from the ENTIRE-TIMI 23 trial, also found a similar pattern — no improvement in early reperfusion, but there was a reduced rate of recurrent myocardial infarction. In streptokinase-treated patients, TIMI grade 3 flow at 20–28 h later tended to be higher in patients treated with dalteparin (68% vs 51% for unfractionated heparin, \(P=0.10\)), and the number of ischaemic episodes on continuous ECG monitoring was lower (16% vs 38%, \(P=0.04\)) \[6\] with similar results recently presented in another study by Simoons and colleagues.

Finally, the Assessment of the Safety and Efficacy of New Thrombolytic Regimens (ASSENT)-3 study compared three strategies in 6095 myocardial infarction patients: full-dose tenecteplase plus enoxaparin; half-dose tenecteplase plus weight-adjusted, reduced-dose, unfractionated heparin plus abciximab; and full-dose tenecteplase plus weight-adjusted, unfractionated heparin \[3\]. Both new antithrombotic regimens showed a reduction in the combined endpoint of 30-day death, myocardial infarction, recurrent ischaemia or major bleeding (17.0% unfractionated heparin, 13.7% enoxaparin, and 14.2% abciximab). Although the rates of intracranial haemorrhage were the same for each group, there was a higher rate of major bleeding with abciximab. Thus, the most simple regimen appeared to have the best efficacy and safety profile — tenecteplase plus enoxaparin. However, this trial did not pre-specify a primary end-point or objective, and thus another large, prospective trial, using all thrombolytic regimens is needed to fully define the role of enoxaparin in ST segment elevation myocardial infarction. This is currently in the planning stages to be carried out by the TIMI group.

References


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Direct stenting: safe with advantages for the patient and for the doctor (less fluoroscopy and procedural time)

See doi: 10.1053/euhj.2001.2893 for the article to which this Editorial refers

In this issue Martínez-Elbal et al. report the result of the DISCO (Direct Stenting of Coronary arteries) trial\[1\]. In this study conducted in 10 centres in Spain, 416 patients with 446 coronary lesions were randomized to balloon pre-dilatation and stenting vs stenting without balloon pre-dilatation (direct stenting). The main objectives of this study were to evaluate the safety, feasibility and the effect on angiographic restenosis of the technique of direct stenting...
compared to the standard approach of stenting with pre-dilatation. There was some selection of patients and lesions, with exclusion of patients older than 75 years, patients with acute and recent myocardial infarction, low left ventricular ejection fraction, left main stenosis, lesions with severe tortuosity or calcifications, bifurcational lesions, restenotic lesions, long lesions (15 mm or longer) or vessels with total occlusion. The operators were allowed to use a variety of second generation tubular balloon expandable stents. There were no differences in clinical and lesion characteristics between the 210 patients randomized to direct stenting and the 206 patients assigned to pre-dilatation and stenting except for a higher prevalence of hypertension in the pre-dilatation and stenting group. It is important to mention that type C lesions were present only in 0·9% of the lesions in the direct stenting group and in 1·4% in the pre-dilatation and stenting group.

The strategy of direct stenting was effectively applied to 97% of the lesions and the patients crossed over to pre-dilatation were all effectively stented. No stent loss or other complications occurred in patients in which there was a failure of direct stenting. The most important differences between the patients treated with the two techniques were a significant reduction in fluoroscopy (6·4 min vs 9·2 min, \(P<0·0005\)) and procedural time (21·2 min vs 27·8 min, \(P<0·0005\)) in direct stenting compared to pre-dilatation and stenting. Patients randomized to direct stenting had half the number of dissections compared to pre-dilatation and stenting (9 vs 18). This fact may explain the 1 mm shorter final stent length implanted in the direct stenting compared to pre-dilatation and stenting group and the incidence of stent thrombosis occurring only in patients who had pre-dilatation (1·8%, \(P=0·04\)). Overall the major adverse cardiac events were higher in patients treated with direct stenting compared to pre-dilatation and stenting (1 vs 4, \(P=0·05\)).

Quantitative angiographic evaluation revealed that the reference vessel size was quite large in both groups: 3 mm or higher. The acute gain of 1·98 mm and 1·94 mm in the direct stenting and in the pre-dilatation and stenting groups, respectively, reflects the effectiveness of direct stenting to achieve an optimal final angiographic result.

Follow-up angiographic evaluation performed in 93-7% of eligible patients showed a binary restenosis rate of 16·5% with direct stenting and 14·3% with pre-dilatation and stenting (\(P=0·53\)) and an expected 0·45 loss index similar for both groups. Clinical follow-up extended to 12 months revealed a similar incidence of MACE (myocardial infarction, death, re-PTCA, CABG) in both groups (15·2% for direct stenting and 16·9% for pre-dilatation and stenting, \(P=0·89\)).

These results are in remarkable accordance with a number of prior observational\[2–7\] and randomized studies\[8–15\].

One of the most important aspects that emerge from this study is that direct stenting can be safely performed with a shorter procedural and fluoroscopy time compared to the more traditional technique of pre-dilatation. More importantly, when the direct stenting procedure is not successful (the stent cannot be advanced to the lesion) the stenosis can be pre-dilated with a regular balloon and then the stent can be re-positioned. No single case of stent loss was reported and no patient experienced any adverse event as a consequence of this strategy. No difference in terms of procedural and in-hospital complications between the two techniques were reported in a large retrospective comparison from the Mayo Clinic involving 777 patients treated with direct stenting and 3176 patients treated with pre-dilatation and stenting\[3\]. No difference in incidence of short-term complications was reported in recently completed randomized trials. In the SLIDE trial\[10\] the total MACE events at 30 days were 2·1% in the 241

### Table 1  Six-month target lesion revascularization rates in some trials evaluating direct stenting

<table>
<thead>
<tr>
<th>Type trial</th>
<th>Patients</th>
<th>TLR-DS</th>
<th>TLR-PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herz et al[11]</td>
<td>Randomized trial</td>
<td>80</td>
<td>7·5%</td>
</tr>
<tr>
<td>Ahmed et al[23]</td>
<td>Retrospective study</td>
<td>319</td>
<td>10·1%</td>
</tr>
<tr>
<td>Khaled et al[12]</td>
<td>Randomized trial</td>
<td>311</td>
<td>9·7%</td>
</tr>
<tr>
<td>Danzi et al[8]</td>
<td>Randomized trial</td>
<td>122</td>
<td>18%</td>
</tr>
<tr>
<td>Legutko et al[16]</td>
<td>Retrospective study</td>
<td>61</td>
<td>9·6%</td>
</tr>
<tr>
<td>Chevalier et al[10]</td>
<td>Randomized trial</td>
<td>341</td>
<td>4·9%</td>
</tr>
</tbody>
</table>

\(P=\text{ns}\) for all comparisons of TLR; TLR=target lesion revascularization; PS=pre-dilatation and stenting; DS=direct stenting.
patients randomized to direct stenting compared to 0·8% in the 120 patients treated with pre-dilatation and stenting (P=ns). A high and comparable clinical success was recently reported in the BET trial (Benefit Evaluation of direct coronary stenting) with 98·3% clinical success rate in the 173 patients randomized to direct stenting vs 97·5% success rate in the 165 patients randomized to pre-dilatation and stenting (P=ns). At the last meeting of the European Society of Cardiology in Stockholm (1–5 September 2001) the results at 30 days of the randomized phase of the Velvet (direct stenting with the Bx VELocity balloon-expandable stent mounted on the Raptor exchange delivery system versus pre-dilatation in an European randomized Trial) study became available. In this study, 401 patients with multiple lesions were randomized to direct stenting vs pre-dilatation and stenting. Along with the other non-randomized and randomized studies, this study reported an incidence of MACE and cerebrovascular complications at 30 days, which were similar in direct stenting and pre-dilatation and stenting (8·9% and 9·2% respectively, P=ns). It is interesting to notice that in this trial, as in the DISCO trial, reported in this issue, that the incidence of angiographic dissection was higher in the lesions treated with pre-dilatation compared to the ones treated with direct stenting (26·2% vs 8·8%, P<0·001). Another important element to take into account is that the strategy of direct stenting does not lead to an inferior immediate quantitative luminal result compared to pre-dilatation and stenting. One study evaluating the post procedural in-stent minimal cross sectional area (in-stent CSA) with intravascular ultrasound reported a mean value of 8·3 mm² with direct stenting vs 8·1 mm² with pre-dilatation and stenting (P=ns) [16]; in another study the minimal in-stent CSA was 6·8 mm² with direct stenting and 7·2 mm² with pre-dilatation and stenting [17].

Even in selected patients with acute coronary syndromes the strategy of direct stenting may prove advantageous, by decreasing the risk of distal embolization [18,19]. The shorter procedural time and avoiding the balloon to pre-dilate the lesion yielded a mean saving of almost 1000 Euros, when direct stenting is applied compared to pre-dilatation and stenting [3]. The DISCO trial incorporated an economical analysis but the results are not yet available and will probably be published in a separate paper.

What about the impact of the strategy of direct stenting on angiographic restenosis and on the need to target lesion revascularization? Among the positive expectations connected to direct stenting there was a reduction in angiographic restenosis. The rationale and experimental support came from a seminal study which evaluated endogenous cell seeding over the stent struts following direct stenting vs pre-dilatation and stenting in a porcine model [20]. The authors found that the endothelization of the stent struts was faster following direct stenting compared to predilatation and stenting due to a higher proportion of remnant endothelium with the first strategy. A faster endothelization led to a 43% reduction in neointimal hyperplasia when stents were implanted without prior balloon dilatation leading to endothelial denudation.

Unfortunately, these hopes did not translate into clinical results when the angiographic restenosis rates and the need for target lesion revascularization following direct stenting were evaluated in humans and prospectively compared to pre-dilatation and stenting. Danzi et al. [3] were among the first to report a similar restenosis rate at a 6 month angiographic follow-up following randomization to direct stenting vs pre-dilatation and stenting (22·8% vs 20·7%, P=ns). Table 1 summarizes the 6 months target lesion revascularization rates of the major trials evaluating this parameter following direct stenting and pre-dilatation and stenting. As can be seen there is no difference between the two strategies. Despite the lack of effect on restenosis rate we cannot dismiss the value of the advantages of direct stenting confirmed by the DISCO trial.

Before closing the door on the balloon, important caveats need to be kept clear. First of all we need to remember that the studies evaluating direct stenting excluded lesions with extensive calcifications, with severe tortuositities or angulations, with angiographically visible thrombus, lesions involving a bifurcation, longer than 15 mm, or total occlusions. When the Interventional Cardiologist faces one of such lesions he or she needs to bear in mind that direct stenting has not been evaluated in that scenario. What has been proven of advantage in some conditions may be detrimental in others. It is also important to consider that long lesions and total occlusions may require a strategy aiming to reduce the total stent length in order to limit the risk of diffuse in-stent restenosis [21,22]. Full lesion pre-dilatation and optimization of the result with a balloon may become a useful initial approach in these situations.

We should not forget the occasional non-dilatable lesion. The careful exclusion criteria present in prospective studies lowered this risk which may present itself as a clinical unsolvable complication if direct stenting is applied indiscriminately.

A final note is that direct stenting leaves out any possibility for provisional stenting. This fact may appear the best attribute of direct stenting to some enthusiastic Interventionists.

Eur Heart J, Vol. 23, issue 8, April 2002
I prefer to remain humble and to know that direct stenting is safe and advantageous when I think it is necessary and feasible.

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References


The stent is here to stay: a note on stenting, ultrasound imaging, and the prevention of restenosis

See doi:10.1053/euhj.2001.2899 for the article to which this Editorial refers

Following percutaneous coronary interventions, a considerable number of patients develop restenosis despite an acute success with initially large lumen dimensions. This serious clinical problem causes hospitalization and recatheterization and represents a substantial economic burden for society. Various novel devices with different modes of operation have been suggested and applied, but most of