Drug-Eluting Stent Thrombosis in Routine Clinical Practice
Two-Year Outcomes and Predictors From the TAXUS ARRIVE Registries

John M. Lasala, MD, PhD; David A. Cox, MD; David Dobies, MD; Kenneth Baran, MD; William B. Bachinsky, MD; Edwin W. Rogers, MD, MBA; Jeffrey A. Breall, MD, PhD; David H. Lewis, MD; Aijun Song, MS; Ruth M. Starzyk, PhD; Stephen R. Mascioli, MD; Keith D. Dawkins, MD; Donald S. Baim, MD; for the ARRIVE 1 and ARRIVE 2 Participating Physicians

Background—Stent thrombosis (ST) is an uncommon but serious complication of drug-eluting and bare metal stents. To assess drug-eluting stent ST in contemporary practice, we analyzed 2-year data from the 7492-patient ARRIVE registry.

Methods and Results—Patients were enrolled at the initiation of percutaneous coronary intervention with no inclusion/exclusion criteria beyond use of the paclitaxel-eluting TAXUS stent. Two-year follow-up was 94% with independent adjudication of major cardiac events. A second, autonomous committee adjudicated Academic Research Consortium (ARC) definite/probable ST. Cumulative 2-year ARC-defined ST was 2.6% (1.0% early ST [<30 days], 0.7% late ST [31 to 365 days], and 0.8% very late ST [>1 year]). Simple-use (single-vessel and single-stent) cases had lower rates than expanded use (broader patient/lesion characteristics, 2-year cumulative: 1.4% versus 3.3%, $P<0.001$; early ST: 0.4% versus 1.4%, $P<0.001$; late ST: 0.5% versus 0.8%, $P=0.14$; very late ST: 0.4% versus 1.0%, $P=0.008$). Within 7 days of ST, 23% of patients died; 28% suffered Q-wave myocardial infarction. Mortality was higher with early ST (39%) than late ST (12%, $P<0.001$) or very late ST (13%, $P<0.001$). Multivariate analysis showed anatomic factors increased early ST (lesion >28 mm, lesion calcification) and late ST (vessel <3.0 mm); biological factors increased very late ST (renal disease, prior brachytherapy). Although early ST (71.4%) and very late ST (23.1%) patients had dual antiplatelet therapy at the time of ST, premature thienopyridine discontinuation was a strong independent predictor of both.

Conclusions—The relative risks of early and late ST differ. Knowledge of ST risk for specific subgroups may guide revascularization options until the completion of randomized trials in these broad populations. **(*Circ Cardiovasc Intervent*. 2009;2:285-293.)**

Key Words: angioplasty ■ coronary disease ■ registries ■ stents ■ thrombosis

Stent thrombosis (ST) is a serious complication following either bare metal stents (BMS) or drug-eluting stents (DES), and its occurrence is associated with significant (40% to 50%) mortality and a composite death/myocardial infarction (MI) rate of 50% to 70%.[1–3] The ST risk is greatest in the first 30 days after stenting (early ST) and higher in patients with complex coronary anatomy beyond that studied in pivotal trials.[2–4] To better understand the incidences and consequences of early ST, late ST (LST), and very late ST (VLST) in a broad population of DES-treated patients, we evaluated 2-year outcomes of 7492 patients receiving the paclitaxel-eluting TAXUS stent in the ARRIVE registries.[5,6]

Clinical Perspective on p 293

Methods

Program Design

The TAXUS Express[2] stent (Boston Scientific Corporation [BSC], Natick, Mass) and the BSC-sponsored TAXUS Peri-Approval Registry: A Multi-Center Safety Surveillance (ARRIVE) Program have been described previously.[5,6] Briefly, ARRIVE 1 (mandated by the US Food and Drug Administration; 2487 analyzed patients, 48 sites), and ARRIVE 2 (voluntary postmarket registry; 5005 analyzed patients, 53 sites) were similarly designed to enroll consecutive consented patients determined by the investigator to be appropriate

Received January 18, 2009; accepted June 1, 2009.

From the Washington University School of Medicine (J.M.L.), St. Louis, Mo; Lehigh Valley Hospital (D.A.C.), Allentown, Pa; Genesys Heart Institute (D.D.), Genesys Regional Medical Center, Grand Blanc, Mich; St. Paul Heart Clinic (K.B.), St. Paul, Minn; Pinnacle Health/Moffitt Heart and Vascular (W.B.B.), Harrisburg, Pa; Cardiology Consultants (E.W.R.), Pensacola, Fla; Krannert Institute of Cardiology (J.A.B.), Indiana University School of Medicine, Indianapolis, Ind; Wisconsin Heart and Vascular Institute (D.H.L.), Madison, Wis; and Boston Scientific Corporation (A.S., R.M.S., S.R.M., K.D.D., D.S.B.), Natick, Mass.

Correspondence to John M. Lasala, MD, PhD, Washington University School of Medicine, Cardiology, Campus Box 8086, 660 South Euclid Ave, St Louis, MO 63110. E-mail jlasala@im.wustl.edu

Circ Cardiovasc Intervent **is available at http://circinterventions.ahajournals.org DOI: 10.1161/CIRCINTERVENTIONS.109.852178.109.852178**

candidates for a DES. Patients were enrolled under a protocol approved by the local institutional review board in full conformity with the US Food and Drug Administration guidelines and the Declaration of Helsinki at procedure start, to minimize potential bias relating to exclusion of complicated/unsuccessful procedures.

Of ARRIVE's 7492-patient population, the majority (4794, 64%) were expanded-use cases whose clinical/anatomic complexity fell beyond the simple-use indications studied in the TAXUS IV pivotal trial.[7] Reference vessel diameter and lesion length were determined visually by the implanting physician, and stents were placed according to the directions for use and/or standard percutaneous coronary intervention practices. Dual antiplatelet therapy (DAPT; clopidogrel/ticlopidine and aspirin) was begun before or immediately after the procedure under directions for use recommendations for aspirin indefinitely and clopidogrel/ticlopidine for at least 6 months. Monitors retained by the sponsor reviewed data from all patients in whom subsequent cardiac events were reported plus an additional 10% to 20% patient sampling per site to confirm the accuracy and completeness of data collection; follow-up was 97% through 1 year and 94% complete through 2 years. This accuracy of ascertainment is supported by the observation that clinical outcomes among simple-use ARRIVE patients closely matched those of similar patients recruited in the randomized clinical trial (RCT) TAXUS arms.[5] An independent Clinical Events Committee adjudicated and determined the relationship of reported cardiac events to the TAXUS stent, and a second committee at the Harvard Clinical Research Institute adjudicated ST per the Academic Research Consortium (ARC) "definite/probable" definitions.[8] The studies are registered with clinicaltrials.gov: NCT00569491 (ARRIVE 1) and NCT00569751 (ARRIVE 2).

Statistical Analysis

Patient/procedural characteristics and event rates were analyzed using descriptive statistics with SAS version 8.0 or higher (SAS Institute, Cary, NC). The 2 ARRIVE registries had similar designs, eligibility criteria, end point definitions, and adjudication processes; data pooling was found to be appropriate. Descriptive statistics (N, mean, SD) were used to summarize continuous variables and frequency tables or proportions for discrete variables. Student *t* test was used to compare continuous variables and χ^2 or Fisher exact test for discrete variables. Kaplan–Meier product method was used to calculate event rates for time-to-event outcomes (log-rank probability value). Rates are provided for 0 to 1 day (acute), 2 to 30 days (subacute), 0 to 30 days (early), 31 to 365 days (LST), and 366 to 730 days (VLST).[8] Annualized rates for each period were also computed. To identify predictors of ST, 42 baseline variables (Table 1) were assessed using backward Cox proportional hazards regression model; the threshold to remain in the model was $P=0.10$.

The sponsor, the principal investigators, and the US Food and Drug Administration designed the ARRIVE registry. Data analyses, carried out by the sponsor, were assessed in a collaborative effort between the principal and coprincipal investigators and the sponsor, who also assisted with writing the report and is included in the author list. The authors had access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

Definite/Probable ST Rates

ST occurred in 184 (2.5%) of 7492 patients; 171 had 1 ST, 12 had 2, and 1 experienced 3 thrombotic events. Overall, 42% were early ST, 28% were LST, and 30% were VLST. Cumulative 2-year ST was 2.6% consisting of 1.0% early ST, 0.7% LST, and 0.8% VLST (Table 2). Rates were higher for the expanded-use versus simple-use cohort (respective 2-year cumulative ST: 3.3% versus 1.4%, $P<0.001$; early ST: 1.4% versus 0.4%, $P<0.001$; LST: 0.8% versus 0.5% $P=0.14$; VLST: 1.0% versus 0.4, $P=0.008$). Patients who ultimately sustained an ST event differed significantly from those who did not in a number of baseline factors (Table 3).

Table 1. Baseline Characteristic Variables Used in Predictor Modeling

Clinical variables		
Acute MI*	Diabetes, insulin treated	MI, previous
Age >70 y	Diabetes, not requiring insulin	PCI, previous
CABG, previous	Gender, male	Renal disease†
Cardiogenic shock	Hypercholesterolemia‡	Smoking at baseline
Congestive heart failure§	Hypertension‡	Stroke, previous
Lesion/angiographic variables		
Bifurcation	In-stent restenosis	Multivessel disease
Brachytherapy, prior	Left main disease	Ostial lesion
Chronic total occlusion	Lesion calcification¶	Preprocedure TIMI=0
LAD as target vessel	Lesion type B2/C	RVD <3 mm
Left main stenting	Multiple overlapping stents	Tortuosity, severe
Lesion >28 mm	Multiple stents per patient	Vein graft
Procedural variables		
IVUS postdeployment	Multivessel stenting	Preprocedure dilatation
IVUS predeployment	Postprocedure dilatation	Stent inflation pressure >14 atm
Adjunctive therapy variables		
Thienopyridine <30 days	Thienopyridine <6 months	Thienopyridine <12 months

Hazard ratios were assessed with the Cox proportional hazards regression model, backward selection was used, and the threshold to stay in the model was set at 0.10. CABG indicates coronary artery bypass graft; IVUS, intravascular ultrasound; LAD, left anterior descending artery; PCI, percutaneous coronary intervention; RVD, reference vessel diameter; TIMI, Thrombolysis in Myocardial Infarction; CK, creatine kinase.

*Included patients presenting with ST-segment elevation MI and non–ST-segment elevation MI. MI was defined as one of the following: CK >2× upper limit of normal with a positive CK(MB), CK >5× upper limit of normal with a positive CK(MB) for post-CABG cases, or ECG evidence of new pathological Q waves (lasting ≥0.04 s) in 2 contiguous leads with positive CK(MB).

†Site reported as serum creatinine >3.0 mg/dL or patient on dialysis.

‡Patient was reported as having this condition and may or may not have been receiving medication for it.

§Site reported as New York Heart Association class ≥III.

¶Moderate and severe.

The difference between ST incidence in the expanded-use versus simple-use subgroups is illustrated in Figure 1, with 1.0% of the difference (δ) becoming evident within 30 days, rising to a δ of 1.3% at 1 year, and 1.9% at 2 years. If ST risk was normalized for exposure time (Figure 2), the annualized hazard rate in the overall population was highest (41% per year) in the 0 to 1 day interval, falling to a relatively constant 0.8% per year from 31 days to 2 years.

Among 9 high risk, expanded-use subgroups interval analysis showed numerically higher ST rates in year 1 than year 2 for all but renal disease patients (Table 2). Early or LST was highest among subgroups with complex lesion morphology: small vessels (reference vessel diameter <2.5 mm), longer lesions (>28 mm), bifurcation lesions, or multivessel stenting. Rates of VLST were highest among patients with renal disease (serum creatinine >3.0 mg/dL or

Table 2. Stent Thrombosis (ARC Definite/Probable) Rates in ARRIVE and Subgroups

				Expanded-Use Subgroups								
Time Point	Overall* (N=7492)	Simple Use† (N=2698)	Expanded Use† (N=4794)	Lesion >28 mm (N=748)	RVD <2.5 mm (N=251)	Multivessel Stenting (N=1208)	Bifurcation Lesion (N=574)	CTO (N=161)	Vein Graft (N=474)	ISR (N=489)	AMI‡ (N=953)	Renal Disease§ (N=191)
0–1 d (acute)	0.2 (17/7492)	0.04 (1/2698)	0.3 (16/4794)	0.7 (5/748)	0.4 (1/251)	0.7 (9/1208)	0.5 (3/574)	0.0 (0/161)	0.6 (3/474)	0.2 (1/489)	0.1 (1/953)	0.5 (1/191)
2–30 d (subacute)	0.8 (60/7462)	0.4 (10/2690)	1.0 (50/4772)	1.9 (14/746)	0.8 (2/251)	1.3 (16/1205)	1.6 (9/570)	1.3 (2/160)	0.6 (3/474)	0.8 (4/487)	1.5 (14/950)	1.1 (2/188)
0–30 d (early)	1.0 (77/7491)	0.4 (11/2697)	1.4 (66/4794)	2.5 (19/748)	1.2 (3/251)	2.1 (25/1208)	2.1 (12/574)	1.2 (2/161)	1.3 (6/474)	1.0 (5/489)	1.6 (15/953)	1.6 (3/191)
31 d–1 y (LST)	0.7 (51/7332)	0.5 (13/2646)	0.8 (38/4686)	1.4 (10/724)	2.0 (5/244)	0.7 (8/1181)	0.7 (4/558)	1.3 (2/155)	1.1 (5/467)	1.0 (5/481)	1.0 (9/925)	0.0 (0/182)
0–1 y	1.8 (128/7274)	0.9 (24/2623)	2.2 (104/4651)	4.0 (29/723)	3.3 (8/240)	2.8 (33/1174)	2.9 (16/557)	2.6 (4/153)	2.4 (11/465)	2.1 (10/479)	2.7 (24/904)	1.6 (3/184)
1–2 y (VLST)	0.8 (56/6882)	0.4 (11/2520)	1.0 (45/4362)	1.8 (12/674)	0.0 (0/225)	1.5 (16/1088)	1.5 (8/518)	2.0 (3/149)	2.3 (10/435)	1.8 (8/450)	1.1 (9/843)	2.7 (4/147)
0–2 y	2.6 (184/7035)	1.4 (35/2545)	3.3 (149/4490)	5.9 (41/698)	3.5 (8/230)	4.3 (49/1128)	4.5 (24/537)	4.8 (7/147)	4.6 (21/457)	3.9 (18/463)	3.9 (33/854)	3.9 (7/179)

Data are presented as % (n/N). Definitions are from Cutlip et al[8]. Event rates presented here were calculated as simple proportions and differ slightly from those in Figure 1, which were calculated by the Kaplan–Meier product method. AMI indicates acute myocardial infarction; CABG, coronary artery bypass graft; CK, creatine kinase; CTO, chronic total occlusion (site reported); ISR, in-stent restenosis; RVD, reference vessel diameter.

*Includes the ARRIVE 1 (patient enrollment February 2004 to May 2004; 2487 analyzed patients) and ARRIVE 2 (patient enrollment October 2004 to October 2005; 5005 analyzed patients) registries. Statistical comparisons (baseline demographic and lesion data, procedural, and postprocedural characteristics) indicated data could be pooled. Of 184 ST patients, 142 had definite ST.

†Simple use cases excluded one or more of the following: AMI, bifurcation lesion, cardiogenic shock, CTO, ISR, large vessel (RVD >3.75 mm), left main disease/stenting, long lesion (>28 mm), moderate/severe calcification, multivessel stenting, ostial lesion, prior brachytherapy, renal disease, severe tortuosity, small vessel (RVD <2.5 mm), vein graft stenting. Expanded use cases are those not classified as simple use. $P<0.05$ for simple use vs expanded use (chi-square test) at all time points but LST.

‡Included patients presenting with STEMI and NSTEMI. Myocardial infarction was defined as one of the following: CK >2× upper limit of normal with a positive CK(MB), CK >5× upper limit of normal with a positive CK(MB) for post-CABG cases, or ECG evidence of new pathological Q waves (lasting ≥0.04 s) in 2 contiguous leads with positive CK(MB).

§Site reported as serum creatinine >3.0 mg/dL or patient on dialysis.

patient on dialysis), vein graft stenting, chronic total occlusion, and in-stent restenosis subgroups (including prior brachytherapy), for whom VLST rates actually exceeded the corresponding early ST rates.

Outcomes Postinitial ST Event

Table 4 shows the occurrence of death, MI, or target lesion revascularization within 7 days of the 184 initial ST events. Only 4 additional events occurred 8 to 30 days after the initial ST (3 deaths, 1 target lesion revascularization). The most common events within 7 days were target lesion revascularization (64%) and MI (63%). Mortality within 7 days was higher with early ST (39%) than LST (12%, $P<0.001$) or VLST (13%, $P<0.001$).

DAPT Use

Among ARRIVE patients, 67.7% (4687 of 6927) were on DAPT at 1 year and 53.1% (3487 of 6569) at 2 years. Antiplatelet therapy status at time of initial ST was available for 80% (148 of 184) of patients; 44.6% (66 of 148) were on DAPT, including 56.3% (54 of 96) who experienced ST during year 1 (Table 5). Use at time of event was higher among patients with early ST (71.4%) than LST (35.0%) or VLST (23.1%), for whom DAPT use had fallen below the 67.7% and 53.1% rates, respectively, in the general ARRIVE population. Expanded-use patients were more likely to be taking DAPT at time of ST: 70% (28 of 40) for early ST, 86% (12 of 14) for LST, and 75% (9 of 12) for VLST.

Multivariate Predictors

Table 6 shows multivariate predictors for early ST, LST, and VLST identified from among 42 assessed variables. Among 15 predictors, only 3 overlapped among time points. Discontinuation of thienopyridine therapy before 30 days was the strongest predictor of early events (14-fold increased risk), whereas discontinuation of thienopyridine before 6 months was associated with a 2-fold risk of LST. Additional factors each associated with increased risk of early or LST included vessel size <3.0 mm, lesion >28 mm, multiple stents and multiple vessels treated and clinical factors such as prior MI and congestive heart failure. In contrast, predictors of VLST tended to be more patient than lesion-based as prior brachytherapy presented the highest risk (7.3-fold, 6.7% rate of VLST [2 of 30]) followed by renal disease (3.9-fold).

Discussion

In the BMS era, ST was thought to be limited to the first 30-day (acute/subacute) period[9] and was effectively reduced to <1% by the addition of ticlopidine to aspirin alone.[10] In 2004 to 2005, sporadic accounts of LST and VLST were reported with DES[11] and attributed to incomplete DES healing.[12] A small but significant increase in ST with DES versus BMS was seen from 1 to 4 years using the original protocol definitions, which excluded ST events following repeat revascularization procedures.[12] But using the ARC definitions of definite/probable ST,[8] data from CYPHER and TAXUS RCTs have shown no significant rate differences between DES and BMS through 1 year, with a similarly low frequency of VLST with TAXUS (0.35% per year) and BMS (0.25% per year, $P=0.40$) from 1 to 5 years.[13] However, these RCT involved mostly "simple-use" procedures with short lesions in vessels of 2.5 to 3.5 mm and avoiding clinical conditions such as acute myocardial infarction (AMI). Yet, as DES were adopted for >80% of percutaneous coronary intervention procedures in the United States, most involved expanded-use situations not included in the pivotal RCTs. In

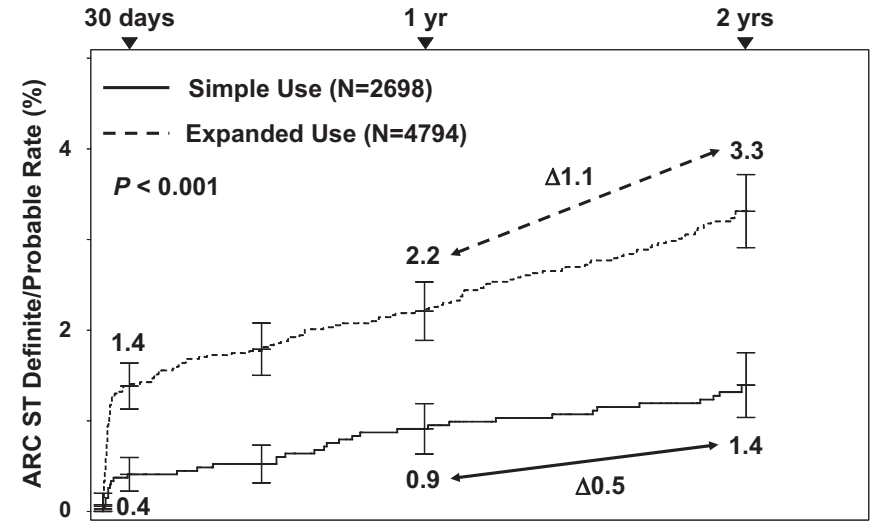
Table 3. Comparison of Baseline Clinical and Procedural Characteristics Between Patients With and Without ARC Definite/Probable Stent Thrombosis

Parameter	Patients With ST* (N=184)	Patients With No ST (N=7308)†	*P*‡
Clinical variables			
AMI	17.9 (33)	12.6 (920)	0.03
Age, y	61.20±12.55	64.33±11.69	<0.001
Congestive heart failure§	13.0 (24)	6.7 (487)	<0.001
Diabetes-insulin treated	16.3 (30)	10.0 (734)	0.006
Expanded use¶	81.0 (149)	63.6 (4645)	<0.001
Hypercholesterolemia‖	75.5 (139)	75.8 (5538)	0.94
Hypertension‖	76.1 (140)	76.0 (5551)	0.97
Male	69.0 (127)	67.3 (4916)	0.62
Myocardial infarction, previous	51.1 (94)	36.0 (2628)	<0.001
Renal disease#	3.8 (7)	2.5 (184)	0.24**
Smoking at baseline	39.7 (73)	23.1 (1691)	<0.001
Lesion/angiographic variables			
Bifurcation lesion	13.0 (24)	7.5 (550)	0.006
Brachytherapy, prior	1.1 (2)	0.4 (31)	0.19**
Calcification (moderate/severe)	26.6 (49)	19.4 (1417)	0.015
Left main stenting	3.3 (6)	2.1 (156)	0.30**
Lesion length >28 mm	22.3 (41)	9.7 (707)	<0.001
Multiple stents per patient	60.3 (111)	38.9 (2845)	<0.001
Multivessel disease	45.7 (84)	36.7 (2681)	0.01
Reference vessel diameter, mm	2.81±0.38	2.94±0.44††	<0.001
Vein grafts	11.4 (21)	6.2 (453)	0.004
Procedural variables			
Direct stenting	42.9 (79)	45.6 (3330)	0.48
Poststent balloon used	52.2 (96)	41.8 (3053)	0.005
Predilatation performed	75.5 (139)	66.7 (4876)	0.01
Stent implantation pressure	14.24±3.52 (184)	14.25±3.27 (7299)	0.97
Stent length per patient, mm	38.91±22.90	29.25±18.99	<0.001
Adjunctive therapy variable			
Thienopyridine therapy <6 months	34.8 (64)	16.2 (1181)	<0.001

Data are presented as % (n) or mean±SD (n).
*Definitions from Cutlip et al.[8]
†Includes 6851 patients with 2-year follow-up and 457 patients without full 2-year follow-up.
‡*P* values are from Student *t* test for continuous variables and from chi-square test for proportions.
§Site reported as New York Heart Association class ≥III.
¶See Table 2 for definitions.
‖Patient was reported as having this condition and may or may not have been receiving medication.
#Site reported as serum creatinine >3.0 mg/dL or patient on dialysis.
**P values from Fisher exact test.
††N=7307.

fact, there are few reports of the rates, consequences, and predictors of ST in the more complex patient mix treated in routine clinical practice.

The combined ARRIVE registries offer a unique opportunity to examine this issue. The large size (7492 patients) and lack of specific inclusion/exclusion criteria provide a broad look at DES performance. Data from 184 ST patients allowed analysis of ST rates (early, late, and VLST) and consequences and the influence of various risk factors that would not be possible in smaller patient cohorts. Principal findings include the following: (1) the 2-year cumulative ARC definite/probable ST rate of 2.6%, higher than in RCTs, included 1.0% early ST, 0.7% LST, and 0.8% VLST; (2) ST was higher at each time point for expanded use than for simple use, with a 2-year cumulative rate of 3.3% versus 1.4%, respectively, $P<0.001$; (3) within 7 days of ST, 23% of patients died and 28% suffered Q-wave MI; (4) multivariate analysis showed that early ST and LST increased with anatomic factors such as long lesions (>28 mm) or small vessels (reference vessel diameter <3.0 mm), respectively, whereas VLST increased with biological factors such as renal disease or prior brachytherapy; and (5) premature discontin-



Number at Risk

Days	0	30	180	365	730
Simple use	2698	2695	2624	2593	2436
Expanded use	4794	4784	4580	4528	4116

Figure 1. Time-to-event curves for ARC stent thrombosis (definite/probable) in ARRIVE simple-use versus expanded-use subgroups. See Table 2 for descriptions of simple-use and expanded-use cases. Bars show CI±1.5 SE; log-rank probability value. Event rates presented here were calculated by the Kaplan–Meier product method and differ slightly from those in Table 2, which were calculated as simple proportions.

uation of thienopyridine use was a strong independent predictor of early ST and LST but offered incomplete protection as 71.4% of early ST and 23.1% of VLST patients suffered ST events while receiving DAPT. The ARRIVE data thus significantly extend our knowledge and highlight factors associated with increased risk of DES early, late, or very late ST, which may be useful to clinicians in estimating relative risk in specific patients.[14]

The estimates of ST rates in ARRIVE agree well with other published evidence. Simple-use ARRIVE ST rates (0.9% for year 1 and 0.5% for year 2, time-to-event analysis) were thus comparable with those of corresponding patients in the RCT TAXUS arms (0.9% and 0.3%, respectively).[5] Expanded-use ARRIVE ST rates also match available data from observational studies, notwithstanding the limitations of different degrees of event ascertainment, monitoring, and adjudication. Thus, higher ST rates at each time point among expanded-use patients in ARRIVE concurs with observations of DES results from the multicenter STENT,[15] EVENT,[16] and DEScover[17] registries as well as smaller studies.[18–21] The 18-month ST rate in the SORTOUT II randomized trial was 2.9% for paclitaxel-eluting stents,[22] but only 1.9% in a 4-center, prospective, observational European cohort study.[23] Conversely, one large US center[18] reported higher early ST (1.9% versus 1.0%) and LST (1.4% versus 0.7%) rates than ARRIVE but comparable VLST rates (0.7% versus 0.8%). As seen in ARRIVE, early ST rates were also higher than late ST rates among the 15 157 patients followed for 1 year in the e-CYPHER registry, although the level of monitoring and end-point ascertainment

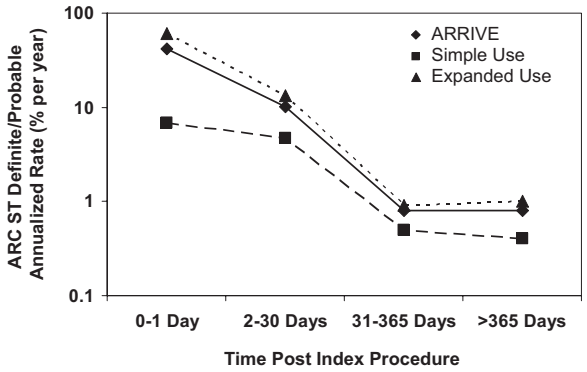


Figure 2. Annualized event rates for ARC stent thrombosis (definite/probable) in ARRIVE (semilog plot). See Table 2 for descriptions of simple-use and expanded-use cases. Calculations for annualized rates of ARC definite/probable ST[8] used binary proportion data. Factors used for time periods less than 1 year: 365/2 (acute, 0 to 1 day); 365/29 (subacute, 2 to 30 days); and 365/334 (late, 31 to 365 days). Annualized rates for the expanded-use group are significantly higher than for the simple-use group for all time intervals except 31 to 365 days. N=7492 for all ARRIVE patients, N=2698 for simple use, and N=4794 for expanded use.

Table 4. Outcomes Within 7 Days Postinitial ST Event in ARRIVE

Time of Initial ST Postindex Procedure*	N†	Events Occurring Within 7 d of Initial ST‡			
		All Death§	All MI	Q-wave MI	TLR¶
ST 0–30 d	77	39.0 (30)	44.2 (34)	20.8 (16)	50.6 (39)
ST 0–1 d	17	29.4 (5)	47.1 (8)	17.6 (3)	70.6 (12)
ST 2–30 d	60	41.7 (25)	43.3 (26)	21.7 (13)	45.0 (27)
ST >30 d–1 y	51	11.8 (6)	74.5 (38)	33.3 (17)	72.5 (37)
ST >1–2 y	56	12.5 (7)	76.8 (43)	32.1 (18)	75.0 (42)
All ST	184	23.4 (43)	62.5 (115)	27.7 (51)	64.1 (118)

Data are presented as % (n).

*Only a patient's first ST event is counted here.

†No. of ST in the time interval.

‡A patient could have >1 event after ST; ST defined as ARC definite/probable.[8]

§All were cardiac deaths except for 1 case in the 30 d to 1 y interval.

¶Target lesion revascularization (TLR) was defined as "TAXUS stent–related" target vessel revascularization, given the absence of a central angiographic core laboratory to perform quantitative coronary angiography.

Table 5. Patient Antiplatelet Therapy Status at Time of Initial Stent Thrombosis

Therapy*	ST 0–1 d (N=17)	ST 2–30 d (N=39)	ST 0–30 d (N=56)	ST >30 d–1 y (N=40)	ST >1–2 y (N=52)
Dual therapy†	70.6 (12)	71.8 (28)	71.4 (40)	35.0 (14)	23.1 (12)
Aspirin only	5.9 (1)	7.7 (3)	7.1 (4)	32.5 (13)	50.0 (26)
Thienopyridine only‡	17.6 (3)	2.6 (1)	7.1 (4)	2.5 (1)	3.8 (2)
No therapy	5.9 (1)	17.9 (7)	14.3 (8)	30.0 (12)	23.1 (12)

Data are presented as % (n). ST is defined as ARC definite/probable.[8]

*Data were collected and assessed based on patient narratives, dossier/medical records, and case report forms. Antiplatelet medication status was available for 80% (148/184) of cases. The directions for use for the TAXUS Express stent recommended DAPT minimally for 6 months.

†Aspirin plus clopidogrel or ticlopidine.

‡Clopidogrel or ticlopidine.

may have led to differences in absolute event rates.[24] In a European 2-institutional cohort study of 8146 patients receiving DES, the incidence of early ST was 3.7% with a 2-year cumulative rate of 4.6%, when compared with the 2.6% rate in ARRIVE.[25] The STENT registry reported a 1.6% 2-year DES ST rate in the off-label group[15] compared with 3.3% in the ARRIVE expanded-use subgroup. The 1-year ARRIVE ST rate of 2.7% in the AMI population is comparable with the 1-year ST rates reported for DES (3.2%) and BMS (3.4%) in the HORIZONS AMI RCT.[26] Differences in methodology notwithstanding, these multisource data lend credence that the higher rates of ST seen in the expanded-use cohort of ARRIVE are realistic estimates.

Despite variances in reported rates, the severe clinical consequences of ST remain similar across studies.[1–3] In ARRIVE, 23% of ST patients died and 28% suffered a Q-wave MI within 7 days of the ST event. In a recent report from a multicenter registry of 431 patients with a definite ST (BMS and DES), the long-term clinical outcome post-ST was also unfavorable, with a high mortality and recurrence rate.[27] Interestingly, in ARRIVE the lethality of later ST seems less than half that of early ST (12% to 13% versus 39%). It is not clear whether this reflects differences in attribution, the fact that sudden death ≤30 days is included in the ARC definition of ST, or a true biological difference in ST lethality at different time points. Confirmation from other large experiences will be required.

The 184 ARRIVE ST patients had significant differences in baseline clinical/procedural characteristics (Table 3) compared with patients who did not suffer ST. Early and LST were most common in subgroups with small vessels, long lesions, multivessel stenting, or bifurcation lesions, as would be expected based on the identification of these same risk factors for BMS ST.[28] In a recent report on patients with acute coronary syndrome, multivariate predictors of early ST (BMS and DES) included absence of preprocedural thienopyridine,

Table 6. Multivariate Predictors of ST

	Hazard Ratio (95% CI)		
Predictor (N=7492 Patients)*	Early (0–30 d; n=77 ST)	Late (31 d–1 y; n=51 ST)	Very Late (1–2 y; n=56 ST)
Thienopyridine <30 d	13.78 (8.77, 21.64)	NS	NS
Multiple stents per patient	2.21 (1.32, 3.69)	NS	2.38 (1.39, 4.08)
Congestive heart failure	2.15 (1.17, 3.92)	NS	NS
Lesion calcification (moderate/severe)	1.83 (1.14, 2.94)	NS	NS
Lesion length >28 mm	1.77 (1.01, 3.08)	NS	NS
Prior MI	1.60 (1.02, 2.52)	NS	2.38 (1.39, 4.06)
Smoking at baseline	NS	5.86 (3.31, 10.38)	1.91 (1.09, 3.34)
RVD <3.0 mm	NS	3.43 (1.82, 6.46)	NS
Insulin-requiring diabetes	NS	2.86 (1.45, 5.64)	NS
Postdilatation	NS	2.16 (1.23, 3.80)	NS
Thienopyridine <6 mo	NS	2.00 (1.07, 3.77)	NS
Multivessel disease	NS	1.79 (1.03, 3.13)	NS
Prior brachytherapy	NS	NS	7.32 (1.75, 30.60)
Renal disease	NS	NS	3.86 (1.39, 10.73)
Vein graft stenting	NS	NS	2.90 (1.44, 5.83)

NS indicates nonsignificant; RVD, reference vessel diameter.

*Predictors are for ARC stent thrombosis, definite plus probable.[8] Variables listed reached statistical significance ($P<0.05$). Baseline variables used for modeling (42) are listed in Table 1. They were screened by univariate and multivariate analyses to identify covariates (5 or 6) that were then included in the final Cox models.

suboptimal angiographic results, and the extent of coronary disease.[29] The recognized factors of small stent diameter and long stent length were also important predictors of early and late ST and have been incorporated in a risk score for ST in the first year that has been developed based on the ARRIVE data.[30] These anatomic risk factors for early ST, however, had little impact on VLST where biological factors such as prior brachytherapy and renal disease were operative.

Several major medical societies have recommended DAPT be taken at least 1 year after DES, if tolerated, noting that patients with ST-associated clinical comorbidity (eg, renal disease) or procedural variables (eg, multiple stents) may be candidates for DAPT >1 year.[31–33] The ARRIVE protocol recommended minimally 6 months DAPT, but 67.7% (4687 of 6927) and 53.1% (3487 of 6569) were on DAPT at 1 and 2 years, respectively. Premature discontinuation of DAPT poses a significant risk to DES-treated patients as seen in ARRIVE (14-fold risk of early ST if discontinued before 30 days; 2-fold risk of LST if discontinued before 6 months) and reported by others.[3,21,23,28,34,35] At the same time, continued DAPT does not confer immunity from ST as most (71%) of ARRIVE patients with early ST were on DAPT at the time of the event, as were 35% of LST patients, similar to another report.[25] However, we did not evaluate platelet inhibition and potential resistance to clopidogrel therapy, which has been implicated in BMS ST,[36] and may have been applicable here. Altered clopidogrel dosing strategies have been associated with improved platelet responsiveness in 2 recent trials.[37,38] Alternatively, a more uniformly effective thienopyridine (prasugrel) may be able to reduce ST events compared with clopidogrel, both for early ST and between 30 days and 15 months.[39] Optimal DAPT duration will be examined further in a large (>20 000 patients) industry-sponsored study to evaluate the comparative benefits of 30 versus 12 months of DAPT, in DES and propensity-matched BMS patients.[40]

It is unknown how many of the ST events observed in ARRIVE were related to potential incomplete DES healing. The high-risk subgroups studied have extensive/aggressive underlying atherosclerotic coronary disease whose progression may lead to plaque rupture that would be indistinguishable from true ST by the ARC definitions or angiography. Distinguishing DES related from non–DES-related etiologies requires randomized or concurrent BMS controls in the same patient sets as seen in the recent HORIZONS study where BMS had the same increased ST rate during the first year after AMI treatment as TAXUS.[26] These high 1-year rates with both stent types may reflect underlying biological risks.

Some limitations should be considered when interpreting these results. Constraints inherent to any registry include lack of randomization, absence of a comparison group, a lower monitoring level than is standard for RCT, no detailed medication records between patient visits, use of site visual assessments (rather than core laboratory measurement) of angiographic data, and the absence of mandated intravascular ultrasound data, each of which may have provided greater insight into the role of procedural risk factors. More specifically, the lack of routine intravascular ultrasound data did not allow the study to evaluate the role of suboptimal stent deployment as a contributor to ST. Evaluation of DAPT also was limited in the 20% (36 of 184) of ST patients for whom antiplatelet therapy status at time of initial ST was not available. Additionally, ST estimates are imprecise even in a large registry, given the low frequency of event and potential limitations of the ARC ST definitions. Nevertheless, the close correlation of observed ST rates in ARRIVE with the simple-use RCT data and more recent complex RCT data in AMI (HORIZONS) suggests that these estimates of differential ST rates in high-risk subgroups are reasonable.

In conclusion, ARRIVE affords a unique look at ST in a large, real-world DES treated population. First-year ST risk reflects mostly DAPT compliance and complex anatomic and clinical factors already known to increase BMS ST risk. Protection from ST by ongoing DAPT is significant but incomplete. Risk factors for VLST seem more related to biological markers than to the anatomic factors related to early/late ST and absent BMS controls for many of the expanded-use subsets it is speculative how many of those late events are related to the DES itself rather than progression of diffuse and aggressive atherosclerosis in these higher risk patients. Either way, there may be reason to continue longer term DAPT in such patients—to protect potentially incompletely healed DES or to protect against natural history—until that question is put into better perspective by trials now being initiated. Until that point, the knowledge of ST incidence, outcomes, and risk factors gained from ARRIVE will hopefully help guide physician management decisions.

Acknowledgments

We thank Yun Lu, MS, and Kevin Najarian, MS, for assistance with the statistical analyses and Mary V. Jacoski, MS, for assistance with data assessment (all BSC).

Sources of Funding

This study was supported by BSC.

Disclosures

Dr Lasala reports receiving Speaker's Bureau fees and consulting fees from BSC; Dr Cox is on the Speaker's Bureau and Medical Advisory Board for BSC; Dr Breall has received research grants from BSC, is on the Xience and Angiomax Speaker's Bureaus, has done medical-legal work, and is a consultant on the Siemans Advisory Board; Dr Lewis was on the Speaker's Bureau for Bristol-Myers Squibb, the manufacturer of Plavix. Drs Baim, Dawkins, Mascioli, Starzyk, and Ms Song are full-time employees and stockholders of BSC. Dr Mascioli has represented BSC as an expert witness. Drs Bachinsky, Baran, Dobies, and Rogers have no conflicts.

References

1. Holmes DR Jr, Kereiakes DJ, Laskey WK, Colombo A, Ellis SG, Henry TD, Popma JJ, Serruys PW, Kimura T, Williams DO, Windecker S, Krucoff MW. Thrombosis and drug-eluting stents: an objective appraisal. *J Am Coll Cardiol*. 2007;50:109–118.
2. Windecker S, Meier B. Late coronary stent thrombosis. *Circulation*. 2007;116:1952–1965.
3. Jaffe R, Strauss BH. Late and very late thrombosis of drug-eluting stents: evolving concepts and perspectives. *J Am Coll Cardiol*. 2007;50:119–127.
4. Farb A, Boam AB. Stent thrombosis redux–the FDA perspective. *N Engl J Med*. 2007;356:984–987.
5. Lasala JM, Cox DA, Dobies D, Muhlestein JB, Katopodis JN, Revtyak G, Baim DS. Usage patterns and 2-year outcomes with the TAXUS express stent: results of the US ARRIVE 1 registry. *Catheter Cardiovasc Interv*. 2008;72:433–445.

6. Lasala JM, Cox DA, Lewis SL, Tadros PN, Haas RC, Schweiger MJ, Chhabra A, Untereker WJ, Starzyk RM, Mascioli SR, Dawkins KD, Baim DS. Expanded use of the TAXUS Express stent: 2-year insights on safety from the 7500-patient ARRIVE registry program. *EuroIntervention*. 2009;5:67–77.
7. Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, Turco M, Caputo R, Bergin P, Greenberg J, Popma JJ, Russell ME. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med*. 2004;350:221–231.
8. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344–2351.
9. Cutlip DE, Baim DS, Ho KK, Popma JJ, Lansky AJ, Cohen DJ, Carrozza JP Jr, Chauhan MS, Rodriguez O, Kuntz RE. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. *Circulation*. 2001;103:1967–1971.
10. Leon MB, Baim DS, Popma JJ, Gordon PC, Cutlip DE, Ho KK, Giambartolomei A, Diver DJ, Lasorda DM, Williams DO, Pocock SJ, Kuntz RE. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. Stent Anticoagulation Restenosis Study Investigators. *N Engl J Med*. 1998;339:1665–1671.
11. Ong AT, McFadden EP, Regar E, de Jaegere PP, van Domburg RT, Serruys PW. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. *J Am Coll Cardiol*. 2005;45:2088–2092.
12. Stone GW, Moses JW, Ellis SG, Schofer J, Dawkins KD, Morice MC, Colombo A, Schampaert E, Grube E, Kirtane AJ, Cutlip DE, Fahy M, Pocock SJ, Mehran R, Leon MB. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N Engl J Med*. 2007;356:998–1008.
13. Allocco DJ, Dawkins KD, Baim DS, Leon MB. The impact of nonstent related progression of underlying coronary artery disease on late clinical outcomes after paclitaxel-eluting stents [TCT Abstract 346]. *Am J Cardiol*. 2008;102:137i–138i.
14. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007;357:2001–2015.
15. Brodie BR, Stuckey T, Downey W, Humphrey A, Bradshaw B, Metzger C, Hermiller J, Krainin F, Juk S, Cheek B, Duffy P, Smith H, Edmunds J, Varanasi J, Simonton CA, Group S. Outcomes and complications with off-label use of drug-eluting stents. Results from the STENT (Strategic Transcatheter Evaluation of New Therapies) Group. *J Am Coll Cardiol Interv*. 2008;1:405–414.
16. Win HK, Caldera AE, Maresh K, Lopez J, Rihal CS, Parikh MA, Granada JF, Marulkar S, Nassif D, Cohen DJ, Kleiman NS. Clinical outcomes and stent thrombosis following off-label use of drug-eluting stents. *JAMA*. 2007;297:2001–2009.
17. Beohar N, Davidson CJ, Kip KE, Goodreau L, Vlachos HA, Meyers SN, Benzuly KH, Flaherty JD, Ricciardi MJ, Bennett CL, Williams DO. Outcomes and complications associated with off-label and untested use of drug-eluting stents. *JAMA*. 2007;297:1992–2000.
18. Pinto Slottow TL, Steinberg DH, Roy PK, Buch AN, Okabe T, Xue Z, Kaneshige K, Torguson R, Lindsay J, Pichard AD, Satler LF, Suddath WO, Kent KM, Waksman R. Observations and outcomes of definite and probable drug-eluting stent thrombosis seen at a single hospital in a four-year period. *Am J Cardiol*. 2008;102:298–303.
19. Mishkel GJ, Moore AL, Markwell S, Shelton ME. Correlates of late and very late thrombosis of drug eluting stents. *Am Heart J*. 2008;156:141–147.
20. Daemen J, Wenaweser P, Tsuchida K, Abrecht L, Vaina S, Morger C, Kukreja N, Juni P, Sianos G, Hellige G, van Domburg RT, Hess OM, Boersma E, Meier B, Windecker S, Serruys PW. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet*. 2007;369:667–678.
21. Yan BP, Duffy SJ, Clark DJ, Lefkovits J, Warren R, Gurvitch R, Lew R, Sebastian M, Brennan A, Andrianopoulos N, Reid CM, Ajani AE. Rates of stent thrombosis in bare-metal versus drug-eluting stents (from a large Australian multicenter registry). *Am J Cardiol*. 2008;101:1716–1722.
22. Galloe AM, Thuesen L, Kelbaek H, Thayssen P, Rasmussen K, Hansen PR, Bligaard N, Saunamaki K, Junker A, Aaroe J, Abildgaard U, Ravkilde J, Engstrom T, Jensen JS, Andersen HR, Botker HE, Galatius S, Kristensen SD, Madsen JK, Krusell LR, Abildstrom SZ, Stephansen GB, Lassen JF. Comparison of paclitaxel- and sirolimus-eluting stents in everyday clinical practice: the SORT OUT II randomized trial. *JAMA*. 2008;299:409–416.
23. Airoldi F, Colombo A, Morici N, Latib A, Cosgrave J, Buellesfeld L, Bonizzoni E, Carlino M, Gerckens U, Godino C, Melzi G, Michev I, Montorfano M, Sangiorgi GM, Qasim A, Chieffo A, Briguori C, Grube E. Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. *Circulation*. 2007;116:745–754.
24. Urban P, Gershlick AH, Guagliumi G, Guyon P, Lotan C, Schofer J, Seth A, Sousa JE, Wijns W, Berge C, Deme M, Stoll HP. Safety of coronary sirolimus-eluting stents in daily clinical practice: one-year follow-up of the e-Cypher registry. *Circulation*. 2006;113:1434–1441.
25. Wenaweser P, Daemen J, Zwahlen M, van Domburg R, Juni P, Vaina S, Hellige G, Tsuchida K, Morger C, Boersma E, Kukreja N, Meier B, Serruys PW, Windecker S. Incidence and correlates of drug-eluting stent thrombosis in routine clinical practice. 4-year results from a large 2-institutional cohort study. *J Am Coll Cardiol*. 2008;52:1134–1140.
26. Stone GW, Lansky AJ, Pocock SJ, Gersh BJ, Dangas G, Wong SC, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Mockel M, Ochala A, Kellock A, Parise H, Mehran R. The HORIZONS-AMI Trial Investigators. Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. *N Engl J Med*. 2009;360:1946–1959.
27. van Werkum JW, Heestermans AA, de Korte FI, Kelder JC, Suttorp MJ, Rensing BJ, Zwart B, Brueren BR, Koolen JJ, Dambrink JH, van't Hof AW, Verheugt FW, ten Berg JM. Long-term clinical outcome after a first angiographically confirmed coronary stent thrombosis: an analysis of 431 cases. *Circulation*. 2009;119:828–834.
28. Honda Y, Fitzgerald PJ. Stent thrombosis: an issue revisited in a changing world. *Circulation*. 2003;108:2–5.
29. Aoki J, Lansky AJ, Mehran R, Moses J, Bertrand ME, McLaurin BT, Cox DA, Lincoff AM, Ohman EM, White HD, Parise H, Leon MB, Stone GW. Early stent thrombosis in patients with acute coronary syndromes treated with drug-eluting and bare metal stents: the Acute Catheterization and Urgent Intervention Triage Strategy trial. *Circulation*. 2009;119:687–698.
30. Baran KW, Lasala JM, Cox DA, Song A, Deshpande MC, Jacoski MV, Mascioli SR. ARRIVE Participating Physicians. A clinical risk score for prediction of stent thrombosis. *Am J Cardiol*. 2008;102:541–545.
31. Grines CL, Bonow RO, Casey DE Jr, Gardner TJ, Lockhart PB, Moliterno DJ, O'Gara P, Whitlow P. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *J Am Coll Cardiol*. 2007;49:734–739.
32. King SB III, Smith SC Jr, Hirshfeld JW Jr, Jacobs AK, Morrison DA, Williams DO, Feldman TE, Kern MJ, O'Neill WW, Schaff HV, Whitlow PL, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Halperin JL, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura R, Page RL, Riegel B, Tarkington LG, Yancy CW. 2007 focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation*. 2008;117:261–295.
33. Paradis JM, Ducrocq G, Tanguay JF. Antiplatelet therapy following drug-eluting stent implantation: new clinical data and recommendations. *Minerva Cardioangiol*. 2008;56:139–154.
34. Iakovou I, Schmidt T, Bonizzoni E, Ge L, Sangiorgi GM, Stankovic G, Airoldi F, Chieffo A, Montorfano M, Carlino M, Michev I, Corvaja N, Briguori C, Gerckens U, Grube E, Colombo A. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA*. 2005;293:2126–2130.
35. Park DW, Park SW, Park KH, Lee BK, Kim YH, Lee CW, Hong MK, Kim JJ, Park SJ. Frequency of and risk factors for stent thrombosis after drug-eluting stent implantation during long-term follow-up. *Am J Cardiol*. 2006;98:352–356.
36. Gurbel PA, Bliden KP, Samara W, Yoho JA, Hayes K, Fissha MZ, Tantry US. Clopidogrel effect on platelet reactivity in patients with stent thrombosis: results of the CREST Study. *J Am Coll Cardiol*. 2005;46:1827–1832.
37. Gladding P, Webster M, Zeng I, Farrell H, Stewart J, Ruygrok P, Ormiston J, El-Jack S, Armstrong G, Kay P, Scott D, Gunes A, Dahl M-L. The antiplatelet effect of higher loading and maintenance dose regimens

of clopidogrel. The PRINC (Plavix Response in Coronary Intervention) trial. *J Am Coll Cardiol Interv*. 2008;1:612–619.
38. Aleil B, Jacquemin L, De Poli F, Zaehringer M, Collet J-P, Montalescot G, Cazenave J-P, Dickele M-C, Monassier J-P, Gachet C. Clopidogrel 150 mg/day to overcome low responsiveness in patients undergoing elective percutaneous coronary intervention. Results from the VASP-02 (vasodilator-stimulated phosphoprotein-02) randomized study. *J Am Coll Cardiol Interv*. 2008;1:631–638.
39. Wiviott SD, Braunwald E, Angiolillo DJ, Meisel S, Dalby AJ, Verheugt FW, Goodman SG, Corbalan R, Purdy DA, Murphy SA, McCabe CH, Antman EM. Greater clinical benefit of more intensive oral antiplatelet therapy with prasugrel in patients with diabetes mellitus in the trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel-thrombolysis in myocardial infarction 38. *Circulation*. 2008;118:1626–1636.
40. Mauri L. Dual anti-platelet therapy (DAPT) randomized trial. Presented at the Transcatheter Cardiovascular Therapeutics Symposium, October 12–17, 2008, Washington, DC. Available at: http://www.hcri.harvard.edu/uploads/news_event_documents/dapt_design_slides_tct. Accessed November 6, 2008.

CLINICAL PERSPECTIVE

Stent thrombosis (ST) is an uncommon but serious complication of both drug-eluting stents and bare metal stents. To understand the incidences, predictors, and consequences of early ST (≤30 days), late ST (31 days to 1 year), and very late ST (>1 year), we evaluated 2-year outcomes in the broad population of 7492 patients who received the paclitaxel-eluting TAXUS Express stent in the ARRIVE registries. Cumulative 2-year Academic Research Consortium-defined ST (definite/probable) was 2.6% (1.0% early ST, 0.7% late ST, and 0.8% very late ST). Simple-use cases (single vessel, single stent) made up 36% of the ARRIVE population and had significantly lower cumulative ST rates through 2 years than did expanded-use cases (broader patient/lesion characteristics, 1.4% versus 3.3%, respectively) due to lower rates of early ST (0.4% versus 1.4%) and very late ST (0.4% versus 1.0%). Within 7 days of ST, 23% of patients died and 28% suffered Q-wave myocardial infarction. Mortality was higher with early ST (39%) than late ST (12%, $P<0.001$) or very late ST (13%, $P<0.001$). Multivariate analysis showed that various anatomic factors increased early ST (lesion >28 mm, lesion calcification) and late ST (vessel <3.0 mm), whereas biological factors increased very late ST (renal disease, prior brachytherapy). Although early ST (71.4%) and very late ST (23.1%) patients had dual antiplatelet therapy at time of ST, premature thienopyridine discontinuation was a strong independent predictor of both. Knowledge of ST risk for specific subgroups may guide revascularization options until the completion of randomized trials in these broad populations.

Circulation
Cardiovascular Interventions

Drug-Eluting Stent Thrombosis in Routine Clinical Practice: Two-Year Outcomes and Predictors From the TAXUS ARRIVE Registries

John M. Lasala, David A. Cox, David Dobies, Kenneth Baran, William B. Bachinsky, Edwin W. Rogers, Jeffrey A. Breall, David H. Lewis, Aijun Song, Ruth M. Starzyk, Stephen R. Mascioli, Keith D. Dawkins and Donald S. Baim
for the ARRIVE 1 and ARRIVE 2 Participating Physicians

Circ Cardiovasc Interv. 2009;2:285-293; originally published online July 22, 2009;
doi: 10.1161/CIRCINTERVENTIONS.109.852178.109.852178
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-7640. Online ISSN: 1941-7632