In-stent restenosis after primary percutaneous coronary intervention: focal versus diffuse pattern. Influence of clinical profile and type of stent

Reestenosis del stent tras una intervención coronaria percutánea primaria: patrón focal frente a difuso. Influencia del perfil clínico y del tipo de stent

Iván Javier Núñez-Gil,* Óscar Vedia, María José Pérez-Vizcayno, Hernán Mejía-Rentería, Pablo Salinas, and Antonio Fernández-Ortiz

Cardiología Intervencionista, Instituto Cardiovascular, Hospital Clínico San Carlos, Madrid, Spain

* Corresponding author: Hospital Clínico San Carlos, Calle Profesor Martín Lagos s/n, 28040 Madrid, Spain.
E-mail address: ibnsky@yahoo.es (I.J. Núñez-Gil).

https://doi.org/10.24875/RECICE.M19000077
2604-7322 / © 2019 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Although the homocoronary retrograde access can be performed using the double catheter technique—the so-called “ping-pong technique”—facilitating the manipulation of materials through antegrade access, we chose a single arterial access since it is the less invasive option. However, it may interfere with the movement of materials in the antegrade direction (this limitation could improve with the use of 7-Fr catheters). In this case and even though we used a 6-FR guidewire we did not find any trouble moving the materials in the antegrade direction (using fewer materials also helped). Although feasible, this should be a last resource technique because of the greater risk involved in cases of perforations. In cases of very long total chronic coronary occlusions that require other techniques such as the controlled antegrade and retrograde subintimal tracking (CART), double vascular access is preferred because it requires materials of a lower profile. Coronary angioplasty through retrograde access has improved the rate of success of total chronic coronary occlusions. Although this technique is conceptually simple, it requires the appropriate tools and experienced heart teams to achieve optimal outcomes.

REFERENCES

To the Editor,

Although the use of new stents has improved the results after coronary angioplasty, the development of in-stent restenosis (ISR) is still one of the leading problems following these interventions. ISR is defined as a stenosis > 50% developing in a segment or border of the stent (up to 5 mm). It is often due to progressive neointimal proliferation and has been reported in up to 30% of the patients with conventional stents and 10% of drug-eluting stent carriers.1-4

ISR can be due to several factors associated with the patient (diabetes, renal failure, acute coronary syndromes), the lesion [type B2-C complexity, length > 20 mm, diameter < 3 mm, chronic occlusions, ostial lesions, bifurcations, and coronary bridges], and the procedure [malapposition, insufficient expansion, luminal areas < 3 mm, multiple stents, stent fractures, border dissections, and type of drug, polymer or stent structure].1,4,5

The most widely used system to describe ISRs is the Mehran angiographic classification. Although it was developed for bare metal stents it is used in all stent types. Restenosis are classified into 4 angiographic patterns: I: focal, II: diffuse, III: proliferative, and IV: occlusive; and these patterns have a prognostic value.1 However, although there are studies on ISR following the implantation of multiple stents, its physiological mechanism after an angioplasty in the setting of ST-segment elevation myocardial infarction (STEMI) is not fully understood. Also, it is a situation prone to the appearance of conditions that may favor the occurrence of ISR [insufficient stent expansion or malapposition, small stents for vessels constricted due to circulating catecholamines, thrombophilia, etc.].2,3

We conducted a study in our unit whose endpoint was the type of ISR (focal vs diffuse) and analyzed its correlation with the patient profile-procedure and type of stent in patients treated with any type of stent in a primary angioplasty.

All patients diagnosed with angiographically significant ISR (> 50% visual stenosis) in a lesion previously treated with a stent angioplasty during a STEMI were retrospectively included between 2004 and 2014. A total of 76 consecutive patients were included. According to the Mehran angiographic classification, the type of ISR was divided into focal (type I, n = 42) or diffuse [II = 5, III = 17, and IV = 12 which were analyzed together; n = 34]. Regarding their position with respect to the stent, focal ISRs were located on the borders in 19 cases (45.2%). Most patients were male (82%) with a mean age of 61.5 years old. The cardiovascular risk factors were common; table 1 shows these stratified according to the type of restenosis. The right coronary artery (53%) was the most commonly compromised vessel followed by the anterior descending artery (32%). The mean follow-up was 88 months [interquartile range, 37.2-111.0] and the mean time until the diagnosis of ISR was 8.7 months [interquartile range: 6.2-24.2]. The comparisons between diffuse and focal patterns, and clinical profiles and procedures were similar [table 1]. Focal ISRs were diagnosed earlier than diffuse ISRs after the STEMI [figure 1]. Also, late ISRs were more common for the diffuse pattern [47.1% vs 21.4%, P = .018] and with higher degrees of angiographic stenosis [mean, 80.56% vs 70.86%, P = .02]. Although overall there were no statistically significant differences on the type of restenosis based on the stent generation [P = .41], the focal pattern was present in a higher percentage of bare-metal stents and first-generation drug-eluting stents. Also, the state-of-the-art second-generation drug-eluting stents showed a tendency towards a higher percentage of diffuse restenosis [figure 2]. Being cautious about the sample size, it is suggested that this may be related to lower doses of antiproliferative drugs, more homogeneous releases, and different polymers (some of them bioresorbable).

Small stents [≤ 2.5 mm] showed a non-significant tendency towards more diffuse disease [64% vs 37%, P = .17]. No significant differences were found on the time elapsed until the diagnosis of ISR stratified according to the type of stent (conventional, first- or second-generation drug-eluting stents).

Figure 1. Number of diagnoses based on the time elapsed from primary angioplasty and stratified according to the type of stent restenosis (mean time to diagnosis in diffuse ISR, 29.5 months; in focal ISR, 14.0 months; P = .015). ISR, in-stent restenosis.

Figure 2. Type of de restenosis according to the Mehran angiographic classification based on the type of stent.
### Table 1. Epidemiological and procedural data of patients analyzed based on their pattern of restenosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diffuse pattern (Mehran II-IV)</th>
<th>Focal pattern (Mehran I)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>26 (76.5%)</td>
<td>36 (85.7%)</td>
<td>.30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.6 ± 13.2</td>
<td>60.6 ± 11.9</td>
<td>.50</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>168.2 ± 6.3</td>
<td>167.5 ± 7.9</td>
<td>.68</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.1 ± 10.5</td>
<td>78.8 ± 11.3</td>
<td>.27</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>24 (61.8%)</td>
<td>21 (57.1%)</td>
<td>.88</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (26.5%)</td>
<td>14 (33.3%)</td>
<td>.51</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>13 (38.2%)</td>
<td>19 (45.2%)</td>
<td>.54</td>
</tr>
<tr>
<td>Smoking</td>
<td>20 (56.8%)</td>
<td>31 (73.8%)</td>
<td>.16</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1 (2.9%)</td>
<td>1 (2.4%)</td>
<td>.87</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>2 (5.9%)</td>
<td>0</td>
<td>.11</td>
</tr>
<tr>
<td>Peripheral vasculopathy</td>
<td>1 (2.9%)</td>
<td>2 (4.8%)</td>
<td>.68</td>
</tr>
<tr>
<td>Chronic nephropathy</td>
<td>0</td>
<td>1 (2.4%)</td>
<td>.36</td>
</tr>
<tr>
<td>Prior angioplasty</td>
<td>5 (14.7%)</td>
<td>5 (11.9%)</td>
<td>.71</td>
</tr>
</tbody>
</table>

**Index procedure (primary angioplasty)**

**Type of stent:**

- Conventional stent: 25 (47.2%) vs. 28 (52.8%)
- First-generation drug-eluting stent: 5 (31.3%) vs. 11 (68.7%)
- Second-generation drug-eluting stent: 4 (57.1%) vs. 3 (42.9%)

**Maximum inflation pressure (atmospheres), mean (interquartile range):**

- Diffuse pattern: 16 (14-18) vs. 14 (14-18)
- Focal pattern: 170 (120-375) vs. 180 (120-360)

**Size:**

- Big (> 2.5 mm): 27 (79.4%) vs. 38 (90.5%)
- Small (≤ 2.5 mm): 7 (20.6%) vs. 4 (9.5%)

**Number of stents:**

- 1.0 ± 0.4 vs. 1.1 ± 0.4

**Time to primary angioplasty, min mean (interquartile range):**

- 170 (120-375) vs. 180 (120-360)

**Thromboaspiration:**

- 13 (38.2%) vs. 12 (28.6%)

**No-reflow:**

- 2 (5.9%) vs. 2 (4.8%)

**Culprit vessel:**

- Left main coronary artery: 1 (2.9%) vs. 0
- Left anterior descending coronary artery: 9 (26.5%) vs. 15 (35.7%)
- Left circumflex artery: 7 (20.6%) vs. 2 (4.8%)
- Right coronary artery: 16 (47.1%) vs. 24 (57.1%)
- Saphenous vein bridge: 1 (2.9%) vs. 1 (2.4%)
- LVEF: 53.0 ± 16.1 vs. 56.0 ± 11.5

**Peak creatine kinase levels, mean (interquartile range):**

- 988 (484-2715) vs. 1446 (480-3808)

**Diagnosis of restenosis**

**Diagnosis for new catheterization:**

- Silent ischemia: 1 (2.9%) vs. 2 (4.8%)
- Asymptomatic*: 12 (35.3%) vs. 21 (50%)
- STEMI: 7 (20.6%) vs. 3 (7.1%)
- NSTEMI: 6 (17.6%) vs. 8 (19%)
- Unstable angina pectoris: 2 (5.9%) vs. 4 (9.5%)
- Stable angina pectoris: 3 (8.8%) vs. 0
- Heart failure: 2 (5.9%) vs. 3 (7.1%)
- Ventricular tachycardia: 1 (2.9%) vs. 1 (2.4%)

**Time correlation:**

- Early ISR (< 1 year): 18 (52.9%) vs. 33 (78.6%)
- Late ISR (≥ 1 year): 16 (47.1%) vs. 9 (21.4%)

**ISR**, in-stent restenosis; **LVEF**, left ventricular ejection fraction; **NSTEMI**, non-ST-segment elevation acute myocardial infarction; **STEMI**, ST-segment elevation acute myocardial infarction.

*Control catheterization is indicated by the treating physician (for academic purposes, clinical studies, preoperative or other reasons).
Given the characteristics of a study with a small number of cases among other limitations, it was difficult to estimate the exact rate of ISR since no follow-up coronary angiography was performed in all the STEMIs treated in our center during the study period. No timeline of the exact moment when the ISRs developed was given either since they are often oligosymptomatic. However, the patients’ clinical characteristics and the behavior of several stents are consistent with data previously published on ISRs in patients in other clinical contexts.1

In conclusion, regarding ISR, both pattern and time may be influenced by the type of stent implanted after a STEMI.

REFERENCES