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Tom Adriaenssens, Julinda Mehilli, Rainer Wessely, Gjin Ndrepepa, Melchior Seyfarth, Anna Wieczorek, Birgit Blaich, Raisuke Iijima, Jürgen Pache, Adnan Kastrati and Albert Schömig

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Does Addition of Estradiol Improve the Efficacy of a Rapamycin-Eluting Stent?

Results of the ISAR-PEACE Randomized Trial

Tom Adriaenssens, MD, Julinda Mehilli, MD, Rainer Wessely, MD, Gjin Ndrepepa, MD, Melchior Seyfarth, MD, Anna Wieczorek, Birgit Blaich, PtHd, Raisuke Iijima, MD, Jürgen Pache, MD, Adnan Kastrati, MD, Albert Schömig, MD

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Objectives
This study aimed to assess the efficacy of a rapamycin plus 17-β-estradiol–eluting stent versus a rapamycin-eluting stent in patients with coronary artery disease.

Background
Estradiol promotes rapid re-endothelialization of coronary stents in animal models, but it is not known whether combining this drug with rapamycin represents an improved drug-eluting stent technology in terms of reduced lumen renarrowing.

Methods
In this randomized study, we enrolled 502 patients with de novo lesions in native coronary arteries who were randomly assigned to receive either a polymer-free, estradiol plus rapamycin-eluting stent (ERES) (n = 252) or a polymer-free, rapamycin-eluting stent (RES) (n = 250). The primary end point was in-stent late lumen loss in the follow-up angiography. Secondary end points were binary angiographic restenosis, target lesion revascularization, combined incidence of death and myocardial infarction, and incidence of stent thrombosis during 1 year after randomization. The study was designed to test for the superiority of the ERES compared with the RES with respect to in-stent late lumen loss.

Results
Late lumen loss (0.52 ± 0.58 mm vs. 0.51 ± 0.58 mm, p = 0.83), the incidence of binary angiographic restenosis (17.6% vs. 16.9%, p = 0.85), the incidence of target lesion revascularization (14.3% vs. 13.2%, p = 0.72), the combined incidence of death and myocardial infarction (7.9% vs. 8.0%, p = 0.98), and the incidence of stent thrombosis (0.8% vs. 1.2%, p = 0.99) were not significantly different between the ERES group and the RES group.

Conclusions
No apparent beneficial effect is obtained by adding estradiol to a polymer-free rapamycin-eluting stent during the first year after the procedure. (The ISAR-PEACE trial; http://clinicaltrials.gov/ct/show/NCT00402636?order=1; NCT00402636) (J Am Coll Cardiol 2007;49:1265–71) © 2007 by the American College of Cardiology Foundation

The use of drug-eluting stents (DES) has reduced the need for reintervention compared with bare-metal stents (BMS) (1). Despite these results, there is an intense ongoing debate on an increased risk of late stent thrombosis, particularly after discontinuation of thienopyridine therapy, and delayed onset of restenosis, or catch-up phenomenon, with DES (2–4). Lack of or delayed endothelialization associated with DES is considered an important factor that may precipitate late stent thrombosis (5). There are limited data regarding the effect of rapamycin on endothelial (re)growth (6). Recent findings from a human study suggest that endothelial dysfunction is frequently apparent after implantation of a sirolimus-eluting stent (7). In addition, there is strong evidence that a rapid re-endothelialization attenuates neointima formation after vascular injury (8,9), and promotion of endothelial recovery is regarded as the next target for restenosis (10). Estradiol has been shown to promote rapid re-endothelialization of the stent and to reduce restenosis after percutaneous coronary interventions (PCIs) in animal models (11–13). Thus, by promoting re-endothelialization, estradiol has the potential of favorably affecting the risk of thrombosis and restenosis after DES implantation. It may serve as a useful adjunct to rapamycin with established pronounced antiproliferative effects.
We designed a randomized study to compare the efficacy of a polymer-free, estradiol plus rapamycin-eluting stent (ERES) with that of a polymer-free, rapamycin-eluting stent (RES) in patients with coronary artery disease. The stent platform used was a microporous stainless steel stent that allows for a polymer-free drug coating.

Methods

Study population and protocol. Patients who were at least 18 years old, had stable or unstable angina or a positive stress test, and were to undergo PCIs for de novo lesions in a native coronary artery were considered eligible for this study. Pregnant women; patients with an acute ST-segment elevation myocardial infarction; malignancies or other comorbid conditions with a life expectancy <12 months; target lesion located in the left main trunk; and a contraindication or known allergy to aspirin, heparin, thienopyridines, rapamycin, estradiol, or stainless steel were considered ineligible for the study. The study protocol was approved by the local ethics committee. All patients gave their written informed consent for participation in this trial.

At least 2 h before undergoing catheterization, patients received a loading dose of 600 mg of clopidogrel. Randomization was performed after wiring of the target vessel using sealed, opaque envelopes containing a computer-generated random sequence. No stratification was performed. Patients were assigned to receive either ERES or RES. The stent platform used in this study has been described in detail previously (14,15). Both rapamycin and estradiolvalerat were in 1% concentrations.

For determination of pharmacologic release kinetics, ERES and RES (n = 3 for each group) were deployed ex vivo and incubated in 1 ml of phosphate-buffered saline at 37°C in screw-cap tubes. Samples harvested at the indicated time points were subjected to ultraviolet spectrophotometric analysis by using a SAFIRE multiplate reader (Tecan Schweiz Trading AG, Männedorf, Switzerland). A calibration curve was established by use of the peak absorbance wavelength of 280 nm (A_{280}) for rapamycin in phosphate-buffered saline and served as a basis for the calculation of respective concentrations and, hence, of total amounts of the substance in each sample. Interference of absorption measurement by estradiolvalerat at 280 nm was ruled out by comparison of A_{280} of stock solutions containing either rapamycin alone (1%) or a mixture of rapamycin and estradiolvalerat (1%/1%) showing virtually the same values for both samples (data not shown). This is due to a considerably lower absorbance level of estradiolvalerat at 280 nm compared with rapamycin at the same concentration. Figure 1 shows a marked slower release of rapamycin from ERES. At 1 month, total release of rapamycin was 95% from RES and 60% from ERES.

Aspirin and unfractionated heparin were administered per standard practice; the use of abciximab (ReoPro, Lilly, Bad Homburg, Germany) was generally restricted to patients with acute coronary syndromes (positive troponin or ST-segment depression on surface electrocardiogram). After the procedure, patients were maintained on aspirin 100 mg twice daily indefinitely, and clopidogrel 75 mg twice daily until discharge and 75 mg daily for at least 6 months. Other medicaments such as beta-blockers, statins, and angiotensin-converting enzyme inhibitors were given as indicated. After enrollment, patients remained in hospital for at least 48 h. Electrocardiograms were recorded, and blood was collected for determination of creatine kinase and its MB isoenzyme before randomization, and every 8 h for the first 24 h after randomization and daily until hospital discharge. Clinical follow-up by phone contact was scheduled at 1 and 12 months. All patients were asked to return for repeat coronary angiography between 6 and 8 months after randomization or earlier, if anginal symptoms had developed.

Data management, end points, and definitions. Relevant data were collected and entered into a computer database by specialized personnel of the ISAR (Intracoronary Stenting and Angiographic Restenosis) Center. All data were verified against source documentation, and all adverse events were adjudicated by an event committee blinded to treatment allocation. Baseline, postprocedural, and follow-up cineangiograms were forwarded to the Quantitative Angiographic Core Laboratory (ISAR Center, Munich, Germany) for assessment by experienced technicians unaware of the treatment allocation. Angiographic image acquisition of the target lesion was done after intracoronary administration of
nitroglycerin, and the same single worst view projection was measured at all time points. Qualitative morphologic lesion characteristics were characterized using standard criteria (16). Off-line quantitative coronary angiographic analysis was performed using the automated edge detection system (QCA-CMS version 6.0, Medis, Medical Imaging Systems, Leiden, the Netherlands). The contrast-filled non-tapered catheter tip was used for calibration. The reference diameter was measured by interpolation. Minimal lumen diameter was measured within the stent and within the 5-mm proximal and distal edges of the stent. Quantitative analysis was performed in the in-stent area (in-stent analysis) and in the in-segment area including the stented segment as well as both 5-mm margins proximal and distal to the stent (in-segment analysis).

The primary end point of the study was in-stent late lumen loss. Secondary end points were the binary angiographic restenosis (diameter stenosis of at least 50% based on in-segment analysis) at follow-up angiography, the need for target lesion revascularization due to restenosis in the presence of symptoms or signs of ischemia, the combined incidence of death and myocardial infarction, and the incidence of stent thrombosis during the 12-month follow-up. The diagnosis of myocardial infarction required the presence of new Q waves in the electrocardiogram and/or elevation of creatine kinase or its MB isoenzyme at least 3 times the upper limit of normal in ≥2 blood samples. Stent thrombosis was defined as a target lesion occlusion with Thrombolysis In Myocardial Infarction flow grade 0 or 1 accompanied by angiographically visible thrombus and/or acute coronary syndrome. Retrospectively, stent thrombosis was also assessed based on the definitions of the Academic Research Consortium (ARC) (17).

Statistical methods. The study hypothesis was that ERES was superior to RES in terms of decreased late lumen loss. Assuming a late lumen loss of 0.48 mm with the RES and choosing a power of 80%, 190 patients were required in each group to demonstrate a significant difference of 0.16 mm in favor of ERES at a 2-sided alpha level of 0.05. We enrolled a total of 502 patients to accommodate for possible missing follow-up angiograms.

The analyses were performed on an intention-to-treat basis. In patients with multilesion interventions, only the first treated lesion that served for randomization was included in the analysis. Categoric variables are summarized as counts or percentages and compared using chi-square or Fisher exact test (when expected cell values were <5). Continuous variables are expressed as mean ± SD and compared with the Student t test. Survival analysis was performed by applying the Kaplan-Meier method; differences in survival parameters were checked for significance by the log-rank test. All analyses were performed using S-Plus 4.5 statistical package (Insightful Corp., Seattle, Washington). A 2-sided p value <0.05 was considered to indicate statistical significance.

Results

Baseline characteristics and procedural results. A total of 502 patients were enrolled in this study; 252 patients were assigned to the ERES group and 250 to the RES group. Figure 2 shows the flow chart of study participants. Baseline demographic and clinical data are shown in Table 1. Angiographic and procedural characteristics are shown in Table 2. Data were well matched between the 2 groups. Implantation of the assigned stent was successful in all but 1 (99.6%) patient in the ERES group and in all patients in the RES group. Only a small proportion of patients received abciximab periprocedurally (Table 2).
At discharge, beta-blockers (97.2% vs. 97.6%, p = 0.80), angiotensin-converting enzyme inhibitors (82.9% vs. 84.0%, p = 0.75), and statins (91.7% vs. 92.4%, p = 0.76) were prescribed in similar proportions of patients in the ERES and RES groups. There were also no significant differences between the 2 groups regarding the actual duration of clopidogrel therapy: 4 weeks in 0.4% and 1.2%, 6 months in 19.4% and 17.2%, and 1 year in 80.2% and 81.6% in the ERES and RES groups, respectively (p = 0.50).

**Angiographic restenosis.** Follow-up angiography was performed in 204 patients (81.0%) in the ERES group and in 201 patients (80.4%) in the RES group (p = 0.97). Reasons for failure to perform follow-up angiography are shown in Figure 2.

In-stent late lumen loss was 0.52 ± 0.58 mm among patients in the ERES group and 0.51 ± 0.58 mm among patients in the RES group (p = 0.83). Figure 3 shows the overlapping cumulative distribution curves of late lumen loss in the 2 study groups. The other quantitative parameters of restenosis were also comparable between the 2 groups (Table 3). The incidence of binary angiographic restenosis was 17.6% in the ERES group and 16.9% in the RES group (p = 0.85) (Fig. 4).

**Stent thrombosis.** According to the protocol-based definition, 2 patients (0.8%) in the ERES group (22 and 249 day after DES implantation, respectively) and 3 patients (1.2%) in the RES group (1, 11, and 13 days after DES implantation, respectively) incurred stent thrombosis (p = 0.99) within 1 year after randomization; all of these patients were on clopidogrel treatment as they incurred this complication.

Using the ARC criteria, definite stent thrombosis was observed in 2 patients (0.8%) in the ERES group and 3 patients (1.2%) in the RES group (p = 0.99). In addition, there were 6 cases of possible stent thrombosis (3 in each group) and no cases of probable stent thrombosis.

### Table 1 Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estradiol Plus Rapamycin Group (n = 252)</th>
<th>Rapamycin Group (n = 250)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>66.3 ± 10.3</td>
<td>67.4 ± 10.5</td>
<td>0.24</td>
</tr>
<tr>
<td>Women</td>
<td>56 (22)</td>
<td>64 (26)</td>
<td>0.37</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>76 (30)</td>
<td>72 (29)</td>
<td>0.74</td>
</tr>
<tr>
<td>Current smoker</td>
<td>48 (19)</td>
<td>45 (18)</td>
<td>0.76</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>156 (62)</td>
<td>166 (66)</td>
<td>0.29</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>154 (61)</td>
<td>172 (69)</td>
<td>0.07</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>79 (31)</td>
<td>73 (29)</td>
<td>0.60</td>
</tr>
<tr>
<td>Non-ST-segment elevation myocardial infarction</td>
<td>59 (23)</td>
<td>50 (20)</td>
<td>0.35</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>80 (32)</td>
<td>84 (34)</td>
<td>0.66</td>
</tr>
<tr>
<td>Prior aortocoronary bypass surgery</td>
<td>23 (9)</td>
<td>18 (7)</td>
<td>0.43</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>55.6 ± 10.9</td>
<td>53.5 ± 13.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.02 ± 0.55</td>
<td>1.08 ± 0.56</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Data are mean ± SD or number of patients (%).

### Table 2 Angiographic and Procedural Data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estradiol Plus Rapamycin Group (n = 252)</th>
<th>Rapamycin Group (n = 250)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target vessel</td>
<td></td>
<td></td>
<td>0.30</td>
</tr>
<tr>
<td>Left anterior descending coronary artery</td>
<td>95 (38)</td>
<td>107 (43)</td>
<td></td>
</tr>
<tr>
<td>Left circumflex coronary artery</td>
<td>75 (30)</td>
<td>60 (24)</td>
<td></td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>82 (33)</td>
<td>83 (33)</td>
<td></td>
</tr>
<tr>
<td>Complex (type B2/C) lesions</td>
<td>175 (69)</td>
<td>192 (77)</td>
<td>0.06</td>
</tr>
<tr>
<td>Chronic total occlusions</td>
<td>6 (2)</td>
<td>6 (2)</td>
<td>0.99</td>
</tr>
<tr>
<td>Vessel size (mm)</td>
<td>2.77 ± 0.5</td>
<td>2.78 ± 0.5</td>
<td>0.90</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>13.5 ± 7.2</td>
<td>12.6 ± 6.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Initial minimal lumen diameter (mm)</td>
<td>1.08 ± 0.46</td>
<td>1.10 ± 0.50</td>
<td>0.63</td>
</tr>
<tr>
<td>Initial diameter stenosis (%)</td>
<td>61.0 ± 14.9</td>
<td>60.3 ± 16.1</td>
<td>0.59</td>
</tr>
<tr>
<td>Maximal balloon pressure (atm)</td>
<td>14.3 ± 2.9</td>
<td>14.3 ± 2.8</td>
<td>0.89</td>
</tr>
<tr>
<td>Maximal balloon diameter (mm)</td>
<td>2.85 ± 0.51</td>
<td>2.90 ± 0.48</td>
<td>0.25</td>
</tr>
<tr>
<td>Length of stented segment (mm)</td>
<td>21.6 ± 7.9</td>
<td>21.3 ± 8.6</td>
<td>0.69</td>
</tr>
<tr>
<td>Final minimal lumen diameter (mm)</td>
<td>2.53 ± 0.44</td>
<td>2.59 ± 0.43</td>
<td>0.12</td>
</tr>
<tr>
<td>Final diameter stenosis (%)</td>
<td>10.8 ± 5.9</td>
<td>9.9 ± 6.1</td>
<td>0.11</td>
</tr>
<tr>
<td>Periprocedural abciximab therapy</td>
<td>22 (8.7)</td>
<td>21 (8.4)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Data are mean ± SD or number of patients (%).
Clinical outcomes. Five patients (2.0%) in the ERES group and 6 patients (2.4%) in the RES group died at 1 year ($p = 0.75$); all of them were on clopidogrel treatment when they died. The combined 12-month incidence of death and myocardial infarction was comparable between the 2 groups (7.9% in the ERES group versus 8.0% in the RES group, $p = 0.98$) (Fig. 5). Target lesion revascularization rate was 14.3% in the ERES group and 13.2% in the RES group ($p = 0.72$) (Fig. 4).

Discussion

In this randomized study, we compared the efficacy of 2 types of polymer-free DES. Using an identical stent platform, the first stent was coated with a combination of 2 drugs, estradiol and rapamycin, and the second stent was coated with rapamycin alone. We could not see any differences in terms of restenosis and clinical outcomes between these 2 DES. Before commenting on these results, we should acknowledge some limitations of the present study. The experimentally shown promotion of endothelialization by estradiol has the potential of reducing the risk of both neointima formation and stent thrombosis. The present study was only powered to assess the additive effects of estradiol on late lumen loss due to neointima formation. Both the relatively limited number of patients and duration of follow-up do not enable any conclusions relative to the possible influence of estradiol in the risk of stent thrombosis in clinical settings. However, we have also to recognize that none of the previous randomized trials on the value of new DES devices has been sufficiently powered to assess the issue of stent thrombosis. Another limitation is also that the present study lacks intravascular imaging modalities such as intravascular ultrasound (IVUS), angiography, and optical coherence tomography that would have allowed evaluation of stent strut coverage in the 2 study groups.

Endothelium, with its inhibitory effects on platelet aggregation, monocyte adhesion, and smooth muscle cell proliferation, has been well recognized for its role in vascular healing after vascular trauma induced by balloon angioplasty or stenting. Pathological studies have shown delayed endothelialization after DES implantation (5). Therefore, strat-

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estradiol Plus Rapamycin Group ($n = 204$)</th>
<th>Rapamycin Group ($n = 201$)</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late lumen loss (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent</td>
<td>0.52 ± 0.58</td>
<td>0.51 ± 0.58</td>
<td>0.83</td>
</tr>
<tr>
<td>In-segment</td>
<td>0.38 ± 0.55</td>
<td>0.38 ± 0.53</td>
<td>0.87</td>
</tr>
<tr>
<td>Minimal lumen diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent</td>
<td>2.01 ± 0.71</td>
<td>2.10 ± 0.74</td>
<td>0.22</td>
</tr>
<tr>
<td>In-segment</td>
<td>1.82 ± 0.63</td>
<td>1.92 ± 0.68</td>
<td>0.15</td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent</td>
<td>28.18 ± 21.20</td>
<td>27.05 ± 21.07</td>
<td>0.59</td>
</tr>
<tr>
<td>In-segment</td>
<td>34.97 ± 18.76</td>
<td>33.50 ± 19.06</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Data are mean ± SD or number of patients (%).
Estradiol-eluting stent, or a moderate-release estradiol-eluting stent (28). The trial demonstrated no benefit among patients treated with estradiol-eluting stents compared with patients treated with a BMS at 6 months. Intravascular ultrasound IVUS measurements performed at 6 months of follow-up did not indicate any statistically significant differences among the 3 arms with respect to neointimal hyperplasia volume, volumetric plaque burden, and in-stent volume obstruction (28). A recent randomized trial of 108 patients with de novo lesions in native coronary arteries did not indicate any superiority of 17-β-estradiol–coated stent over control phosphorylcholine-coated stent regarding angiographic and clinical outcomes (29). In another recent randomized placebo-controlled trial, 299 patients were assigned to either local delivery of estradiol or placebo (infused in the coronary artery) at the time of stenting (30). The study showed that the procedure was safe and that the infusion of estradiol led to a reduction in the need for urgent PCI at 6 months, but it did not significantly reduce angiographic late loss at 6 months (30).

The present study represents the largest clinical experience with 17-β-estradiol–eluting stents for the prevention of restenosis and the first clinical trial to assess a combination of drugs such as estradiol and rapamycin in the settings of DES technology. The clinical outcomes at 1 year confirm our earlier reports regarding the safety and efficacy of the polymer-free, RES platform (15,31,32); however, the present study failed to provide evidence in favor of an additional effect of estradiol coating on top of that of rapamycin regarding inhibition of neointimal proliferation. It is highly improbable that the lack of additional positive effects by adding estradiol to rapamycin is related to the slowing down of the release kinetics of rapamycin by estradiol. A slower release of rapamycin is expected to potentiate its inhibitory effect on neointima formation. This is suggested by both direct (33) and indirect (31,34) comparisons of neointima measures between slow- and fast-release RES. In fact, both groups in the present study showed late lumen loss measures greater than those observed for polymer-based sirolimus-eluting stents (34) but lower than the in-stent late lumen loss of 0.61 mm observed for phosphorylcholine polymer-based zotarolimus-eluting stents (35). On the other hand, the in-stent late lumen loss of 0.52 mm in the ERES group of our study is similar to the 0.54 mm value of this index in the estradiol group of the EASTER trial (27) and much lower than the 0.82 and 0.86 mm values reported recently for moderate- and fast-release estradiol–eluting stents (28).

The disparate results between the animal models and recent clinical studies regarding the efficacy of estrogen-coating stents remain hard to explain. However, several explanations may be offered for the failure of estrogen-coating to improve angiographic and clinical outcomes in our study. First, in the presence of powerful inhibitory actions of rapamycin on vascular smooth muscle cells, there may be no further inhibition of smooth muscle cell prolif-
eration by locally delivered estrogen. Although the re-endothelialization-promoting properties of estrogen have been demonstrated (11–13), they may not be sufficient to counteract the inhibitory effects of rapamycin on the re-endothelialization process. Second, estrogen promotion of the re-endothelialization process may depend on its concentration at the site of vascular injury, but the optimal local dose in humans is still not known (12). Finally, we cannot exclude that a follow-up longer than 1 year might be required to detect the advantages provided by estradiol regarding prevention of late stent thrombosis after cessation of thienopyridine therapy.

In conclusion, no apparent beneficial effect is obtained by adding estradiol to a polymer-free RES during the first year of thienopyridine therapy.

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REFERENCES


28. Abizaid A. ETHOS I: no incremental benefit with estradiol eluting stents. Paper presented at: Transcatheter Cardiovascular Therapeutics; October 24, 2006; Washington, DC.


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