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Presence and characteristics of coronary artery fistulas among patients undergoing coronary angiography in the Polish population

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Abstract

Background

A coronary artery fistula (CAF) is defined as a connection between one or more coronary artery or heart chamber.

Aim

To determine the overall incidence of CAF among Polish patients undergoing diagnostic coronary artery angiography, frequency of particular origin and draining sites.

Methods

The data were obtained from the National Polish Percutaneous Interventions Registry (ORPKI), among patients hospitalized between 01 January 2014 and 31 December 2016 in invasive cardiology departments in Poland.

Results

The study included 298,558 patients. Presence of a coronary artery fistula was noted in 261 (0.087%) patients in our study group. There were 131 female patients with a coronary artery fistula (50.19%) and 130 male patients (49.81%). The most frequent origin of a coronary artery fistula was the left anterior descending artery (LAD) (n= 167; 59.22%). The pulmonary artery was the most frequent drainage site for fistulas originating from the LAD and right coronary artery (RCA) (84 cases, 50.30% and 25 cases, 31.65%, respectively). Fistulas originating from the circumflex artery most frequently drained into another artery (27.78%)

Conclusions
Left anterior descending coronary is the origin site for more than half of all detected coronary artery fistulas. Pulmonary artery is the most frequent origin and drainage sites for coronary artery fistulas.

What is new:

The aim was to evaluate the prevalence of coronary artery fistulas (CAF) in coronary arteries among patients, who were diagnosed using coronary angiography in Poland. Study included 298 558 patients. Presence of a coronary artery fistula was noted in 261 (0.087%) patients in our study group. This is the largest registry of CAFs. Our study showed that left anterior descending artery (LAD) is the most frequent origin of coronary artery fistulas in contrast to the previously published results. The study also indicated that pulmonary artery was the most frequent drainage site for fistulas, however prior angiographic evaluations revealed the right atrium and right ventricle to be more common drainage sites.

Introduction

Coronary artery fistulas are defined as abnormal connections between one or more coronary arteries and heart chambers (coronary cameral fistula) or with the great thoracic vessel (coronary artery or arteriovenous fistula) bypassing the capillary bed [1]. The vast majority of these are congenital but can also appear after trauma, infection, or iatrogenic injury following intracardiac congenital heart operations or cardiac biopsy following heart transplantation [1,2,3]. Available sources also report the presence of a coronary artery fistula as a complication of percutaneous coronary intervention of a totally occluded coronary vessel
The incidence in the general population stands at 0.002% but is higher among patients who have undergone coronary angiography and varies from 0.05 to 0.25% [6,7,8]. Interestingly, the incidence of coronary artery fistulas detected with coronary CT angiography is even higher and amounts to 0.9% [7].

Management of coronary artery fistulas is a challenging task, especially in asymptomatic patients. Some sources recommend closure of the fistula in asymptomatic patients to prevent long-term complications [3,8,9]. Onset of typical symptoms such as dyspnoea or chest pain, large left to right overload, myocardial ischaemia, left ventricular systolic dysfunction or its overload, and as a consequence, progression of congestive heart failure, are primary indications for closure of a fistula [1,6]. Detailed recommendations for managing coronary artery fistulas are provided by ACC/AHA Guidelines for the Management of Adults With Congenital Heart Disease, released in 2008. According to the mentioned recommendations, large coronary artery fistulas should be closed using transcatheter or surgical methods after estimation of its course and potential of treatment to close the fistula completely. Closing small or moderate coronary artery fistulas should be reserved for cases where myocardial ischaemia, unexplained systolic or diastolic impairment, or arrhythmia have been documented (recommendations class I, level of evidence C) [10].

According to the Clinical Classification of Rare Cardiovascular Diseases and Disorders, released in 2018, coronary artery fistulas are assigned to Class IV, Group I (Rare congenital cardiovascular diseases, abnormalities of the position and connection of the heart and vessels) [11].

In our study, we present results obtained from the National Percutaneous Coronary Intervention Registry (ORPKI). This is a national registry of all percutaneous procedures in interventional cardiology in Poland, operated by the Jagiellonian University Medical College.
Presence of coronary artery fistulas has been noted during diagnostic coronary artery angiography. Records from the registry were presented in previous studies [12].

The aim of our study was to determine the overall incidence of coronary artery fistulas among Polish patients undergoing diagnostic coronary artery angiography, frequency of particular origin and draining sites, and determination of potential predisposing factors.

Methods

The study group was comprised of 298,558 patients admitted to Polish hospitals who had undergone coronary artery angiography between 01 January 2014 and 31 December 2016. Presence of a coronary artery fistula was assessed during diagnostic coronary angiography. Three main coronary arteries were considered as the origin of a coronary artery fistula: left anterior descending, circumflex artery, and right coronary artery. Possible drainage sites were the left ventricle, right ventricle, right atrium, pulmonary artery, or another artery. Invasive diagnostics were performed due to different indications such as stable coronary artery disease, acute coronary syndromes (unstable angina, non–ST segment elevation myocardial infarction, ST segment elevation myocardial infarction), cardiac arrest, congenital heart defects, and other indications. Additionally, the frequency of several risk factors of atherosclerosis such as diabetes, smoking status, hypertension, other comorbidities including previous stroke, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, and coexisting kidney disease or chronic obstructive pulmonary disease were assessed.

Statistical analysis

Descriptive analysis was performed. P values of less than 0.05 were regarded as statistically significant. Nominal variables were presented as numbers and percentages, and compared using the likelihood ratio test, while continuous variables were presented as means
and standard deviations and compared using the Student’s t-test. P-values less than 0.05 were assumed to indicate statistical significance, however, clinical significance of obtained results should be interpreted with respect to expert knowledge of the particular parameter. The analyses were conducted in JMP® 14.0.0 (SAS Institute Inc. Cary, NC, USA, 2018).

Results

Presence of a coronary artery fistula was noted in 261 (0.087%) patients in our study group. The mean age of patients with a coronary artery fistula was 65.27 (SD 10.99) with a range from 19-88 years. Mean weight was 76.57 kg (SD 15.77) ranging from 30-145 kg. Among patients without a coronary artery fistula, mean age was 66.59 (SD 10.86) ranging from 15-105 years. Mean weight was 80.64 kg (SD 16.42). The study population consisted of 182,873 males (61.25%) and 112,212 females (37.58%). In the case of 3,473 (1.16%) patients, the gender was not recorded. The exact number of patients with multiple fistulas was not determined.

There was no significant difference in age between groups with and without a coronary artery fistula (65.27 SD 10.00 vs. 66.59 SD 10.86 P= 0.0545). There were 131 female patients with a coronary artery fistula (50.19%) and 130 male patients (49.81%). Regarding the whole study group, the presence of coronary artery fistulas was more frequent among females (0.12%), than among males (0.07%, P< 0.0001). Moreover, patients with coronary artery fistulas weighed less than other patients (76.57 SD 15.77 vs. 80.64 kg SD 16.42 respectively, P< 0.0001).

The most frequent origin of a coronary artery fistula was the left anterior descending artery (n= 167; 59.22%). The right coronary artery was affected in 79 cases (28.01%) and
circumflex artery in 36 cases (12.77%). Percentage values for individual fistula origin sites are shown on figure 1.

The pulmonary artery was the most frequent drainage site for fistulas originating from the left anterior descending and right coronary artery (84 cases, 50.30% and 25 cases, 31.65%, respectively). Fistulas originating from the circumflex artery most frequently drained into another artery (27.78%). Percentage values of drainage sites for analysed coronary artery fistulas significance in figures 2 – 4.

Acute coronary syndrome occurred in the case of 171,112 patients (57.31%). Presence of a coronary artery fistula was described in 97 cases (0.06%) and was significantly less frequent than in the group of patients diagnosed due to other indications (n= 164, 0.13%, P< 0.0001). In the case of unstable angina, presence of a fistula was noted in 63 cases (0.06%, P= 0.0024). Regarding acute myocardial infarctions, fistulas were present in the case of 24 (0.06%, P= 0.0534) patients diagnosed due to non–ST–elevation myocardial infarction and 10 (0.03%) cases of patients treated due to of ST–segment elevation myocardial infarction (P< 0.0001). Regarding the entire study group and indications to perform coronary angiography, fistulas were the most common finding among patients diagnosed due to indications classified as other and comprised 0.17% of the cases. Exact details of fistula presence and its incidence are shown in Table 1.

Interestingly, taking into account comorbidities, only chronic obstructive pulmonary disease associated with coronary artery fistulas more frequently than other groups. Coronary artery fistulas were present in 18 cases (0.23% from the group of patients with chronic obstructive pulmonary disease) and incidence was higher than among the rest of patients (243 patients, 0.08%, P= 0.0004). Coronary artery fistulas were also diagnosed more frequently among patients suffering from hypertension, kidney disease and those who were cigarette
smokers, but these results did not reach statistical significance. The exact details of investigated comorbidities are shown in Table 2.

**Discussion**

Most patients with coronary artery fistulas remain asymptomatic in the first two decades of life, but as the size of the fistula increases, symptoms may appear. Clinical presentation and symptoms depend on the size, shunt direction, and location of the fistula. Typically, patients experience exertional dyspnoea, fatigue, angina, or palpitations [1,3,13]. Angina occurs in the presence of the “coronary steal phenomenon”, which appears when systemic to pulmonary blood flow lowers the distal diastolic pressure and leads to ischaemia of adjacent myocardium, even in the absence of coronary artery disease. Obviously, in some cases, coronary fistulas may coexist with atherosclerotic changes of an artery and cause ischaemia simultaneously [13]. Other studies showed that fistulas originating from the proximal part of a coronary artery can even increase the likelihood of atherosclerotic coronary artery disease [14] but in most cases symptoms are rather associated with “steal phenomenon”.

Large left to right shunts predispose patients to evolution of congestive heart failure through volume overload of the heart chambers and pulmonary vascular bed. Other relatively rare complications of fistulas are thrombosis or embolism, which may lead to acute ischaemia and cause myocardial infarction [1]. Moreover, progressive enlargement of the fistula may result in aneurysm formation and can put patients at risk of rupture and occurrence of haemopericardium and cardiac tamponade [3,15,16,17]. Coronary artery fistulas also predispose patients to infective endocarditis and some sources suggest that as long as the shunt persists, proper endocarditis prophylaxis should be considered [3,13,17].
The most common finding in the physical examination is presence of a continuous murmur induced by systolic–diastolic flow in large fistulas. Diagnostic investigations include basic tests such as electrocardiogram, which can reveal left ventricular volume overload or ischaemic changes, and chest x–ray, which may reveal cardiomegaly in the case of a significant left to right shunt, however, these findings are not pathognomonic [1,3,17]. In some cases, coronary artery fistulas can be visualised by transthoracic echocardiography and doppler imaging which may disclose heart chamber or coronary artery enlargement, the origin, and drainage site. It is not, however, a suitable tool for functional assessment [1,3,8,17]. Other non–invasive techniques such as magnetic resonance imaging and computed tomography provide excellent anatomical delineation and are useful in confirming the origin site and patency of the fistula. Additionally, a myocardial perfusion scan could be useful in the assessment of myocardial ischaemic territory and determining whether invasive treatment should be undertaken among asymptomatic patients [17]. The non-invasive diagnosis is sometimes difficult, especially in symptomatic patients. Therefore in some cases Fractional Flow Reserve (FFR) was used for clinical evaluation of the fistula severity and significance. Data from such cases, especially with long term follow up is limited and further investigation on this field is needed. Coronary angiography remains the principal diagnostic technique for the precise evaluation of haemodynamic significance of the fistula, its origin, course, presence of stenosis or aneurysm, and drainage site [17]. Both coronary arteries should be visualised selectively to confirm diagnosis, exact anatomy and presence of multiple fistulas [1].

Coronary artery fistulas are a rare finding. The overall incidence of coronary artery fistulas reported in our study is in line with previous studies [6,7,14]. Large reports from various study groups and angiographic evaluations demonstrate the presence of coronary artery fistulas at around 0.1% [18,19]. On the other hand, one of the largest reports, with an assessment of 126 595 angiograms suggests a higher incidence of coronary artery fistulas and
puts this number at 0.18% of patients [20]. However, the data was collected between the years 1960-1988, and since then, diagnostic techniques, imaging quality, and the ability to delineate anatomical structures have significantly improved. The incidence of coronary artery congenital anomalies revealed by angiographic evaluations was also performed among a central European population and coronary artery fistula was present in five angiograms (0.065%) [21]. Interestingly, a study conducted in Turkey revealed a much higher incidence, on the level of 0.37% [22].

An even higher incidence of coronary artery fistulas was reported via Coronary Computed Tomography angiography studies and reached 0.9% [7]. This discrepancy may be explained by limitations of coronary angiography such as difficulties in cannulation of arteries with a fistulous origin and in the reliable assessment of anatomic relations of complex, anomalous vessels based on two-dimensional fluoroscopic images [7].

Previous studies report the right coronary artery as the most frequent origin site for coronary artery fistulas (52%), with the left anterior descending coronary artery being involved in 30% of cases, while the circumflex artery is affected in approximately 18% of cases [1]. Other reports, which deliver a wide range of percentages, also describe the right coronary artery as the most frequent origin site [17]. These results are in opposition to our findings, which revealed the left anterior descending coronary artery as the origin site for more than half of all detected coronary artery fistulas (59.22%). Drainage sites are also surprising, since prior angiographic evaluations showed the right atrium and right ventricle to be more common drainage sites of coronary artery fistulas (19-26% for right atrium and 14–40% for right ventricle) [17]. In our study, the most common drainage site was the pulmonary artery, and some previous reports also support this finding [7]. Moreover, a study conducted by Verdini et al. also suggests the left anterior descending coronary artery and pulmonary
artery as the most frequent origin and drainage sites for coronary artery fistulas, respectively [23]. Some cases describe also superior vena cava as one of the possible drainage sites [24].

Acute coronary syndrome is a rare clinical presentation among patients with CAF. However, CAF might be a place of higher likelihood of thrombus formation due to turbulent blood flow. Thrombus originating from CAF may be a cause of systemic and coronary embolisation [25].

In our study, we determined that female sex could be a predisposing factor for coronary artery fistulas. This finding is also contradictory to prior evaluations which suggested a higher incidence of coronary artery anomalies among females, but at the same time, citing non-gender differences in fistula occurrence [17, 26]. The correlation between higher incidence of COPD in patients group with fistulas and its influence on drainage site need further investigation.

Study limitations

The greatest limitation of the presented study is its retrospective character. Data was submitted by all Interventional Centers in Poland with different grade of completeness and was not monitored. All data regarding comorbidities was based on medical records, and no additional laboratory tests or long-term follow up including type of treatment were performed during data collection. Coronary angiograms were not assessed directly for the conducted study, but written descriptions were analysed.
Conclusions

In our study, we investigated a large population of patients who had undergone coronary angiography and determined the incidence of coronary artery fistulas to be 0.087%. Additionally, our report sheds new light on the most frequent origin and drainage sites of coronary fistulas and suggests that female sex could be a predisposing factor. Regarding assessed comorbidities, only the occurrence of chronic obstructive pulmonary disease was more frequent, while other factors require further investigations.

References:


Table 1. Comparison of indications to perform coronary angiography and incidence of coronary artery fistula ($P<0.0001$).

<table>
<thead>
<tr>
<th>Indication</th>
<th>Stable angina</th>
<th>Unstable angina</th>
<th>Non-ST elevation myocardial infarction</th>
<th>ST elevation myocardial infarction</th>
<th>Cardiac arrest</th>
<th>Congenital heart defect</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery fistula</td>
<td>138 (0.12%)</td>
<td>63 (0.06%)</td>
<td>24 (0.06%)</td>
<td>10 (0.03%)</td>
<td>2 (0.12%)</td>
<td>14 (0.16%)</td>
<td>10 (0.17%)</td>
</tr>
<tr>
<td>absent</td>
<td>111103 (99.88%)</td>
<td>97656 (99.94%)</td>
<td>38893 (99.94%)</td>
<td>34466 (99.97%)</td>
<td>1732 (99.88%)</td>
<td>8532 (99.84%)</td>
<td>5914 (99.83%)</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>111241</td>
<td>97719</td>
<td>38917</td>
<td>34476</td>
<td>1734</td>
<td>8546</td>
<td>5924</td>
</tr>
</tbody>
</table>
Table 2. Occurrence of comorbidities in the presence of coronary artery fistulas.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Present - number of cases</th>
<th>Absent - number of cases</th>
<th>Total occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>41 (0.06%)</td>
<td>220 (0.09%)</td>
<td>64403 (P=0.0168)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>6 (0.07%)</td>
<td>255 (0.09%)</td>
<td>8796 (P=0.7128)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>41 (0.06%)</td>
<td>220 (0.09%)</td>
<td>65322 (P=0.0163)</td>
</tr>
<tr>
<td>Previous percutaneous coronary</td>
<td>40 (0.05%)</td>
<td>221 (0.10%)</td>
<td>76892 (P&lt;0.0001)</td>
</tr>
<tr>
<td>intervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous coronary artery bypass graft</td>
<td>3 (0.02%)</td>
<td>258 (0.09%)</td>
<td>16740 (P=0.0002)</td>
</tr>
<tr>
<td>Smokers</td>
<td>53 (0.11%)</td>
<td>208 (0.08%)</td>
<td>50398 (P=0.1494)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>192 (0.09%)</td>
<td>69 (0.07%)</td>
<td>205703 (P=0.0983)</td>
</tr>
<tr>
<td>Condition</td>
<td>Cases</td>
<td>Controls</td>
<td>N</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------</td>
<td>----------</td>
<td>----</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>17</td>
<td>244</td>
<td>14979</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>18</td>
<td>243</td>
<td>7977</td>
</tr>
</tbody>
</table>

Figure 1. Percentage values of coronary artery fistula origin.
Figure 2. Percentage values of drainage sites for fistulas originating from the left anterior descending coronary artery.

Figure 3. Percentage values of drainage sites for fistulas originating from the circumflex coronary artery.
Figure 4. Percentage values of drainage sites for fistulas originating from the right coronary artery.