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Is postoperative calcium channel blocker therapy needed in patients with radial artery grafts?

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Background: Chronic calcium channel blocker therapy has traditionally been considered necessary in patients carrying a radial artery graft, even in the absence of objective data to support it. This report was conceived to evaluate the angiographic and clinical effects of calcium channel blocker therapy during the first postoperative year.

Patients and Results: A total of 100 consecutive patients who received a radial artery graft at our institution were randomly assigned to receive (n = 53) or not receive (n = 47) calcium channel blocker therapy with oral diltiazem 120 mg/daily started in the early postoperative period. At 1-year follow-up, all patients were reassessed clinically and by Tl^{201} myocardial scintigraphy, and 83 of them underwent control angiography. In 12 cases we also evaluated the response of the radial artery to the endovascular infusion of serotonin. No difference in terms of clinical outcome, scintigraphic results, and patency rate was found between patients who received or did not receive calcium channel blocker therapy. Endovascular serotonin infusion evoked an evident spastic reaction of radial artery grafts, not attenuated by calcium channel blocker therapy.

Conclusion: Calcium channel blocker therapy started immediately after surgery and continued for the first postoperative year does not affect radial artery graft patency and clinical and scintigraphic outcomes. On the basis of these data, the prophylactic use of calcium channel blocker therapy in patients with radial artery grafts seems unsubstantiated.

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Since the reintroduction of radial artery (RA) grafts in coronary surgery in the mid-1990s, a chronic antispastic therapy (usually using calcium channel blockers) has traditionally been considered necessary.

However, to date only scant objective data on the optimum duration of postoperative chronic calcium channel blocker therapy (CCBT) have been published, so the modalities of the antispastic therapy are actually empirically established by the single centers.

In a previous study we showed that beyond the first postoperative year CCBT does not ensure substantial advantages in terms of both clinical results and RA graft patency.[1] However, concerns still exist about the role of CCBT in the initial period after surgery, when the spastic tendency of the RA is thought to be maximal.[2]

This report was conceived to evaluate the angiographic and clinical effects of CCBT during the first postoperative year.

TABLE 1. Preoperative characteristics of patients of the two groups

	CCBT group	No-CCBT group	*P* value
No. of cases	53	47	—
Mean age (y)	63.8 ± 4.6	63.2 ± 3.5	.46
Male/female	38/15	32/15	.86
Cardiac risk factors			
Diabetes	11	10	.89
Smoking	23	21	.94
Dyslipidemia	19	22	.36
Hypertension	12	10	.93
Previous myocardial infarction	29	25	.96
Three-vessel disease	41	39	.65
Left-main disease	2	1	1.00*
Radial artery target vessel			
OM	25	21	.96
PDA	15	13	.65
RCA	11	12	.74
Diag	2	1	1.00*

CCBT, Calcium channel blocker therapy; *Diag,* diagonal branch; *OM,* obtuse marginal branch; *PDA,* posterior descending artery; *RCA,* right coronary artery.
*Two-tailed exact Fisher *t* test.

TABLE 2. One-year clinical and scintigraphic results in the two groups of patients

	CCBT group	No-CCBT group	*P* value
No. of cases	53	47	—
Mean follow-up (mo)	11.8 ± 0.5	11.9 ± 0.3	.23
Death	0	0	—
Angina recurrence	1	0	1.00*
Scintigraphic evidence of residual ischemia	2	1	1.00*
RA-related residual ischemia	1	0	1.00*

RA, Radial artery; *CCBT,* calcium channel blocker therapy.
*Two-tailed exact Fisher *t* test.

Methods

Patient Population

Our experience with RA grafting started in January 1993; since the beginning of our series, the antispastic therapy consisted of oral diltiazem (120 mg/daily) started in the early postoperative period.[3]

The early, midterm, and long-term clinical and angiographic results, as well as the early and midterm alterations of the forearm circulation and the midterm vasodilatory profile of the RA grafts, have been the object of previous publications.[1-7]

The present report is intended to describe the clinical and angiographic effect of CCBT in the first postoperative year.

For this purpose, 100 consecutive patients who received an RA graft at our institution between January 2000 and March 2001 were randomly assigned to receive (n = 53) or not receive (n = 47) CCBT started in the early postoperative period.

In patients assigned to receive CCBT, oral diltiazem (120 mg/daily) was started the day of extubation (the first postoperative day in 49 cases and the following day in the remaining cases); no intravenous diltiazem was used in this series. Patients assigned to the no-CCBT group did not receive CCBT in any form during the hospital stay and follow-up period.

Follow-up

After 6 months and 1 year all cases were submitted to clinical and scintigraphic control; 83 of them (42 from the CCBT group and 41 from the no-CCBT group) also agreed to be submitted to 1-year angiographic control.

Graft morphology was graded according to the 4 grades scale in use at our institution[2,7]: perfectly patent graft, patent graft with irregularities, stringed graft, and occluded graft.

All angiograms were reviewed blindly by 2 expert observers. In case of disagreement, a third external blinded review was requested.

Moreover, to verify the effect of CCBT therapy on the spastic attitude of the RA grafts, we evaluated the response of the RA to the endovascular infusion of serotonin in 12 patients submitted to angiography after a previously described method.[6]

Serotonin hydrochloride 10^{-5} mol/L (ICN Pharmaceuticals Inc, Costa Mesa, Calif) was selectively injected into the graft at a rate of 3 mL/min for 3 minutes; at the end of the serotonin challenge 2 mg of isosorbide dinitrate were injected into the conduit.

Drug infusion was always performed under electrocardiography and invasive blood pressure monitoring.

At the end of each step of the protocol a cine run was performed, keeping a fixed angiographic view.

Digital angiograms were then analyzed using computerized quantitative angiography (Medis, Neuen, The Netherlands).

Statistical Analysis

Results are expressed as mean value ± SD. Statistical analysis comparing 2 groups was performed with parametric or nonparametric tests for independent samples (Student *t* test and Mann-Whitney *U* test for continuous or ordinal data, respectively), whereas χ^2 or 2-tailed Fisher exact tests were used to compare nominal data of the 2 groups. Yates correction was applied when required (Statistical Package for the Social Science Program, SPSS Inc, Chicago, Ill).

Results

The mean preoperative clinical and angiographic characteristics of patients of the 2 groups are summarized in Table 1; the 2 groups were similar with regard to all the examined variables.

Follow-up was 100% complete, and mean follow-up time was 11.8 ± 0.5 months for patients who received CCBT and 11.9 ± 0.3 for patients who did not receive CCBT ($P = .23$).

No patients died during the follow-up. As depicted in Table 2, symptomatic angina was reported by only 1 patient

TABLE 3. One-year angiographic results in the two groups of patients

	CCBT group	No-CCBT group	*P* value
No. of cases	42	41	—
Perfect RA	40	40	1.00*
Stringed RA	1	0	1.00*
Irregular RA	1	0	1.00*
Occluded RA	0	1	1.00*

RA, Radial artery; *CCBT,* calcium channel blocker therapy.
*Two-tailed exact Fisher *t* test.

TABLE 4. One-year radial artery response to endovascular serotonin infusion in the two groups of patients

	Continued group	Suspended group	*P* value
No. of cases	6	6	—
Baseline RA diameter (mm)	2.10 ± 0.10	2.11 ± 0.10	.86
RA diameter after serotonin (mm)	1.69 ± 0.32	1.70 ± 0.31	.95
Mean diameter reduction (mm)	0.41 ± 0.22	0.41 ± 0.21	.99

RA, Radial artery.

(in the CCBT group; $P = .95$). One-year myocardial scintigraphy demonstrated inducible ischemia in 3 cases including the symptomatic one; 2 of these cases were from the CCBT series, and 1 was from the control group ($P = .91$). All of the patients with angina or scintigraphic evidence of ischemia recurrence were submitted to re-angiography; in only 1 case (from the CCBT group; $P = .95$) an RA malfunction (anastomotic stenosis) was the cause for the ischemia recurrence.

One-year angiography was performed in 83 patients (42 of the CCBT group and 41 of the no-CCBT group). The angiographic results are summarized in Table 3. No differences in terms of both patency and perfect patency rates were found between patients who received or did not receive CCBT.

Endovascular serotonin infusion evoked an evident spastic reaction of RA grafts, not significantly attenuated by CCBT (Table 4).

Discussion

Since the early day of its reintroduction in coronary surgery, the RA propensity for vasospasm has been worrisome.

In fact, in contrast with almost all conduits used for surgical myocardial revascularization and in particular with the gold-standard internal thoracic artery, the RA has a thick muscular wall and only limited amount of elastic tissue in its media.[8] This abundant muscular component is the anatomic background of the hyperspastic attitude of the artery that has been well documented both in vivo and in vitro. In a classic organ-bath study, Chardigny and colleagues[9] reported that the contractile response elicited on RA rings by a variety of vasoconstricting stimuli is markedly superior to that exhibited by both the internal thoracic artery and gastroepiploic artery, and our group confirmed this finding in vivo.[6] Furthermore, almost all series of early angiographic control of RA grafts reported cases of catheter-induced artery spasm.[10,11]

For this reason, the necessity for pharmacologic intervention to prevent RA spasm when this artery is used as a coronary artery bypass conduit has been emphasized by many authors, and the good patency rates obtained in the current era (opposed to the alarming incidence of graft failure in the 1970s) are often explained on the basis of the systematic adoption of vasodilating agents.

However, no convincing clinical evidence on the optimum modalities and length of the antispastic therapy is actually available, and the type of drug and duration of the treatment are usually established on an empiric basis by the single authors.

In a previous study, we showed how beyond the first postoperative year CCBT does not ensure substantial advantages in terms of both clinical results and RA graft patency.[1] These data are possibly explainable on the basis of the described morpho-functional remodeling of RA grafts that, in the years after surgery, tend to lose their peculiar hyperreactivity and assume a vasoactive profile more similar to that of an elastic-walled artery.[7]

However, the role of CCBT in the early postoperative period, when RA spastic tendency is thought to be maximal,[2] has yet to be clarified, and its use remains routine in many centers.

The present study protocol was designed with the aim of providing objective data on the clinical, scintigraphic, and angiographic effects of CCBT in the months immediately after surgery. Our results show how the adoption of calcium channel blockers does not lead to significant benefits in terms of clinical and scintigraphic results and RA angiographic status.

Furthermore, data derived from the subset of patients submitted to endovascular serotonin challenge testifies how CCBT had no effect on the early vasoreactive profile of the RA.

On the basis of our data, the role and efficacy of CCBT seems at least debatable.

A possible explanation for these findings is the inappropriateness of diltiazem to prevent RA graft spasm. In recent years several authors have suggested the poor efficacy of diltiazem on the RA and suggested the use of different vasodilators (including nitroglycerin, isosorbide dinitrate, nicorandil, nifedipine, verapamil, and amlodipine)[12-16]; al-

though the majority of these studies were conducted in vitro or had a limited follow-up period, the research of the ideal antispastic drug for RA grafts seems worthwhile in view of the growing use of this artery in coronary surgery and the lack of scientific data to support the use of diltiazem.

In conclusion, our data provide substantial evidence that CCBT with oral diltiazem 120 mg/daily started immediately after surgery and continued for the first postoperative year does not affect RA graft patency and clinical and scintigraphic outcomes.

On the basis of these data, the prophylactic use of diltiazem in patients with RA grafts seems unsubstantiated.

The more appropriate antispastic drug for patients with RA grafts and, more in general, the opportunity of adopting a vasodilating therapy in case of RA grafting should be further investigated.

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