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Original article

Coronary in-stent restenosis in diabetic patients after implantation of sirolimus or paclitaxel drug-eluting coronary stents

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Abstract

It is now emerging that, in patients who are at high risk for cardiovascular complications and, in particular, those with diabetes, the occurrence of late restenosis and thrombosis after treatment of coronary artery disease with drug-eluting stents is higher than earlier reports have suggested.

Therefore, the aim of this study was to assess the prevalence of in-stent restenosis in a cohort of consecutive patients with diabetes treated for coronary disease in 2005 with drug-eluting stents [either sirolimus (58%) or paclitaxel (42%)]. The duration of follow-up was 9.0 ± 3.4 months [mean ± 1 standard deviation (S.D.)]. A total of 154 patients (type 2 diabetes: 91%) were included in the study (age: 66 ± 10 years), and the total number of implanted stents was 184. Two subjects died from cardiac causes, while myocardial infarction and (un)stable angina were observed in 3 (2%) and 39 (25%) patients, respectively. In-stent restenosis, appraised by angiography, was observed in 17 individuals (11%) after a mean follow-up of five months. Mean HbA_{1c} in patients with restenosis was 7.6 ± 1.8%. There was no difference in the rate of restenosis with sirolimus – ($n = 8$) compared with paclitaxel – ($n = 9$) eluting stents. Male gender, oral therapy for diabetes and stent diameter were predictors of in-stent restenosis.

In conclusion, even over a medium-term period, in-stent restenosis remains a potential risk for coronary diabetic patients treated with drug-eluting devices.

Résumé

Resténoses coronaires après stents actifs (sirolimus ou paclitaxel) dans un groupe de diabétiques.

Les resténoses tardives et thromboses, après mise en place de stents à élution médicamenteuse chez des patients coronariens à haut risque cardiovasculaire, en particulier diabétiques, semblent être des complications plus fréquentes que les données de la littérature médicale ne le suggéraient initialement.

Le but de notre étude a été d'analyser la fréquence des resténoses intra-stent dans une cohorte de patients diabétiques chez lesquels un stent à élution médicamenteuse (sirolimus [58 %] ou paclitaxel [42 %]) avait été mis en place en 2005 (durée du suivi : 9,0 ± 3,4 mois ; moyenne ± 1 S.D.). Cent cinquante quatre patients, dont une majorité de diabétiques de type 2 (91 %), ont été inclus (âge : 66 ± 10 ans). Le nombre de stents implantés a été de 184. Au cours du suivi, deux patients sont décédés de cause cardiovasculaire. Un infarctus du myocarde ou une récidive d'angor a été observé chez trois (2 %) et 39 sujets (25 %) respectivement. Une resténose intra-stent a été constatée sur base d'une angiographie chez 17 malades (11 %), après un délai moyen de 5,0 mois. Le taux d'HbA_{1c}, en cas de resténose, était de 7,6 ± 1,8 %. Il n'y avait pas de différence significative de fréquence de resténose en fonction du type de stent implanté (sirolimus : $n = 8$; paclitaxel : $n = 9$). Le sexe masculin, un traitement oral du diabète ainsi que le diamètre du stent ont été des facteurs prédictifs de resténose.

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En conclusion, même à moyen terme, la resténose reste un risque potentiel chez des diabétiques coronariens traités par stents à élution de médicament.

Keywords: Cardiovascular disease; Drug-eluting stents; Restenosis; Diabetes; Predictors

Mots clés : Maladie cardiovasculaire ; Stent à élution médicamenteuse ; Resténose ; Diabète sucré ; Facteurs prédictifs

1. Introduction

Both type 1 and 2 diabetes mellitus subjects have a two- to fourfold increased cardiovascular risk when compared with the general population. Moreover, coronary artery disease (CAD) accounts for up to 75% of all-cause mortality in diabetic patients, with myocardial infarction involved in up to 30% of all deaths [1–4]. The typically diffuse pattern of coronary artery atheroma observed in diabetes makes revascularization technically difficult and a satisfactory outcome less clear-cut than in non-diabetic individuals [5–7]. The use of bare-metal coronary-artery stents during percutaneous intervention has clearly decreased the incidence of acute complications and improved patients short-term outcome [8–10]. While within-stent restenosis is likely to compromise any positive long-term benefits [6,7,11], on a relatively short-term basis, sirolimus- or paclitaxel-eluting stent implantation markedly reduces in-stent restenosis compared with bare-metal stents [12–18]. It is, however, emerging that the rates of late-occurrence restenosis and thrombosis, despite drug-eluting stent use, are higher than those initially reported, particularly in patients who are at high risk of cardiovascular complications [19–21]. Recent data have even questioned the long-term safety of drug-eluting stents in patients with diabetes, as indicated by Spaulding et al. [22].

Therefore, the aims of this study were to assess the incidence of in-stent restenosis over a medium-term follow-up period in a cohort of all consecutive patients with diabetes treated for coronary disease with drug-eluting stents (either sirolimus or paclitaxel) in the year 2005, as well as to identify predictors of restenosis.

2. Patients and methods

This retrospective study included all diabetic patients (type 1 and 2 diabetes) in whom percutaneous coronary intervention and implantation of drug-eluting stents were performed, according to standard techniques, between 1 January 2005 and 31 December 2005. The primary study endpoint was the demonstration of in-stent angiographic restenosis, defined as within-segment restenosis greater or equal to 50% during the follow-up interval. Secondary endpoints were number of deaths, as well as any other major cardiovascular events occurring during the follow-up period.

Considered for inclusion were 160 patients admitted to the Department of Cardiology of Saint-Luc Academic Hospital. Six subjects were excluded due to incomplete data files. Only patients with known diabetes were included. Their baseline clinical characteristics, as well as their cardiovascular risk factors, are indicated in Table 1. Type 2 diabetes was present in 91% of individuals. Table 2 shows the baseline angiographic characteristics of the study population. Initial angiography followed by implantation of drug-eluting stents was primarily performed in the aftermath of myocardial infarction ($n = 75$), stable ($n = 34$) or unstable angina ($n = 31$), or silent ischaemia ($n = 14$), after confirmation of clinically significant stenosis. Implantation of sirolimus- (Cypher, Cordis, Johnson & Johnson) or paclitaxel- (Taxus, Boston Scientific) eluting stents was considered successful at discharge in all cases. In 30 patients, more than one

Table 1
Baseline characteristics of the patients

n	154
Age (years)	66 ± 10[a]
M/F (%)	79/21
BMI (kg/m^2)	29 ± 5
Type 2 diabetes (%)	91
Cardiovascular risk factors (other than diabetes) (%)	
Arterial hypertension	83
Current smoking	32
Dyslipidemia	70
Positive familial history	43
Personal history of coronary artery disease	55
Personal history of PTCA, stenting or CABG	38
Heart failure	4
Antihyperglycaemic treatment (%)	
Diet alone	2
Insulin sensitizers[b] (1)	22
Insulin secretagogues (2)	23
(1) + (2)	15
Insulin	33
Insulin + [1 and/or 2]	5
HbA_{1c}	7.7 ± 1.5
Plasma creatinine > 1.2 mg/dl	30

M: male; F: female; BMI: body mass index; PTCA: percutaneous transluminal coronary angioplasty; CABG: coronary artery bypass grafting.
[a] Values are means ± 1 S.D.
[b] Metformin.

Table 2
Baseline angiographic findings

Coronary artery disease	*n* (%)
Single-vessel disease	54 (35)
Two-vessel disease	58 (38)
≥ three-vessel disease	42 (27)
Vessels affected	***n* (%)**
Main left coronary	18 (12)
Left anterior descending	114 (74)
Left circumflex	82 (53)
Right coronary	97 (63)
Multivessel disease	100 (65)