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Coronary Artery Disease Progression Late After Successful Stent Implantation

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Objectives This study sought to define the importance of 5-year coronary artery disease (CAD) progression after successful stenting.

Background Safety concerns regarding first-generation drug-eluting stents mandate 5-year follow-up studies. However, only limited data exist on the long-term importance of CAD progression relative to late stent–related problems.

Methods This study followed for 5 years, 428 consecutive patients randomized to drug-eluting versus bare-metal stents with successful stenting documented by freedom from symptoms/events and no ischemic perfusion defects (PDs) after 6 months. Rest/stress scintigraphic scans were repeated after 60 months. Late events and new PDs in areas remote from stented vessels indicated CAD progression.

Results During follow-up, 110 of 428 (25.7%) patients had 150 clinical events: 43 patients (10%) died, 36 (8.4%) suffered a myocardial infarction, and 71 (16.6%) needed repeat revascularization. Event rates were lower in remote versus target-vessel areas (9.8% vs. 14.3%, $p = 0.019$). Remote myocardial infarction and repeat revascularization accounted for 46 of 124 (37.1%) nonfatal events and were similar for both stent types. Five-year scintigraphic studies in patients without follow-up events showed 23.3% new PDs, 71% of which were asymptomatic. Remote defects accounted for 37.5% PDs and were similar for both stent types.

Conclusions Even 5 years after stenting, target-vessel events and/or new PDs remained more frequent than CAD progression assessed by remote events and/or new PDs. Still, remote events accounted for almost 40% of all events with a similar rate of additional new PDs, often silent, and independent of stent type. This documents the importance of CAD progression and stresses the need to differentiate remote from target-vessel events/PDs in long-term stent safety studies. (Basel Stent Kosten-Effektivitäts Trial [BASKET]; ISRCTN75663024) (J Am Coll Cardiol 2012;59:793–9) © 2012 by the American College of Cardiology Foundation

Safety concerns regarding late cardiac death or nonfatal myocardial infarction (MI) related to late stent thrombosis mandate prolonged follow-up after implantation of first-generation drug-eluting stents (DES) (1). Late stent thromboses occurring after 6 to 12 months after the intervention, first observed in individual patients (2), were found to occur more often after DES than after bare-metal stent (BMS) use in the "all-comer" angioplasty population of the BASKET (Basel Stent Kosten-Effektivitäts Trial) (3). The rate was low and did not affect overall mortality. This was confirmed in several studies and registries (4,5) with rates of definite stent thrombosis according to the Academic Research Consortium's definitions (6) after DES implantation of approximately 0.6% per year, steadily increasing up to 4 years of follow-up (7). Still, 5-year follow-up reports of the pivotal DES trials (8,9) confirmed the benefits of first-generation DES, compared with BMS, in reducing target-vessel (TV) revascularization without increasing overall death or MI rates.

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In view of the progressive nature of coronary artery disease (CAD), it could be expected that during prolonged follow-up investigations after stenting, cardiac events would occur irrespective of this procedure in vessels or locations

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Abbreviations and Acronyms

BMS = bare-metal stent(s)
CAD = coronary artery disease
DES = drug-eluting stent(s)
MI = myocardial infarction
PDs = perfusion defects
SPECT = single-photon emission computed tomography
TV = target vessel

not touched by the intervention. In a low-risk clinical trial population treated with BMS, hazard rates for late non-TV events were about 3 times higher than for TV events (10). In long-term follow-up investigations of pooled early DES trials (11,12), events attributed to non-TVs were estimated at 26% during years 2 to 5 after the intervention, with similar rates in DES- and BMS-treated patients. However, these findings were based on observations of low-risk patients and influenced by protocol-driven repeat coronary angiographies and limited follow-up rates. Importantly, in a broader population of patients including those with multivessel disease, the importance of CAD progression can only be assessed if the initial revascularization is shown to be successful and complete. In addition, disease progression may not only manifest as death, remote MI, and angina-driven non-TV revascularization, but also as symptomatic or silent new perfusion defects (PDs).

Thus, the aim of the present prospective investigation was to define the importance of CAD progression over a 5-year period after successful complete revascularization by angioplasty and stenting in a comprehensive manner capturing clinically symptomatic and silent disease and comparing it between patients randomized to DES versus BMS. We hypothesized that during late follow-up, clinical CAD progression could become as relevant as symptomatic late stent problems occurring irrespective of stent type implanted.

Methods

Patients and study design. BASKET included 826 consecutive patients treated with angioplasty and stenting between May 2003 and May 2004 at the University Hospital of Basel, Switzerland, excluding only those with restenotic lesions, in need of ≥4-mm stents and those not consenting (13). Patients presented with stable symptoms in 42%, unstable angina in 36%, and with ST-segment elevation MI in 21% of cases, whereas 69% had multivessel CAD and 66% at least 1 "off-label" indication. Patients were randomized 2:1 to DES or BMS. Follow-up findings have been reported after 18 (3) and 36 months (14). In addition, all patients surviving the initial 6 months were invited for a rest/stress myocardial perfusion scintigraphy using single-photon emission computed tomography (SPECT) (15).

This patient population and dataset provided a unique opportunity for the present prospective outcome study, the BASKET-PRO (BASKET-PROgression of CAD study). Based on a new protocol with a new ethical approval and a new written informed patient consent, all BASKET patients without clinical CAD manifestations up to 6 months after the intervention, no ischemic perfusion defects at this point in time, and surviving up to 5 years after stenting were invited to undergo a further follow-up examination including history, current therapy, clinical examination, electrocardiography as well as a second rest/stress myocardial perfusion scintigraphy performed 5.5 ± 0.25 years after stent implantation. Follow-up was performed in the outpatient clinic in all patients. The patient flow is detailed in Figure 1.

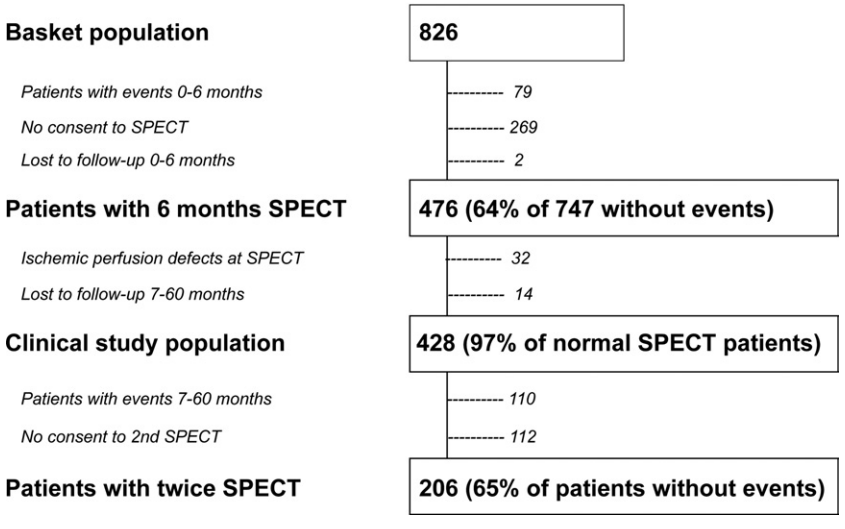

Figure 1 Patient Flow Chart

The flow chart shows the derivation of the study population from 826 consecutive patients for the clinical follow-up and the repeat scintigraphic studies.
BASKET = Basel Stent Kosten-Effektivitäts Trial; SPECT = single-photon emission computed tomography.