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Author's response to Dr. Kern's letter

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Letters to the Editor

LIMA Thoracic Branch Coronary Steal Syndrome

To the Editor

As a devotee of the controversy of LIMA side branches and their possible contribution to myocardial ischemia [1], I read with great interest the well-documented case report of Abdo et al. [2] who described a patient with angina and a radionuclide scan with a reversible anterior defect, which normalized after coil emobilization of the LIMA side branch associated with resolution of chest pain.

The discussion accurately reflects the controversy of whether the syndrome of LIMA side branch steal does or does not exist. In review of the available literature, Abdo et al. [2] points out that only 14 of the 43 patients with a presumed LIMA branch steal syndrome culled from many studies [1] had some kind of objective resolution of their ischemia after side branch closure. Most of the others had only subjective or no improvement, with a high likelihood of placebo effect.

I complement the authors and wish to address one of the principal points. The physiology of the LIMA and its side branch demonstrates out-of-phase blood flow patterns with predominant diastolic flow in the LIMA as it anastomses to the LAD, while the thoracic side branch flow remains largely, if not entirely, systolic over its course to the chest wall. The LAD flow and coronary flow reserve remain unchanged by side branch occlusion in each of the 3 patients in whom we performed these maneuvers [1].

Abdo et al. [2] believe that Doppler velocity measurements are insufficient to resolve the controversy. While I agree that Doppler flow does not measure volumetric flow or myocardial perfusion and hence does not necessarily represent myocardial ischemia, the flow velocity does accurately estimate flow when the vessel cross-section is constant and does accurately reflect the physiologic responses to the potential diversion of flow before and during side branch occlusion.

The accuracy of using radionuclide perfusion imaging to reflect flow changes among the different coronary regions has been questioned, especially in patients with multivessel disease. Moreover, the use of perfusion imaging to prove ischemia should also give one pause when considering the abundant examples of false positives, persistent positives, and false negatives before and after percutaneous coronary interventions that can be observed in every day practice. Unlike physiologic measurements, the reproducibility of single perfusion imaging studies to demonstrate accuracy is rarely performed or included in case reports [1], including that of Abdo et al. [2].

Since the incidence of the side branch steal syndrome is uncommon, many of our impressions come from a single case or small case series. In support of the controversy, Abdo et al. [2] cited the potential flaws in the measurements of CVR after side branch occlusion made by Luise et al. [3] and remarked on the likely spurious basal flow signals representing systolic flow reversal phenomenon of Abhyankar et al. [4], thus making the controversy all the more pointed.

Lastly, as the authors know, without stenoses (or a subclavian narrowing) the use of FFR in a LIMA will not yield any pertinent information regarding steal. Flow alterations need to be assessed by a flow measuring tool, hence the use of the Doppler flow wire.

At this point, I believe that a few patients appear to benefit by side branch occlusion, but we have no way to determine who these individuals are or why benefit should occur in some patients and not in others. Without better data, I still believe that the bulk of physiologic and clinical information indicates that the thoracic LIMA side branch does not and cannot produce true steal from the coronary circulation unless specific hemodynamic conditions exist, which drive flow to the region of lowest resistance away from the myocardium.

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Author's Response to Dr. Kern's Letter

This is a response to a letter to the editor entitled LIMA thoracic branch coronary steal syndrome, by Morton Kern. Our original article was in CCI 66: 360–363, 2005.

We appreciate the experience and judgment of our oftentimes mentor, Dr. Kern. However, there are some subtleties of statements regarding this controversy of whether a large LIMA side branch may be responsible on occasion for ischemia in the anastomosed LAD distribution. Dr. Kern still believes that Doppler velocity measurements accurately estimate flow and that it ''does accurately reflect the physiologic responses to the potential diversion of flow before and during side branch occlusion.'' The purpose of our case report was to demonstrate that this may not always be correct.

Although no test is perfect in medicine, we think that radionuclide imaging was accurate in showing ischemia in the LAD distribution distal to the LIMA anastomosis, and the reversal to normal on the radionuclide image following coil embolization of the LIMA side branch, corresponded with the patient's relief of symptoms. Perhaps, this discrepancy is due to the possible importance of systolic flow to the coronary circulation, which was discounted in the Doppler velocity analysis. By analogy, this may be similar to the decrease in systolic flow due to myocardial bridging, which is also controversial, but many people believe that this condition can also cause ischemia.

Dr. Kern concludes that, ''I believe that a few patients appear to benefit by side branch occlusion but we have no way to determine who these individuals are.'' We agree that Doppler velocity measurements do not appear to be able to determine this; but an assessment of perfusion may be more reliable to predict which patients may benefit. The proof is whether the objective evidence for ischemia reverses in addition to relief of the patient's symptoms. If we are willing to perform coronary angioplasty on the basis of an abnormal perfusion study, why not use this as objective data for ischemia induced by a large LIMA side branch?

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Oral Sirolimus After Bare Metal Stent Implantation

To the Editor

We read with interest the article of our friends from Brazil about the use of oral Sirolimus after bare metal stent implantation [1], published in the December issue of the journal.

The authors reported angiographic and clinical outcome of 15 patients with *de novo* lesions treated with bare metal stents plus one moth of oral Sirolimus.

The authors concluded that the oral Sirolimus therapy do not improve angiographic parameters of restenosis compared to historical reports, and the use of 5 mg per day during 30 days was associated with high incidence of side effects and ''... this results do not encourage further trials evaluating the current protocol for the prevention of in stent restenosis.''

We have some concerns and comments related with the findings and conclusions of this small report:

1. First, the authors reported 6.6% and 13% of angiographic binary in stent and in segment restenosis

with 0.61 mm of in segment late loss, those numbers are far from the average of in stent and in segment restenosis and late loss reported by control arm in recent drug eluting stent trials. In fact, control arm of SIRIUS, C SIRIUS, E SIRIUS, and TAXUS IV reported an average of binary restenosis over 35% with 1.0 mm of late loss [2–5]. Furthermore, the amount of late loss (0.61 mm) was similar to those recently reported by the ENDEAVOR II trial (0.62 mm). All these findings are in favor to the immunosuppressive effects of oral Sirolimus therapy. Besides, both patients who had binary restenosis, restenosis was mild (among 50–70%) and after 2 years of follow up, no patient developed death, myocardial infarction, stent thrombosis, TLR, or TVR meaning 0% of MACCE !!!!. If we compare results of the control arm of SIRIUS trial with the results presented by Chaves et al. [1] it represented an 81.4% reduction of in stent restenosis, 64.5% reduction of in segment restenosis, and 95% reduction in MACCE !!!. These positive numbers are also in agreement with others pilots experiences such as ORBIT and ORAR trials [6,7] and also with randomized data from Germany and Argentina with oral Sirolimus therapy, which also demonstrated a significant reduction of clinical and angiographic parameters of restenosis [8,9].

2. The amount of side effects was higher than previous data [6–9]; however, as the ORBIT trial demonstrated [6], it is unnecessary to give 5 mg per day during 1 month, in fact angiographic and clinical results do not improve using high maintenance dose for a longer period of time. Two or three mg per day appears to be the ideal maintenance doses and not longer to 14 days after the procedure. With this therapeutic scheme, all the earlier mentioned investigators achieved significant lower side effects than was reported by Chaves et al. [1].

Even though oral sirolimus administration have less immunosuppressive effects than the local administration, there are other issues with the use of drug-eluting stents, such as cost, incidence of stent thrombosis; although not well established, a call for caution was reported recently [10] in patients unfit for long-term antiplatelet therapy etc., indicating that other alternative therapies including oral immunosuppressive, should not be discarded in order to improve the outcome of patients with *at moderate risk of restenosis* (as presented by the authors in this issue of the Journal [1].

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Reply to the Letter: Oral Sirolimus After Bare Metal Stent Implantation

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To the Editor

We thank Dr. Rodriguez and colleagues for their interest in our article. We have several comments in response regarding their concerns.

First, we conducted a pilot study with 15 patients to assess intimal hyperplasia inhibition with a new oral rapamycin protocol (15-mg loading dose 24 hr before PCI, followed by a daily dose of 5 mg for 4 weeks) in patients subjected to elective bare metal coronary stent implantation for the novo lesions [1]. In such a small sample size, we choose to analyze two continuous and statistical powerful variables (angiographic late loss and IVUS percent neointimal volume) as surrogate end points for restenosis. Categorical variables (binary restenosis and MACE rates) are known to require larger sample sizes to draw any valid conclusions on treatment effect.

Second, multiple risk factors have an independent impact on restenosis, including diabetes, reference diameter, and lesion length. Therefore, it seemed inappropriate to compare our patients (13% diabetics, 3.04 ± 0.38 mm reference diameter and 14 ± 2 mm lesion length) with the control arm of the more recent drug-eluting stent trials mentioned by Dr. Rodriguez, which presented patients with a much higher risk of restenosis (higher incidence of diabetes, longer lesions, and smaller vessels). The in-stent late loss (0.61 mm) and IVUS percent neointimal volume (28.5%) found in our patients were, in fact, quite similar to those reported for patients with a similar risk of restenosis, treated with bare metal stents (0.71–0.80 mm and 20.5%–29%, respectively) [2–4].

Third, the in-stent late-loss plateau achieved for de novo lesions in most published oral rapamycin protocols (0.60–0.71 mm) [1,5–7] coupled with undesirable side-effects, dampened our enthusiasm with oral rapamycin as an alternative treatment option for the prevention of in-stent restenosis. These disappointing results were, in our view, responsible for the poor recruitment of the ORBIT II trial comparing oral rapamycin with placebo and interrupted prematurely due to a slow enrollment.

Finally, we maintain our assertion that considering the efficacy/safety balance, the aforementioned results do not encourage further trials evaluating oral rapamycin for the prevention of restenosis in de novo lesions.

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