Effect of Obesity on Coronary Atherosclerosis and Outcomes of Percutaneous Coronary Intervention

Grayscale and Virtual Histology Intravascular Ultrasound Substudy of Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents

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Background—Obesity is a cardiovascular risk factor, but the obesity paradox in patients undergoing percutaneous coronary intervention is poorly understood.

Methods and Results—Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) was a prospective, multicenter study of patients undergoing drug-eluting stent implantation. Overall, 780 patients (916 culprit lesions) were evaluated by grayscale and virtual histology-intravascular ultrasound pre—percutaneous coronary intervention. Poststenting intravascular ultrasound was done in 780 patients (894 treated lesions). Patients were divided into body mass index (BMI) tertiles. The high-BMI group had more diabetes mellitus, hypertension, and hyperlipidemia and more frequent plaque ruptures compared with the low-BMI group. At the minimal lumen area site, the high-BMI group had a larger plaque area (11.7 [11.0–12.4] versus 9.8 [9.3–10.4] mm²) and a greater plaque burden (77.3% [76.1%–78.5%] versus 74.4% [73.1%–75.8%]) compared with the low-BMI group; however, a larger external elastic membrane area (14.6 [13.8–15.3] versus 12.7 [12.1–13.3] mm²) resulted in a similar minimal lumen area compared with the low-BMI group. Post stenting, the high-BMI group had a significantly larger stent area versus the lower-BMI group. At 1-year follow-up, the high-BMI group was associated with less clinically driven target lesion revascularization compared with the low-BMI group in both the overall and the propensity-matched cohorts.

Conclusions—A high BMI was associated with a greater plaque burden; however, a larger external elastic membrane preserved lumen dimensions and was associated with a larger stent area during intravascular ultrasound-guided stent implantation. Thus, despite more comorbidities, greater plaque burden, and more plaque rupture, a high BMI was not associated with worse outcomes after drug-eluting stent implantation.

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

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Key Words: atherosclerosis ■ obesity
WHAT IS KNOWN

- Obesity contributes to the development and progression of coronary artery disease.
- Although recent studies have shown a reduced risk of mortality and major adverse cardiac events after percutaneous coronary intervention in patients with high body mass index, the mechanism of the so-called obesity paradox is not yet understood.

WHAT THE STUDY ADDS

- A high body mass index was more frequently associated with plaque rupture along with more necrotic core and greater plaque volume.
- In the high–body mass index group, a larger external elastic membrane contributed to preserving lumen, which led to a larger stent area during intravascular ultrasound guidance.
- Despite more comorbidities and plaque rupture, target lesion revascularization at 1 year was less frequent in the high–versus low–body mass index group.

ultrasound (IVUS) substudy, culprit lesions were prospectively evaluated using grayscale and virtual histology (VH)-IVUS, and patients were treated with IVUS-guided DES implantation. The aims of the current analysis were (1) to compare morphological lesion characteristics relative to BMI and (2) to observe the prognostic effect of obesity on immediate PCI results and 1-year clinical outcomes.

Methods

Patient Selection and Imaging

The design, major inclusion and exclusion criteria, end points, and definitions from the ADAPT-DES study have been described in detail. In brief, ADAPT-DES was a prospective, multicenter, observational study of consecutive patients who were treated successfully with ≥1 Food and Drug Administration- or Conformité Européenne (CE)-mark-approved DES regardless of patient or lesion complexity. Procedural IVUS use was per operator discretion; however, the operator was required to report the timing of IVUS imaging and how the IVUS information influenced the procedure. In the current analysis, 780 patients had presenting grayscale and VH-IVUS of 916 culprit lesions in native coronary arteries. Clinical follow-up was done at 1 year. The study was approved by the Institutional Review Board at each participating center, and all eligible patients signed the informed written consent.

Diagnosis of stent thrombosis was based on the Academic Research Consortium criteria. All-cause and cardiac mortality, myocardial infarction, and stent thrombosis were adjudicated by an independent clinical events committee. Target lesion and vessel revascularization were site-reported but not centrally adjudicated.

Grayscale and VH-IVUS Analysis

Pre- and poststenting grayscale and VH-IVUS image acquisition was performed using a synthetic aperture array, 20 MHz, and 3.2 Fr catheter (Eagle Eye; Volcano Corporation, Rancho Cordova, CA) after intracoronary nitroglycerin. The IVUS catheter was advanced distal to the lesion and was pulled back to the aorto-ostial junction using an R-100 motorized catheter pullback system (0.5 mm/s). During pullback, grayscale IVUS was recorded, raw radiofrequency data were captured at the top of the R wave, and reconstruction of the color-coded map by a VH-IVUS data recorder (S5; Volcano Corporation, Zaventem, Belgium) was performed. IVUS studies were archived onto a digital video disk. Using computerized planimetry software (echoPlaque; INDEC Systems Inc, Mountain View, CA) contouring and data output, off-line grayscale and VH-IVUS analyses of all imaged segments were performed prospectively at an independent IVUS core laboratory (Cardiovascular Research Foundation, New York, NY) that was blinded to the clinical events.

Grayscale and VH-IVUS Analysis

Quantitative IVUS measurements included external elastic membrane (EEM), lumen, plaque+media (EEM minus lumen) areas, and plaque burden (plaque+media divided by EEM). Volumes were calculated using Simpson rule and reported as total and normalized volumes (volume divided by analysis length). The slice with the minimal lumen area (MLA) was identified and assessed (Figure 1).

A culprit lesion was defined as the lesion that was stented. Proximal and distal 5-mm-long segments from each stent edge but before a significant (>1.5 mm in diameter) side branch, were defined as the reference segments.

Pre-PCI qualitative grayscale IVUS morphology analysis included plaque rupture (intraplaque cavity that communicated with the lumen with an overlying residual fibrous cap fragment) and attenuated plaque (ultrasound attenuation of deeper arterial structures despite the absence of bright calcium). VH-IVUS plaque components were color-coded as dense calcium (white), necrotic core (red), fibrofatty (light green), or fibrous tissue (dark green) and reported as normalized volume. A fibroatheroma had >10% confluent necrotic core (spotty red color was not considered as confluent necrotic core). If there was >30° of necrotic core abutting the lumen in 3 consecutive slices, the fibroatheroma was classified as a VH thin-cap fibroatheroma; otherwise, it was classified as a thick-cap fibroatheroma.

Post-PCI quantitative IVUS analysis included measurements at every 1 mm of the EEM, stent, and lumen area. Volumes were calculated using Simpson rule and reported as total volumes and normalized volumes (volume divided by analysis length). The slices with the MLA and the minimal stent area were identified and assessed. Stent expansion was defined as a minimal stent area divided by the average of the proximal and distal reference lumen areas. Qualitative analysis included (1) stent malapposition (blood speckle behind stent struts not overlaying a side branch), (2) intrastent plaque or thrombus protrusion, and (3) edge dissection (intimal, medial, intramural hematoma, or outside of the EEM).

Statistical Analysis

Categorical variables were summarized using percentages and counts and were compared using χ² statistics or Fischer exact test where appropriate. For tertile analysis by BMI, low versus intermediate BMIs were separated by 25.80 kg/m² and intermediate versus high BMIs were separated by 29.26 kg/m². For lesion-level data, a model with a generalized estimating equation approach was used to compensate for potential cluster effects of multiple lesions in the same patient and presented as least square means with 95% confidence intervals. Continuous variables were compared using ANOVA and unpaired t-tests or nonparametric Wilcoxon-rank sum test and shown as median and interquartile ranges. To adjust for differences in patient demographics, we performed multivariate linear or logistic regression analysis, including age, sex, diabetes mellitus, hypertension, hyperlipidemia, and renal insufficiency as covariates. Including variables such as age, male sex, BMI, creatinine clearance ≤60 mL/min, current smoking, hypertension, left anterior descending artery location, statin treatment before admission, ST-segment–elevation myocardial infarction, angiographic diameter stenosis, bifurcation, and calcification, multivariable logistic regression analysis was performed to identify the independent predictors of plaque rupture. To identify the clinical factors independently predicting the normalized EEM volume, multivariable analysis included age, BMI, creatinine clearance ≤60 mL/min, and current smoking. Time-to-event data were as
Kaplan–Meier estimates and were compared between groups with the log-rank test. P value of <0.05 was considered statistically significant. Statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC).

Results
Baseline Clinical and Procedural Characteristics
Baseline clinical and procedural characteristics in 780 patients are summarized in Table 1. Patients with a high BMI were younger and more frequently had diabetes mellitus, hypertension, and hyperlipidemia.

Preprocedural IVUS Findings
The normalized plaque+media volume was greater in the high-BMI versus the low-BMI group; however, a larger normalized EEM volume preserved the normalized lumen volume in the high-BMI group (adjusted ANOVA P=0.51; Table 2; Figure 2). Similarly, at the MLA site, the high-BMI group had a greater plaque burden and a larger EEM area but a similar MLA when compared with the lower-BMI groups. Moreover, BMI (unstandardized coefficient, 0.177; P value adjusted by generalized estimating equation, <0.001) and creatinine clearance <60 mL/min (unstandardized coefficient, −2.38; P value adjusted by generalized estimating equation, 0.012) were the independent clinical predictors of normalized EEM volume.

The normalized plaque volume (r=0.144) and normalized EEM volume (r=0.140) significantly correlated with BMI. However, BMI correlated with body surface area, and normalized plaque volume (r=0.211) and normalized EEM volume (r=0.223) also correlated with body surface area (all P<0.001).

High BMI (versus low BMI) was more frequently associated with plaque rupture. The highest BMI tertile showed greater normalized volumes of VH-IVUS necrotic core and dense calcium.

There was no interaction between diabetes mellitus and BMI tertiles with regard to lesion characteristics (interaction P=0.59 for normalized vessel volume, interaction P=0.012 for % plaque volume, interaction P=0.36 for normalized necrotic core volume, interaction P=0.98 for MLA, interaction P=0.88 for thin-cap fibroatheroma, and interaction P=0.70 for plaque rupture).

On multivariable analysis, it was found that the independent predictors of plaque rupture were male sex (odds ratio, 1.85; 95% confidence interval, 1.26–2.71; P=0.002), angiographic diameter stenosis (10% increment; odds ratio, 1.87; 95% confidence interval, 1.57–2.23; P<0.001), and BMI (odds ratio, 1.05; 95% confidence interval, 1.01–1.08; P=0.005).

In the propensity-matched cohort (matched for age, sex, diabetes mellitus, and renal insufficiency), a high BMI (versus a low BMI) was related to a greater normalized EEM volume (14.69 [interquartile range, 13.88–15.50] versus 13.38 mm³ [interquartile range, 12.74–14.01]) and necrotic core volume (1.39 [interquartile range, 1.24–1.54] versus 1.12 mm³ [interquartile range 1.01–1.22]) and more plaque rupture (42% versus 31%; all P<0.05), similar to the overall cohort.

Both acute coronary syndrome and nonacute coronary syndrome subgroups showed that a high BMI (versus a low BMI) was associated with larger normalized EEM and plaque+media volumes and with more necrotic core and more plaque ruptures (in the acute coronary syndrome group), which was similar to the overall cohort.

Poststenting IVUS Findings
During PCI, IVUS was used to guide and optimize the DES implantation procedure in 94.3%; it was used only to
document the final results in the remaining 5.7%. Larger stents were implanted in lesions in the high-BMI group. Poststenting IVUS findings are summarized in Table 3. Post PCI, the high-BMI tertile had a larger stent area and MLA compared with the lower-BMI tertiles.

The frequency of acute malapposition was 10.1% in the low-BMI tertile, 12.1% in the intermediate-BMI tertile, and 13.7% in high-BMI tertile (ANOVAP = 0.38). There was no significant difference in frequency of tissue protrusion among the tertiles (33.0% in low-BMI tertile, 38.0% in intermediate-BMI tertile, and 41.4% in high-BMI tertile; ANOVAP = 0.13), as well as no difference in frequency of proximal edge dissections (3.9% in low BMI, 3.5% in intermediate BMI, and 2.9% in high BMI; ANOVAP = 0.75) or distal edge dissections (4.4% in low BMI, 5.7% in intermediate BMI, and 3.1% in high BMI; ANOVAP = 0.27).

**Immediate and 1-Year Follow-Up Clinical Outcomes**

Immediate PCI outcomes and 1-year adverse cardiac events after DES implantation are summarized in Table 4. The incidence of death, myocardial infarction, or stent thrombosis was similar among the BMI tertiles. However, a high BMI (versus a low BMI) showed a trend of being associated with less clinically driven target lesion revascularization in the propensity-matched cohort (1.8% versus 5.8%; P = 0.051) and in the overall group of patients (2.0% versus 5.0%; P = 0.053). Figure 3 shows the corresponding Kaplan–Meier curves.

**Discussion**

The major findings of this study evaluating culprit lesions in patients undergoing DES implantation are the following: (1) in the high-BMI tertile, plaque rupture was more frequent along with a greater amount of necrotic core and greater normalized plaque+media, although a larger EEM contributed to preserving lumen volume and MLA. (2) After DES implantation, the high-BMI group had a larger stent area when compared with the lower-BMI tertiles. (3) At 1-year follow-up, a high BMI (versus a low BMI) showed a trend of being associated with less clinically driven target lesion revascularization.

Previous angiographic data demonstrated no significant effect of BMI on coronary stenosis severity; however, in the current study, a high BMI was associated with a greater culprit lesion plaque volume and plaque burden. This analysis also helped to explain this contradiction. In the current study, a high BMI was associated with a larger EEM both at the MLA.
site and diffusely, extending into the adjacent reference segments, so that the normalized EEM volume was also increased. Although there might be potential links between obesity and other risk factors, these findings were consistent in the propensity-matched cohort, and there was no interaction of diabetes mellitus with the lesion characteristics in relation to BMI. The larger EEM area and volume (i.e., positive remodeling) indicated a greater compensatory response to plaque accumulation that preserved the lumen area and volume, as seen in the current study. This helped to explain why lumen-based angiographic observations failed to show any relationship between obesity and the extent of coronary atherosclerosis.

### Table 2. Preprocedural IVUS Findings of 916 Culprit Lesions

<table>
<thead>
<tr>
<th>Lesion number</th>
<th>Low-BMI Tertile</th>
<th>Intermediate-BMI Tertile</th>
<th>High-BMI Tertile</th>
<th>P Value Adjusted</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length, mm</td>
<td>308</td>
<td>26.7 (24.9–26.8)</td>
<td>29.0 (27.1–30.9)</td>
<td>0.16</td>
<td>0.14</td>
</tr>
<tr>
<td>Normalized volume, mm³/mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEM</td>
<td>13.2 (12.7–13.7)</td>
<td>14.1 (13.5–14.7) *</td>
<td>14.9 (14.2–15.5) *&lt;0.001</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Lumen</td>
<td>5.6 (5.4–5.8)</td>
<td>5.8 (5.6–6.1)  *</td>
<td>6.0 (5.7–6.3) * 0.10</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>P+M</td>
<td>7.6 (7.2–8.0)</td>
<td>8.3 (7.8–8.7) *</td>
<td>8.9 (8.4–9.4) *&lt;0.001</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>% Plaque volume</td>
<td>56.2 (55.1–57.3)</td>
<td>57.3 (56.2–58.3)</td>
<td>58.3 (57.2–59.4) * 0.03</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Necrotic core</td>
<td>1.11 (1.02–1.21)</td>
<td>1.23 (1.12–1.34) *</td>
<td>1.41 (1.29–1.54) * 0.001</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Dense calcium</td>
<td>0.51 (0.45–0.56)</td>
<td>0.55 (0.49–0.62) *</td>
<td>0.61 (0.54–0.67) * 0.11</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Fibrous tissue</td>
<td>2.55 (2.38–2.72)</td>
<td>2.89 (2.67–3.11) *</td>
<td>3.16 (2.93–3.40) *&lt;0.001</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Fibrofatty</td>
<td>0.65 (0.57–0.72)</td>
<td>0.73 (0.64–0.82) *</td>
<td>0.76 (0.67–0.85) 0.13</td>
<td>0.85</td>
<td></td>
</tr>
</tbody>
</table>

At the MLA site

<table>
<thead>
<tr>
<th>Low-BMI Tertile</th>
<th>Intermediate-BMI Tertile</th>
<th>High-BMI Tertile</th>
<th>P Value Adjusted</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM area, mm²</td>
<td>12.7 (12.1–13.3)</td>
<td>13.5 (12.8–14.2)</td>
<td>14.6 (13.8–15.3) *†&lt;0.001</td>
<td>0.02</td>
</tr>
<tr>
<td>MLA, mm²</td>
<td>2.8 (2.7–2.9)</td>
<td>2.9 (2.8–3.0)</td>
<td>2.9 (2.7–3.0)   0.67</td>
<td>0.72</td>
</tr>
<tr>
<td>P+M area, mm²</td>
<td>9.8 (9.3–10.4)</td>
<td>10.6 (10.0–11.2)</td>
<td>11.7 (11.0–12.4) *†&lt;0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Plaque burden, %</td>
<td>74.4 (73.1–75.8)</td>
<td>75.4 (74.1–76.6)</td>
<td>77.3 (76.1–78.5) *† 0.005</td>
<td>0.008</td>
</tr>
</tbody>
</table>

| Area stenosis | 0.76 (0.74–0.77) | 0.77 (0.76–0.78) | 0.78 (0.77–0.79) * 0.009 | 0.02 |

Qualitative data

| Atenuated plaque, n, % | 197 (64.0%) | 183 (58.8%) | 192 (64.6%) | 0.28 | 0.24 |
| Plaque rupture, n, %  | 87 (28.2%) | 101 (32.5%) | 116 (39.1%) * 0.02 | 0.03 |
| Thin-cap fibroatheroma within lesion, n, % | 162 (52.6%) | 158 (47.6%) | 160 (53.9%) | 0.29 | 0.36 |
| Thick-cap fibroatheroma at the MLA site, n, % | 177 (57.5%) | 192 (61.7%) | 176 (59.5%) | 0.56 | 0.61 |
| Thin-cap fibroatheroma at the MLA site, n, % | 44 (14.3%) | 35 (11.3%) | 37 (12.5%) | 0.52 | 0.84 |

Values are generalized estimating equation least square mean (95% confidence interval) or n (%). BMI indicates body mass index; EEM, external elastic membrane; IVUS, intravascular ultrasound; MLA, minimal lumen area; and P+M, plaque plus media.

*P<0.05 vs low-BMI group.
†P<0.05 vs intermediate-BMI group; adjusted P values considered age, sex, diabetes mellitus, hypertension, hyperlipidemia, and renal insufficiency as covariates.
Although obesity is a major risk factor of coronary disease, its relationship with adverse cardiac events, including repeat revascularization, has remained unclear in patients with established coronary artery disease.3–6 Clinical studies have reported that obese patients have better clinical outcomes, especially after PCI.7,8 The current study suggests 1 plausible explanation for the so-called obesity paradox. Even in the setting of a greater plaque burden, a larger EEM in the high-BMI group allows for the use of larger stents and larger balloons to achieve greater stent expansion and a larger minimum stent area, especially under the IVUS guidance that was used in 95% of the patients. Previous studies have shown that stent expansion, as defined by the minimum stent area, is the greatest determinant of 1-year target lesion revascularization because greater stent expansion provides more room for intimal hyperplasia.14–17 Thus, as shown in the current study, patients with a high BMI who, in fact, have greater plaque burden, more frequent plaque rupture, larger amounts of necrotic core, and

Table 3. Poststenting Intravascular Ultrasound Findings in 894 Treated Lesions

<table>
<thead>
<tr>
<th>Lesion number</th>
<th>Low-BMI Tertile</th>
<th>Intermediate-BMI Tertile</th>
<th>High-BMI Tertile</th>
<th>P Value</th>
<th>Adjusted P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior descending</td>
<td>297 (27.8–31.7)</td>
<td>296.6 (27.4–31.8)</td>
<td>302.3 (28.3–32.1)</td>
<td>0.89</td>
<td>0.30</td>
</tr>
<tr>
<td>Left circumflex artery</td>
<td>6.2 (5.9–6.4)</td>
<td>6.4 (6.1–6.7)</td>
<td>6.9 (6.6–7.2)</td>
<td>0.003</td>
<td>0.007</td>
</tr>
<tr>
<td>Minimal stent area, mm²</td>
<td>2.6 (2.5–2.6)</td>
<td>2.6 (2.6–2.7)</td>
<td>2.8 (2.7–2.8)</td>
<td>0.002</td>
<td>0.02</td>
</tr>
<tr>
<td>MLA, mm²</td>
<td>6.1 (5.9–6.4)</td>
<td>6.4 (6.1–6.7)</td>
<td>6.8 (6.5–7.1)</td>
<td>0.005</td>
<td>0.01</td>
</tr>
<tr>
<td>EEM area at the MLA, mm²</td>
<td>7.8 (7.0–8.4)</td>
<td>7.1 (6.9–7.0)</td>
<td>7.3 (7.0–7.6)</td>
<td>0.008</td>
<td>0.01</td>
</tr>
<tr>
<td>Normalized stent volume, mm³/mm²</td>
<td>7.7 (7.4–8.0)</td>
<td>7.9 (7.6–8.2)</td>
<td>8.5 (8.2–8.9)</td>
<td>0.001</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Values are generalized estimating equation least square mean (95% confidence interval) or n (%). BMI indicates body mass index; EEM, external elastic membrane; and MLA, minimal lumen area.

*P < 0.05 vs low-BMI group.
†P < 0.05 vs intermediate-BMI group; adjusted P values considered age, sex, diabetes mellitus, hypertension, hyperlipidemia, and renal insufficiency as covariates.
‡Stent expansion (%) equals the stent area at the MLA site/average of lumen areas in proximal and distal references.

Table 4. Immediate Percutaneous Coronary Intervention Outcomes and 1-Year Adverse Cardiac Events

<table>
<thead>
<tr>
<th>Immediate procedural outcomes</th>
<th>Overall</th>
<th>Propensity-Matched Cohort</th>
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<tbody>
<tr>
<td></td>
<td>Low-BMI</td>
<td>Intermediate-BMI</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>No reflow</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Perforation</td>
<td>0 (0%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Periprocedural myocardial infarction</td>
<td>3 (1.2%)</td>
<td>3 (1.2%)</td>
</tr>
</tbody>
</table>

1-year adverse events

| All cause of death            | 1 (0.4%)| 3 (1.2%) | 5 (1.9%) | 0.256    | 1 (0.6%)| 1 (0.6%)                 | 5 (2.9%)| 0.10    |
| Cardiac cause of death        | 1 (0.4%)| 1 (0.4%) | 1 (0.4%) | 1.0      | 0 (0%)  | 0 (0%)                 | 1 (0.6%)| 1.0     |
| Myocardial infarction         | 1 (0.4%)| 2 (0.8%) | 0 (0%)  | 0.134    | 0 (0%)  | 0 (0%)                 | 2 (1.2%)| 0.37    |
| Stent thrombosis              | 5 (1.9%)| 6 (2.3%) | 5 (1.9%) | 0.935    | 0 (0%)  | 0 (0%)                 | 2 (1.2%)| 0.13    |
| Clinically driven target lesion revascularization | 13 (5.0%) | 9 (3.5%) | 5 (2.0%) | 0.164    | 10 (5.8%)| 7 (4.1%)                 | 3 (1.8%)| 0.15    |
| Clinically driven target vessel revascularization | 20 (7.7%) | 15 (5.9%) | 13 (5.1%) | 0.435    | 15 (8.7%)| 13 (7.6%)                 | 8 (4.7%)| 0.33    |

Values are n (%). BMI indicates body mass index.
*P = 0.057 vs low-BMI group (Kaplan–Meier estimates).
†P = 0.051 vs low-BMI group (Kaplan–Meier estimates).
more comorbidities, such as diabetes mellitus, hypertension, and hyperlipidemia, did not have worse outcomes, possibly because of greater stent expansion.

Although the differences in normalized EEM volume and % plaque volume between high- and low-BMI groups were relatively small, they might be clinically meaningful. In a previous study, a greater increase in percent atheroma volume was observed in patients who experienced major adverse cardiac events compared with those who did not (0.95±0.19% versus 0.46±0.16%), although the difference was subtle.18

In a previous study, abdominal obesity was an independent predictor of rupture of a culprit plaque.19–21 Our current data also demonstrated more frequent plaque rupture of culprit lesions in patients with high BMI along with a greater plaque burden and a larger necrotic core. Similar to the previous data, BMI was the independent predictor of plaque rupture. Further studies are needed to clarify how obesity contributes to the plaque vulnerability.

**Limitations**

First, this is a cross-sectional analysis, not serial IVUS data. Second, with the lack of hard events, the sample size was underpowered to observe the effect of BMI on stent thrombosis and mortality. Although metabolic syndrome and abdominal obesity seem to be related to worse prognosis and mortality, the current study was unable to demonstrate this effect. Additionally, the current study was underpowered to observe the effect of BMI on stent thrombosis.

**Conclusions**

Obesity as evidenced by a high BMI was associated with a greater plaque volume and more plaque rupture in culprit lesions; however, in high-BMI groups, positive remodeling allowed lumen volume and MLA to remain as large as that in lower-BMI groups. With a larger EEM, achievement of a greater stent area under IVUS guidance in patients with a high BMI may have mitigated against worse outcomes.

**Sources of Funding**

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**Disclosures**

Dr Mintz has received grant support and is a consultant for Volcano Corporation and Boston Scientific. Dr Witzenbichler has received speaker honoraria from Boston Scientific, Abbott Vascular, and Volcano Corporation. Dr Metzger is a consultant for Abbott Vascular, Cordis, IDEV, Medtronic, and Volcano. Dr Rinaldi is a consultant for Abbott, Boston Scientific, St. Jude Medical, and Volcano. Dr Duffy has received speaker honoraria from Volcano Corporation. Dr Weisz is a consultant for InfraReDx. Dr Stuckey is an advisory board member of Boson Scientific and has received speaker honoraria from Boston Scientific and Eli Lilly/Daiichi-Sankyo. Dr Stone is a consultant for Boston Scientific, InfraReDx, and Volcano Corporation. Dr Maehara has received grant support and is a consultant for Boston Scientific, and he has received lecture fees from St. Jude Medical and Volcano Corporation. The other authors report no conflicts.

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