Direct Stent Implantation in Acute Myocardial Infarction. The DISCO 3 Study

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Introduction and objectives. An association has been reported between direct stenting in primary angioplasty and low incidences of the no-reflow phenomenon and distal embolization. The aims of this study were to determine the proportion of patients who can be treated by direct stent implantation and to identify factors that establish when the technique should be used in acute myocardial infarction in clinical practice.

Patients and methods. This prospective descriptive and multicenter study (DISCO 3) included 189 patients. Angiographic reperfusion parameters were recorded and resolution of the ST-segment elevation was monitored. Adverse clinical events, such as death, non-fatal reinfarction, and repeat revascularization of the culprit vessel, were recorded at discharge, and after 1 and 6 months.

Results. Direct stenting was performed in 56% of patients, and stenting after predilatation in 44%. The main predictors of direct stenting were short postinfarction delay, non-zero initial TIMI flow, and preinfarction angina. The most common reasons for balloon predilatation were TIMI flow zero on traversing the lesion with a guidewire (92%), involvement of a major bifurcation or tortuous vessel, and severe calcification. Indices of myocardial reperfusion were better with direct stenting: TIMI myocardial perfusion grade 2-3 flow was present in 84% vs 69% (P = 0.005), and >70% ST-segment resolution occurred in 66% vs 42% (P = 0.003). No difference in adverse clinical events was found.

Conclusions. Direct stenting is feasible for treating acute myocardial infarction in more than half of patients. The lesions should not be severely calcified nor involve tortuous vessels, and there should be sufficient flow following passage of a guidewire to define the lesion’s characteristics.

Key words: Myocardial infarction. Coronary angioplasty. Stent. Reperfusion. Microcirculation.

Implante directo del stent en el infarto agudo de miocardio. Estudio DISCO 3

Introducción y objetivos. El implante directo del stent en la angioplastia primaria se ha asociado con una menor incidencia de no reflujo y embolización distal. El objetivo de este estudio fue evaluar la proporción de pacientes que puede ser tratada y los factores que determinan la implantación directa del stent en el infarto agudo de miocardio en la práctica habitual.

 Pacientes y método. Se incluyó a 189 pacientes en este estudio descriptivo, prospectivo y multicéntrico (DISCO 3). Se analizaron los resultados angiográficos y de resolución de la elevación del segmento ST. Se registraron los acontecimientos clínicos (muerte, reinfarto no mortal y nueva revascularización del vaso causante) en el momento del alta, al mes y a los 6 meses.

Resultados. Se trató con stent directo (SD) al 56% de los pacientes y con stent tras predilatación (SP) al 44%. Los mejores predictores de SD fueron: menor tiempo de evolución del infarto, flujo TIMI inicial distinto de 0 y presencia de angina preinfarto. Los motivos para la predilatación fueron: presencia de un flujo TIMI 0 tras cruzar la lesión (92%), bifurcación mayor, calcificación y tortuosidad severas. Los índices de reperfusión miocárdica fueron mejores en el grupo de SD, con un grado de perfusión miocárdica TIMI 2-3 (el 84 frente al 69%; p = 0,005) y una resolución del segmento ST > 70% (el 66 frente al 42%, p = 0,003). No hubo diferencias significativas en la presencia de eventos clínicos adversos en el seguimiento.
Patients were included if they had acute coronary syndrome with an ST-segment elevation of >30 min and <12 h evolution and over 1 mV in 2 contiguous leads, as well as stenosis of >50% in the culprit artery based on a visual coronary arteriography reading. Patients were excluded if they suffered cardiogenic shock, if the culprit vessel was the left main coronary artery or saphenous vein graft, or if thrombectomy or distal protection devices were used.

**Procedure**

Direct stenting (DS) was ruled out if, after traversing with the angioplasty guide-wire, it was impossible to define a lesion (TIMI flow zero) or when anatomic conditions such as severe calcification revealed by fluoroscopy, severe tortuosity, major bifurcation (secondary vessel ≥2 mm), and aorto-ostial stenosis, increased the likelihood of failure. Zeta or Pixel® stents (Guidant Inc.) were used, and the aim was to cover the stenosis with a single stent deployed at nominal pressure to ensure a 1:1 stent/artery ratio. Overdilatation was to be avoided, except in cases of suboptimal outcome.

Acetylsalicylic acid (250 mg, intravenously) and clopidogrel (300 mg, orally, except in previously treated patients) were administered unless contraindicated. During preparation for catheterisation, abciximab (Reopro®, Lilly Inc.) was administered in the form of a 0.25 mg/kg bolus, followed by continuous perfusion for 12 h at 0.125 µg/kg/min, up to a maximum of 10 µg/min. Abciximab was administered in the emergency department whenever possible, and otherwise in the coronary care unit or catheterization laboratory. Verapamil or adenosine were used at the operator’s discretion in cases of slow flow or no-reflow. All patients were stented. Success was defined as <20% residual stenosis after angioplasty, and an epicardial TIMI (thrombolysis in myocardial infarction) grade ≥3 flow in the culprit vessel. The type of post-infarction medical treatment prescribed (beta-blockers, angiotensin-converting enzyme inhibitors, statins) was left to the discretion of the attending clinician.

Angiographic analysis and resolution of the ST-segment elevation were performed at a central laboratory.

**Methods**

In the electrocardiogram, elevation was determined at 20 ms after the J-point in the total number of leads affected by the infarction, i.e. anterior (V1-V6, I, and aVL) and nonanterior infarctions (II, III, aVF, V5V6). ST-segment resolution from baseline ECG (baseline $\sum TS$) to 1 h post-intervention (post $\sum TS$) was calculated as follows:

$$\text{A resolution of } >70\% \text{ was considered complete.}$$

### ABBREVIATIONS

- DS: direct stent implantation.
- SP: stent implantation after balloon predilatation.
- TIMI: thrombolysis in myocardial infarction cTFC: corrected TIMI frame count.
- TMPG: TIMI myocardial perfusion grade.

### INTRODUCTION

In hospitals with a well-established program and staff experienced in percutaneous interventions, primary angioplasty is the treatment of choice for acute myocardial infarction (AMI). Several randomized studies have shown that, when compared with angioplasty and balloon dilatation alone, systematic stenting of the culprit vessel leads to lower rates of recurrent ischemia and repeat revascularization.

Direct stenting is not only safe but can also reduce the duration and costs of angioplasty, as well as decreasing exposure to radiation in patients with stable ischemic heart disease and acute coronary syndrome without ST-segment elevation. Studies in patients with acute coronary syndrome and ST-segment elevation have shown that direct stenting can reduce the incidence of no-reflow and distal embolization.

In the electrocardiogram, elevation was determined at 20 ms after the J-point in the total number of leads affected by the infarction, i.e. anterior (V1-V6, I, and aVL) and nonanterior infarctions (II, III, aVF, V5V6). ST-segment resolution from baseline ECG (baseline $\sum TS$) to 1 h post-intervention (post $\sum TS$) was calculated as follows:

$$\text{A resolution of } >70\% \text{ was considered complete.}$$

### CONCLUSIONS

El uso del SD en el tratamiento del infarto agudo de miocardio de menos de 12 h de evolución es factible en más de la mitad de los casos, cuando las lesiones no presentan calcificación y/o tortuosidad severas, y cuando se consigue, tras el paso de la guía, un flujo mínimo que permita definir las características de la lesión.

### Palabras clave:


### PATIENTS AND METHODS

#### Patient Selection

DISCO 3 was a descriptive, prospective, non-randomized study carried out in 13 Spanish centers with a primary angioplasty program, between November 2002 and June 2003.
Angiographic results were analyzed offline by an experienced observer. Epicardial blood flow (TIMI grade flow before and after traversing the lesion with the guidewire, and post-intervention, and corrected TIMI frame count [cTFC]) were estimated using Gibson et al’s definition. 9,10 The TIMI myocardial perfusion grade (TMPG) was also analyzed using Gibson et al’s criteria. 11 The latter analysis was performed after classification of the results as either closed (TMPG 0-1) or open microvasculature (TMPG 2-3). No-reflow was defined as an acute reduction in epicardial blood flow (from TIMI 2 or 3 to TIMI 0 or 1) without thrombus, dissection, spasm, or high-grade residual stenosis in the culprit vessel. Distal embolization was defined as a post-procedure abrupt interruption in filling of one of the distant peripheral branches of the culprit vessel. Enzyme elevation and creatine kinase MB isoenzyme (CK-MB) maximum peak were measured on admission, and systolic ventricular function was measured at discharge by echocardiogram. Adverse clinical events (death, non-fatal reinfarction and repeat revascularization of the culprit vessel due to ischemia) were assessed at discharge, and at 1 and 6 months after discharge.

Statistical Analysis
The χ² test and Fisher’s exact test were used for the comparison of proportions. Student’s t test and the Mann-Whitney U test were used for comparisons of quantitative and categorical variables, as appropriate. A stepwise multivariate logistic regression analysis was performed to identify variables which independently predicted the use of direct stenting and the level of myocardial reperfusion achieved. Level of myocardial reperfusion achieved was measured using TMPG and resolution of the ST-segment elevation. At each step in the logistic regression analysis, variables with a P value <.05 were retained and those with a P value >0.10 were excluded. Event-free survival time was analyzed using the Kaplan-Meier method, and survival curves were compared using the log-rank test. P values <.05 were considered statistically significant.

RESULTS
A total of 189 patients with acute coronary syndrome and ST-segment elevation were treated with primary angioplasty during the study period and were included in the analysis. Direct stenting was performed in 106 (56%) patients and stenting after balloon predilatation in 83 (44%). There were very few differences in demographic and clinical characteristics between the 2 study groups at baseline. The DS group had a higher proportion of patients with preinfarction angina (defined as angina occurring in the 24 h prior to infarction onset), but there were no differences in terms of infarction site or Killip class. The symptom-onset-to-door time was significantly greater in the SP group (150 vs 110 min; P=.003), but there were no differences between groups in terms of door-to-abciximab or door-to-balloon times (Table 1).

Procedure
Direct stenting was successful in 98.1% of cases. In 2 patients in the DS group, balloon predilatation was necessary (as it was not possible to traverse the lesion), although these patients were included within the DS group.
group in the analysis. The reasons for balloon predilatation were: TIMI flow zero on traversing the lesion with a guidewire (92%), severe calcification (5.3%), involvement of a major bifurcation (1.4%), and tortuosity (1.3%). There were no differences between groups regarding the site of the culprit artery or the number of diseased or treated vessels. Stents used in the DS group had a greater diameter and were shorter. There were no differences in inflation pressure, use of overdilatation, or the need for additional stents during the procedure (Table 2), nor were there any differences in terms of occlusive coronary dissection. No stents were lost and there were no cases of acute intrastent occlusion (Table 3).

In a multivariate model which included demographic variables, presence of preinfarction angina, infarction site, Killip class, length of postinfarction delay, non-zero initial TIMI flow and vessel size, only presence of preinfarction angina, short postinfarction delay, and initial TIMI flow were found to be independent predictors of direct stent implantation (Table 4).

**Epicardial and Myocardial Reperfusion**

A higher percentage of patients in the SP group had a non-zero initial TIMI flow (85.2% vs 73.5%; P=0.001) and, with regard to epicardial reperfusion, more patients in the DS group had a TIMI grade 3 flow after the procedure (87.2% vs 75.3%; P=0.03). Between group differences on the cTFC were not statistically significant (19.8 vs 26.9; P=0.1) (Figure 1).

There were 3 cases of no-reflow and 6 cases of distal embolization in the SP group, and none in the DS group. Angiographic indices of myocardial reperfusion (TMPG) were better in the DS group, both in patients with optimal perfusion (TMPG 3; 58.8% vs 44.9%; P=0.04) and in

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**TABLE 2. Procedure Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Direct Stenting</th>
<th>Stenting After Predilatation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial TIMI flow 0, %</td>
<td>73.5</td>
<td>85.2</td>
<td>.001</td>
</tr>
<tr>
<td>Culprit artery, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADA</td>
<td>50.5</td>
<td>56.8</td>
<td>.6</td>
</tr>
<tr>
<td>CCA</td>
<td>12.9</td>
<td>13.6</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>36.6</td>
<td>29.6</td>
<td></td>
</tr>
<tr>
<td>Nb. of diseased vessels, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>58.1</td>
<td>62.2</td>
<td>.6</td>
</tr>
<tr>
<td>2</td>
<td>28.6</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>13.3</td>
<td>15.8</td>
<td></td>
</tr>
<tr>
<td>Nb. vessels treated, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>89.5</td>
<td>92.9</td>
<td>.1</td>
</tr>
<tr>
<td>2</td>
<td>9.5</td>
<td>7.0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Stent diameter, mean±SD, mm</td>
<td>3.22±0.45</td>
<td>3.04±0.48</td>
<td>.009</td>
</tr>
<tr>
<td>Stent length, mean±SD, mm</td>
<td>16.72±4.31</td>
<td>18.96±4.58</td>
<td>.001</td>
</tr>
<tr>
<td>Maximum pressure, mean±SD, atm</td>
<td>13.53±2.86</td>
<td>13.01±3.24</td>
<td>.1</td>
</tr>
<tr>
<td>Postdilatation, %</td>
<td>9.7</td>
<td>9.4</td>
<td>.3</td>
</tr>
</tbody>
</table>

**TABLE 3. Complications During the Procedure**

<table>
<thead>
<tr>
<th>Complications, n</th>
<th>Direct Stenting</th>
<th>Stenting After Predilatation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute intrastent occlusion</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Loss of stent</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Dissection</td>
<td>1</td>
<td>2</td>
<td>.2</td>
</tr>
<tr>
<td>No reflow at end of procedure</td>
<td>0</td>
<td>3</td>
<td>.03</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>0</td>
<td>6</td>
<td>.04</td>
</tr>
</tbody>
</table>

**TABLE 4. Factors Predicting Direct Stent Implantation**

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-zero initial TIMI flow</td>
<td>4.07</td>
<td>1.86-8.92</td>
<td>.001</td>
</tr>
<tr>
<td>Time from symptom onset, h</td>
<td>0.72</td>
<td>0.59-0.89</td>
<td>.002</td>
</tr>
<tr>
<td>Preinfarction angina</td>
<td>3.19</td>
<td>1.29-7.81</td>
<td>.01</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; OR, odds ratio. Independent variables: age, sex, diabetes mellitus, preinfarction angina, site of infarction, Killip class, length of postinfarction delay, non-zero initial TIMI flow, and vessel size.*
patients with TMPG 2-3, which would be equivalent to open microvasculature (83.5% vs 68.9%; \( P = .005 \)) (Figure 1). This difference persisted when only patients with an initial TIMI flow of 0 were analyzed (78.8% vs 67.2%; \( P = .05 \)). In a multivariate logistic regression model which included possible predictors of myocardial reperfusion (age, sex, diabetes mellitus, preinfarction angina, prior infarct, infarction site, Killip class, vessel size, length of postinfarction delay, and initial TIMI flow), only DS was found to be an independent predictor of the level of myocardial reperfusion achieved (odds ratio [OR]=2.63; 95% confidence interval [CI], 1.24-5.58; \( P = .01 \)) (Table 5).

The percentage of patients with complete ST-segment resolution (>70%) was greater in the DS group (65.5% vs 42%; \( P = .003 \)) (Figure 1). This difference persisted when only patients with an initial TIMI flow of 0 were analyzed (62.2% vs 41.4%; \( P = .04 \)). In the multivariate analysis (which included the same variables as described above), the use of DS (OR=2.19; 95% CI, 1.11-4.34; \( P = .02 \)) and the presence of diabetes mellitus (OR=1.39; 95% CI, 1.15-1.99; \( P = .04 \)) were independent predictors of a complete resolution of the ST-segment (Table 5).

Clinical Evolution

There were no differences in CK-MB on admission, though the SP group had a higher CK-MB peak (367 vs 237 U/L; \( P = .04 \)). The DS group showed better systolic ventricular function at discharge (55% vs 50%; \( P = .003 \)), and the mean length of hospital stay in this group was also shorter. There were no differences in pharmacological treatment at discharge (Table 6), and there were no differences between groups in terms of adverse clinical events during hospital stay and follow-up (Table 7) (Figure 2).

### DISCUSSION

In patients with stable ischemic heart disease and acute coronary syndrome without ST-segment elevation, technical improvements in the design and quality of stents in recent years (improved crossing profile, deliverability, and drug release systems) mean that they can be used without predilatation in increasingly complex lesions. The objective of the present study was to determine the percentage of patients who could be treated with this technique and to study the factors influencing the use of DS during primary angioplasty in conditions of usual clinical practice in a catheterization laboratory.

The results show that the culprit lesion could be treated with DS in 56% of patients receiving primary angioplasty, with a success rate of 98%. There was no increase in the
number of acute complications, need for overdilatation, or use of additional stents when compared with patients in which predilatation was used.

The most common motive for predilatation was the impossibility of defining the lesion (TIMI flow 0) after traversing it with a guide-wire (92%). In the remaining cases, predilatation was used because of calcification, tortuosity, or major bifurcation. The major limitation on the use of DS in primary angioplasty therefore appears to be the presence of a thrombus which prevents adequate stent selection, rather than anatomical factors.

In this series, the best predictors of the use of DS were short postinfarction delay, non-zero initial TIMI flow, and the presence of preinfarction angina. In the first case, a short postinfarction delay might lead to poorer organization of the thrombus and increase the likelihood of fragmentation when the lesion is traversed with the guide-wire. This in turn would provide sufficient TIMI flow to limit the length and diameter required for the implanted stent. Preinfarction angina, on the other hand, has been associated with a lower reperfusion time after fibrinolysis, possibly because occlusive thrombus formation in patients with prior episodes of angina is a dynamic process, with repeated episodes of occlusion and reperfusion giving the thrombus a multi-layered, heterogeneous structure which may be less resistant to fibrinolytic agents and the passage of the guide-wire. This in turn would facilitate direct stent implantation.

Nevertheless, we had insufficient data to be able to confirm this hypothesis.
Epicardial and Myocardial Reperfusion and Clinical Evolution

Reperfusion of the epicardial vessel, assessed using the TIMI flow grade and the cTFC, has been associated with improvements in ventricular function and increased survival.11-14 In the present study, the percentage of patients with a final TIMI grade 3 flow was higher in the DS group although, as in earlier studies, the quantitative analysis of epicardial flow using cTFC values showed no statistically significant differences between the study groups.11,15

In revascularized patients with AMI, myocardial perfusion may be insufficient even when reperfusion of the culprit artery is achieved. Insufficient myocardial perfusion can have several causes, including spasm, local edema, damage from leucocyte activation and liberation of oxygen-free radicals, as well as macro- and microembolization of ruptured plaque and, particularly, thrombus.6,7,15

It has been suggested that direct stent implantation is of greatest use when thrombus is present, as the reduction in the number of inflations decreases the likelihood of thrombus break-up and subsequent distal embolization.6 At least 3 earlier studies have examined the use of DS in primary angioplasty; 2 of these (including one randomized study in patients who had received prehospital fibrinolysis)6,7 reported a reduction in cases of no-reflow and distal embolization in patients treated with DS. However, another randomized study found no statistically significant differences between patients receiving direct stent and those who were stented after balloon predilatation.11 In our study, all cases of no-reflow and distal embolization occurred in the balloon predilatation group. Angiographic and electrocardiographic indices of myocardial reperfusion were also analyzed in the DISCO 3 study. The TMPG provides an angiographic index of the degree of microvascular permeability achieved, whilst ST-segment resolution is a validated method for assessing myocardial reperfusion, as it indicates the degree of functional recovery of the myocyte. Both have been shown to be associated with infarct size and mortality.8,11,16,17 In the present study, both the percentage of patients with TMPG 2-3 and those with >70% resolution of the ST-segment elevation were higher in the DS group (83.5% vs 68.9%, and 65.5% vs 42%, respectively), indicating better tissue reperfusion on both measures. Patients in the DS group also had lower enzyme elevation and better systolic ventricular function. In the SP group, the mean postinfarction delay was longer and there was a higher proportion of patients with initial TIMI flow 0. Both of these can produce poorer myocardial perfusion as well as episodes of no-reflow and/or distal embolization and can therefore lead to an increase in the size of the infarction. However, in the multivariate analysis performed to control for this effect, as well as for other variables which could impact on myocardial perfusion, use of DS remained an independent predictor of myocardial reperfusion.

There were no significant differences in adverse clinical events (death, re-infarction and revascularization due to ischemia of the culprit vessel) between the 2 study groups during hospital stay and at 6 months follow-up. An earlier study suggested that DS might be associated with higher rates of intrastent restenosis and additional revascularization15; however, we found no differences in the need for additional revascularization between groups during follow-up.

Limitations

The study’s principal limitation with regard to the results on reperfusion was that patients were not randomized to the 2 study groups. Patients stented after predilatation had longer postinfarction delays and poorer coronary flow at the start of the procedure, and after traversing the lesion with the guide-wire, and both of these factors may be correlated with the reperfusion grade achieved and the final size of the infarct. Although multivariate analysis was performed to control for possible confounding variables, the results of the present study should still be treated with caution.

CONCLUSIONS

The use of DS in the treatment of AMI of less than 12 h evolution is feasible in over 50% of cases, as long as calcification and/or tortuosity are not present and as long as it is possible to achieve a minimal flow after traversing with the guide-wire, so that the lesion’s characteristics can be defined. The main predictors of DS are short postinfarction delay, non-zero initial TIMI flow, and angina in the 24 h prior to the infarction.

DISCO 3 STUDY INVESTIGATORS

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