Maximal Hyperemia in the Assessment of Fractional Flow Reserve

Intracoronary Adenosine Versus Intracoronary Sodium Nitroprusside Versus Intravenous Adenosine: The NASCI (Nitroprussiato Versus Adenosina nelle Stenosi Coronariche Intermedie) Study

Antonio Maria Leone, MD, PhD, Italo Porto, MD, PhD, Alberto Ranieri De Caterina, MD, Eloisa Basile, MD, Andrea Aurelio, MD, Andrea Gardi, MS, Dolores Russo, MS, Domenico Laezza, RVT, Giampaolo Niccoli, MD, PhD, Francesco Burzotta, MD, PhD, Carlo Trani, MD, Mario Attilio Mazzari, MD, Rocco Mongiardo, MD, Antonio Giuseppe Rebuzzi, MD, Filippo Crea, MD

Rome, Italy

Objectives This study sought to compare increasing doses of intracoronary (IC) adenosine or IC sodium nitroprusside versus intravenous (IV) adenosine for fractional flow reserve (FFR) assessment.

Background Maximal hyperemia is the critical prerequisite for FFR assessment. Despite IV adenosine currently representing the recommended approach, IC administration of adenosine or other coronary vasodilators constitutes a valuable alternative in everyday practice. However, it is surprisingly unclear which IC strategy allows the achievement of FFR values comparable to IV adenosine.

Methods Fifty intermediate coronary stenoses (n = 45) undergoing FFR measurement were prospectively and consecutively enrolled. Hyperemia was sequentially induced by incremental boli of IC adenosine (ADN) (60 μg ADN60, 300 μg ADN300, 600 μg ADN600), by IC sodium nitroprusside (NTP) (0.6 μg/kg bolus) and by IV adenosine infusion (IVADN) (140 μg/kg/min). FFR values, symptoms, and development of atrioventricular block were recorded.

Results Incremental doses of IC adenosine and NTP were well tolerated and associated with fewer symptoms than IVADN. Intracoronary adenosine doses (0.881 ± 0.067, 0.871 ± 0.068, and 0.868 ± 0.070 with ADN60, ADN300, and ADN600, respectively) and NTP (0.892 ± 0.072) induced a significant decrease of FFR compared with baseline levels (p < 0.001). Notably, ADN600 only was associated with FFR values similar to IVADN (0.867 ± 0.072, p = 0.28). Among the 10 patients with FFR values ≤ 0.80 with IVADN, 5 were correctly identified also by ADN60, 6 by ADN300, 7 by ADN600, and 6 by NTP.

Conclusions Intracoronary adenosine, at doses higher than currently suggested, allows obtaining FFR values similar to IV adenosine. Intravenous adenosine, which remains the gold standard, might thus be reserved for those lesions with equivocal FFR values after high (up to 600 μg) IC adenosine doses. (J Am Coll Cardiol Intv 2012;5:402–8) © 2012 by the American College of Cardiology Foundation
Accurate assessment of the severity of intermediate coronary stenoses represents an everyday challenge for the interventional cardiologist. Although many quantitative anatomic tools have been proposed, their clinical relevance is still matter of debate. In the last few years, the physiological assessment of coronary stenoses using fractional flow reserve (FFR) has emerged as a powerful diagnostic and prognostic tool (1). FFR, which is simply derived by the ratio between distal and proximal pressures under conditions of maximal hyperemia, represents a reliable and reproducible tool to functionally assess the severity of coronary lesions. Specifically, FFR has been proven to identify ischemia-inducing lesions (2–7), as well as to predict prognosis, especially when used to guide percutaneous coronary intervention (PCI) (8,9). Using the cutoff value of 0.80, in the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) study, FFR-guided PCI has been shown to be associated with a better clinical outcome and to reduce costs compared with angiography-guided PCI in patients with multivessel coronary artery disease (10,11).

Maximal hyperemia is a critical prerequisite to correctly assess FFR, because suboptimal microcirculatory vasodilation might result in underestimation of the functional severity of coronary stenoses (1,12). Intravenous (IV) adenosine infusion is currently considered the gold standard for FFR evaluation (10). However, intracoronary (IC) administration of vasodilator agents, such as adenosine, papaverine, or sodium nitroprusside, represents a valuable alternative in everyday practice, theoretically allowing the delivery of a higher drug concentration into the coronary circulation and reducing the occurrence of systemic symptoms. Nevertheless, it is surprising that, despite its wide use, a recommended dose for IC adenosine is not yet established (13–21). Similarly, the efficacy of IC sodium nitroprusside (22), which is frequently used to improve microvascular perfusion in ST-segment elevation myocardial infarction, has not been systematically tested in the setting of FFR measurement. Thus, we designed a study to evaluate the safety and efficacy of a strategy of incremental bolus of IC adenosine, as well as IC sodium nitroprusside, for the assessment of FFR in comparison with IV adenosine infusion.

Methods

Patient population. The NASCI (Nitroprussiato vs Adenosina nelle Stenosi Coronariche Intermedie) study is a prospective study designed to compare different strategies to induce coronary vasodilation for FFR measurements. From May 2010 to February 2011, 45 consecutive patients (50 lesions) undergoing diagnostic cardiac catheterization for suspected coronary artery disease showing angiographically intermediate lesions (diameter stenosis 50% to 70% at visual estimation) in at least 1 main coronary artery were consecutively and prospectively enrolled. Lesions localized on left and right coronary ostia were excluded. Clinical exclusion criteria were recent myocardial infarction (within 7 days) or prior myocardial infarction in the territory supplied by the target vessel, severe valvular heart disease, acutely decompensated chronic heart failure, or advanced renal failure (estimated glomerular filtration rate ≤30 ml/min). Clinical features, cardiovascular risk factors, and left ventricular function were recorded. Cardiovascular medications were not withheld before the study. The study was approved by the local ethical committee and conformed to the Declaration of Helsinki on human research, and informed consent was obtained after complete explanation of the protocol and potential risks.

Coronary angiography. Diagnostic coronary angiography was performed through radial or femoral percutaneous approach. Nonionic contrast medium was used for all patients. At least 2 different projections differing more than 30° were recorded for each assessed lesion. Coronary stenoses were visually assessed by 2 expert independent reviewers (A.M.L. and I.P.).

Pressure measurements. After administration of heparin 100 IU/kg IV, a 0.014-inch pressure monitoring guidewire (Pressure Wire, Radi Medical Systems, Upssala, Sweden) was calibrated and introduced into the guiding catheter. The pressure transducer was advanced just outside the tip of the guiding catheter, and the pressure measured by the sensor was then equalized to that of the guiding catheter. The wire was then advanced distally to the target coronary stenosis. Special attention was paid to avoid arterial pressure wave damping, unsel ective catheterization of coronary ostia and variation in the position of the pressure wire. FFR was calculated as the ratio of distal coronary pressure divided by aortic pressure obtained after achievement of maximal hyperemia. Femoral or brachial vein were used for systemic drug administration. An FFR value of ≤0.80 was considered the significant ischemic threshold.

Study protocol. After checking the correct position of both the guiding catheter and the pressure wire, 0.2 mg of intracoronary isosorbide dinitrate were administered. The study consisted of 3 sequential steps.

1. Incremental bolus of IC adenosine (60 μg [ADN60], 300 μg [ADN300], 600 μg [ADN600]) were admin-
istered with each next dose given at least 60 s apart from the previous or after returning to baseline hemodynamic conditions. Each administration was performed in 5 to 10 s and rapidly flushed by saline solution. Next higher dose was not administered in case of an atrioventricular block (AVB) lasting more than 5 s.

2. Hyperemia was then induced by a 0.6 μg/kg bolus of IC sodium nitroprusside (NTP).

3. Finally, continuous adenosine IV infusion (140 μg/kg/min) (IVADN) was started and maximal hyperemia was assumed at least after 60 s in the presence of stable systemic blood pressure decrease compared with baseline levels remaining for at least 10 beats.

Heart rate, aortic pressure, and distal coronary pressure were continuously recorded and digitally stored throughout all the phases of the study. Patient’s symptoms (namely an angina-like sensation, dyspnea, or flushing), development of complete AVB, or any other complication were carefully recorded. Mean FFR values as well as the number of patients with the lowest FFR and with an FFR ≤0.80 with the different strategies were considered as efficacy endpoints.

**Statistical analysis.** Normality was assessed by D’Agostino and Pearson test. Categorical variables were expressed as percentages and analyzed by Fisher exact test. Continuous variables were expressed as mean ± SD and/or median (interquartile range) and compared using the paired t test or the nonparametric Wilcoxon test, as appropriate. Considering that all analyses were performed comparing 1 variable to a standard reference (e.g., baseline systolic blood pressure), no corrections for multiple comparisons were made. The primary endpoint of the present study was to test the noninferiority of IC adenosine or NTP in comparison with IVADN in inducing maximal hyperemia measured as the lowest possible FFR value. Sample size was calculated hypothesizing a noninferiority threshold as a difference of <0.02 ± 0.05 in the FFR value between those calculated inducing maximal hyperemia with IVADN and those with IC adenosine to sodium nitroprusside. According to this calculation, 39 lesions were required to have the 80% power to identify a significant difference between different approaches. Considering the possibility that not all patients would be able to tolerate high doses of IC adenosine, a final number of 50 lesions was chosen. In particular, assuming the FFR value obtained by IVADN as the standard reference and hypothesizing that this value was the lowest possible to detect small differences, a 1-sided paired t test was used for the comparisons among ADN60, ADN300, ADN600, or NTP and IVADN. All statistical analyses were performed with the Statistical Package for the Social Sciences (version 19.0, SPSS Inc., Chicago, Illinois). A p value of 0.05 was considered significant.

**Results**

**Patient characteristics.** The characteristics of the patients are summarized in Table 1. The mean age was 65 ± 9 years and 82% of patients were men. They were referred for coronary angiography for chronic stable angina (38%), atypical chest pain (20%), acute coronary syndrome (29%), and silent ischemia (13%). Twenty-two patients (49%) had a previous PCI. The average angiographic percentage stenosis was 58 ± 19%, and the target vessels were left anterior descending (74%), circumflex (16%), right coronary artery (8%), and saphenous vein graft (2%).

**Systemic hemodynamic, feasibility, and safety.** Data are presented in Table 2. Intracoronary adenosine was feasible in 50 (100%), in 48 (96%), and in 43 (86%) lesions at doses of 60, 300, and 600 μg, respectively. In all cases, the reason for not completing IC adenosine protocol was related to the development of complete AVB >5 s. NTP was not administered in 2 patients due to systolic blood pressure <90 mm Hg before drug administration, so that 48 lesions (96%) were finally tested.

Intracoronary adenosine had a modest effect on blood pressure (Table 2), whereas IVADN decreased mildly but significantly both systolic and diastolic pressure without symptoms. By contrast, NTP was associated with a marked reduction of systolic and diastolic blood pressure that hesitated in 2 (4%) episodes of symptomatic hypotension. Conversely, whereas IV adenosine and NTP slightly increased heart rate, IC adenosine was associated with a reduction of heart rate that was significant at the higher doses (Table 2). Complete AVB was developed in 8 of 50

| Age, yrs | 65 ± 9 |
| Men | 37 (82) |
| Diabetes | 20 (44) |
| Hypertension | 38 (84) |
| Active smoking | 7 (15) |
| Dyslipidemia | 28 (62) |
| Family history of coronary artery disease | 15 (33) |

**Medications**

| ASA | 42 (93) |
| Clopidogrel | 31 (69) |
| Beta-blockers | 31 (69) |
| RAAS antagonist | 41 (91) |
| Calcium-channel blockers | 12 (27) |
| Statins | 33 (73) |
| Chronic stable angina | 17 (38) |
| Prior MI—remote area | 17 (38) |
| Previous PCI | 22 (49) |
| % stenosis visual estimation | 58 ± 19 |

**Values are mean ± SD or n (%).**

ASA = acetylsalicylic acid; MI = myocardial infarction; PCI = percutaneous coronary intervention; RAAS = renin-angiotensin-aldosterone system.
patients (16%) with ADN60, in 13 of 48 (27%) with ADN300, and in 10 of 43 (23%) with ADN600. Importantly, AVB was always transient and spontaneously reversible, thus never requiring atropine administration or temporary pacemaker implantation. Both IC adenosine and NTP, as compared to IVADN, were associated with a lower rate of development of systemic symptoms. In particular, in 40% of cases, patients experienced flushing and more rarely angina-like sensation or dyspnea. Importantly, all symptoms promptly disappeared with drug discontinuation.

**Efficacy in inducing hyperemia: IC versus IV adenosine.** As expected, all 3 IC adenosine doses induced a significant decrease in FFR compared with baseline distal coronary pressure/aortic pressure (p < 0.001 for all 3 doses). More importantly, increasing IC adenosine doses allowed obtaining progressively lower values of FFR (0.881 ± 0.067 with ADN60, 0.871 ± 0.068 with ADN300, and 0.868 ± 0.070 with ADN600). Notably, as regards to the primary endpoint of the study, only ADN600 was associated with an FFR value not significantly different from IVADN (0.867 ± 0.072, p = 0.28 for noninferiority), whereas, compared with IVADN, ADN60 and ADN300 were associated with significantly higher FFR values (p < 0.001 and p = 0.01, respectively). Considering each lesion separately, ADN60 obtained the lowest values in 24% of cases (12 of 50), ADN300 in 42% (20 of 48), and ADN600 in 53% (23 of 43), whereas IVADN obtained the lowest values in 66% of tested lesions (33 of 50). However, the global strategy of incremental bolus of IC adenosine allowed collectively the obtainment of the lowest values in 70% (35 of 50) of all cases (p = 0.83 vs. IV adenosine).

IVADN identified 10 patients with a positive FFR (FR = 0.80). Not all these patients were correctly diagnosed by IC adenosine: ADN60 identified 5 patients, ADN300 identified 6 patients, and ADN600 identified 7 patients. In particular, this dosage was unable to correctly diagnose 3 patients: In 1 patient, FFR was 0.81, in another 0.83, and in the last, FFR could not be performed for AVB with ADN300 (Fig. 1).

**IC sodium nitroprusside versus IV adenosine.** NTP was associated with a significantly higher mean FFR value than IVADN was (0.892 ± 0.072 vs. 0.867 ± 0.072 respectively, p < 0.001). Specifically, only in 12 cases (of 48, 25%) were FFR values with NTP equal (n = 6) or inferior (n = 6) to those obtained with IVADN. NTP was associated with the lowest FFR value in 7 of 48 tested lesions (15%) compared with 33 of 50 cases (66%) with IVADN (p < 0.0001). NTP identified 7 patients with an FFR ≤ 0.80, among whom 6 had FFR = 0.80 with IVADN also, and 1 an FFR value of 0.80 with NTP and 0.81 with IVADN (Fig. 1, Online Fig. 1).

---

### Table 2. Results: Effect of Different Doses of IC or IV Adenosine and IC Sodium Nitroprusside on Profile, Symptoms, Atrioventricular Block, and FFR

<table>
<thead>
<tr>
<th>n</th>
<th>HR (beats/min)</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
<th>MBP (mm Hg)</th>
<th>Symptoms</th>
<th>AVB</th>
<th>FFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>70 ± 8</td>
<td>144 ± 20</td>
<td>79 ± 9</td>
<td>101 ± 11</td>
<td>0 (0%)</td>
<td>0 (0)</td>
<td>0.98 ± 0.04</td>
</tr>
<tr>
<td>ADN60</td>
<td>50</td>
<td>68 ± 12</td>
<td>142 ± 22</td>
<td>75 ± 10</td>
<td>97 ± 12†</td>
<td>2 (2%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>ADN300</td>
<td>48</td>
<td>64 ± 12</td>
<td>144 ± 21</td>
<td>74 ± 9</td>
<td>97 ± 10†</td>
<td>4 (8.3%)†</td>
<td>13 (27%)</td>
</tr>
<tr>
<td>ADN600</td>
<td>43</td>
<td>62 ± 12</td>
<td>145 ± 25</td>
<td>76 ± 9</td>
<td>96 ± 19†</td>
<td>5 (9.3%)†</td>
<td>10 (23%)</td>
</tr>
<tr>
<td>NTP</td>
<td>48</td>
<td>74 ± 11</td>
<td>123 ± 19†</td>
<td>67 ± 8</td>
<td>84 ± 16†</td>
<td>8 (16%)</td>
<td>4 (8.4%)</td>
</tr>
<tr>
<td>IVADN</td>
<td>50</td>
<td>75 ± 12</td>
<td>137 ± 23†</td>
<td>75 ± 12†</td>
<td>96 ± 14†</td>
<td>20 (40%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

Values are mean ± SD, median (interquartile range), or n (%). Two-sided t test versus baseline: *p = 0.05; †p < 0.05.

ADN60 = intracoronary bolus of 60 μg of adenosine; ADN300 = intracoronary bolus of 300 μg of adenosine; ADN600 = intracoronary bolus of 600 μg of adenosine; AVB = atrioventricular block; DBP = diastolic blood pressure; FFR = fractional flow reserve; HR = heart rate; IC = intracoronary; IQR = interquartile range; IV = intravenous; IVADN = IV = 140 μg/kg/min intravenous infusion of adenosine; MBP = mean blood pressure; NTP = intracoronary bolus of 0.6 μg/kg sodium nitroprusside; SBP = systolic blood pressure.

---

### Figure 1. Efficacy in Inducing Maximal Hyperemia in FFR Assessment

Baseline and fractional flow reserve (FFR) values obtained with incremental bolus of intracoronary adenosine (intracoronary bolus of 60 μg of adenosine [ADN60], of 300 μg [ADN300], of 600 μg [ADN600]), intracoronary bolus of 0.6 μg/kg sodium nitroprusside (NTP), or 140 μg/kg/min intravenous infusion of adenosine (IVADN).
Discussion

The induction of maximal coronary hyperemia represents a critical prerequisite to correctly assess FFR (1,12,23). With this aim, although IV adenosine is currently considered the gold standard approach, in everyday practice, IC adenosine administration is frequently used as a cheaper, simpler, and more rapid alternative. However, despite its wide use and its documented safety and efficacy, a clear recommended dosage for IC adenosine is still lacking (13,15,21). Similarly, the reliability of FFR assessment using IC sodium nitroprusside has not been appropriately tested in a prospective trial. In the present study, we thus compared safety and efficacy of high doses of IC adenosine or sodium nitroprusside with IV adenosine. Of note, our data show that both IC approaches were feasible and safe in most patients, but that only the highest dose of adenosine, 600 μg, was not significantly different from IV adenosine. Moreover, a strategy of increasing IC adenosine dose until the maximum dose of 600 μg allowed detection of the lowest FFR value in a similar proportion of lesions as compared to continuous IV infusion.

IV versus IC adenosine. Intravenous administration of adenosine at a dose of 140 μg/kg/min represents the gold standard for FFR assessment (14). Indeed, the IV route provides several practical advantages, such as an effective and safe stress protocol, the induction of a prolonged vasodilator stimulus allowing the achievement of a stabilization of pressure traces, and the possibility to perform a pressure wire pullback in case of multiple lesions or diffusely diseased coronary arteries. However, IV adenosine administration is a time-consuming and costly procedure for the large amount of adenosine used for each FFR assessment. Furthermore, patients often experience the typical known side effects related to systemic adenosine infusion. Conversely, IC adenosine administration allows an easily feasible and rapid procedure that requires a much lower amount of adenosine, thus also reducing costs. Although commonly used in clinical practice in a large number of catheterization laboratories worldwide, IC adenosine administration has the major drawback of a possible suboptimal induction of maximal hyperemia. This is mainly due, on the one hand, to the possible nonselective drug administration into the target coronary artery and, by contrast, to the uncertainty regarding the dose needed to achieve maximal coronary vasodilation (18,20). The former issue might be addressed by selective IC injection by microcatheter. Using this technique, Yoon et al. (24) have demonstrated that, compared with IV or IC (in bolus) adenosine at commonly suggested doses, the dose of 240 to 360 μg administered IC in 1 min (and not in bolus) was more effective to induce maximal coronary hyperemia. However, this procedure is more invasive than the standard technique and the issue of safety might limit its widespread use. With regard to the second issue, doses lower than 50 μg have been used in several previous studies, although they allow physicians to reliably measure FFR value in less than one-fourth of patients (18,20). Casella et al. (21) have shown that a 150-μg bolus resulted in mean FFR values comparable to those obtained after IV adenosine. Conversely, Lopez-Palop et al. (15) have demonstrated that 210 μg, the highest tested dose in their study, was necessary to reach the lowest FFR value in almost one-fifth of cases.

While designing the NASCI study, we selected the dose of 60 μg as the standard dose, according to the current thinking (18), and then we multiplied it by 5 (300 μg, similarly to the highest doses reported several times in literature) or 10 times (600 μg) to test the feasibility and the effect of very high doses of IC adenosine on FFR. Of note, the use of these high IC doses of adenosine is not uncommon in daily practice, especially in the setting of primary PCI for the pharmacological treatment of no-reflow, where even higher doses have been safely administered (25–27). In addition, the step-by-step approach avoided further increase of dose in cases of AVB lasting more than 5 s and allowed the prevention of excessive bradycardic reactions in individuals very sensitive to adenosine and us to reach the maximum dose of 600 μg in the majority (86%) of patients with minor hemodynamic changes (with the exception of a transient heart rate decrease), with a much lower rate of systemic symptoms and significantly lower costs than those associated with IV adenosine.

Our study demonstrates that conventional doses of IC adenosine are insufficient to induce maximal hyperemia and that only the very high dose of 600 μg was not inferior to IV adenosine. Although the IV approach was associated with the lowest value in most cases compared with each IC dose, the strategy of increasing IC dose, aimed at reaching the maximum tolerated dose for each patient, made it possible to obtain the minimum FFR, and thus presumably maximal hyperemia, in 70% of cases. Using the cutoff of the FAME study (10), however, IV adenosine was associated with a lower FFR value in a higher percentage of cases than of those using the IC strategy. Although technical pitfalls due to catheter dislodgement and unselective administration of adenosine might have played a role, this might indicate that the IV approach is still superior in inducing maximal hyperemia and finally in identifying functionally significant stenosis. In this view, the IV route might represent an alternative to IC administration only in those cases where the FFR value approaches 0.80 (0.81 to 0.83).

IC sodium nitroprusside versus IV adenosine. Given its potent arteriolar vasodilator capability, sodium nitroprusside is recommended and often used in the treatment of no-reflow in the setting of ST-segment elevation myocardial infarction (25). To date, only 1 small study tested sodium nitroprusside in the induction of maximal hyperemia in FFR assessment (22). In this study, sodium nitroprusside–induced hyperemia was...
shown to be equivalent to that induced by adenosine, while providing a more sustained duration of the hyperemic response. Specifically, the dose of 0.6 μg/kg was shown to be equivalent and to strictly correlate with IC adenosine, which, however, was given to doses ranging between 30 and 50 μg. We cannot exclude that higher doses would have been able to induce an even more pronounced vasodilation, but the significant drop in systemic blood pressure in all patients suggests that probably hyperemia was successfully induced and more importantly that higher doses might have been harmful due to excessive hypotensive effect. Despite this evidence, in our study, mean FFR value with NTP was significantly higher than that for IVADN and allowed us to obtain the lowest FFR value in a minority of patients only. With the exception of 1 case, in which NTP identified the lowest FFR value compared with both adenosine strategies, our data are generally consistent with a suboptimal efficacy of NTP to obtain maximal hyperemia in most patients. Thus, NTP should be reserved for those patients with a clear contraindication to adenosine, such as drug hypersensitivity or severe chronic obstructive pulmonary disease.

Conclusions

On the basis of the results of this study, we suggest following the flow chart (Fig. 2) to perform a safe and cost-effective functional evaluation of intermediate stenosis with FFR. Maximal hyperemia might be initially induced by incremental bolus of IC adenosine until a maximum dose of 600 μg if tolerated. PCI can be safely deferred if FFR is >0.83 (that was the highest value of FFR found with ADN600 resulting in a positive FFR with IVADN) and performed if <0.80. Conversely, if FFR is equivocal, that is, FFR value is between 0.83 and 0.81, or when the patient develops a clinically relevant AVB, FFR evaluation should be repeated with IV adenosine and then a decision made on the basis of the cutoff value of 0.80. Alternatively, in the rare case in which a patient does not tolerate both IC and IV administration of adenosine, IC sodium nitroprusside can be used in a relatively safe and accurate manner.

For example, if we had applied the proposed flow chart to the 50 lesions of the present study, we would have safely and correctly diagnosed 70% of the intermediate stenoses with IC adenosine. This might have economical implications also. Considering the current Italian prices and an average patient of 70 kg for the evaluation of the 50 lesions of the present study using the current gold standard represented by IVADN, we would have spent €3,957.50. With this proposed flow chart, we would have spent €1,504, saving €2,453.50.

In conclusion, our study clearly indicates that generally suggested dosages of IC adenosine, compared with IV administration, are insufficient to induce maximal arteriolar vasodilation in most cases. High doses of IC adenosine can be relatively safely administered to most patients and a strategy of increasing dose until 600 μg allows obtaining the minimum FFR value in a similar proportion of patients compared with the gold standard IV route that thus still might be reserved to those cases of equivocal FFR after IC adenosine. Finally, IC sodium nitroprusside could be considered a potential alternative in patients with contraindications to adenosine administration.

Reprint requests and correspondence: Dr. Antonio Maria Leone, Department of Cardiovascular Medicine, Catholic University of the Sacred Heart, Largo Agostino Gemelli 8, 00168 Rome, Italy. E-mail: antoniomariacleone@gmail.com.

REFERENCES


Key Words: adenosine ■ fractional flow reserve ■ intermediate coronary stenosis ■ sodium nitroprusside.

For the supplementary figure, please see the online version of this article.