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Outcome of ST-elevation myocardial infarction *versus* non-ST-elevation acute coronary syndrome treated with titanium-nitride-oxide-coated *versus* everolimus-eluting stents: insights from the BASE-ACS trial

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Aim. The BASE-ACS trial demonstrated an outcome of titanium-nitride-oxide-coated bioactive stents (BAS) that was statistically non-inferior to that of everolimus-eluting stents (EES) at 12-month follow-up, in patients presenting with acute coronary syndrome (ACS) who underwent early percutaneous coronary intervention (PCI). We explored a *post-hoc* analysis of the 12-month outcome of the BASE-ACS trial in the subgroup of patients with ST-elevation myocardial infarction (STEMI) *versus* non-ST-elevation ACS (non-STEACS).
Methods. A total of 827 patients with ACS (321 STEMI) were randomly assigned to receive either BAS or EES. The primary endpoint was a composite of cardiac death, non-fatal myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) at 12-month follow-up.
Results. The 12-month cumulative incidence of the primary endpoint was similar between the two subgroups (9% *versus* 9.5%, in STEMI *versus* non-STEACS patients respectively, P=0.90). The 12-month rate of cardiac death was significantly higher in the STEMI subgroup as compared with the non-STEACS subgroup (2.8 *versus* 0.6%, respectively, P=0.01). However, the rates of non-fatal MI, ischemia-driven TLR, definite stent thrombosis, and non-cardiac death were all statistically matched between the two subgroups (P>0.05 for all).
Conclusion. In the current post-hoc analysis of the BASE-ACS trial based on the infarction type, the 12-month outcome of patients who underwent early PCI for ACS was slightly worse in the setting of STEMI as compared with non-STEACS, as reflected by a significantly higher rate of cardiac death.

Key words: **Percutaneous coronary intervention - Titanium - Drug-eluting stents - myocardial infarction.**

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Primary percutaneous coronary intervention (PCI) with stenting is currently the state-of-the-art means of restoring reperfusion of the culprit artery in patients presenting with acute ST-segment elevation myocardial infarction (STEMI).[1-3] However, since the introduction of coronary stents, restenosis resulting from neointimal hyperplasia has always been the "Achilles Heel" of this technique, frequently ending up with repeat intervention and, consequently, increased healthcare cost.[4, 5] Several clinical

trials and meta-analyses demonstrated that the use of drug-eluting stents (DES) in patients presenting with acute STEMI, is safe and improves clinical outcome, chiefly by reducing the rate of re-intervention, as compared with bare metal stents (BMS).[6-10] Nevertheless, data from meta-analyses and registries have questioned the long-term safety of DES, raising concerns about a higher risk of late - and very late - stent thrombosis (ST), a potentially life-threatening complication.[11-13] Recently, the safety of the titanium-nitride-oxide-coated bioactive stents (BAS) has been established in several reports from real-life unselected populations.[14, 15] Interestingly, a randomized study has demonstrated a rather "better" outcome with BAS in comparison with paclitaxel-eluting stents the setting of acute myocardial infarction (MI).[16]

Evidence for a divergence of outcome in patients with STEMI treated with primary PCI and those with non-STEMI treated with the early invasive strategy is still unclear. In a *post-hoc* analysis of the CADILLAC randomized controlled trial; non-STEMI patients had a similar late mortality, but a significantly higher rate of ischemia-driven target vessel revascularization, despite favourable baseline angiographic characteristics and similar procedural success rates.[17] Further insights from the NHLBI registry data indicated a higher in-hospital mortality rate in patients with STEMI; yet, a similar outcome at one year follow-up.[18] In the multicenter large randomized controlled BASE-ACS trial, BAS proved non-inferior to everolimus-eluting stents (EES) at 12-month follow-up in patients presenting with acute coronary syndrome (ACS) including both STEMI and non-ST-segment elevation ACS (non-STEACS).[19] We performed a *post-hoc* analysis of the 12-month outcome of the BASE-ACS trial based on the subgroups presenting with STEMI versus non-STEACS.

Materials and methods

Patient selection and study design

The design of the original trial has been previously reported.[19] Briefly, the BASE-ACS (A prospective randomized comparison of titanium-nitride-oxide-coated bioactive stents with everolimus-eluting stents in acute coronary syndrome) trial is a prospective multicenter randomized controlled clinical trial, with the chief aim to evaluate non-inferiority in clinical outcomes of BAS (Titan2®, Hexacath, Paris, France) as compared with EES (Xience V, Abbott Vascular, Santa Clara, CA, USA) in patients presenting with the whole spectrum of ACS. The study enrolled a total of 827 patients above 18 years, presenting with ACS, with at least one significant *de novo* lesion (defined as at least 50% diameter stenosis by visual estimation) in a native coronary artery or coronary bypass graft. Chief exclusion criteria were limited to unprotected left main disease or aorto-ostial lesions, intolerance to the study medications, planned surgery within 12 months of the index procedure, and life expectancy less than 12 months. Enrolled patients were randomly assigned in a 1:1 fashion to receive either BAS or EES. The operators were be necessity aware of the assigned study stent, but patients and the staff involved in follow-up assessment were blinded to the allocated stent type.

Ethical issues

The study was initiated by the investigators and conducted according to the ethical guidelines of the 1964 Declaration of Helsinki, as revised in 2002. An informed written consent was obtained from every patient after full explanation of the study protocol. The study protocol was approved by the Ethics Committees of the coordinating center, Satakunta Central Hospital, and the other participating hospitals. The BASE-ACS trial is registered with ClinicalTrials.gov, number NCT00819923.

Pharmacological interventions

Patients already maintained on aspirin received no additional aspirin loading dose. Those not maintained on aspirin were pre-treated with aspirin at a loading dose of 250 mg orally or 250-500 mg intravenously dur-

ing PCI, and continued thereafter at a daily dose of at least 75-150 mg indefinitely. Oral clopidogrel was initiated at a loading dose of at least 300 mg before or immediately after the procedure and continued thereafter at a daily dose of 75 mg. According to the protocol, patients in either group were prescribed oral clopidogrel for a minimum of 6 months, and thereafter, for extended periods (maximum 12 months) according to the operator's discretion. During the procedure, low-molecular weight heparin (enoxaparin sodium) or unfractionated heparin was administered intravenously in the standard dosage recommended by the guidelines. Use of peri-procedural glycoprotein IIb/IIIa inhibitors or bivalirudin was left up to the operator's discretion.

Study endpoints and definitions

Diagnostic criteria for STEMI and non-STEACS have been previously described in detail.[19] The primary endpoint was the first occurrence of major adverse cardiac events (MACE), defined as a composite of cardiac death, non-fatal MI, or ischemia-driven target lesion revascularization (TLR) at 12-month follow-up. Secondary endpoints included all-cause death, a composite of cardiac death or non-fatal MI, and definite ST at 12-month follow-up. Cardiac death was defined as death from cardiovascular causes or any death without another known cause. ST was adjudicated according to the criteria of definite and probable ST described by the Academic Research Consortium (ARC).[20] An independent Clinical Events Committee whose members were blinded to stent group allocation throughout the study period adjudicated all clinical events for analysis. Outcomes were examined across the randomized groups as a function of the type of ACS (non-STEACS or STEMI) and stent type.

Statistical analysis

Continuous variables were presented as mean ± SD, while categorical variables were described with absolute and relative (percentage) frequencies. Comparisons between the two groups were performed using the unpaired two-tailed t-test for continuous, and the Pearson chi-square test or Fisher's exact test for categorical variables. All data were presented on the basis of the intention-to-treat principle, which included all patients who underwent randomization, regardless of the treatment actually received. Selected baseline characteristics and 1-year clinical outcomes were compared between the two subgroups (STEMI versus non-STEACS), and no adjustments were made for multiple comparisons. All tests were two-sided and statistical significance was set at 5%. All data were analyzed with the use of SPSS version 11, and SAS system for Windows version 9.1 (SAS Institute Inc., Cary, NC, USA).

Results

Baseline clinical, angiographic and procedural data

Of the 827 enrolled patients, 417 were assigned to receive BAS (including 162 [38.8%] STEMI patients), and 410 to EES (including 159 [38.8%] STEMI patients). Baseline clinical characteristics are shown in Table I. Patients with STEMI were significantly younger, more likely to be smoker, but less likely to have hypertension, hyperlipidemia, prior MI, and prior PCI and coronary bypass surgery as compared with those with non-STEACS. Baseline angiographic and procedural data are shown in Table II. Patients with STEMI had less lesions treated per patient; however, they were significantly more likely to have type C lesions, thrombus-containing lesions, underwent more direct stenting and thrombus aspiration, and received more glycoprotein IIb/IIIa inhibitors and bivalirudin, but less low-molecular weight heparin as compared with those with non-STEACS.

Clinical outcome of the BASE-ACS at 12-month follow-up

BAS were non-inferior, as compared with EES, with respect to the occurrence of the

TABLE I.—*Baseline clinical characteristics of the two individual subgroups.*

Variable	STEMI subgroup (N.=321)	Non-STEACS subgroup (N.=506)	P value
Age (years)	61.7 ± 12.2	63.8 ± 11.6	0.011
Male gender	249 (77.6)	380 (75.1)	0.45
Diabetes mellitus	47 (14.6)	93 (18.4)	0.18
Insulin-treated	13 (4.0)	23 (4.5)	0.86
Current smoking	139 (43.3)	139 (27.5)	0.0001
Hyperlipidemia	105 (32.7)	283 (55.9)	0.0001
Hypertension	115 (35.8)	298 (58.9)	0.0001
Prior MI	21 (6.5)	75 (14.8)	0.0001
Prior PCI	17 (5.3)	66 (13.0)	0.0001
Prior CABG	7 (2.2)	30 (5.9)	0.015

Continuous variables are presented as mean ± SD, while categorical variables are presented as frequency (percentage). CAD: coronary artery disease; PCI: percutaneous coronary revascularization; CABG: coronary artery bypass grafting; GP: glycoprotein; non-STEACS: non-ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction.

TABLE II.—*Angiographic and procedural characteristics of the two individual subgroups.*

Variable	STEMI subgroup (N.=321)	Non-STEACS subgroup (N.=506)	P value
Radial access	178 (55.5)	305 (60.3)	0.19
Number of lesions treated per patient	1.15±0.4	1.22±0.5	0.042
Number of stents per culprit lesion	1.15±0.4	1.14±0.4	0.89
Lesion type			
A	17 (5.3)	79 (15.6)	0.0001
B	237 (73.8)	363 (71.7)	0.52
C	67 (20.9)	64 (12.6)	0.002
Thrombus	239 (74.5)	125 (24.7)	0.0001
Calcified lesions	133 (41.4)	219 (43.3)	0.614
Bifurcation lesions	54 (16.8)	123 (24.3)	0.012
Reference vessel diameter (mm)	3.12±0.4	3.14±0.4	0.45
Lesion length (mm)	14.8±6.3	14.1±5.7	0.08
Stent diameter (mm)	3.14±0.4	3.16±0.5	0.53
Stent length (mm)	18.6±5.2	17.9±5.5	0.12
Total stent length per lesion (mm)	21.3±9.1	20.3±8.7	0.10
Direct stenting	140 (43.6)	120 (25.7)	0.0001
Thrombus aspiration	137 (42.7)	17 (3.4)	0.0001
Post-dilatation	135 (42.1)	222 (43.9)	0.61
Procedural success	320 (99.7)	505 (99.8)	1.00
Unfractionated heparin	89 (27.7)	126 (24.9)	0.37
Low-molecular weight heparin	130 (40.5)	353 (69.8)	0.0001
GP IIb/IIIa inhibitor	131 (40.8)	111 (21.9)	0.0001
Bivalirudin	100 (31.2)	21 (4.2)	0.0001

Continuous variables are presented as mean±SD, while categorical variables are presented as frequency (percentage). TIMI: thrombolysis in myocardial infarction; non-STEACS: non-ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction.

primary composite endpoint of MACE at 12-month follow-up (9.6% *versus* 9%, respectively; relative risk for EES, 0.94; 95% confidence interval [CI], 0.59-1.5; P=0.81 for superiority; P=0.001 for non-inferiority) (Figure 1). Non-fatal MI was significantly less frequent in the BAS group as compared with the EES group (2.2% *versus* 5.9%, respectively; P=0.007). Among the secondary endpoints, the rate of definite ST trended

to be less frequent in patients who received BAS (0.7% *versus* 2.2%, respectively; P=0.07).

Clinical outcome at 12 months in patients with STEMI versus *those with non-STEACS*

The 12-month cumulative incidence of MACE was similar between the two subgroups (9% *versus* 9.5%, in STEMI *versus*
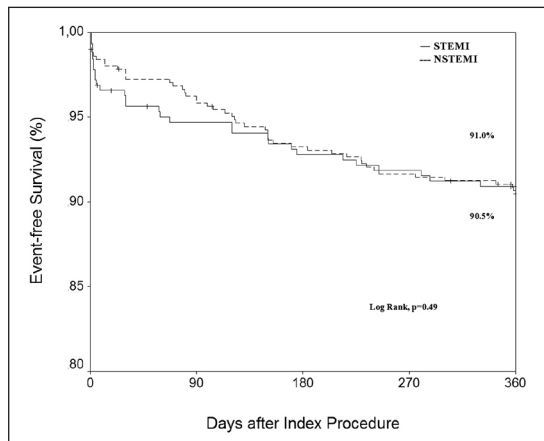
Figure 1.—Event-free survival curves for the 2 infarction-type subgroups. Non-STEACS, non-ST-elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction; ST.

P=0.89). Similarly, the rates of cardiac death were not significantly different between the two stent arms (3.7% *versus* 1.9%, respectively, P=0.50). Yet, the rates of non-fatal MI and those of definite ST showed a trend to reduction in the BAS arm (1.2% *versus* 4.4%, and 0.6% *versus* 3.8%; P=0.09, and P=0.053; respectively). The rates of ischemia-driven TLR were also statistically similar between the two stent arms (5.6% *versus* 5.1%, respectively, P=0.85) (Figure 2A). Likewise, among patients presenting with non-STEACS, the primary composite endpoint of MACE was statistically similar between the two stent arms (9.8% *versus* 9.2%, respectively, P=0.81). Similarly, the rates of cardiac death and definite ST were statistically similar between the two stent arms (0.8% *versus* 0.4%; and 0.8% *versus* 1.2%; P=0.57, and P=0.68; respectively). Non-fatal MI was significantly lower in patients assigned to BAS as compared with those assigned to EES (2.7% *versus* 6.8%, respectively, P=0.03). Ischemia-driven TLR was statistically similar between the two stent arms (7.1% *versus* 4.8%, respectively, P=0.35) (Figure 2B).

Infarction-type-based analysis of the two stent arms

Among patients assigned to receive the BAS, the primary composite endpoint of MACE was statistically similar in patients presenting with STEMI as compared with those presenting with non-STEACS (9.3% *versus* 9.8%, respectively, P=0.85). The rate of cardiac death was significantly higher in patients with STEMI (3.7% *versus* 0.8%, re-

non-STEACS patients respectively, P=0.90). However, the rate of cardiac death was significantly higher in patients with STEMI (2.8% *versus* 0.6%, respectively, P=0.01). Otherwise, the 12-month rates of non-fatal MI, ischemia-driven TLR, definite ST and non-cardiac death were all statistically matched between the two subgroups (P>0.05 for all) (Table III).

Stent-based analysis of the two infarction-type subgroups

Among patients presenting with STEMI, the primary composite endpoint of MACE was statistically similar in patients assigned to receive BAS and those assigned to receive EES (9.3% *versus* 8.8%, respectively,

TABLE III.—*Clinical outcome in the two individual subgroups at 12-month follow-up.*

Variable	STEMI subgroup (N.=321)	Non-STEACS subgroup (N.=506)	OR	95% CI	P value
Cardiac death	9 (2.8)	3 (0.6)	0.51	0.36 - 0.72	0.01
Non-fatal MI	9 (2.8)	24 (4.7)	1.44	0.82 - 2.53	0.17
Ischemia-driven TLR	17 (5.3)	30 (5.9)	1.08	0.73 -1.59	0.76
MACE	29 (9.0)	48 (9.5)	1.03	0.77 - 1.40	0.90
Definite ST	7 (2.2)	5 (1.0)	0.66	0.41 - 1.07	0.16
Non-cardiac death	4 (1.2)	9 (1.8)	1.27	0.56 - 2.87	0.78

Variables are presented as frequency (percentage). MI: myocardial infarction; TLR: target lesion revascularization; MACE: major adverse cardiac events; ST: stent thrombosis; non-STEACS: non-ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction; OR: odds ratio; CI: confidence interval.
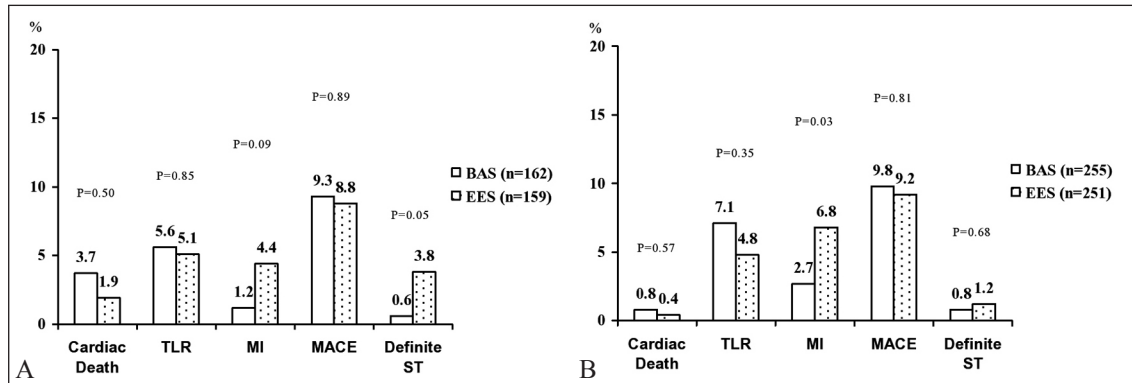
Figure 2.—Stent type-based analysis of the 2 infarction-type subgroups: A) STEMI; B) non-STEACS. BAS: bioactive stents; EES: everolimus-eluting stent; MACE: major adverse cardiac events; MI: myocardial infarction; non-STEACS: non-ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularization.
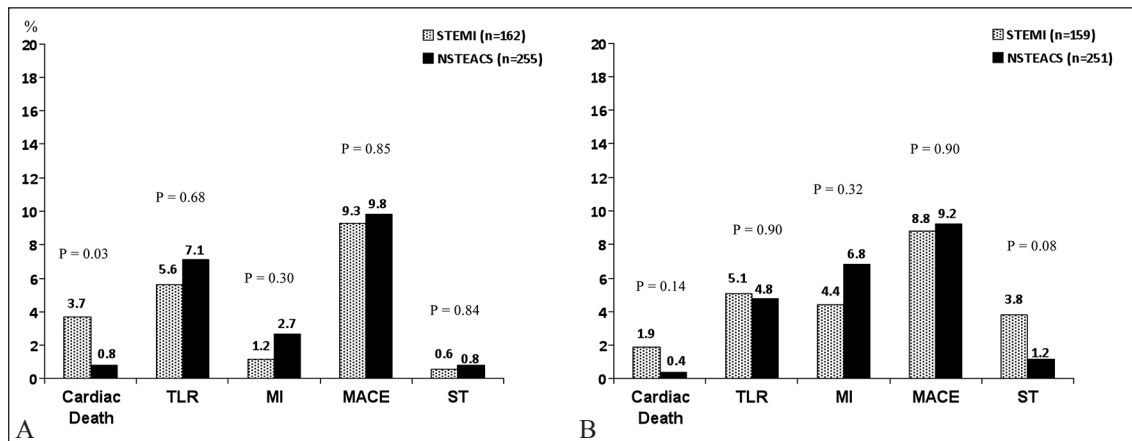

Figure 3.—Infarction-type-based analysis of the 2 stent treatment arms: A) BAS, B) EES. BAS: bioactive stents; EES: everolimus-eluting stent; MACE: major adverse cardiac events; MI: myocardial infarction; non-STEACS: non-ST-elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularization.

spectively, P=0.034). However, the rates of non-fatal MI, definite ST, and ischemia-driven TLR were all similar between the two subgroups (P>0.05 for all) (Figure 3A). Comparatively, among patients assigned to receive the EES, the primary composite endpoint of MACE was statistically similar in the two subgroups (8.8% *versus* 9.2%, respectively, P=0.90). Patients who presented with STEMI showed a trend toward a higher rate of ST (3.8% *versus* 1.2%, respectively, P=0.08). Otherwise, other secondary endpoints were statistically matched between the two subgroups (P>0.05 for all) (Figure 3B).

Discussion

Main findings

The current *post-hoc* analysis of the BASE-ACS trial based on the type of ACS (STEMI *versus* non-STEACS) demonstrated that the 12-month outcome of patients presenting with ACS and undergoing early PCI (irrespective of stent type) was slightly worse in patients presenting with STEMI, as reflected by a significantly higher rate of cardiac death, in comparison with those presenting with non-STEACS; yet, the composite incidence of MACE at 12-month

follow-up was similar between the two subgroups (P>0.05). To the best of the authors' knowledge, this is the first systematic analysis of outcome based on the type of ACS at presentation in patients treated with BAS.

Clinical outcome in STEMI patients: BASE-ACS trial

Despite the fact that patients with STEMI fared as well as those with non-STEACS concerning the one-year primary composite endpoint of MACE; yet, cardiac mortality was significantly higher in the STEMI subgroup. Not surprisingly, however, the two subgroups were substantially different regarding the baseline clinical and angiographic characteristics. Although patients with STEMI were younger and – apart from more frequent smoking – had fewer cardiovascular risk factors and less extensive coronary affection, and were less likely to have prior coronary events; they were substantially more likely to have complex coronary lesions and angiographically evident thrombosis over their plaques. Similarly, previous studies demonstrated that patients presenting with non-STEMI were older, with more comorbidities, and more extensive coronary artery disease. Prior evidence also demonstrated significantly higher early mortality rates in patients with STEMI *versus* those with non-STEMI, which persisted even after risk adjustment.[17, 18, 21] At least some of the difference in mortality might be attributed to larger infarct size or anterior infarct location in STEMI, with a subsequently compromised left ventricular systolic function, the single most important predictor of long-term survival following MI. Furthermore, ischemic preconditioning and perhaps more importantly, adequate collateral circulation in patients presenting with non-STEACS – who were older and had more past coronary events – might have reduced the impact of the index acute ischemic event. Owing to the retrospective nature of this post-hoc subgroup analysis, data relevant to left ventricular systolic function, collat-

eral circulation, along with other data relevant to outcome such as the time from symptom onset to intervention and bleeding complications, have been overlooked. Interestingly, increased cardiac death rates in the STEMI subgroup was not related to procedural success or procedure-related complications, which were similar by MI type.

Although the 12-month rates of nonfatal MI were slightly higher in patients presenting with non-STEACS *versus* those presenting with STEMI; yet, the difference did not meet statistical significance (4.7% *versus* 2.8%, respectively, P=0.17). And despite the higher prevalence of complex type C lesions and thrombus-containing stenoses in the subgroup of STEMI, this subgroup was significantly more likely to undergo mechanical thrombus aspiration, and to receive periprocedural glycoprotein IIb/IIIa inhibitors and bivalirudin, all of which would contribute to a lower rate of early thrombotic events. In accordance with our results, other reports observed similar rates of recurrent MI following the early invasive approach for patients with STEMI *versus* non-STEMI.[17, 18]

Likewise, the rates of ischemia-driven TLR were comparable based on MI type at 12-month follow-up. Despite the higher frequency of type C lesions in the subgroup of STEMI, those with non-STEACS had more lesions treated per patient and more bifurcation lesions. Ultimately, the mean stent length and diameter were similar between the two subgroups. Our findings are in agreement with a previous registry of patients with acute MI who underwent early PCI, in which STEMI and non-STEMI patients had analogous rates of recurrent MI.[18] Nevertheless, a substudy of the large randomized controlled CADILLAC trial demonstrated that ischemia-driven target vessel revascularization rates were higher for patients with non-STEMI *versus* those with STEMI.[17] The higher prevalence of insulin-dependent diabetes mellitus among the non-STEMI subset in that trial might underlie the higher rates of re-intervention.

Limitations of the study

The BASE-ACS trial was not designed *a priori* to particularly explore subgroup differences in outcome, whether as a pooled subgroup analysis or as regards subgroup and type of stent implanted. Furthermore, as already stated earlier, due to the retrospective nature of this *post-hoc* analysis, some data relevant to the outcome of PCI may have been missed. In addition, the trial may have been underpowered for specific subgroup analysis; therefore any conclusions drawn from the analysis data should be taken cautiously. Finally, the findings of the current *post-hoc* analysis should be interpreted with the recognition that it was a non-randomized subset analysis, which might limit the conclusiveness of its findings.

Conclusions

In the current post-hoc analysis of the BASE-ACS trial based on the infarction type, the 12-month outcome of patients presenting with ACS who underwent early PCI was slightly worse in the setting of STEMI as compared with non-STEACS, as reflected by a significantly higher rate of cardiac death.

Riassunto

Esito dell'infarto miocardico con sopraslivellamento del tratto ST rispetto alla sindrome coronarica acuta senza sopraslivellamento ST, trattati con stent a rivestimento di ossido di titanio-nitruro rispetto a stent a rilascio di everolimus: dati del trial BASE-ACS

Obiettivo. Lo studio BASE-ACS ha dimostrato che l'esito di stent bioattivi a rivestimento di ossido di titanio-nitruro (BAS) era statisticamente non inferiore a quello degli stent a rilascio di everolimus (EES) a 12 mesi di follow-up, in pazienti affetti da sindrome coronarica acuta (ACS) sottoposti a intervento coronarico percutaneo precoce (PCI). Abbiamo esaminato un'analisi a posteriori dell'esito a 12 mesi dello studio BASE-ACS nel sottogruppo di pazienti colpiti da infarto miocardico con sopraslivellamento del tratto ST (STEMI), rispetto ad ACS senza sopraslivellamento ST (non STEACS).

Metodi. Un totale di 827 pazienti con ACS (321 STEMI) è stato assegnato in modo casuale alla somministrazione di BAS o SEE. L'endpoint primario era un composito di morte cardiaca, infarto miocardico (MI) non fatale e rivascolarizzazione della lesione target da ischemia (TLR) a 12 mesi di follow-up.

Risultati. L'incidenza cumulativa a 12 mesi dell'endpoint primario è risultata simile tra i due sottogruppi (9% contro il 9,5%, rispettivamente, nei pazienti STEMI rispetto ai non STEACS, P= 0,90). La percentuale di morte cardiaca a 12 mesi era significativamente maggiore nel sottogruppo STEMI rispetto al sottogruppo non STEACS (rispettivamente 2,8 contro 0,6%, P =0,01). Tuttavia, le percentuali di infarto miocardico non fatale, TLR da ischemia, trombosi definita dello stent e morte non cardiaca erano statisticamente compensaea fra i due sottogruppi (P> 0,05 per tutti).

Conclusione. Nell'attuale analisi a posteriori dello studio BASE-ACS basata sul tipo di infarto, l'esito a 12 mesi dei pazienti sottoposti a PCI per sindrome coronarica acuta precoce era lievemente peggiore nel contesto di STEMI, rispetto ai pazienti non STEACS, come si riflette nella percentuale significativamente più elevata di morte cardiaca.

Parole chiave: Percutaneous coronary intervention - Titanio - Stent medicati - Miocardio, infarto.

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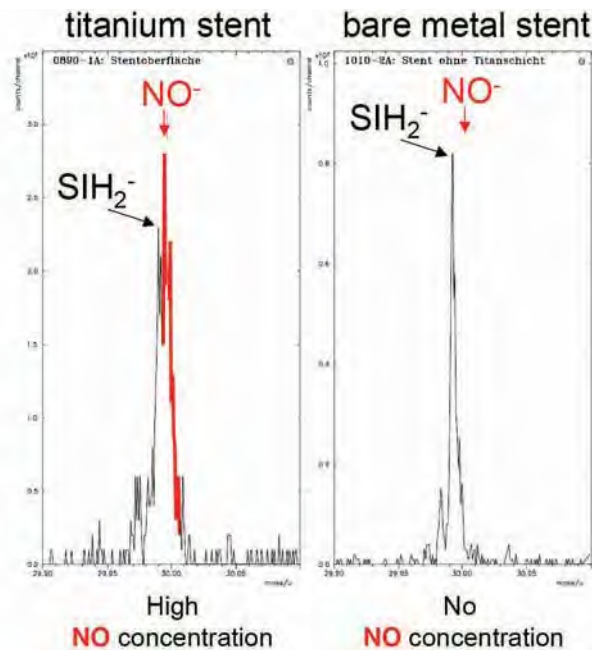
Figure 1. Typical spectrogram of a titanium-nitride-oxide coated stent (left) and an uncoated bare-metal stent (right). The titanium-coated stent shows a large NO-peak on its surface which is not present in the bare-metal stent.

Registry experience with a titanium-nitride-oxide coated stent

In the current issue of *EuroIntervention*, two registries are published showing experience with the commercially available Titan™ (Hexacath, France) stent in everyday clinical practice: a nine-month-follow-up report from the Titan Pori registry, and the multi-centre Titan registry from Israel. In the Pori registry, 193 patients with 212 lesions were included at a single centre and followed for 6 months. The registry comprised approximately one third of all patients derived from routine clinical practice, with a high proportion of acute coronary syndromes (57%) and complex lesions (Type B and C: 88%). The mean reference vessel diameter (2.9±0.3 mm) and lesion length (12.9±3.0 mm) are indicative of vessels with a moderate risk of restenosis. The rate of major adverse cardiac events (MACE) at 9 months was 10.4% with a low target lesion revascularisation (TLR) of 5.2%. Notably, there was no case of stent thrombosis up to 9 months, but clopidogrel was administered for a mean duration of 8 months.

In the Israeli registry, 296 patients were included, 36% had diabetes mellitus and 81% acute coronary syndromes. The vessel characteristics revealed a high proportion of complex lesions (Type B2 or C: 61%) and long lesions (49% > 15 mm, mean lesion length: 17.5±14.8 mm). The overall rate of MACE at 6 months was 7%, consisting of TLR in 5.4% of patients, myocardial infarction in 0.7% of patients, and death in 0.7% of patients. Myocardial infarction was related to acute and subacute stent thrombosis in two patients, but clopidogrel was administered for only one month.

The two studies indicate that stent coating with titanium is associated with favourable clinical outcome. The need for repeat revascularisation was low as was the incidence of stent thrombosis. Due to the absence of a drug and polymer, there is no need for prolonged clopidogrel administration. Indeed, clopidogrel was administered for only one month in the study by Mosseri et al, similar to bare metal stents. The Titan stent platform is further characterised by a very low stent profile, high flexibility, and low strut thickness of 80 µm, and therefore provides for excellent deliverability especially in calcified, tortuous vessels out-performing current generation drug-eluting stents. Clinical studies comparing thick- with thin- strut stent designs revealed reduced restenosis and target lesion revascularisation[16,17]. Therefore, the combination of titanium-nitride-oxide stent coating with this thin strut construction might have allowed a reduction in restenosis. Finally, the cost for the Titan stent is only approximately half that of current drug-eluting stents. In a cost-conscious health care environment, the incremental benefit of drug-eluting stents compared with the Titan stent deserves consideration especially in light of the recent BASKET trial[18], where drug-eluting stents proved only cost-effective in high-risk groups.

Future directions

While the present registry data with the Titan™ (Hexacath, France) stent are encouraging, the following limitations have to be considered. Both registries included only a moderate number of patients and lesions with a limited follow-up period of 6 to 9 months. Patient selection was at the discretion of the operator, and assessment of clinical outcome was not adjudicated. Therefore, comparison of these data with other registries of bare metal stents and drug-eluting stents may be of limited value. What is then the role of the Titan™ stent in the current era of drug-eluting stents?

First, coronary artery stenoses at low to moderate risk for restenosis, i.e. lesions in vessels with a reference vessel diameter >3.0 mm and length of <15 mm may be more cost-effectively treated with a titanium-nitride-oxide coated stent than drug-eluting stents.

Second, there is increasing concern that drug-eluting stents are associated with late stent thrombosis requiring long-term dual antiplatelet therapy. Accordingly, patients who are not candidates for long-term dual antiplatelet therapy such as those scheduled for elective surgery after the index procedure, patients at increased risk of bleeding, those requiring oral anticoagulation, and the elderly may be more appropriately treated with a titanium-nitride-oxide coated stent.

Third, in light of the favourable angiographic and ultrasonic measures of restenosis with the titanium-nitride-oxide coated stent in concert with its promising safety profile, the time might have come to compare this stent directly with drug-eluting stents in randomised, clinical trials.

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