Analysis of coronary artery anomalies in adults: morphology, atherosclerosis, and cardiovascular risks

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ABSTRACT

Aims: Despite their rarity, coronary artery anomalies (CAAs) warrant careful consideration during percutaneous or surgical interventions due to their potential influence on clinical outcomes. The objective of this study was to ascertain the prevalence and characteristics of CAAs in adult patients undergoing coronary angiography.

Methods: A retrospective analysis was conducted on 12.457 coronary angiography records from a tertiary hospital, encompassing the period from May 2007 to October 2010. The classification of anomalies adhered to the system proposed by Dr. Angelini and approved by the Congenital Heart Surgery Committee. Statistical comparisons were performed through the application of Student's t-test, Pearson's chi-square test, and Fisher's exact test.

Results: An analysis of angiographies identified CAAs in 134 cases, consisting of 89 males and 45 females, with an age range spanning from 21 to 87 years. Myocardial bridging was identified in 62 instances (0.49%), coronary artery exit anomalies in 17 instances (0.14%), coronary artery aneurysms in 30 instances (0.24%), coronary artery fistula in 18 instances (0.14%) , and coronary artery atresia in one instance (0.01%). There were no substantial gender variations observed among the different types of anomalies.

Conclusion: The findings of this study align closely with previous research concerning the prevalence and characteristics of CAAs. Prompt diagnosis and angiographic assessment of congenital CAAs are essential for optimal management and minimizing procedural risks. Anatomical knowledge is indispensable in elucidating pathophysiological mechanisms, optimizing surgical strategies, and advancing diagnostic imaging techniques.

Keywords: Coronary angiography, coronary artery anomalies, myocardial bridging, sudden death, congenital anomalies

INTRODUCTION

The prevalence of coronary artery anomalies (CAAs) within the general population is estimated to be between 0.2% and 1.2%.^{1,2} Though rare and usually asymptomatic, CAAs can lead to angina, myocardial infaction (MI), heart failure, heart attacks, and sudden death.^{3,4} Myocardial bridge (MB), a condition typically seen in the left anterior descending coronary artery (LAD), can be managed using both medical and surgical approaches.⁵

The occurrence of an exit anomaly of the circumflex artery, exhibiting an anomalous coronary artery outflow originating from the right coronary sinus, is documented at a rate of 0.32-0.67%.⁶ This anomaly represents the most frequently observed coronary artery outflow variation. Recognition of the anomaly is essential to avoid potential arterial injury during surgical procedures.⁷ The presence of a single coronary artery, a congenital anomaly characterized by a single opening in the aorta supplying the entire heart, also poses a serious risk of sudden death.⁸

Accurate assessment of abnormal coronary artery anatomy, based on data obtained through coronary angiography or other imaging modalities, is paramount in clinical followup, treatment regimens, and the avoidance of complications during surgical interventions. The study aimed to ascertain the incidence of congenital CAAs through an examination of coronary angiographies.

METHODS

Study Design

This retrospective study involved the examination of 12.457 coronary angiography records obtained from a tertiary hospital during the period from May 2007 to October 2010. A cardiologist and an anatomist undertook the assessment of the data , with the goal of identifying any irregularities in the coronary arteries. Ethical approval for this retrospective study has been obtained from the Kırıkkale University Non-interventional Clinical Researches Ethics Committee (Date: 02/25/2021, Decision No: 2021.01.24). All procedures were

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carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study included 134 cases diagnosed with CAAs through coronary angiography and 139 cases in the control group. However, patients with CAAs who had other potential causes of angina, such as heart transplantation, coronary artery bypass surgery, pulmonary hypertension, hypertrophic cardiomyopathy, liver or kidney failure, congestive heart failure, acute coronary syndrome, or valvular heart diseases, were excluded from the study.

The study's focus was on exploring various abnormalities present in the coronary arteries. These anomalies encompassed abnormal drainage into the coronary sinus, drainage structures near the aortic root or the sinus of Valsalva, and coronary arteries positioned above the heart's apex. Furthermore, the study addressed other cardiovascular anomalies including MB, coronary artery fistula (CAF), coronary artery aneurysms, and coronary artery atresia. The defects observed in this study were classified using the Angelini system, which is approved by the Congenital Heart Surgery Committee and is more frequently utilized than other classification systems due to its comprehensive approach and broad acceptance.⁹

Imaging Procedure

Coronary angiograms were performed using the Judkins technique. Images were acquired using a Philips Allura Xper FD10 angiography unit equipped with a Flat Image Detector, a Philips TG 21 monitor, and a 40-85kW Philips MRC 200 x-ray tube. Radiographic angles were adjusted to achieve the optimal image for every case, ensuring flexibility in image acquisition. The data was processed utilizing the Philips digital heart imaging system integrated with the angiography equipment

Statistical Analysis

Descriptive statistics were utilized to summarize the demographic and clinical features of the study population. Continuous variables with normal distributions were summarized using means and standard deviations. Categorical variables are reported as frequencies (n) and percentages (%).

Appropriate statistical analyses comparing the CAAs and control groups were performed using tests chosen based on the nature of the variables. Continuous variables, such as age, were compared across groups using Student's t-test, assuming normality. Categorical variables-gender, hypertension, and family history of cardiovascular disease-were analyzed using Pearson's chi-square test. To preserve statistical validity in instances of categorical variables with small cell counts, such as those pertaining to CAF or aneurysms, the Fisher's exact test was utilized. Statistical significance was defined as a p-value below 0.05. R software, version 4.4.0, was utilized for statistical analysis.

RESULTS

An in-depth analysis of 12,457 coronary angiography cases was conducted to evaluate the prevalence and clinical presentation of CAA, with 134 patients (1.08%) exhibiting the anomaly. Myocardial bridging was the most prevalent anomaly, observed in 62 patients (0.49% of the total cohort). Coronary artery aneurysms were the second most prevalent anomaly, observed in 30 patients (0.24%), while CAF were identified in 18 patients (0.14%). Coronary artery exit anomalies were also identified in 17 participants (0.14%). Less prevalent anomalies included right coronary artery atresia (n=1, 0.01%) and a single coronary artery (n=1, 0.01%) (Table 1).

	Number of cases (n)	Percentage (%)
Myocardial bridge	62	0.49
Aneurysm	30	0.24
Fistulae	18	0.14
Atresia (right coronary)	1	0.01
Exit anomalies	17	0.14
LMCA-to-RS (type IV)	2	0.02
LAD-to-RS (type I)	2	0.02
Cx-to-RS (type IV)	11	0.09
RCA-to-LS (type I)	2	0.02
Single coronary artery (type III)	1	0.01

Comparison of Clinical and Demographic Characteristics of Anomaly and Control Groups

For comparative analysis, a control group, matched by age and gender to the anomaly group, was randomly selected from the remaining non-CAA patients. Both groups exhibited similar age distributions; the anomaly group's mean age was 52.43 ± 12.43 years, and the control group's mean age was 52.43 ± 12.43 years. Both groups had similar male proportions (66.42% vs. 66.19%), confirming successful matching (p>0.999). The clinical and demographic characteristics for the CAA group (n=134) and the control group (n=139) are presented in Table 2.

Compared to the anomaly group, the control group exhibited a significantly higher prevalence of diabetes mellitus (11.94% vs. 21.58%, p=0.049), hyperlipidemia (9.70% vs. 24.46%, p=0.002), and a family history of cardiovascular disease (25.37% vs. 41.01%, p=0.009). These findings suggest a potentially weaker association between diabetes, hyperlipidemia, family history of heart disease, and the occurrence of CAA.

While the anomaly group exhibited nearly double the rate of atherosclerosis (20.15%) compared to the control group (12.95%), this difference was not statistically significant (p=0.150). Between the groups, there were no statistically significant differences in other major cardiovascular risk factors including hypertension (35.82% vs. 29.50%, p=0.324), smoking (41.79% vs. 30.22%, p=0.062), and MI (29.85% vs. 25.90%, p=0.553).

Gender-Specific Analysis of Coronary Artery Anomalies with in the CAA Group

Gender-based stratification of the CAA group (n=134) was performed to analyze potential differences in the type and frequency of anomalies. Of the anomalies observed, myocardial bridging constituted the most frequent, affecting 41.04% of the CAA cohort.

Table 2. Demographic and clinical char	acteristics: case (coronary artery anoma	aly) vs. control (normal) grouj	ps	
	Overall (n=273)	Normal (n=139)	Anomaly (n=134)	р
Age				0.777
Mean (SD)	52.65±12.5	52.43±12.43	52.86±12.6	
Median (IQR)	53 (19-87)	52.5 (19-82)	53 (21-87)	
Gender				>0.999
Male	181 (66.30%)	92 (66.19%)	89 (66.42%)	
Female	92 (33.70%)	47 (33.81%)	45 (33.58%)	
Hypertension	89 (32.60%)	41 (29.50%)	48 (35.82%)	0.324
Diabetes mellitus	46 (16.85%)	30 (21.58%)	16 (11.94%)	0.049
Hyperlipidemia	47 (17.22%)	34 (24.46%)	13 (9.70%)	0.002
Smoking history	98 (35.90%)	42 (30.22%)	56 (41.79%)	0.062
Family history	91 (33.33%)	57 (41.01%)	34 (25.37%)	0.009
Atherosclerosis	45 (16.48%)	18 (12.95%)	27 (20.15%)	0.150
Myocardial infarction	76 (27.84%)	36 (25.90%)	40 (29.85%)	0.553
Continuous variables are presented as mean±standa (IQR) are presented. Statistical comparisons between significance				

Myocardial bridges were present in 44.94% of males, compared to a slightly lower prevalence of 33.33% in females. The left anterior descending artery was the predominant location for myocardial bridges, with the circumflex and right coronary arteries (RCA) exhibiting a lower frequency; gender did not significantly influence occurrence or location (p=0.532).

In 15 cases (11.19%), aneurysms were detected most often in the LAD, with almost identical rates in males (11.24%) and females (11.11%) (p=0.733). Aneurysms in other coronary arteries, like the left main coronary artery (LMCA), circumflex (Cx), and RCA, were rare and did not exhibit any notable gender variations.

CAF analysis indicated the LMCA (5.22%), LAD (2.99%), and RCA (5.22%) as the most involved sites, with no significant

gender disparity in frequency (p=0.696). The analysis of exit anomalies showed a male-exclusive presence of rare events, namely LMCA-to-RCS, LAD-to-RCS, and RCA-to-LCS. Because of the low frequency of these events (two occurrences per event), meaningful statistical analysis was not possible. No significant difference (p>0.999) was detected in the prevalence of the Cx-to-RCS anomaly between males (7.87%) and females (8.89%). The observed single coronary artery anomaly and atresia were present in only one male patient, limiting the statistical significance of the findings (Table 3).

The comparison of atherosclerosis and MI occurrence between CAA patients and the control group (Table 4). Among the control group (n=139), 25.9% exhibited atherosclerosis, and 12.95% had a history of MI. In CAA patients, a significantly

	Overall	Male	Female	р	
	(n=134)	(n=89)	(n = 45)	_	
Myocardial bridge				0.532	
LAD	55 (41.04%)	40 (44.94%)	15 (33.33%)		
Cx	6 (4.48%)	4 (4.49%)	2 (4.44%)		
RCA	1 (0.75%)	1 (1.12%)	0 (0.00%)		
Aneurysm				0.733	
LMCA	2 (1.49%)	2 (2.25%)	0 (0.00%)		
LAD	15 (11.19%)	10 (11.24%)	5 (11.11%)		
Сх	3 (2.24%)	1 (1.12%)	2 (4.44%)		
RCA	10 (7.46%)	7 (7.87%)	3 (6.67%)		
Fistulae				0.696	
LMCA	7 (5.22%)	4 (4.49%)	3 (6.67%)		
LAD	4 (2.99%)	2 (2.25%)	2 (4.44%)		
RCA	7 (5.22%)	4 (4.49%)	3 (6.67%)		
Atresia (right coronary)	1 (0.75%)	1 (1.12%)	0 (0.00%)	>0.999	
Exit anomalies				>0.999	
LMCA-to-RCS (type IV)	2 (1.49%)	2 (2.25%)	0 (0.00%)		
LAD-to-RCS (type I)	2 (1.49%)	1 (1.12%)	1 (2.22%)		
Cx-to-RCS (type IV)	11 (8.21%)	7 (7.87%)	4 (8.89%)		
RCA-to-LCS (type I)	2 (1.49%)	1 (1.12%)	1 (2.22%)		
Single coronary artery	1 (0.75%)	1 (1.12%)	0 (0.00%)	>0.999	

Table 4. Comparison of atherosclerosis and myocardial infarction occurrence between CAA patients and control group								
	Overall (n)	I	Atherosclerosis		Myocardial infarction			
	Overall (II)	Present	Absent	р	Present	Absent	р	
Control group	139	36 (25.9%)	103 (74.1%)	-	18 (12.95%)	121 (87.05%)	-	
Patients								
Aneurysm	30	14 (46.67%)	16 (53.33%)	0.024	11 (36.67%)	19 (63.33%)	0.002	
Exit anomaly	17	8 (47.06%)	9 (52.94%)	0.067	2 (11.76%)	15 (88.24%)	0.890	
Fistula	18	3 (16.67%)	15 (83.33%)	0.394	2 (11.11%)	16 (88.89%)	0.826	
Myocardial bridge	62	23 (37.1%)	39 (62.9%)	0.107	9 (14.52%)	53 (85.48%)	0.764	
Categorical variables are represented as count (percentage). Statistical comparisons between coronary artery anomaly patients and control group chi-square test for categorical data. P-values below 0.05 were bolded to indicate statistical significance, CAA: Coronary artery anomalie								

higher prevalence of atherosclerosis was observed in the aneurysm group (46.67%) compared to the control group (p=0.024). Conversely, MI was more common in the aneurysm group (36.67%) compared to the control group (12.95%) (p=0.002). Exit anomalies showed a similar trend for atherosclerosis (47.06% vs. 25.9%) but did not reach statistical significance (p=0.067). MI occurrence in this group was rare (11.76%) and did not show a significant difference compared to the control group (p=0.890). CAFs were associated with lower rates of both atherosclerosis (16.67%) and MI (11.11%), with no significant difference from the control group (p=0.394 and p=0.826, respectively).

For myocardial bridges, 37.1% of patients exhibited atherosclerosis, while 14.52% had a history of MI. However, neither atherosclerosis (p=0.107) nor MI (p=0.764) showed statistically significant differences when compared to the control group. Statistical significance was defined as p<0.05.

DISCUSSION

CAAs represent a critical intersection between cardiovascular clinical practice and anatomical understanding. From an anatomical perspective, these anomalies highlight the importance of congenital vascular development and its implications for functional pathology. Anatomical variations, such as abnormal origins, courses, and terminations of coronary arteries, play a vital role in assessing surgical and interventional risks.¹⁰

Despite their low incidence, CAAs present a notable clinical concern, as they can result in myocardial dysfunction, angina, syncope, arrhythmias, MI, and even sudden death.⁴ A total of 12.457 coronary angiograms were analyzed, identifying various abnormalities including outflow anomalies, atresia, CAFs, aneurysms, and MBs. CAAs were detected in 134 cases. CAAs, including CAFs, were found in 0.3% (40 cases). In a comprehensive analysis of 126.595 coronary angiograms, Yamanaka and Hobbs¹¹ documented the presence of coronary artery outflow anomalies, course anomalies, and CAFs in 1,686 cases, equivalent to 1.3% of the total cohort. Kardos and colleagues¹² identified CAFs, concurrent with origin and course anomalies, in 1.34% (103 cases) of 7,694 coronary angiograms. Aydınlar et al.¹³ discovered that out of 12,059 cases, 100 (0.82%) exhibited CAFs with origin and course anomalies. Tuncer et al.¹⁴ reported similar findings, identifying CAFs in 56 cases among 70,850 coronary angiograms. Findings align with existing research on the prevalence of CAAs in the Turkish population.

In this study, we compared a cohort of patients with CAAs to an age- and gender-matched control group, ensuring no significant differences in baseline characteristics. This matching facilitated a reliable comparison of cardiovascular risk factors and outcomes. The control group exhibited significantly higher rates of diabetes mellitus, hyperlipidemia, and family history of cardiovascular disease key risk factors for CAD.¹⁵ Additionally, while the anomaly group's higher atherosclerosis rate was notable, other traditional risk factors, such as hypertension, smoking, and family history, may have a more substantial role in CAD.¹⁶ Prior studies have highlighted these risk factors' stronger correlation with CAD compared to coronary anomalies. In summary, CAAs might modestly contribute to atherosclerosis risk, but their overall impact on major cardiovascular events remains unclear. Larger, long-term studies are needed to explore the multifactorial relationship between CAAs, atherosclerosis, and cardiovascular outcomes.

This study found no statistically significant gender differences in CAAs, consistent with evidence suggesting these anomalies are largely independent of gender-specific factors. Anatomical and functional variations, such as myocardial bridges, aneurysms, and exit anomalies, are more influenced by individual hemodynamic conditions and genetic predispositions than by sex.⁹ A study concluded that both genders similarly influence the prevalence, clinical presentation, and atherosclerotic burden of CAAs, with RCA originating from LCX being more common in males than females. These findings emphasize the need for personalized evaluation and management of CAAs, regardless of gender. Future research with larger cohorts and advanced imaging methods is necessary to explore any subtle gender-related variations in outcomes.¹⁷

The circumflex artery originating from the right coronary sinus is the most common CAAs, with an incidence of 0.32-0.67% in coronary angiograms. Located behind the aorta, this anomaly is a significant concern for cardiovascular surgeons, as it increases the risk of damaging the circumflex artery during valve replacement procedures.^{4,7,18} In our study, cases with this anomaly exhibited a retroaortic course and a short, sharp angle of origin. This anatomical variation can lead to complications during surgical procedures such as aortic valve replacement and mitral valve repair due to potential vascular injury and improper positioning of the artery.^{9,19} These findings underscore the importance of preoperative imaging and careful intraoperative monitoring.

Rare anomalies, such as the LMCA originating from the right coronary sinus, can result in an abnormal course of the

coronary artery in cases with interarterial outlet anomalies. This deviation may lead to structural changes that could disrupt blood flow or obstruct coronary perfusion, predisposing individuals to myocardial ischemia and sudden cardiac death. Rooted in embryological errors, these anomalies, including abnormal aorta-pulmonary pathways, disrupt normal blood flow and increase the risk of CAD. In our study, two cases were observed in which the coronary arteries passed behind the aorta without the risk of interarterial compression, both of which did not exhibit myocardial ischemia (Figure 1).²⁰⁻²²



Figure 1. Left main coronary artery originating from the right coronary sinüs (type IV)

The origin of the right coronary artery (RCA) from the left coronary sinus is a rare anatomical variant, observed in 0.03-0.17% of coronary angiographic examinations. Arterial compression near the aorta can lead to various cardiac complications, including myocardial ischemia, rapid heart rate, fainting, and sudden death. Specifically, the interarterial course, where the RCA arises from the left coronary sinus and passes between the aorta and pulmonary artery, may worsen myocardial ischemia and infarction. Although less common, retroaortic coronary artery origin can also increase the risk of MI.^{16,23,24} In our study, MI was detected in three cases, one with an interarterial and two with retroaortic coronary artery origin anomalies.

The LAD originating from the right coronary sinus is an extremely rare anatomical variant, with a prevalence of less than 0.01%. Normally, the LAD arises from the left coronary sinus, supplying the anterior wall of the left ventricle and the interventricular septum. In our series, two cases exhibited LAD originating from the right aortic sinus, a rarer variant than the RCA-originating LAD, with no hemodynamic changes or complications observed. However, LAD origin from the right coronary sinus may increase the risk of myocardial ischemia, infarction, and other CAD due to artery compression or altered blood flow.^{3,11,25}

Single coronary artery anomaly, occurring in 0.024% of individuals, presents with a single ostium originating from the aortic arch. The presence of this anomaly has been reported in 0.2-1.6% of coronary angiographic examinations. This study identified a single-ostium coronary artery anomaly in one case. Although this anomaly typically has no impact on blood flow, it might raise the risk of sudden death in a few instances (Figure 2).^{8,26,27}



Figure 2. Single coronary artery

Among 1,495 patients examined through 64-slice multidetector computed tomography coronary angiography, only one case of circumflex artery atresia was observed, highlighting the low prevalence of this anomaly.²⁸ Conversely, our series identified only one instance of RCA atresia. Despite the examination of this cohort, coronary artery atresia remains a rare anomaly, as confirmed by angiographic scans.

In addition, the prevalence of atherosclerosis and MI in the control group was consistent with general population rates, supporting previous data. This provides a relevant baseline for comparing cardiovascular risks in patients with CAAs.²⁹ CAAs are characterized by abnormal vessel dilation, posing risks due to potential hemodynamic stress, which may lead to further dilation or rupture. CAA aneurysms have a prevalence of 0.3%-5% in coronary angiography patients.^{30,31} Our study's frequent LAD artery aneurysms align with previous findings emphasizing the LAD's functional dominance in coronary circulation (**Figure 3**). While CAAs are not directly caused by atherosclerosis, they can promote it, especially in individuals with cardiovascular risk factors.^{28,32} Our findings suggest CAA aneurysms increase the risk of atherosclerosis and MI, likely due to hemodynamic stress, structural weakness, and



Figure 3. Left anterior descending arter aneurysms

morphological changes in the arterial wall.³² MB, found in 0.5-16% of coronary angiograms, are characterized by an epicardial coronary artery segment running through the myocardium. While usually benign, MB can occasionally lead to significant cardiac issues.³³⁻³⁵ In our study, the LAD artery was most commonly affected, consistent with the literature. However, MB showed no significant association with atherosclerosis or MI compared to the control group. This is in line with studies suggesting that while MB may alter blood flow and cause vascular damage, its role in atherosclerosis and MI remains debated, with some studies showing no increased risk, while others propose mechanical stress on the vessel wall as a potential risk factor.³⁶

The prevalence of coronary artery fistulas (CAF) in this study aligns with previous reports, which document an incidence of 0.1% and 0.08% in adult patients undergoing coronary angiography.³⁷ CAFs are a rare CAAs with pathophysiological significance, as they can lead to myocardial ischemia by diverting blood to heart chambers or large vessels, a phenomenon known as "coronary steal." This bypass impairs myocardial perfusion, particularly during periods of increased oxygen demand.³⁸ In our study, lower rates of atherosclerosis and MI were observed in patients with CAF compared to previous reports linking these anomalies to higher coronary event rates. This discrepancy may be attributed to the limited sample size, and further research is needed to clarify the role of fistulas in the development of atherosclerosis and MI.

The exit anomaly group showed a potential association with increased atherosclerosis risk, though not statistically significant. Previous studies suggest that exit anomalies may affect coronary flow, but their direct impact on atherosclerosis and MI remains unclear. The low MI frequency in this group indicates the complexity of these anomalies and suggests other unmeasured factors may contribute to cardiovascular risk. Further research is needed to clarify the mechanisms linking exit anomalies to coronary artery disease.^{39,40}

CONCLUSION

Through a comprehensive analysis of CAAs in a large population, this study confirms the consistency of its findings with previously established prevalence and types of anomalies. Although the study did not reveal substantial variations in anomaly distribution or associated clinical features based on gender, the results underscore the critical need for early identification and precise classification to inform clinical decision-making. It is essential to recognize these anomalies to optimize treatment strategies, minimize complications, and improve outcomes, especially within the context of percutaneous or surgical interventions. These findings highlight the importance of coronary angiography in the identification and treatment of CAAs. Given these findings, it is crucial to emphasize the role of coronary angiography not only in identifying but also in determining the best treatment strategies for CAAs.

In addition to highlighting the significance of early detection, our study also examines the relationship between CAAs and key cardiovascular risk factors, such as atherosclerosis and MI. The findings suggest that aneurysms and certain coronary anomalies, such as exit anomalies, may be associated with an increased risk of atherosclerosis and MI, while other anomalies like myocardial bridges and CAFs show more varied associations. These results highlight the need for further research into the mechanisms through which coronary anomalies contribute to cardiovascular disease and suggest that clinicians should consider these anomalies in the broader context of patient cardiovascular risk management.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this retrospective study has been obtained from the Kırıkkale University Non-interventional Clinical Researches Ethics Committee (Date: 02/25/2021, Decision No: 2021.01.24).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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