Relationship Between Intravascular Ultrasound Guidance and Clinical Outcomes After Drug-Eluting Stents

The Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) Study

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Background—Prior small to modest-sized studies suggest a benefit of intravascular ultrasound (IVUS) guidance in noncomplex lesions. Whether IVUS guidance is associated with improved clinical outcomes after drug-eluting stent (DES) implantation in an unrestricted patient population is unknown.

Methods and Results—Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) was a prospective, multicenter, nonrandomized "all-comers" study of 8583 consecutive patients at 11 international centers designed to determine the frequency, timing, and correlates of stent thrombosis and adverse clinical events after DES. Propensity-adjusted multivariable analysis was performed to examine the relationship between IVUS guidance and 1-year outcomes. IVUS was utilized in 3349 patients (39%), and larger-diameter devices, longer stents, and/or higher inflation pressures were used in 74% of IVUS-guided cases. IVUS guidance compared with angiography guidance was associated with reduced 1-year rates of definite/probable stent thrombosis (0.6% [18 events] versus 1.0% [53 events]; adjusted hazard radio, 0.40; 95% confidence interval, 0.21–0.73; P=0.003), myocardial infarction (2.5% versus 3.7%; adjusted hazard radio, 0.66; 95% confidence interval, 0.49–0.88; P=0.004), and composite adjudicated major adverse cardiac events (ie, cardiac death, myocardial infarction, or stent thrombosis) (3.1% versus 4.7%; adjusted hazard radio, 0.70; 95% confidence interval, 0.55–0.88; P=0.002). The benefits of IVUS were especially evident in patients with acute coronary syndromes and complex lesions, although significant reductions in major adverse cardiac events were present in all patient subgroups those with including stable angina and single-vessel disease.

Conclusions—In ADAPT-DES, the largest study of IVUS use to date, IVUS guidance was associated with a reduction in stent thrombosis, myocardial infarction, and major adverse cardiac events within 1 year after DES implantation.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00638794.

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Intravascular ultrasound (IVUS) has been used for >2 decades to guide percutaneous coronary intervention (PCI) and is currently most frequently used to optimize stent expansion and apposition.[1–16] Nonetheless, definitive randomized trials to demonstrate whether IVUS guidance improves clinical outcomes after stent implantation have not been performed, with most prior trials being underpowered and restricted to noncomplex lesions. The benefits of IVUS after drug-eluting stent (DES) use are particularly controversial given the improved

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outcomes with DES compared with bare metal stents. This issue is especially important because stent thrombosis (ST) still occurs even with second-generation DES (especially in complex lesions) and is associated with high rates of myocardial infarction (MI) and mortality.[17,18] A recent meta-analysis from 11 studies (only 1 of which was randomized) suggested that IVUS-guided DES implantation compared with angiographic guidance alone might reduce the incidence of death, ST, and major adverse cardiac events (MACE) but not MI or target vessel revascularization (TVR). However, most of the studies included in this meta-analysis were modest in size, and none reported how IVUS was used to actually guide the procedure.[19]

The Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) study was a large-scale, prospective, multicenter study designed to assess the relationship between platelet reactivity and other clinical and procedural variables with subsequent ST and adverse clinical events in patients treated with coronary DES. The present study reports a prespecified substudy from ADAPT-DES comparing the outcomes of IVUS guidance versus angiographic guidance of DES implantation.

Methods

Study Design and Protocol

The design, major inclusion and exclusion criteria, end points, and definitions from the ADAPT-DES study have been described in detail.[20] In brief, in the ADAPT-DES study, up to 11 000 consecutive patients at 11 US and German sites successfully treated with ≥1 Food and Drug Administration– or CE Mark–approved DES were eligible for enrollment, regardless of patient or lesion complexity. The only major exclusion criteria were the occurrence of a major complication during the procedure or before platelet function testing or planned bypass surgery after PCI. All patients were loaded with aspirin and clopidogrel. Platelet reactivity was assessed after successful PCI, usually on the morning after the procedure, with the use of the VerifyNow Aspirin, P2Y12, and IIb/IIIa assays (Accumetrics, San Diego, CA).[21] A prescribed washout period for glycoprotein IIb/IIIa inhibitors was required before platelet function testing. After PCI, patients were treated with aspirin indefinitely, and clopidogrel was recommended for at least 1 year. Clinical follow-up was scheduled at 30 days, 1 year, and 2 years by telephone contact. At the time of the present analysis, all patients had reached the 1-year follow-up period.

Procedural IVUS use was per operator discretion. When IVUS was used, the operator was required to report the timing of IVUS imaging (eg, before intervention, after DES, after adjunct balloon inflation) and how the IVUS information influenced the procedure. The study was approved by the institutional review board at each participating center, and all eligible patients signed written informed consent.

End Points and Definitions

Study monitors traveled at regular intervals to the enrolling sites to independently assess the accuracy of data entry and to collect original source documents in patients with adverse events. An independent committee of 3 physicians met routinely to adjudicate all deaths and MI and ST events, reviewing hospital charts, ECGs, coronary angiograms, and other data as required.

Clopidogrel hyporesponsiveness was defined as VerifyNow P2Y12 >208 platelet reaction units. Aspirin hyporesponsiveness was defined as VerifyNow aspirin ≥550 aspirin reaction units.

The primary end point was definite or probable ST according to the Academic Research Consortium definitions.[22] Additional end points included all-cause mortality, MI, revascularization, and major bleeding. Cardiac biomarkers were assessed before and after the procedure for evidence of adverse clinical events, according to the local standard of care. Periprocedural MI was defined as total creatine kinase (CK) >2 times the upper limit of normal with a positive CK-MB or troponin I or T. If the total CK was not available, then CK-MB >3 times the upper limit of normal was considered evidence of a periprocedural MI. If neither CK nor CK-MB was available, then troponin elevation >5 times the 99th percentile of the upper reference limit or upper limit of normal for the specific institution was considered evidence of periprocedural MI. MI unrelated to the PCI procedure was defined as (1) typical rise and fall of biochemical markers (troponin or CK-MB) of myocardial necrosis with either ischemic symptoms, development of new pathological Q waves, or ECG changes indicative of ischemia; (2) development of new pathological Q waves; or (3) pathological findings of an acute MI. ST, MI, and death were adjudicated by an independent clinical events committee using original source documents without knowledge of whether IVUS was used during the index procedure. Major bleeding was defined as a Thrombolysis in Myocardial Infarction (TIMI) major or minor bleed, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) bleed, and Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) bleed or any postdischarge bleeding event requiring medical attention. Stroke was defined as an acute neurological deficit lasting >24 hours, as diagnosed by a physician, with supporting information, including brain imaging and neurological/neurosurgical evaluation.[23,24] Ischemia-driven target lesion revascularization (TLR), TVR, major bleeding, and stroke were site reported but not centrally adjudicated.

Statistical Methods

As described previously, with an anticipated 1-year ST rate of 1.0%, a sample size of 11 000 patients was estimated to provide >99% power to identify variables associated with ST with a hazard ratio of >3.[20] Enrollment was terminated after 8665 patients were enrolled given financial considerations; this reduced sample size still provided 99% power.[20] Categorical variables were compared between groups by χ^2 or Fisher exact test. Continuous variables were presented as mean±SD and were compared between groups by Student *t* test. Time-to-event data are summarized as Kaplan-Meier estimates and were compared between groups with the log-rank test. Landmark analysis was used to determine the time-to-event rates from 0 to 30 days and >30 days to 1 year. A propensity score was constructed by modeling IVUS guidance in a logistic regression model with the following variables: age, gender, race, body mass index, current smoker, history of diabetes mellitus, insulin dependence, renal insufficiency, hemodialysis, hypertension, hyperlipidemia, peripheral artery disease, history of congestive heart failure, previous brachytherapy, prior MI, prior coronary artery bypass, Killip class at presentation, cardiac diagnosis, all medications preadmission through PCI, all laboratory data, hemodynamic support, access site, closure device, number of diseased vessels, number of lesions, number of stents, prediameter and postdiameter stenosis, prestent and final TIMI flow, maximum vessel diameter, calcium, ostial location, bifurcation, chronic total occlusion, total lesion and stent length, maximum device diameter, maximum balloon pressure, dissection, DES use only, stent type, and site. Then, to determine the predictors of outcomes, platelet reactivity plus other baseline variables considered clinically relevant were entered into multivariable Cox proportional hazards regression models stratified by the quintiles of the propensity score. The Supremum test verified that the proportional hazards assumption was valid for modeling both early and late ST (P=0.57 and P=0.13, respectively). A P value <0.05 was considered significant for all analyses. Statistical analyses were performed with the use of SAS version 9.1.3 (SAS Institute, Cary, NC).

Results

From July 2008 to September 2010, 8665 patients were enrolled in ADAPT-DES at 11 sites in the United States and Germany. Eighty-two patients (0.9%) were excluded because

platelet function testing was performed before the protocol-required glycoprotein IIb/IIIa inhibitor washout period. Thus, the final study population consisted of 8583 patients. IVUS-guided stenting was performed in 3349 patients (39%), and angiography-guided stenting was performed in 5234 patients (61%). The follow-up rate at 1 year was 96%, including 97% with IVUS guidance versus 96% with angiography guidance (*P*=0.10).

Patient and Procedural Characteristics According to IVUS Use

Compared with patients stented with angiography guidance alone, those in whom IVUS was used were slightly younger, were more likely to be smokers, and more frequently presented with ST-segment elevation MI (STEMI) but were less likely to have hypertension, hyperlipidemia, and prior coronary artery bypass grafting (Table 1). As shown in Table 2, heparin was used more frequently and bivalirudin less frequently in the IVUS-guided group compared with the angiography-guided group. Clopidogrel hyporesponsiveness was also slightly more frequently observed in the IVUS-guided group, as was thienopyridine use at 1 year. Although 3-vessel disease was less common and fewer lesions per patient were treated in the IVUS-guided group, total stent length was longer than in the angiography-guided group (Table 3). Everolimus-eluting stents and larger stents were more commonly used in the IVUS-guided group.

Table 1. Baseline Characteristics

	IVUS Guided (n=3349)	Angiography Guided (n=5234)	*P*
Age, y	62.9±10.8	64.1±10.9	<0.0001
Male, No. (%)	2457 (73)	3901 (75)	0.23
Diabetes mellitus, No. (%)	1048 (31)	1735 (33)	0.07
Insulin-treated, No. (%)	358 (11)	640 (12)	0.03
Hypertension, No. (%)	2616 (78)	4218 (81)	0.006
Hyperlipidemia, No. (%)	2287 (68)	4093 (78)	<0.0001
Current smoking, No. (%)	851 (25)	1088 (21)	<0.0001
Renal insufficiency, No. (%)*	536 (16)	894 (17)	0.19
Prior MI, No. (%)	824 (25)	1340 (26)	0.30
Prior percutaneous coronary intervention, No. (%)	1434 (43)	2242 (43)	0.99
Prior coronary artery bypass graft surgery, No. (%)	425 (13)	1042 (20)	<0.0001
Body mass index	29.2±5.7	29.7±5.7	0.0001
Left ventricular ejection fraction, %†	56.9±13.4	53.2±11.3	<0.0001
Killip class 1, No. (%)	3282 (98)	5120 (98)	1.00
Presenting clinical syndrome, No. (%)			
ST-segment elevation MI	421 (13)	392 (8)	<0.0001
Non–ST-segment elevation MI	506 (15)	744 (14)	0.25
Unstable angina	909 (27)	1464 (28)	0.40
Stable ischemic heart disease	1513 (45)	2634 (50)	<0.0001

IVUS indicates intravascular ultrasound; MI, myocardial infarction.
*Creatinine clearance <60 mL/min calculated with the Cockcroft-Gault formula.
†Available only in 78% of patients.

Procedural IVUS Use

In the IVUS-guided group, IVUS was used only before PCI in 7% of patients, only after PCI in 30% of patients, and both before and after PCI in 63% of patients. Solely on the basis of the IVUS evaluation, the operator changed the PCI strategy in 74% (2484/3349) of patients to choose (1) a larger stent or balloon (in 38% [943/2484] of cases); (2) higher inflation pressures (in 23% [564/2484] of cases); (3) a longer stent (in 22% [546/2484] of cases); (4) additional poststent dilatation because of incomplete expansion (in 13% [329/2484] or incomplete stent apposition (in 7% [166/2484]); and/or (5) additional stent placement (in 8% [197/2484]).

Clinical Outcomes

As shown in Table 4, the unadjusted 1-year rate of definite/probable ST was significantly lower in the IVUS-guided group compared with the angiography-guided group (0.6% [18 events] versus 1.0% [53 events]; hazard ratio [HR], 0.53; 95% confidence interval [CI], 0.31–0.90; *P*=0.017) (Figure, left). This difference was present within 1 month of stent implantation, with continued divergence of the curves apparent between 1 month and 1 year. Findings of both definite and probable ST were less in the IVUS-guided group.

The 1-year unadjusted rates of MI were also significantly lower in IVUS-guided compared with angiography-guided patients (2.5% versus 3.7%; HR, 0.67; 95% CI, 0.51–0.87; *P*=0.002) (Table 4 and Figure, middle). IVUS guidance

Table 2. Platelet Function and Antiplatelet Medications

	IVUS Guided (n=3349)	Angiography Guided (n=5234)	*P* Value
PRU	191±95	186±98	0.045
PRU >208, No. (%)*	1461/3289 (44)	2149/5160 (42)	0.01
ARU	418±54	420±56	0.15
ARU ≥550*, No. (%)	169/3330 (5)	309/5197 (6)	0.09
Use of thienopyridine, No. (%)			
On admission	1611/3349 (48)	2070/5234 (40)	<0.0001
At discharge	3348/3349 (100)	5227/5229 (100)	1.0
At 1 y	2873/3228 (89)	4028/4998 (81)	<0.0001
Use of aspirin, No. (%)			
On admission	2719/3349 (81)	4322/5234 (83)	0.10
At discharge	3304/3349 (99)	5206/5229 (100)	<0.0001
At 1 y	3045/3206 (95)	4771/4984 (96)	0.11
In-hospital medication, No. (%)			
Bivalirudin	1985/3349 (59)	3339/5234 (64)	<0.0001
Unfractionated heparin	3263/3349 (97)	5018/5234 (96)	0.0001
Low-molecular-weight heparin	1041/3349 (31)	523/5234 (10)	<0.0001
Glycoprotein IIb/IIIa inhibitor, No. (%)	76/3349 (2)	199/5234 (4)	<0.0001

ARU indicates aspirin reaction units; IVUS, intravascular ultrasound; and PRU, P2Y12 reaction units.
*Prespecified cutoff value for hyporesponsiveness.

Table 3. Lesion and Procedural Characteristics

	IVUS Guided (n=3349)	Angiography Guided (n=5234)	*P* Value
Three-vessel disease, No. (%)*	830 (25)	1634 (31)	<0.0001
Bifurcation lesion, No. (%)	473 (14)	844 (16)	0.01
In-stent restenotic lesion, No. (%)	377 (11)	507 (10)	0.02
Left main lesion, No. (%)	146 (4)	171 (3)	0.009
Lesions treated per patient	1.48±0.75	1.52±0.81	0.02
Stents implanted per patient	1.73±0.97	1.71±1.05	0.63
Total stent length per patient, mm	33.6±21.9	31.7±22.6	0.0002
Maximum vessel diameter, mm	3.2±0.8	3.0±0.7	<0.0001
Maximum device diameter, mm†	3.4±0.6	3.2±0.5	<0.0001
Maximum balloon pressure, atm	16.9±3.7	16.7±3.5	0.13
Maximum diameter stenosis before stent, %	87.1±10.8	88.8±9.4	<0.0001
Maximum diameter stenosis after stent, %	1.9±6.4	1.5±7.1	0.02
Prestent TIMI flow 0/1, No. (%)	462 (12)	706 (11)	0.15
Final TIMI flow 3, No. (%)	3789 (100)	6260 (99)	0.054
Drug-eluting stent implanted, No. (%)	3347 (100)	5230 (100)	1.0
Everolimus-eluting	2442 (73)	3096 (59)	<0.0001
Paclitaxel-eluting	452 (14)	963 (18)	<0.0001
Sirolimus-eluting	259 (8)	896 (17)	<0.0001
Zotarolimus-eluting fast release	206 (6)	329 (6)	0.80
Zotarolimus-eluting slow release	85 (3)	102 (2)	0.07

IVUS indicates intravascular ultrasound; TIMI, Thrombolysis in Myocardial Infarction.

*Visual diameter stenosis >50%.

†Either stent or balloon.

compared with angiography guidance was associated with lower rates of target vessel–related MI (1.7% versus 2.9%; *P*=0.0004), with similar rates of non–target vessel–related MI. Moreover, the type of MI that was most reduced with IVUS guidance was spontaneous MI (0.8% versus 1.5% with angiography guidance; HR, 0.53; 95% CI, 0.34–0.82; *P*=0.004), with nonsignificantly different rates of periprocedural MI and ST-related MI. The 1-year rates of ischemia-driven TLR and TVR were also lower with IVUS guidance (Table 4).

The overall 1-year rate of adjudicated MACE, defined as cardiac death, definite/probable ST, or MI, was significantly less in the IVUS-guided group compared with the angiography-guided group (3.1% versus 4.7%; HR, 0.67; 95% CI, 0.53–0.84; *P*=0.0006) (Figure, right). Rates of MACE were significantly lower with IVUS guidance in patients treated with complex disease (left main lesions, bifurcation lesions, and/or multivessel disease) as well as in those with noncomplex disease, although the absolute reduction in 1-year MACE was greater in complex patients (Figure I in the online-only Data Supplement). Similarly, the absolute reduction in MACE was greatest in patients presenting with STEMI, intermediate in those with non-STEMI or unstable angina, and least (but still significantly lower) in those with stable angina (Figure II in the online-only Data Supplement). To examine potential causes for this gradient in effect, we compared the lesion characteristics among patients with STEMI, non-STEMI or unstable angina, and stable angina. Across the 3 groups, (1) STEMI lesions had the least prevalence of complex lesion morphology such as 3-vessel disease, calcification, bifurcation, in-stent restenosis, or left main disease; and (2) STEMI lesions showed the most prevalence of thrombus with prestent TIMI grade 0/1 and largest vessel size, but no difference was observed for the incidence of final TIMI grade 3 compared with the lesions in the patients with non-STEMI, unstable angina, or stable angina.

IVUS use varied across the 11 sites from <1% to 90% of cases (median, 33%). A total of 115 operators enrolled patients from the 11 sites, with the median IVUS use per operator ranging from 0% to 94.1% of cases. There was no significant interaction between IVUS guidance versus angiography guidance for the 1-year occurrence of the primary end point of definite/probable ST between the sites that used IVUS greater than versus less than the median (*P* for interaction=0.66). The multivariable predictors of IVUS use appear in Table I in the online-only Data Supplement. By propensity-adjusted multivariable analysis (which accounted for site, specific DES type, and other variables related to IVUS use), IVUS guidance was a predictor of definite/probable ST, MI, and MACE (Tables 5–7).

Discussion

The principal findings from this study are as follows: (1) Longer stent lengths and larger stent sizes were used in the IVUS-guided group compared with angiography guidance alone without increasing periprocedural MI; (2) IVUS guidance was strongly associated with lower 1-year rates of definite/probable DES thrombosis, MI, and MACE, as well as ischemic TLR and TVR; and (3) the greatest absolute benefits of IVUS-guidance were present in patients with acute coronary syndromes and complex coronary anatomy, although significantly better event-free survival was observed in all patient groups.

In prior randomized trials of IVUS-guided versus angiography-guided bare metal stent implantation, IVUS resulted in greater acute lumen gains with reductions in subsequent restenosis and repeat revascularization but not MI or mortality.[1] In the DES era, a meta-analysis including this trial and 10 registries reported that IVUS guidance may reduce ST and cardiac death after DES, although TVR rates were reduced only in complex lesion cohorts.[2–16] The present study reports by far the largest experience with IVUS guidance of DES implantation, with a major strength being enrollment of an all-comers population. In this population, IVUS guidance was associated with lower rates of ST, MI, and ischemia-driven TLR and TVR compared with angiography guidance alone. Moreover, whereas the event-free survival curves showed the greatest separation in the first month, the advantage of IVUS guidance was maintained and even increased at 1 year, a finding not seen in the earlier smaller studies.[12,13]

In the present study, although MACE rates were lower in all patient groups in which IVUS guidance was used, the greatest absolute benefit of IVUS was present in patients

Table 4. Clinical Outcomes at 1 Year

Event Rate at 1 y	IVUS Guided (n=3349)	Angiography Guided (n=5234)	Unadjusted Hazard Ratio (95% CI)	*P* Value
Definite or probable stent thrombosis	0.6 (18)	1.0 (53)	0.53 (0.31–0.90)	0.02
Early (0–30 d)	0.3 (11)	0.6 (31)	0.61 (0.28–1.31)	0.09
Late (>30 d to 1 y)	0.3 (9)	0.5 (23)	0.54 (0.24–1.20)	0.20
Definite stent thrombosis	0.5 (15)	0.8 (39)	0.60 [0.33–0.90]	0.09
Probable stent thrombosis	0.1 (3)	0.3 (14)	0.33 [0.10–1.16]	0.07
Major adverse cardiac events*	3.1 (103)	4.7 (238)	0.67 (0.53–0.84)	0.0006
Early (0–30 d)	1.6 (53)	2.1 (109)	0.76 (0.55–1.05)	0.10
Late (>30 d to 1 y)	1.7 (55)	2.7 (133)	0.64 (0.47–0.87)	0.005
Death	1.8 (58)	2.0 (103)	0.87 (0.63–1.20)	0.40
Cardiac	0.8 (27)	1.2 (60)	0.71 (0.45–1.12)	0.12
MI	2.5 (81)	3.7 (188)	0.67 (0.51–0.87)	0.002
Periprocedural MI	1.3 (42)	1.6 (81)	0.82 (0.57–1.19)	0.26
ST-related MI	0.4 (14)	0.6 (32)	0.68 (0.36–1.27)	0.22
Spontaneous MI	0.8 (26)	1.5 (76)	0.53 (0.34–0.82)	0.004
Target vessel–related MI†	1.7 (55)	2.9 (148)	0.58 (0.42–0.79)	0.0004
Non–target vessel–related MI†	0.6 (20)	0.7 (34)	0.91 (0.52–1.58)	0.74
Major bleeding	4.3 (144)	7.4 (387)	0.58 (0.48–0.70)	<0.0001
Stroke	0.6 (20)	0.5 (21)	1.30 (0.72–2.35)	0.38
Ischemic TLR	1.5 (51)	2.4 (124)	0.64 (0.46–0.88)	0.007
Ischemic TVR	2.4 (81)	4.0 (207)	0.60 (0.17–0.78)	0.0001

Values are percentage (number) unless indicated otherwise. CI indicates confidence interval; IVUS, intravascular ultrasound; MI, myocardial infarction; TLR, target lesion revascularization; and TVR, target vessel revascularization.

*Cardiac death, MI, or definite/probable stent thrombosis.

†Twelve MIs were indeterminate in origin and are not included in these subgroups.

with acute coronary syndromes, with a gradient of effect from STEMI to non-STEMI/unstable angina to stable coronary artery disease. In the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) IVUS substudy, early ST after primary PCI in STEMI was associated with small luminal areas within the stent and/or at the stent edge because of stent underexpansion, thrombus protrusion, and/or edge dissection.[25] The present study suggests that IVUS may substantially improve outcomes in patients with STEMI. Similarly, greater absolute benefits of IVUS were present in patients undergoing DES implantation in complex or multiple lesions compared with noncomplex single lesions. This may explain in part why earlier modest-sized studies evaluating IVUS guidance versus angiography guidance in mostly noncomplex patients and lesions were negative.

The 60% reduction in the rate of DES ST with the use of IVUS guidance (after adjustment for baseline differences, including site and stent type) in the present report is notable. Previous studies have demonstrated that the strongest predictors of DES thrombosis and restenosis are stent underexpansion and reference segment disease (including edge dissections, large untreated plaque burden, and small lumen area).[26–28] In the present study, a larger stent or balloon and/or higher inflation pressures (that would have minimized underexpansion) were used in ≈60% of IVUS-guided procedures, and additional stents (that would have mitigated inflow/outflow issues) were used in ≈20% of patients. These responses are most likely responsible for the lower rates of ST and clinical restenosis (TLR and TVR) observed in the IVUS cohort in the present study.

The 1-year rates of ST and MI, however, were significantly lower in the IVUS-guided group. Of note, the principal reduction in MI with IVUS was adjudicated to spontaneously occurring MIs and not to events related to either the procedure itself or ST. Although further study is required to understand the mechanisms through which IVUS reduced spontaneous MIs in the present study, identification and treatment of angiographically unapparent high-risk plaques adjacent to and in the same vessel as the stented segment may have contributed. In addition, in-stent restenosis may present as acute MI in 4% to 10% of cases,[29,30] and procedures for restenosis may result in MI. Reducing TLR and TVR with IVUS may thereby have also contributed to preventing subsequent MIs.

Of note, although larger stents and balloons, longer stents, and/or higher inflation pressures were used in 74.2% of IVUS-guided patients, the rate of periprocedural MI was not increased in the IVUS group. In contrast, in the randomized Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) trial of everolimus- versus sirolimus-eluting stents, IVUS was used in 619 patients (43.6%) and was associated with a significantly higher rate of periprocedural MIs compared with angiography guidance alone.[10] A sensitive definition of periprocedural MI (troponin >3 times normal, as suggested in the second universal definition of MI) was used in EXCELLENT, whereas the

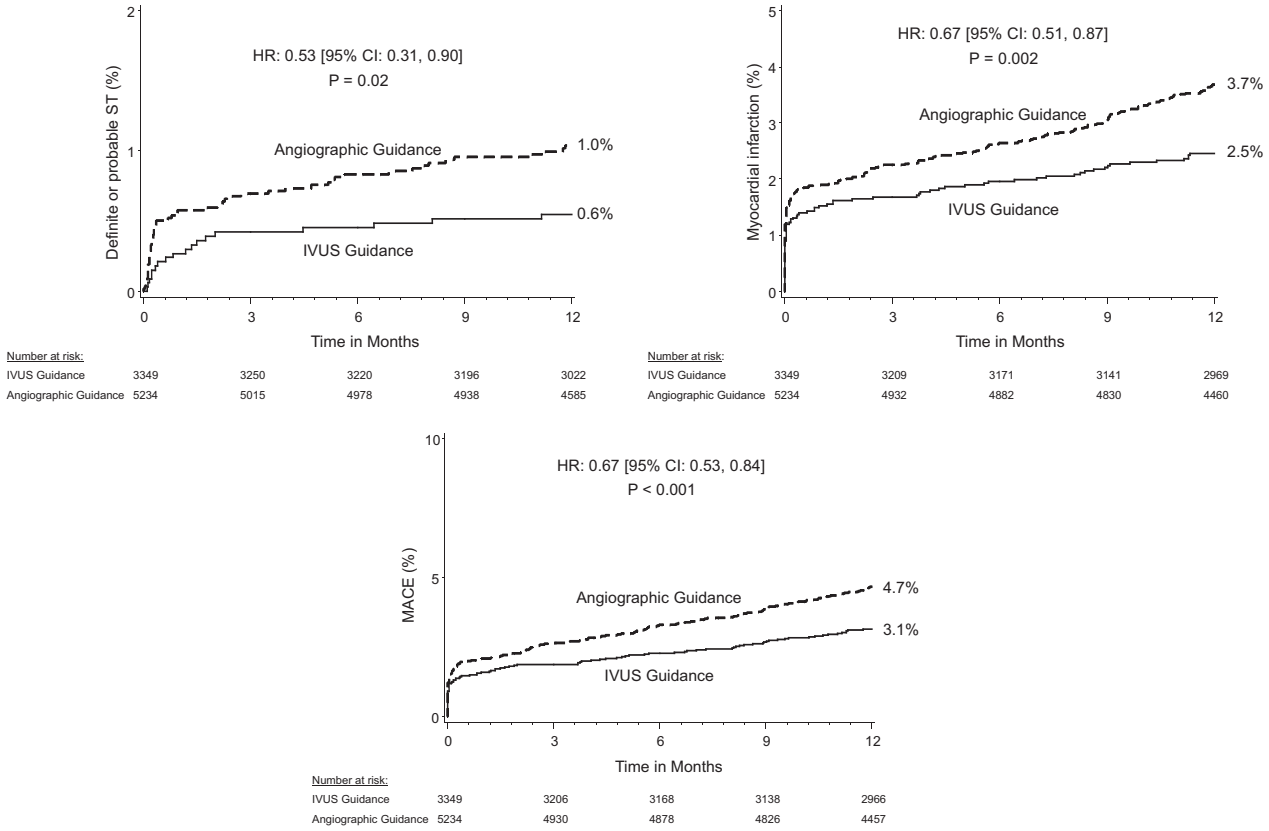

Figure. Time-to-event curves through 1 year for definite/probable stent thrombosis (ST) (**left**), myocardial infarction (**middle**), and major adverse cardiac events (MACE) (**right**) according to intravascular ultrasound (IVUS) guidance vs angiography guidance. CI indicates confidence interval; HR, hazard ratio.

present analysis used the World Health Organizatino definition (total CK >2 times the upper limit of normal with elevated CK-MB), which identifies larger MIs. Moreover, the higher rate of periprocedural MI in the EXCELLENT trial was not reported in any of the other IVUS-guided versus angiography-guided studies.

Study Limitations

The present study, although the largest to date examining the potential utility of IVUS guidance during stenting, was not a randomized trial. The decisions of whether to use IVUS and how to respond to the IVUS images were left to each operator's discretion, with no specific guidelines for optimal stenting. There was modest variation between the IVUS-guided versus angiography-guided patients; however, differences in clinical outcomes favoring IVUS persisted after propensity-adjusted multivariable analysis. Nonetheless, possible bias from unmeasured confounders cannot be excluded. The results of the present report should thus be considered hypothesis generating. The present study also cannot determine which procedural choices that IVUS influenced (eg, larger devices, longer stents) were associated with improved outcomes. Routine core laboratory analysis was not performed, and thus

Table 5. Multivariable Predictors of Definite or Probable Stent Thrombosis

	Adjusted Hazard Ratio (95% CI)	χ^2	*P* Value
IVUS guidance	0.40 (0.21–0.73)	8.76	0.003
Maximum device diameter (per 1 mm)	0.59 (0.35–1.00)	3.79	0.05
Premature DAPT discontinuation	3.57 (1.85–7.14)	14.16	0.0002
STEMI presentation	2.97 (1.63–5.42)	12.55	0.0004
Hyporesponsiveness to thienopyridine*	2.25 (1.36–3.72)	9.93	0.002
Diabetes mellitus	1.72 (1.06–2.80)	4.74	0.03
Total stent length (per 1 mm)	1.01 (1.00–1.02)	4.99	0.03

CI indicates confidence interval; DAPT, dual antiplatelet therapy; IVUS, intravascular ultrasound; and STEMI, ST-segment elevation myocardial infarction.

*Platelet reaction units >208.

Table 6. Multivariable Predictors of Myocardial Infarction

	Adjusted Hazard Ratio (95% CI)	χ^2	*P* Value
IVUS guidance	0.66 (0.49–0.88)	8.21	0.004
Renal insufficiency*	1.64 (1.19–2.26)	9.05	0.003
Three-vessel coronary artery disease	1.59 (1.23–2.04)	12.87	0.0003
Diabetes mellitus	1.48 (1.15–1.90)	9.52	0.002
Acute coronary syndrome presentation	1.40 (1.10–1.79)	7.39	0.007
Prior myocardial infarction	1.34 (1.04–1.73)	4.95	0.03

CI indicates confidence interval; IVUS, intravascular ultrasound.

*Baseline creatinine clearance <60 mL/min calculated with the Cockcroft-Gault formula.

Table 7. Multivariable Predictors of Major Cardiac Adverse Events

	Adjusted Hazard Ratio (95% CI)	χ^2	*P* Value
IVUS guidance	0.70 (0.55–0.88)	7.56	0.002
Hemoglobin (per 1 g/dL)	0.88 (0.82–0.95)	10.00	0.001
Renal insufficiency*	1.61 (1.21–2.13)	10.97	0.001
Diabetes mellitus	1.54 (1.24–1.92)	14.89	0.0001
Three-vessel coronary artery disease	1.46 (1.17–1.83)	11.37	0.001
Prior myocardial infarction	1.40 (1.12–1.76)	8.18	0.004
Acute coronary syndrome presentation	1.36 (1.10–1.69)	7.92	0.005

CI indicates confidence interval; IVUS, intravascular ultrasound.

*Baseline creatinine clearance <60 mL/min calculated with the Cockcroft-Gault formula.

we cannot determine the exact differences in stent expansion and other parameters that resulted from IVUS use. Moreover, IVUS was not performed in the control arm. Because angiographic changes in diameter often underestimate differences in minimal stent area, the modest increase in postprocedural luminal dimensions in the IVUS group likely underestimated the improvement in stent expansion in the IVUS-guided arm. Cardiac biomarkers were assessed after PCI only for evident adverse clinical events. As such, asymptomatic MIs may not have been detected, although given the fact that the present protocol excluded patients with major angiographic complications and unsuccessful procedures, it is unlikely that such occurrences would be prognostically relevant.[31] Finally, TVR, TLR, stroke, and bleeding events were not adjudicated by an independent clinical events committee, and thus we focused most of our analysis on ST, MI, and MACE.

Conclusions

The present study, drawn from the largest prospective study of IVUS use to date, suggests that IVUS guidance may reduce the rates of ST and MI within 1 year after DES implantation, with the greatest benefits present in patients with acute coronary syndromes and complex target lesions.

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The ADAPT-DES study was sponsored by the Cardiovascular Research Foundation, with funding provided by Boston Scientific, Abbott Vascular, Medtronic, Cordis, Biosensors, The Medicines Company, Daiichi-Sankyo, Eli Lilly, Volcano, and Accumetrics.

Disclosures

Dr Witzenbichler has received speaker honoraria from Boston Scientific, Abbott Vascular, and Volcano Corporation. Dr Maehara has received grant support and is a consultant for Boston Scientific, and has received speaker honoraria from St Jude Medical and Volcano. Dr Weisz is a consultant to InfraReDx. Dr Rinaldi is a consultant to Abbott, Boston Scientific, St Jude Medical, and Volcano. Dr Metzger is a consultant to Abbott Vascular, Cordis, IDEV, Medtronic, and Volcano. Dr Henry is on the Scientific Advisory Board for Abbott Vascular, Boston Scientific, and The Medicines Company and is on the Steering Committee for TRANSLATE, sponsored by Eli Lilly and Company/Daiichi Sankyo. Dr Cox is a consultant to Abbott Vascular, Boston Scientific, and The Medicines Company. Dr Stuckey is on the Advisory Board for Boston Scientific and has received speaker honoraria from Boston Scientific and Eli Lilly/Daiichi-Sankyo. Dr Mehran has received institutional grant support from The Medicines Company, Bristol-Myers Squibb/Sanofi, and Eli Lilly and Company/Daiichi Sankyo and is a consultant to Abbott Vascular, AstraZeneca, Boston Scientific, Covidien, Janssen Pharmaceuticals, Regado Biosciences, Maya Medical, Merck & Col, and The Medicines Company. Dr Mintz has received grant support from and is a consultant to Volcano Corporation and Boston Scientific Corporation. Dr Stone is a consultant to Volcano Corporation, InfraReDx, and Boston Scientific. The remaining authors have nothing to disclose.

References

1. Parise H, Maehara A, Stone GW, Leon MB, Mintz GS. Meta-analysis of randomized studies comparing intravascular ultrasound versus angiographic guidance of percutaneous coronary intervention in pre-drug-eluting stent era. *Am J Cardiol*. 2011;107:374–382.
2. Agostoni P, Valgimigli M, Van Mieghem CA, Rodriguez-Granillo GA, Aoki J, Ong AT, Tsuchida K, McFadden EP, Ligthart JM, Smits PC, de Jaegere P, Sianos G, Van der Giessen WJ, De Feyter P, Serruys PW. Comparison of early outcome of percutaneous coronary intervention for unprotected left main coronary artery disease in the drug-eluting stent era with versus without intravascular ultrasonic guidance. *Am J Cardiol*. 2005;95:644–647.
3. Jakabcin J, Spacek R, Bystron M, Kvasnák M, Jager J, Veselka J, Kala P, Cervinka P. Long-term health outcome and mortality evaluation after invasive coronary treatment using drug eluting stents with or without the IVUS guidance: randomized control trial: HOME DES IVUS. *Catheter Cardiovasc Interv*. 2010;75:578–583.
4. Roy P, Steinberg DH, Sushinsky SJ, Okabe T, Pinto Slottow TL, Kaneshige K, Xue Z, Satler LF, Kent KM, Suddath WO, Pichard AD, Weissman NJ, Lindsay J, Waksman R. The potential clinical utility of intravascular ultrasound guidance in patients undergoing percutaneous coronary intervention with drug-eluting stents. *Eur Heart J*. 2008;29:1851–1857.
5. Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW; MAIN-COMPARE Investigators. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv*. 2009;2:167–177.
6. Kim JS, Hong MK, Ko YG, Choi D, Yoon JH, Choi SH, Hahn JY, Gwon HC, Jeong MH, Kim HS, Seong IW, Yang JY, Rha SW, Tahk SJ, Seung KB, Park SJ, Jang Y. Impact of intravascular ultrasound guidance on long-term clinical outcomes in patients treated with drug-eluting stent for bifurcation lesions: data from a Korean multicenter bifurcation registry. *Am Heart J*. 2011;161:180–187.
7. Kim SH, Kim YH, Kang SJ, Park DW, Lee SW, Lee CW, Hong MK, Cheong SS, Kim JJ, Park SW, Park SJ. Long-term outcomes of intravascular ultrasound-guided stenting in coronary bifurcation lesions. *Am J Cardiol*. 2010;106:612–618.
8. Claessen BE, Mehran R, Mintz GS, Weisz G, Leon MB, Dogan O, de Ribamar Costa J Jr, Stone GW, Apostolidou I, Morales A, Chantziara V, Syros G, Sanidas E, Xu K, Tijssen JG, Henriques JP, Piek JJ, Moses JW, Maehara A, Dangas GD. Impact of intravascular ultrasound imaging on early and late clinical outcomes following percutaneous coronary intervention with drug-eluting stents. *J Am Coll Cardiol Cardiovasc Interv*. 2011;4:974–981.
9. Hur SH, Kang SJ, Kim YH, Ahn JM, Park DW, Lee SW, Yun SC, Lee CW, Park SW, Park SJ. Impact of intravascular ultrasound-guided percutaneous coronary intervention on long-term clinical outcomes in a real world population. *Catheter Cardiovasc Interv*. 2013;81:407–416.
10. Park KW, Kang SH, Yang HM, Lee HY, Kang HJ, Cho YS, Youn TJ, Koo BK, Chae IH, Kim HS. Impact of intravascular ultrasound guidance in routine percutaneous coronary intervention for conventional lesions: data from the EXCELLENT trial. *Int J Cardiol*. 2013;167:721–726.
11. Chen SL, Ye F, Zhang JJ, Tian NL, Liu ZZ, Santoso T, Zhou YJ, Jiang TM, Wen SY, Kwan TW. Intravascular ultrasound-guided systematic two-stent techniques for coronary bifurcation lesions and reduced late stent thrombosis. *Catheter Cardiovasc Interv*. 2013;81:456–463.
12. Maluenda G, Lemesle G, Ben-Dor I, Collins SD, Syed AI, Torguson R, Kaneshige K, Xue Z, Suddath WO, Satler LF, Kent KM, Lindsay J, Pichard AD, Waksman R. Impact of intravascular ultrasound guidance in patients with acute myocardial infarction undergoing percutaneous coronary intervention. *Catheter Cardiovasc Interv*. 2010;75:86–92.

13. Ahmed K, Jeong MH, Chakraborty R, Ahn Y, Sim DS, Park K, Hong YJ, Kim JH, Cho KH, Kim MC, Hachinohe D, Hwang SH, Lee MG, Cho MC, Kim CJ, Kim YJ, Park JC, Kang JC; Other Korea Acute Myocardial Infarction Registry Investigators. Role of intravascular ultrasound in patients with acute myocardial infarction undergoing percutaneous coronary intervention. *Am J Cardiol*. 2011;108:8–14.
14. Patel Y, Depta JP, Novak E, Yeung M, Lavine K, Banerjee S, Lin CH, Zajarias A, Kurz HI, Lasala JM, Bach RG, Singh J. Long-term outcomes with use of intravascular ultrasound for the treatment of coronary bifurcation lesions. *Am J Cardiol*. 2012;109:960–965.
15. Ahn JM, Han S, Park YK, Lee WS, Jang JY, Kwon CH, Park GM, Cho YR, Lee JY, Kim WJ, Park DW, Kang SJ, Lee SW, Kim YH, Lee CW, Kim JJ, Park SW, Park SJ. Differential prognostic effect of intravascular ultrasound use according to implanted stent length. *Am J Cardiol*. 2013;111:829–835.
16. De la Torre Hernandez JM, Alfonso F, Sanchez Recalde A, Jimenez Navarro MF, Perez de Prado A, Hernandez F, Abdul-Jawad Altisent O, Roura G, Garcia Camarero T, Elizaga J, Rivero F, Gimeno F, Calviño R, Moreu J, Bosa F, Rumoroso JR, Bullones JA, Gallardo A, Fernandez Diaz JA, Ruiz Arroyo JR, Aragon V, Masotti M; ESTROFA-LM Study Group. Comparison of paclitaxel-eluting stents (Taxus) and everolimus-eluting stents (Xience) in left main coronary artery disease with 3 years follow-up (from the ESTROFA-LM Registry). *Am J Cardiol*. 2013;111:676–683.
17. Bangalore S, Kumar S, Fusaro M, Amoroso N, Attubato MJ, Feit F, Bhatt DL, Slater J. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. *Circulation*. 2012;125:2873–2891.
18. Armstrong EJ, Feldman DN, Wang TY, Kaltenbach LA, Yeo KK, Wong SC, Spertus J, Shaw RE, Minutello RM, Moussa I, Ho KK, Rogers JH, Shunk KA. Clinical presentation, management, and outcomes of angiographically documented early, late, and very late stent thrombosis. *J Am Coll Cardiol Cardiovasc Interv*. 2012;5:131–140.
19. Zhang Y, Farooq V, Garcia-Garcia HM, Bourantas CV, Tian N, Dong S, Li M, Yang S, Serruys PW, Chen SL. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: a meta-analysis of one randomised trial and ten observational studies involving 19,619 patients. *EuroIntervention*. 2012;8:855–865.
20. Stone GW, Witzenbichler B, Weisz G, Rinaldi MJ, Neumann FJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Mazzaferri E, Gurbel PA, Xu K, Parise H, Kirtane AJ, Brodie BR, Mehran R, Stuckey TD; ADAPT-DES Investigators. Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study. *Lancet*. 2013;382:614–623.
21. Bangalore S, Kumar S, Fusaro M, Amoroso N, Attubato MJ, Feit F, Bhatt DL, Slater J. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. *Circulation*. 2012;125:2873–2891.
22. 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; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344–2351.
23. Stone GW, Bertrand M, Colombo A, Dangas G, Farkouh ME, Feit F, Lansky AJ, Lincoff AM, Mehran R, Moses JW, Ohman M, White HD. Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial: study design and rationale. *Am Heart J*. 2004;148:764–775.
24. Mehran R, Brodie B, Cox DA, Grines CL, Rutherford B, Bhatt DL, Dangas G, Feit F, Ohman EM, Parise H, Fahy M, Lansky AJ, Stone GW. The Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial: study design and rationale. *Am Heart J*. 2008;156:44–56.
25. Choi SY, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, Kellett MA Jr, Dressler O, Parise H, Mehran R, Dangas GD, Mintz GS, Stone GW. Intravascular ultrasound findings of early stent thrombosis after primary percutaneous intervention in acute myocardial infarction: a Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) substudy. *Circ Cardiovasc Interv*. 2011;4:239–247.
26. Cheneau E, Leborgne L, Mintz GS, Kotani J, Pichard AD, Satler LF, Canos D, Castagna M, Weissman NJ, Waksman R. Predictors of subacute stent thrombosis: results of a systematic intravascular ultrasound study. *Circulation*. 2003;108:43–47.
27. Fujii K, Carlier SG, Mintz GS, Yang YM, Moussa I, Weisz G, Dangas G, Mehran R, Lansky AJ, Kreps EM, Collins M, Stone GW, Moses JW, Leon MB. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. *J Am Coll Cardiol*. 2005;45:995–998.
28. De Labriolle A, Bonello L, Lemesle G, Steinberg DH, Roy P, Xue Z, Kaneshige K, Suddath WO, Satler LF, Kent KM, Pichard AD, Lindsay J, Waksman R. Clinical presentation and outcome of patients hospitalized for symptomatic in-stent restenosis treated by percutaneous coronary intervention: comparison between drug-eluting stents and bare-metal stents. *Arch Cardiovasc Dis*. 2009;102:209–217.
29. Chen MS, John JM, Chew DP, Lee DS, Ellis SG, Bhatt DL. Bare metal stent restenosis is not a benign clinical entity. *Am Heart J*. 2006;151:1260–1264.
30. Pervaiz MH, Sood P, Sudhir K, Hermiller JB, Hou L, Hattori K, Su X, Cao S, Wang J, Applegate RJ, Kereiakes DJ, Yaqub M, Stone GW, Cutlip DE. Periprocedural myocardial infarction in a randomized trial of everolimus-eluting and paclitaxel-eluting coronary stents: frequency and impact on mortality according to historic versus universal definitions. *Circ Cardiovasc Interv*. 2012;5:150–156.
31. Jeremias A, Baim DS, Ho KK, Chauhan M, Carrozza JP Jr, Cohen DJ, Popma JJ, Kuntz RE, Cutlip DE. Differential mortality risk of postprocedural creatine kinase-MB elevation following successful versus unsuccessful stent procedures. *J Am Coll Cardiol*. 2004;44:1210–1214.

CLINICAL PERSPECTIVE

Prior small to modest-sized studies suggest a benefit of intravascular ultrasound (IVUS) guidance in noncomplex lesions. Whether IVUS guidance is associated with improved clinical outcomes after drug-eluting stent (DES) implantation in an unrestricted patient population is unknown. Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) was a prospective, multicenter, nonrandomized "all-comers" study of 8583 consecutive patients at 11 international centers designed to determine the frequency, timing, and correlates of stent thrombosis and adverse clinical events after DES. Propensity-adjusted multivariable analysis was performed to examine the relationship between IVUS guidance and 1-year outcomes. IVUS was utilized in 3349 patients (39%), and larger-diameter devices, longer stents, and/or higher inflation pressures were used in 74% of IVUS-guided cases. IVUS guidance compared with angiography guidance was associated with reduced 1-year rates of definite/probable stent thrombosis (0.6% versus 1.0%; adjusted hazard ratio, 0.40; 95% confidence interval, 0.21–0.73; P=0.003), myocardial infarction (2.5% versus 3.7%; adjusted hazard ratio, 0.66; 95% confidence interval, 0.49–0.88; P=0.004), and composite adjudicated major adverse cardiac events (cardiac death, myocardial infarction, or stent thrombosis) (3.1% versus 4.7%; adjusted hazard ratio, 0.70; 95% confidence interval, 0.55–0.88; P=0.002). The benefits of IVUS were especially evident in patients with acute coronary syndromes and complex lesions, although significant reductions in major adverse cardiac events were present in all patient subgroups including stable angina and single-vessel disease. In ADAPT-DES, the largest study of IVUS use to date, IVUS guidance was associated with a reduction in stent thrombosis, myocardial infarction, and major adverse cardiac events within 1 year after DES implantation.

Relationship Between Intravascular Ultrasound Guidance and Clinical Outcomes After Drug-Eluting Stents: The Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) Study

Bernhard Witzenbichler, Akiko Maehara, Giora Weisz, Franz-Josef Neumann, Michael J. Rinaldi, D. Christopher Metzger, Timothy D. Henry, David A. Cox, Peter L. Duffy, Bruce R. Brodie, Thomas D. Stuckey, Ernest L. Mazzaferri, Jr, Ke Xu, Helen Parise, Roxana Mehran, Gary S. Mintz and Gregg W. Stone

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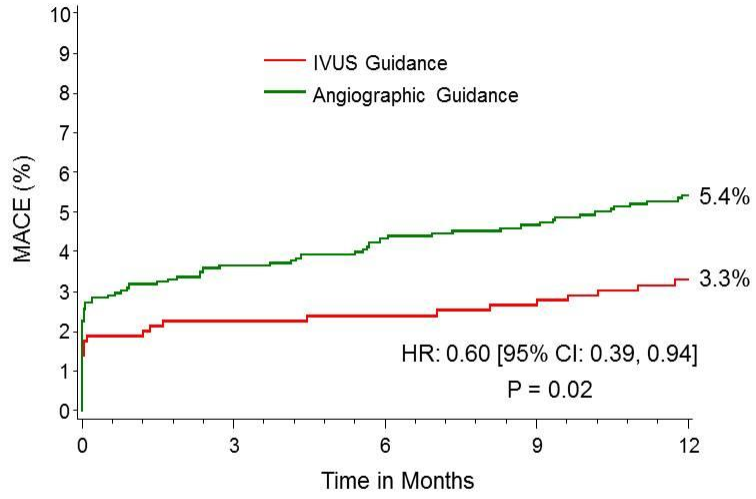
SUPPLEMENTAL MATERIAL

Supplemental Table 1. Multivariable predictors of IVUS use (prior to propensity adjustment)

Variable	Hazard Ratio [95% CI]	P-value
Male	0.87 [0.77, 0.97]	0.01
Caucasian	0.76 [0.65, 0.89]	0.0005
Body mass index >30 kg/m^2	0.82 [0.74, 0.91]	0.0001
History of renal insufficiency	1.26 [1.04, 1.53]	0.02
Hyperlipidemia	0.66 [0.57, 0.75]	<0.0001
History of congestive heart failure	0.55 [0.45, 0.68]	<0.0001
Prior coronary bypass grafting	0.75 [0.64, 0.88]	0.0006
ST-segment elevation MI presentation	1.55 [1.27, 1.89]	<0.0001
Anemia	0.87 [0.77, 0.99]	0.04
Three vessels treated	0.41 [0.26, 0.63]	<0.0001
Left anterior descending artery location	1.33 [1.20, 1.47]	<0.0001
Baseline -stenosis >= median (90%)	0.81 [0.72, 0.90]	0.0001
Post-PCI stenosis >= median (0%)	1.41 [1.18, 1.68]	0.0001
Calcified lesion	1.18 [1.05, 1.33]	0.007
Ostial lesion	1.44 [1.23, 1.68]	<0.0001
Bifurcation lesion	0.65 [0.56, 0.76]	<0.0001
Graft lesion	0.57 [0.42, 0.76]	0.0001
Max device diameter >= median (3.25 mm)	2.74 [2.48, 3.04]	<0.0001
Max balloon pressure >= median (16 atm.)	1.12 [1.01, 1.24]	0.03
Patients with drug-eluting stents only	1.69 [1.12, 2.56]	0.0122
Everolimus-eluting stent usage	1.55 [1.40, 1.73]	<0.0001
Closure device used	2.64 [2.37, 2.94]	<0.0001
Thienopyridine pre-hospital admission	1.44 [1.29, 1.60]	<0.0001
Thienopyridine loading dose	0.55 [0.47, 0.64]	<0.0001
Aspirin loading dose	1.23 [1.03, 1.47]	0.02
Bivalirudin use	0.84 [0.75, 0.94]	0.002
Heparin use	1.52 [1.16, 1.98]	0.003
Low molecular weight heparin use	2.18 [1.85, 2.57]	<0.0001
Glycoprotein IIb/IIIa inhibitor use	0.56 [0.41, 0.76]	0.0002
Angiotensin converting enzyme inhibitor or receptor blocker use	1.16 [1.04, 1.30]	0.007
Diuretic use	1.12 [1.01, 1.26]	0.04
Proton pump inhibitor use	1.14 [1.02, 1.27]	0.02
TNK (rtPA) use	0.50 [0.32, 0.78]	0.002

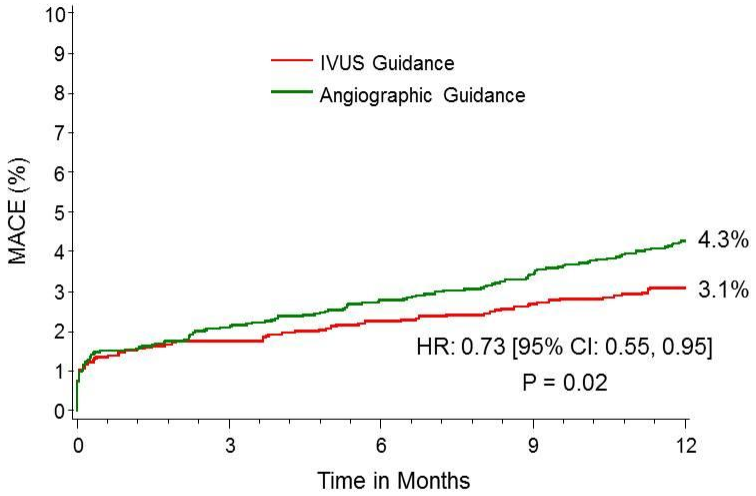
Supplemetnal Figure 1, left.



Number at risk:

IVUS Guidance	802	768	760	753	702
Angiographic Guidance	1520	1424	1409	1399	1305

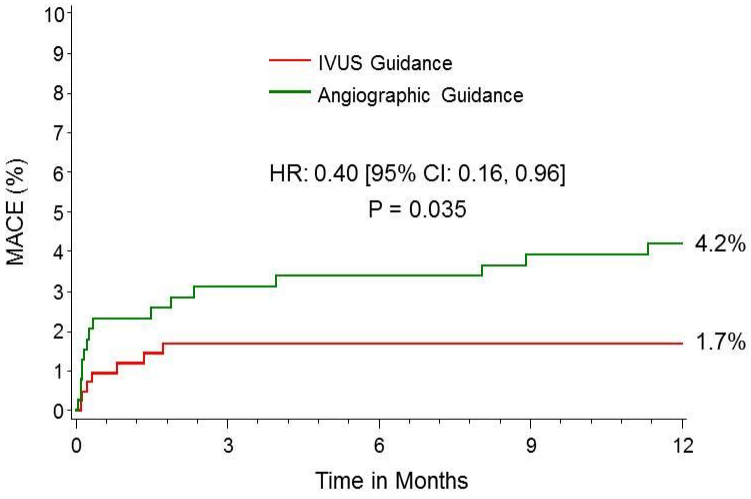
Supplemental Figure 1, right



Number at risk:

IVUS Guidance	2538	2429	2399	2376	2256
Angiographic Guidance	3669	3466	3429	3387	3113

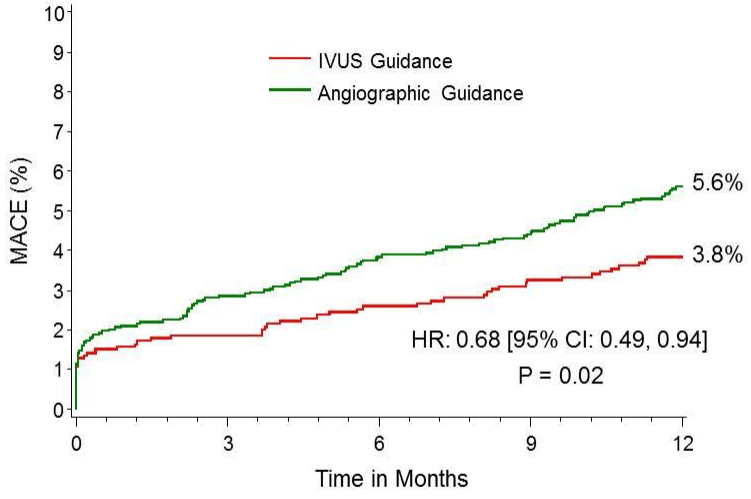
Supplemental Figure 2, left



Number at risk:

IVUS Guidance	421	407	406	403	390
Angiographic Guidance	392	361	357	353	329

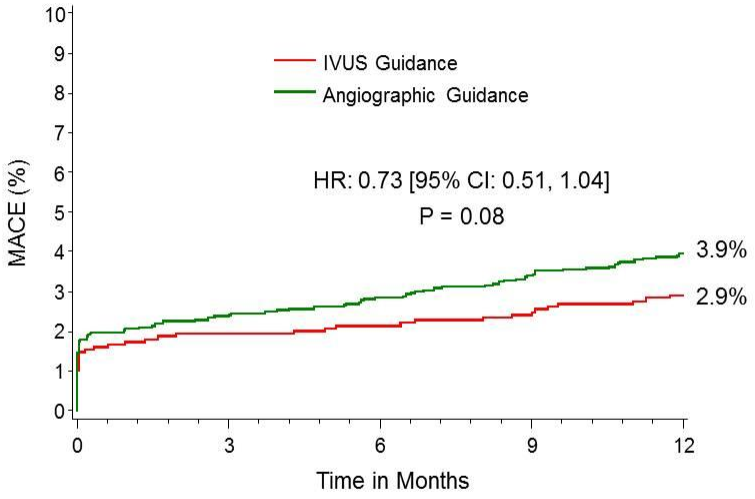
Supplemental Figure 2, middle



Number at risk:

IVUS Guidance	1415	1352	1331	1317	1253
Angiographic Guidance	2208	2070	2042	2022	1840

Supplemental Figure 2, right



Number at risk:

IVUS Guidance	1513	1447	1431	1418	1323
Angiographic Guidance	2634	2499	2479	2451	2288