been suffered from angina in long term. Microvascular dysfunction, the supplied myocardium,

and optimal use of anti-anginal drugs might contribute these results.

Medina 001 lesions required PCI in some patients together with medical treatment; however, intervention to this lesion has particular importance because of the relation with the main vessel. Possible issues of PCI of the ostial diagonal artery lesions include ostial miss of stents, extension to the main vessel, potential injury to the main vessel, and compromising the flow. Most of the studies about bifurcation excluded 001 lesions, as it is difficult to obtain restenosis ratio in these patients.

There was not much data to guide the interventional management of medina 001 lesions, especially severe ostial diagonal stenosis. Weinstein et al<sup>4</sup> have evaluated 39 300 coronary

angiographies and found 22 patients with severe ostial stenosis of the diagonal artery. They included artery diameter above 1.5 mm and a degree of stenosis of  $\geq 70\%$ .<sup>4</sup> They found that the larger in diameter arteries were more frequently dilated; however, in the present study, higher degrees of stenosis were more frequently dilated. They did not find any difference between conservative treatment and PCI as anginal severity at follow-up; however, the patients who underwent PCI had angina more than 50% rate.

In another non-randomized study conducted, Brueck et al<sup>3</sup> compared PCI of isolated ostial stenosis of the diagonal artery with a diameter  $>2.0$  mm with medical treatment. Interestingly, they showed that the patients treated percutaneously showed a significantly greater incidence of rehospitalization for severe angina and re-catheterization. The number of patients included in that study was high. However, the follow-up period was relatively shorter than that in the present study. They claimed that the reason for the higher ratio of angina episodes in the PCI group could be a significant increase in the use of nitrates and a trend toward the increased use of calcium antagonists in the medical therapy group at 12-month follow-up.<sup>3</sup> Significant ostial stenosis of the diagonal artery was defined as a luminal reduction assessed by quantitative coronary angiography (QCA). The diagonal stenosis was evaluated quantitatively, and the diagonal stenosis with  $>75\%$  was included in their study.<sup>3</sup> We did not routinely use QCA software for stenosis degree. This software was mainly developed for single, straight coronary segments, and variability could be higher in bifurcation lesions. The dedicated bifurcation QCA software could be used when appropriate.

Functional assessment was not performed in this study. Koo et al<sup>13</sup> have shown that diagonal branch occlusion caused fewer anginas, minor electrocardiogram change, less arrhythmogenic potential, and higher coronary wedge pressure than did a LAD occlusion. It might be helpful to consider the blood supply area to the diagonal artery when making the treatment decision. A multicenter study included 482 patients who underwent coronary computed tomography angiography and fractional flow reserve measurement. Comparing similar stenosis of the main vessel, side branch supplied a smaller myocardial mass and showed less physiological severity. The vessel length  $>73$  mm was an independent predictor of myocardial mass of  $>10\%$ , which could benefit from revascularization.<sup>14</sup>

If it is decided to place the stent, flush ostial technique, stent draw-back technique,<sup>15</sup> Szabo technique,<sup>16</sup> inverted provisional stenting/crossover technique,<sup>17</sup> the modified flower petal technique<sup>18</sup> could be used. However, it should be noted that in any case where the angle is not  $90^\circ$ , ostial miss or protrusion to the main vessel is inevitable. Although inverted provisional technique provides complete ostial coverage, disruption of blood flow can occur and may require a second stent placement to the main vessel. In this study, most of the patients underwent direct stenting to the ostium with flush ostial technique. The procedural success was 100%, and no apparent stenosis was seen at follow-up.

An analysis determined that this suboptimal location was found in a significant proportion of 54% of patients who underwent

aorta-ostial vessel PCI.<sup>19</sup> It will be beneficial to find the most suitable angle by examining the localization of the lesion from several different angles and, if possible, to use methods that assist intravascular imaging with optical coherence tomography or intravascular ultrasound to minimize this risk.

Angina persisted in most of the patients in the PCI group in our study. The reason for this may be less use of antianginal treatment other than beta-blocker treatment, although it does not reach statistical significance. Another reason could be the ostial miss, but we did not use any intravascular imaging method. The patients with no angina at the beginning of the study were excluded to objective assessment during follow-up. Angina was more common in patients with wider diagonal arteries whether a percutaneous procedure was performed when the patients were evaluated according to angina. Wider coronary arteries supply larger area, and therefore, medical treatment should be optimized in these patients.

### Study Limitations

This is a non-randomized observational study, and the results should be interpreted with caution. The number of the patients in the PCI group was relatively lower. Intravascular imaging methods were not used during stent implantation. Ischemic evaluation was not present in most patients after the selection of treatment modality.

### Conclusion

Isolated ostial diagonal lesions should be carefully evaluated, and PCI reserved for most patients with acute coronary syndrome or refractory angina despite optimal medical therapy. The percutaneous intervention was not superior to medical therapy in isolated ostial diagonal artery disease, and the patient with wider diagonal artery tends to suffer anginal episodes in higher frequency. The procedural success was mainly acceptable; however, conservative treatment with current anti-anginal drugs with appropriate dosage should be initially started.

**Ethics Committee Approval:** Ethics Committee approval was obtained from Kocaeli University Non-Interventional Clinical Research Ethics Committee (Approval no: KÜ GOKAEK-2021/06.17, Project no: 2021/108, Date: 18.03.2021).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Conception – A.T., B.A.; Design – A.T., B.A.; Supervision – B.A., G.K., T.K., A.A., U.Y., E.U.; Data Collection and/or Processing – A.T., G.K., A.A., U.Y., E.U.; Analysis and/or Interpretation – A.T.; Literature Review – A.T.; Writing – A.T.; Critical Review – B.A., G.K., T.K., A.A., U.Y., E.U.

**Acknowledgments:** The data about the patients who were enrolled in the present study were also introduced in the master thesis of Doctor Akin Torun.

**Declaration of Interests:** The authors declare that they have no competing interest.

**Funding:** The authors declare that this study had received no financial support.

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