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Four-year results after brachytherapy for diffuse coronary in-stent restenosis: will coronary radiation therapy survive?

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Abstract

Background: Prior to the introduction of drug-eluting stents (DES), diffuse coronary in-stent restenosis (ISR) was mainly treated by brachytherapy (BT), with good short-term and mid-term results. However, there exist limited data on the long-term effects of BT that justify its continuous use.

Materials and methods: Two hundred patients with diffuse ISR treated with intravascular BT were retrospectively followed over 4 years. Group A (n=134) was treated with the noncentered ^{90}Sr/Y BetaCath radiation system, whereas Group B (n=66) was treated with the centered ^{32}P Galileo source wire system. Primary endpoints after 4 years were target lesion restenosis (TLS) and target lesion revascularization (TLR). Secondary endpoints were target vessel revascularization (TVR) and nontarget vessel revascularization (NTVR), as well as major adverse cardiac events (MACE).

Results: Follow-up at 4 years yielded a TLS rate of 37.6% (Group A, 40.8%; Group B, 31.1%; P=.48). TLR was performed in 34.8% of patients (37.5% in Group A vs. 29.5% in Group B; P=.55). Ten percent of patients underwent coronary bypass surgery. Percutaneous coronary intervention was performed more often in Group A (27.5%) than in Group B (19.7%), while TVR was less frequent in Group A (10.0%) than in Group B (18.0%). NTVR was undertaken in 25.0% of Group A patients versus 21.3% of Group B patients, and MACE occurred in 1.7% of Group A patients versus 3.3% of Group B patients. These differences were not statistically significant (P>.05).

Conclusions: While excellent short-term and mid-term results after coronary BT are widely accepted, a high TLS rate can be observed after 4 years. The potential superiority of DES to BT will depend on the availability of long-term clinical data.

Keywords: In-stent restenosis; Coronary brachytherapy; Reintervention; Drug-eluting stents

1. Introduction

Until recently, coronary brachytherapy (BT) was considered the most effective approach for the treatment of in-stent restenosis (ISR). This was based on the favorable results of BT over those of percutaneous coronary intervention (PCI) using bare metal stents [1–3]. However, both the recent SISR trial and the TAXUS V ISR trial suggest the potential superiority of drug-eluting stents (DES) to BT for the treatment of ISR [4,5]. While the benefit of DES for de novo stenoses is well documented, it now appears that DES also might be the best treatment for ISR. However, only short-term data are available. Even for the well-established approach of intracoronary BT, there exist only limited data on long-term clinical and angiographic outcomes. In order to evaluate the potential of BT in its struggle for existence, we analyzed the clinical results of BT for ISR over 4 years.

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2. Materials and methods

2.1. Study population

From October 2000 to April 2002, a total of 200 patients with diffuse coronary ISR were treated with repeat PCI and BT at our institution. Diffuse ISR was defined as a visually determined stenosis that was >50% in diameter and >10 mm in length, and was associated with clinical symptoms and/or objective evidence of myocardial ischemia.

2.2. PCI with BT and medical therapy

All procedures, including radiation protocol and dosimetry, were performed as described previously [6]. Patients in Group A (n=134) were treated with the noncentered BetaCath radiation system (Novoste, Narcross, USA), with an ^{90}Sr/Y source in a closed noncentered coronary catheter [7]. Patients in Group B (n=66) were treated with the centered Galileo source wire β-radiation system (Guidant, Indianapolis, USA), with a ^{32}P source in a closed spiral-shaped coronary centering balloon catheter [8]. All patients received dual platelet inhibition with clopidogrel and aspirin for 12 months followed by aspirin alone (100 mg/day), together with angiotensin-converting enzyme inhibitors, statins, and β-blockers.

2.3. Study endpoints

The primary study endpoints were target lesion restenosis (TLS) and target lesion revascularization (TLR) at 4 years. TLR was defined as repeat revascularization driven by symptoms or by noninvasive testing, with PCI or bypass surgery, of a stenosis >50% of the previously treated lesion. Secondary endpoints were target vessel revascularization (TVR) and nontarget vessel revascularization (NTVR), as well as major adverse cardiac events (MACE) at 4 years. MACE included myocardial infarction and cardiac death. Clinical follow-up 4 years after BT was performed by either a review of hospital records (including coronary angiography findings) or a telephone interview with the patient or the referring physician.

Table 1
Baseline and angiographic characteristics

	Total (N=200)	Group A (BetaCath) (n=134)	Group B (Galileo) (n=66)	P
Age [mean (S.D.)]	67.2 (10.4)	67.5 (10.9)	66.6 (9.3)	.54
Male [n (%)]	164 (82.0)	113 (84.3)	51 (77.3)	.78
Diabetes [n (%)]	43 (21.5)	28 (20.9)	15 (22.7)	.95
Prior CABG [n (%)]	43 (21.5)	26 (19.4)	17 (25.8)	.53
Location of lesion [n (%)]				
Left descending coronary artery	74 (37.0)	47 (35.1)	27 (40.9)	.69
Left circumflex coronary artery	36 (18.0)	26 (19.4)	10 (15.2)	.67
Right coronary artery	70 (35.0)	50 (37.3)	20 (30.3)	.59
Left main coronary artery	3 (1.5)	2 (1.5)	1 (1.5)	.54
Saphenous vein graft	19 (9.5)	11 (8.2)	8 (12.1)	.58

Table 2
Follow-up data at 4 years: primary endpoints

	Total	Group A (BetaCath)	Group B (Galileo)	P
Original patients [n (%)]	200 (100)	134 (100)	66 (100)	
Patients lost to follow up [n (%)]	12 (6.0)	7 (5.2)	5 (7.6)	.76
Death (noncardiac) [n (%)]	7 (3.5)	7 (5.2)	0 (0.0)	.15
Patients remaining in the study [n (%)]	181 (100)	120 (100)	61 (100)	
Primary endpoints [n (%)]				
TLS	68 (37.6)	49 (40.8)	19 (31.1)	.48
Conservative treatment	5 (2.8)	4 (3.3)	1 (1.6)	.87
TLR	63 (34.8)	45 (37.5)	18 (29.5)	.55
CABG	18 (9.9)	12 (10.0)	6 (9.8)	.82
PCI	45 (24.9)	33 (27.5)	12 (19.7)	.47
Balloon only	34 (18.9)	27 (22.5)	7 (11.5)	.19
Cutting balloon	2 (1.1)	1 (0.8)	1 (1.6)	.79
Bare metal stent	5 (2.8)	3 (2.5)	2 (3.3)	.85
DES	4 (2.2)	2 (1.7)	2 (3.3)	.88
Repeat PCI (>1)	10 (5.5)	8 (6.7)	2 (3.3)	.58

2.4. Statistical analysis

Binary variables are presented as rates, and continuous variables are presented as mean±S.D. Binary variables were compared by chi-square analysis. The frequency of TLR-free survival was calculated by the Kaplan–Meier method. Statistical significance was accepted with P<.05.

3. Results

Out of 200 patients with diffuse ISR, 134 were treated with the BetaCath system (Group A) and 66 were treated with the Galileo system (Group B). Patient baseline and angiographic characteristics were similar in both treatment groups and are listed in Table 1. Diabetes mellitus was present in 21.5% of patients, and 21.5% had prior coronary artery bypass grafting (CABG). No lesion-specific differences were detected as described previously [6].

Table 3
Follow-up data at 4 years: secondary endpoints

	Total	Group A (BetaCath)	Group B (Galileo)	P
Patients remaining in the study [n (%)]	181 (100)	120 (100)	61 (100)	
Secondary endpoints [n (%)]				
TVR	23 (12.7)	12 (10.0)	11 (18.0)	.27
NTVR	43 (23.8)	30 (25.0)	13 (21.3)	.80
MACE				
Myocardial infarction	6 (3.3)	4 (3.3)	2 (3.3)	.67
Cardiac death[a]	4 (2.2)	2 (1.7)	2 (3.3)	.88

[a] Cardiac death unrelated to target lesion.