PROCEDURAL CHARACTERISTICS OF PRIMARY CORONARY ANGIOPLASTY IN DIABETIC PATIENTS WITH ACUTE ANTERIOR MYOCARDIAL INFARCTION

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SUMMARY - Background: Mortality and morbidity rates are higher in diabetics compared to non-diabetics after acute myocardial infarction (AMI). Previous angiographic studies regarding primary angioplasty for the treatment of AMI found that angioplasty was similarly successful in diabetics and non-diabetics. However, it is noteworthy that patients of "real life" are often far from the population randomised in prospective protocols. The aim of this study was to examine the procedural characteristics of consecutive diabetic patients hospitalised for anterior AMI and treated with primary angioplasty as compared to non-diabetics.

Method: We analysed 28 consecutive diabetics and 74 non-diabetics who underwent primary angioplasty for anterior AMI (<12 h from the onset of symptoms) during 15 consecutive months between 2000 and 2001 in our institution, depending on the presence or absence of diabetes.

Results: Among analysed data, we found that in diabetics compared to non diabetics: (i) the delay before arrival in the cath-lab was significantly longer (5.5 ± 2.7 vs 4.2 ± 2.8 h); (ii) there was a less important collateral flow coming from the non-culprit arteries towards the culprit artery; (iii) there was a less important rate of recovery of a normal flow (TIMI 3) in the culprit artery after coronary angioplasty (67% vs 91%).

Conclusion: Our study demonstrates that several procedural characteristics could explain the poorer prognosis of AMI treated by primary angioplasty in the diabetic population. The longer delay found in diabetics before arrival in hospital could probably be improved.

Key-words: diabetes mellitus, acute myocardial infarction, collateral circulation, coronary angiography, coronary angioplasty.

RÉSUMÉ - Particularités de l'angioplastie primaire pour infarctus antérieur aigu chez les diabétiques.

Contexte: La mortalité et la morbidité de l'infarctus aigu du myocarde est plus élevée chez les diabétiques comparés aux non diabétiques. Des études angiographiques ont montré que l'angioplastie primaire était aussi efficace chez les diabétiques que chez les non diabétiques. Toutefois, il est bien admis que les patients que nous prenons quotidiennement en charge sont différents de ceux qui sont randomisés dans les grandes études. Le but de notre étude est de comparer les caractéristiques procédurales de l'angioplastie primaire pour infarctus antérieur chez les diabétiques et les non diabétiques.

Méthode: Nous avons analysé 28 diabétiques et 74 non diabétiques consécutifs hospitalisés pour angioplastie primaire pour infarctus antérieur aigu (<12 h après le début des symptômes) pendant 15 mois consécutifs entre 2000 et 2001.

Résultats: Les caractéristiques suivantes ont été retrouvées chez les diabétiques comparés aux non diabétiques: (i) le délai avant l’arrivée en salle de cathétérisme est significativement plus élevé chez les diabétiques (5,5 ± 2,7 vs 4,2 ± 2,8 h respectivement); (ii) il y a moins de collatérales provenant des autres artères coronaires vers l’artère coronaire occluse chez les diabétiques; (iii) l’obtention d’un flux normal (TIMI 3) en fin de procédure est moins fréquent chez les diabétiques comparé aux non diabétiques après angioplastie (67 % vs 91 % respectivement).

Conclusion: Notre étude démontre qu’un certain nombre de caractéristiques procédurales peuvent expliquer le moins bon pronostic des diabétiques comparé aux non diabétiques après angioplastie. Le plus long délai qui est retrouvé chez les diabétiques avant l’arrivée en salle de cathétérisme lors d’un infarctus aigu pourrait certainement être amélioré.

Mots-clés: diabète, infarctus aigu, circulation collatérale, coronarographie, angioplastie coronaire.

The prevalence of diabetes mellitus is growing exponentially and diabetes is a strong risk factor for cardiovascular disorders, including coronary heart disease [1]. Several studies have demonstrated that patients with diabetes mellitus have higher mortality and morbidity rates than non diabetic patients after acute myocardial infarction (AMI) [1, 2]. Several explanations have been proposed to account for these higher mortality and morbidity rates found in diabetics after AMI, including a more severe coronary artery disease or the presence of a diabetic cardiomyopathy [3].

Previous angiographic studies regarding primary angioplasty for the treatment of AMI found that angioplasty was similarly successful in diabetics and non diabetics [4]. It is noteworthy that patients of “real life” are often far from the population randomised in selective prospective protocols. Moreover, the angiographic and procedural characteristics of diabetic patients treated by primary angioplasty for AMI have never been carefully compared to non diabetics. For example, the presence of less coronary collateral vessels has been previously described in diabetic patients compared to non-diabetic patients with stable or unstable angina [5]. Such a decrease in collateral vessel formation could induce a more severe ischemia in the area of infarction. Unfortunately, the extent of coronary collateral vessel has never been examined in the diabetic population with AMI.

The aim of this study was to examine the procedural characteristics of consecutive diabetic patients compared to non diabetic patients, hospitalised in a single center for acute anterior myocardial infarction treated by primary coronary angioplasty.

■ METHODS

From January 2000 to March 2001, 345 consecutive patients underwent urgent coronary angiography for suspicion of acute myocardial infarction in a single center (Lariboisiere hospital, Paris, France). Inclusion criteria of our study were the presence of an acute anginal chest pain (≤12 h from the beginning of symptoms) associated with ST segment shift in anterior leads at ECG (at least V1 to V3 leads – anterior AMI) with a culprit lesion located on the left anterior descending (LAD) artery and treated with primary angioplasty. Patients were excluded when a thrombolytic therapy was started before the arrival at the hospital, when AMI was not related to a lesion located on the left anterior descending artery, when the coronary flow was normal (TIMI 3) in the culprit artery before angioplasty, when the right coronary artery was not visualized before the beginning of angioplasty and in case of severe heart failure or shock at arrival (Killip score > 2).

Diabetes mellitus was defined as the existence, before admission, of a treatment for diabetes (insulin or oral antidiabetic drugs). Patients with unknown diabetes mellitus and a glucose level > 180 mg/dl at arrival were excluded from the study. Patients with a glucose level between 126 and 180 mg/dl were considered as non diabetics if the level of glycated haemoglobin was normal.

A total of 102 consecutive patients, fulfilling inclusion and exclusion criteria, where analysed. Coronary angiograms were retrospectively and independently reviewed by two experienced observers and the following angiographic data were studied: location of the culprit lesion on the LAD, TIMI flow [6] in the LAD before and after angioplasty (TIMI 0: no flow downstream the culprit lesion – TIMI 1: partial filling of the coronary artery downstream the culprit lesion – TIMI 2: complete but slow filling of the coronary artery downstream the culprit lesion – TIMI 3: complete and normal filling of the coronary artery downstream the culprit lesion), collateral flow towards the culprit artery using the Rentrop score [7] (Rentrop 0: no collateral flow – Rentrop 1: filling of side branches of the culprit artery to be perfused by collateral vessels without visualization of the epicardial segment – Rentrop 2: partial filling of the epicardial culprit artery by collateral vessels – Rentrop 3: complete filling of the epicardial culprit artery by collateral vessels).

Each arterial segment (ACC/AHA classification) was studied and the following data were recorded for each segment: visual stenosis quantification (quantitative coronary assessment in case of significant mismatch between the 2 observers), TIMI flow downstream the lesion. Calcification severity of each segment was also visually estimated (0: no calcification – 1: minor calcification – 2: moderate calcification – 3: massive calcification). Angioplasty technique used (balloon and/or stent diameter and length, inflation pressure), use of GPIIb/IIIa blocker abciximab and post-procedural lesion quantification were also recorded. Abciximab was administered when the angiography demonstrated the presence of a large thrombus in the coronary artery before or during the procedure. Abciximab was also administered in case of no or low-reflow phenomenon. We used a single bolus followed by a 12 h-infusion.

All values were expressed as mean ± SEM or percentage in each group (diabetic and non-diabetic). Comparisons between groups were assessed using Student t-test, comparison of percentages and χ². Statistical significance was defined as a value of P < 0.05.

■ RESULTS

The characteristics of the population are presented on Table I. In the overall population studied, 28 were diabetics and 74 were non diabetics. Diabetics were more often women, more often overweight (BMI > 27 kg/m²) and more than 40% of diabetic patients were treated with insulin. Interestingly, the delay before
arrival in the cath-lab was significantly longer in the diabetic population compared to non diabetic population (5.5 ± 2.7 h vs 4.2 ± 2.8 h, p < 0.05). Peak CPK was lower in diabetics compared to non diabetics. Table II summarises the pre-procedural angiographic characteristics of the population. The location of the culprit lesion on the LAD as the flow in the culprit artery downstream the lesion were similar in diabetics and non diabetics. In diabetic patients, we found more often no collateral vessels (Rentrop 0) towards the culprit artery as compared to non diabetics. This decrease in collaterality was not explained by the degree of the residual flow in the culprit artery, since there was a similar rate of patients with no collaterality and no flow in the culprit artery (Rentrop 0 and TIMI 0) in diabetics compared to non diabetics. This decrease in collateral flow was not explained by the presence of severe lesions on the other arteries from which collateral vessels could be born. The calcification score was higher, even if not significant, in diabetics.

Table III summarises the procedural characteristics and results of the angioplasty procedure. No significant differences were found between diabetics and non diabetics. There was a trend towards more frequent use of abciximab in diabetic patients. However, the rate of recovery of a normal flow (TIMI 3) in the LAD downstream the culprit lesion after the procedure was lower in diabetics compared to non diabetics with a more frequent slow flow (TIMI 2).

**DISCUSSION**

Our results demonstrate that, in our population of diabetics compared to non diabetics: (i) the delay before the arrival in the cath-lab is longer (1.3 h); (ii) the collateral flow towards the culprit artery is decreased; (iii) there is a less important rate of recovery of a normal flow in the culprit artery after coronary angioplasty. The decrease in collateral flow and the
more frequently impaired flow after the angioplasty procedure cannot be explained by anatomical or procedural characteristics. These results could, in part, explain the higher rate of mortality and morbidity rates previously described in diabetics after AMI [2]. The lower peak CPK found in diabetics could appear surprising. However, if the area of CPK under the curve is correlated with the size of necrosis, the peak CPK value is more correlated with the efficacy of reperfusion. Then, this result is concordant with the lower rate of recovery of a normal flow found in diabetics.

It is noteworthy that the delay between the beginning of symptoms and the start of reperfusion therapy is a critical point in the management of AMI. Thus, the longer delay found in diabetics before arrival to hospital could clearly explain the higher incidence of morbidity and mortality rates after AMI in diabetics. Previous studies have demonstrated that the delay before decision to provide medical assistance was longer in diabetics [8]. More recently, Berton et al. [9] found that in case of AMI, the time interval between the onset of symptoms and patient’s arrival to hospital is delayed in older patients with diabetes and in patients with a history of coronary disease or chronic atrial fibrillation. This longer pre-hospital time delay could be explained by the higher frequency of silent or near silent ischemia. The propensity of diabetic patients to present either silent, near silent or unrecognized myocardial infarction is well established [10]. Atypical symptoms such as confusion, dyspnea, fatigue or nausea and vomiting have been found to be the presenting complaints in 32 to 42% of diabetic patients with AMI compared to 6-15% of non diabetic patients [10, 11]. A common explanation for painless infarction in diabetics is autonomic neuropathy. In autopsies of diabetic patients who died of silent myocardial infarction, typical diabetic neuropathic changes were found in the intracardiac sympathetic and parasympathetic fibers [12]. Moreover, the anginal perception threshold, the time from the onset of myocardial ischemia is prolonged in diabetic patients compared to non diabetics. Whatever the reasons, the time interval between the onset of symptoms and a patient’s arrival to hospital is far from being optimal in diabetic patients and then need to be optimised possibly by a more careful educational action on patients and/or physicians.

AMI is responsible for 30% of deaths in the diabetic population. Before thrombolytic era, mortality rate was as high as 30 to 40% after 1 month compared to less than 20% in the non diabetic population and higher in women compared to men [13]. Thrombolytic treatment has markedly decreased mortality in diabetic and non diabetic patients [14]. However, despite a large use of thrombolytic therapy in this population, mortality and morbidity rates remain significantly higher in the diabetic population [14]. In the GUSTO I trial [3], a study which aim was to compare two thrombolytic treatments in AMI, 14.5% of patients were diabetics. In this study, diabetic patients compared to non diabetics were older, more often women, had more frequently an history of vascular disease, a location of AMI in the anterior wall, heart failure and thrombolysis was started later. All these characteristics make the diabetic group more at risk of morbidity and mortality. After 30 days, mortality was 10.5% in diabetic patients compared to 6.2% in non diabetics. Previous studies regarding primary coronary angioplasty in diabetic patients found that primary angioplasty was similarly successful in diabetics and non diabetics and appears to be more effective than thrombolytic therapy among diabetics with AMI [4]. Despite more severe stenosis and poorer flow in the culprit artery, procedural success (residual stenosis < 50% and TIMI 3 flow) after angioplasty was similar in diabetics compared to non diabetics. However, in this study, 70.4% of diabetics had a procedural success and 72.4% in non diabetics. The rate of procedural success was similar to this study in our diabetic population but was clearly higher in the non diabetic population and similar to that found in recent studies [15]. This discrepancy could be explained by a better result of primary coronary angioplasty in non diabetic pa-

### Table III. Procedural angiographic characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>No Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent use (%)</td>
<td>81</td>
<td>72</td>
</tr>
<tr>
<td>Stenting length (mm)</td>
<td>18.6 ± 6.6</td>
<td>18.9 ± 7.2</td>
</tr>
<tr>
<td>Stent diameter (mm)</td>
<td>3.06 ± 0.26</td>
<td>3.19 ± 0.3</td>
</tr>
<tr>
<td>Number of stent</td>
<td>1.25 ± 0.4</td>
<td>1.19 ± 0.45</td>
</tr>
<tr>
<td>Maximal pressure inflation (mmHg)</td>
<td>10.7 ± 2.7</td>
<td>11.4 ± 2.5</td>
</tr>
<tr>
<td>Abciximab use (%)</td>
<td>50</td>
<td>34</td>
</tr>
<tr>
<td>End of the procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI Flow (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI 3</td>
<td>67</td>
<td>91</td>
</tr>
<tr>
<td>TIMI 2</td>
<td>22</td>
<td>*</td>
</tr>
<tr>
<td>TIMI 0 or TIMI 1</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Residual stenosis &gt;50 % on the culprit lesion (%)</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>TIMI 0 or 1 and residual stenosis &gt; 50 % (%)</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SEM or percentage (%) in each group. * p < 0.05 in Diabetic group compared to non diabetic group.
tients, may be related to a larger use of stents and abciximab. However, the diabetics remain with a lower procedural success rate. We have no clear explanations for the lower successful procedural rate found in diabetics of our study. We can hypothesize that the longer delay before arrival and/or the presence of severe coagulation and platelet dysfunction could explain this difference.

The magnitude of coronary collateral flow is one of the principal determinant of infarct size [16]. A decrease in coronary collateral formation has been described previously in diabetic patients with stable and unstable angina [5]. We found similar results regarding our population of acute anterior myocardial infarction. Such a decrease in collateral vessel could participate to a more profound ischemia in the area at risk and then a more important infarct size. The mechanisms leading to such a decrease in coronary collateral flow in diabetics compared to non diabetics remain unclear. There has been increasing interest in the literature in the functional impact of diabetes mellitus on coronary vascular function. It has been demonstrated that elevated glucose level causes endothelial cell dysfunction [17]. Because the function of the endothelium is important in collateral development, endothelial dysfunction could explain the decrease in collaterals found in diabetic patients.

Study limitations

There are several limitations to these study. First, only anterior myocardial infarction with an impaired TIMI flow on the culprit artery were analysed. Our results cannot be extrapolated to all AMI. However, anterior myocardial infarction is much more frequently complicated by heart failure or cardiogenic shock than inferior or lateral locations. The restriction of our analysis to anterior myocardial infarction could lead to a better understanding in the determinants of complicated AMI and to accurately compare diabetics to non diabetics. Second, visible angiographic collaterals represent only a fraction of the total collateral vessels. Moreover, angiography may not detect most collaterals located intramurally. Therefore, the collaterals visualized by angiography may not accurately quantify collateral circulation. However, this limitation is similar in the diabetic and non diabetic groups. We cannot exclude that the decrease in collateral flow found in our diabetic patients could be due to the longer delay before reperfusion, compared to non diabetics. However, it is noteworthy that collateral flow increase with time when a coronary artery is occluded and reverse in case of reperfusion. Third, we do not present results regarding mortality. However, we found that, taking account of the relative low number of patients of this study, the statistical power will be too low to make accurate comparisons concerning mortality. Fourth, this study is a retrospective study.

However, the angiographic and clinical data belong to the same period and concern consecutive patients.

CONCLUSION

Our study demonstrates that, in our population of diabetics compared to non diabetics treated by primary coronary angioplasty for AMI, several procedural characteristics can explain the poorer prognosis previously described in diabetics: (i) the delay before the arrival in the cath-lab is longer; (ii) the collateral flow toward the culprit artery is decreased; (iii) there is a less important rate of recovery of a normal flow in the culprit artery after coronary angioplasty. A more careful educational action on patients and/or physicians could probably decrease the delay before arrival in the cath-lab. Moreover, we can hypothesize that a more systematic use of GP IIb/IIa blockers and direct stenting or future pharmacological approaches could be proposed in diabetics in order to finally obtain, more frequently, a normal flow at the end of the procedure.

REFERENCES

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