BACKGROUND: Coronary bifurcation lesions (CBLs) are frequently encountered in clinical practice and are associated with worse outcomes after percutaneous coronary intervention. However, there are limited data around the prognostic impact of different CBL distributions.

METHODS AND RESULTS: All CBL percutaneous coronary intervention procedures from the prospective e-Ultimaster (Prospective, Single-Arm, Multi Centre Observations Ultimaster Des Registry) multicenter international registry were analyzed according to CBL distribution as defined by the Medina classification. Cox proportional hazards models were used to compare the hazard ratio (HR) of the primary outcome, 1-year target lesion failure (composite of cardiac death, target vessel–related myocardial infarction, and clinically driven target lesion revascularization), and its individual components between Medina subtypes using Medina 1.0.0 as the reference category. A total of 4003 CBL procedures were included. The most prevalent Medina subtypes were 1.1.1 (35.5%) and 1.1.0 (26.8%), whereas the least prevalent was 0.0.1 (3.5%). Overall, there were no significant differences in patient and procedural characteristics among Medina subtypes. Only Medina 1.1.1 and 0.0.1 subtypes were associated with increased target lesion failure (HR, 2.6 [95% CI, 1.3–5.5] and HR, 4.0 [95% CI, 1.6–9.0], respectively) at 1 year, compared with Medina 1.0.0, prompted by clinically driven target lesion revascularization (HR, 3.1 [95% CI, 1.1–8.6] and HR, 4.6 [95% CI, 1.3–16.0], respectively) as well as cardiac death in Medina 0.0.1 (HR, 4.7 [95% CI, 1.0–21.6]). No differences in secondary outcomes were observed between Medina subtypes.

CONCLUSIONS: In a large multicenter registry analysis of coronary bifurcation percutaneous coronary intervention procedures, we demonstrate prognostic differences in 1-year outcomes between different CBL distributions, with Medina 1.1.1 and 0.0.1 subtypes associated with an increased risk of target lesion failure.

Key Words: bifurcation • drug-eluting stent • Medina classification • outcomes • percutaneous coronary intervention

Coronary bifurcation lesions (CBLs) are some of the most challenging and frequently encountered lesion subsets in interventional practice, representing nearly 20% of all percutaneous coronary intervention (PCI) procedures.1,2 Although several classifications of CBLs exist, the Medina classification, endorsed by major bodies such as the European Bifurcation Club, is the most widely used.2–5 This classification assigns a binary value (0 or 1) to the proximal and distal main branches (MBs) as well as the side branch (SB), in that respective order, based on the presence (1) or absence (0) of significant plaque burden (≥50% stenosis) in that vascular segment.4 Furthermore, CBLs can be classified into true bifurcation lesions, if both the MB and SB have...
significant stenosis, and nontrue bifurcation lesions if either the MB or SB is not significantly stenosed.

Although previous studies have examined clinical outcomes of CBL PCI according to lesion complexity (simple versus complex bifurcations) or true versus nontrue bifurcations,6–9 none have systematically examined the prognostic impact of disease distribution within the CBL on mid- or long-term outcomes following PCI.10–12

The present study sought to compare the impact of disease distribution according to Medina classification on 1-year clinical outcomes adjudicated by an independent clinical events committee among patients undergoing bifurcation PCI within the e-Ultimaster (Prospective, Single-Arm, Multi Centre Observations Ultimaster Des Registry).

METHODS

Study Data Set

The e-Ultimaster study is a large, international, prospective observational study that enrolled 37 198 patients between October 2014 and June 2018 in 378 hospitals from 50 countries including sites in Europe, Asia, Africa, the Middle East, South America, and Mexico. Eligibility criteria were minimal to enroll an all-comer population, and included (1) age ≥18 years and (2) an indication for a PCI according to routine hospital practice. The Ultimaster sirolimus-eluting coronary stent (Terumo, Tokyo, Japan) is made of cobalt-chromium with a strut thickness of 80 μm. Sirolimus is released from an abluminal applied bioreabsorbable polymer coating (poly-D,L-lactic acid polycaprolactone) that is fully metabolized through dl-lactide and caprolactone into carbon dioxide and water in 3 to 4 months. The study was approved by the ethical committees of the participating sites, and all patients provided written informed consent. The clinicaltrials.gov identifier is NCT02188355. The data used for the purpose of this study are only available to designated researchers and cannot be shared with other researchers. However, all efforts were made to describe the methods in detail.

Study Population and Follow-Up

All patients with a single CBL at the index procedure from the e-Ultimaster study were included, stratified into 7 permutations according to their Medina classification (true bifurcations: 0.1.1, 1.0.1, 1.1.1; nontrue bifurcations: 0.0.1, 0.1.0, 1.0.0, 1.1.0) (Figure S1). There were no restrictions on the clinical indication, the number of lesions to be treated, or number of stents to be implanted. Because the Medina classification was not available for 56 (1.4%) patients, they were excluded from our analysis. Follow-up was up to 1 year, except

CLINICAL PERSPECTIVE

What Is New?

• This is the first study to examine the prognostic difference in 1-year clinical outcomes after coronary bifurcation lesion percutaneous coronary intervention according to Medina subtype in a large multinational cohort.
• Our findings demonstrate that the most prevalent coronary bifurcation lesion subtypes are Medina 1.1.1 (35.5%) and 1.1.0 (26.8%), whereas the least prevalent is Medina 0.0.1 (3.5%).
• Only 2 Medina subtypes (1.1.1 and 0.0.1) were associated with increased target lesion failure at 1 year, whereas no prognostic differences were observed for other subtypes.

What Are the Clinical Implications?

• Greater caution is warranted for patients with specific coronary bifurcation lesion distributions, namely Medina 1.1.1 and 0.0.1, who may need to be followed up more closely given their increased risk of target lesion failure at 1 year following intervention.
• Further research is needed to further optimize outcomes of patients with isolated side branch lesions (Medina 0.0.1) who are at a 4-fold higher risk of target lesion failure at 1 year.

Nonstandard Abbreviations and Acronyms

CBL coronary bifurcation lesion
MB main branch
SB side branch
TLF target lesion failure
TLR target lesion revascularization
TVF target vessel failure

Figure 1. Distribution of coronary bifurcation lesions as per the Medina classification subtype.
Table 1. Baseline Patient and Procedural Characteristics According to Medina Classification Subtype

| Characteristic                        | True bifurcation | Nontrue bifurcation | P value |
|---------------------------------------|------------------|---------------------|---------|
|                                       | Medina 1.0.1     | Medina 1.1.1        | Medina 0.1.0 | Medina 1.0.0 | Medina 1.1.0 |       |
|                                       | n=356            | n=1420              | n=291     | n=137        | n=399        | n=1064 |
| Age, y, mean±SD [n]                   | 65.1±11.3 [356]  | 65.7±11.4 [1420]    | 64.9±10.7 [291] | 65.9±10.8 [137] | 65.2±11.2 [399] | 65.0±11.6 [336] | 65.8±10.8 [1064] | 0.709 |
| Men, % [n]                            | 73.3 [261/356]   | 77.5 [1101/1420]    | 74.2 [216/291] | 75.9 [303/399] | 77.1 [259/336] | 77.4 [824/1057] | 0.338 |
| Diabetes, % [n]                       | 25.1 [89/356]    | 28.7 [405/1410]     | 29.3 [84/287] | 31.4 [43/137] | 26.6 [106/399] | 21.9 [73/334] | 0.111 |
| Insulin-dependent diabetes, % [n]     | 4.8 [17/354]     | 5.3 [74/1410]       | 8.0 [23/287] | 5.8 [8/137] | 4.5 [18/399] | 4.2 [14/334] | 0.412 |
| Hypertension, % [n]                   | 68.7 [233/339]   | 69.1 [940/1420]     | 71.4 [200/291] | 72.9 [97/133] | 71.1 [273/364] | 66.3 [212] | 0.588 |
| Hypercholesterolemia, % [n]           | 57.9 [188/325]   | 62.2 [825/1326]     | 61.3 [171/279] | 58.9 [76/129] | 63.9 [246/399] | 61.5 [193/314] | 0.555 |
| Current smoking, % [n]                | 23.7 [70/356]    | 23.7 [288/1215]     | 19.6 [49/287] | 23.1 [80/347] | 27.3 [76/278] | 23.6 [211/894] | 0.608 |
| Previous MI, % [n]                    | 24.3 [83/341]    | 25.4 [347/1410]     | 26.3 [75/285] | 27.3 [36/132] | 21.0 [82/391] | 20.7 [67/324] | 0.318 |
| Previous PTCA, % [n]                  | 26.5 [93/351]    | 29.5 [410/1326]     | 30.3 [87/287] | 30.9 [123/398] | 28.7 [94/328] | 32.0 [337/1052] | 0.179 |
| Previous CABG, % [n]                  | 5.2 [18/347]     | 5.4 [75/133]        | 4.5 [13/287] | 3.7 [5] | 4.4 [9/323] | 4.4 [46/1046] | 0.210 |
| Chronic coronary syndrome, % [n]      | 48.0 [171/356]   | 49.0 [696/1420]     | 55.9 [162/290] | 49.6 [68/137] | 55.8 [222/398] | 49.4 [166/336] | 0.020 |
| Acute coronary syndrome, % [n]        | 52.0 [185/356]   | 51.0 [724/1420]     | 44.1 [128/290] | 50.4 [69/137] | 44.2 [176/398] | 50.6 [170/336] | 0.020 |
| Unstable angina                       | 13.8 [49/356]    | 13.3 [189/1420]     | 10.7 [31/290] | 23.4 [32/137] | 13.1 [52/398] | 9.8 [33/336] | 11.7 [124/1063] | 0.004 |
| NSTEMI                                 | 24.7 [88/356]    | 23.0 [327/1420]     | 24.1 [70/290] | 16.1 [22/137] | 20.6 [82/391] | 25.9 [87/336] | 21.9 [233/1063] | 0.237 |
| STEMI                                  | 13.5 [48/356]    | 14.7 [208/1420]     | 9.3 [27/290] | 11.0 [15/137] | 10.6 [42/398] | 14.9 [50/336] | 11.9 [126/1063] | 0.064 |
| Femoral access, % [n]                 | 211.1 [375/356]  | 213 [302/1420]      | 19.9 [58/291] | 18.3 [25/137] | 15.8 [63/399] | 15.5 [52/398] | 17.9 [190/1064] | 0.059 |
| Radial access, % [n]                  | 79.5 [283/356]   | 79.4 [127/1420]     | 80.8 [235/291] | 81.0 [11/137] | 85.2 [340/399] | 83.9 [282/336] | 83.5 [888/1064] | 0.042 |
| Intracoronary imaging use, % [n]      | 7.6 [27/356]     | 10.4 [148/1420]     | 10.7 [31/291] | 11.0 [15/137] | 12.8 [51/399] | 13.1 [44/336] | 14.5 [154/1064] | 0.008 |
| Lesion preparation, % [n]             |                  |                     |            |               |               |                  |                          |
| Atherectomy                           | 0.6 [2/356]      | 2.0 [29/1420]       | 0.0 [0/291] | 0.0 [0/137] | 1.0 [4/399] | 0.6 [2/336] | 1.5 [16/1064] | 0.020 |
| Cutting balloon                       | 0.8 [3/356]      | 1.6 [23/1420]       | 3.4 [10/291] | 1.5 [2/137] | 1.5 [8/399] | 1.2 [4/336] | 1.3 [14/1064] | 0.190 |
| Thrombus aspiration                   | 3.1 [11/356]     | 2.8 [40/1420]       | 1.7 [5/291] | 1.5 [2/137] | 3.0 [12/399] | 3.9 [13/336] | 2.8 [30/1064] | 0.720 |
| Overall no. of lesions treated, meansD [N] | 1.5±0.7 [356]  | 1.4±0.7 [1420]    | 1.5±0.8 [291] | 1.4±0.8 [137] | 1.3±0.6 [399] | 1.4±0.6 [336] | 1.4±0.7 [1063] | 0.056 |
| No. of stents implanted, meansD [N]   | 1.8±1.0 [356]    | 2.0±1.1 [1420]      | 2.1±1.1 [291] | 1.7±0.9 [137] | 1.5±0.8 [399] | 1.5±0.8 [336] | 1.8±1.0 [1063] | <0.001 |

(Continued)
for patients in whom no Ultimaster stent was implanted, in which follow-up was only available to discharge. The event rates (see Outcomes) at 1-year follow-up were calculated based upon the number of patients who had a 1-year follow-up visit or experienced a clinical event. All primary outcome-related adverse events were adjudicated by an independent clinical events committee.

**Outcomes**

The primary outcome measure was target lesion failure (TLF), defined as the composite of cardiac death, target vessel–related myocardial infarction, and clinically driven target lesion revascularization. Secondary outcomes included target vessel failure (TVF), composite of cardiac death, target vessel myocardial infarction and clinically driven target vessel revascularization, and patient-oriented composite end point, defined as a composite of all-cause death, any myocardial infarction (MI), and any revascularization. For MI, the extended historical definition was applied that primarily uses creatine kinase myocardial band, or if not available troponin, as a cardiac biomarker criterion. All deaths, MI, target lesion revascularizations (TLRs) or target vessel revascularizations, and stent thrombosis were adjudicated by an independent clinical events committee.

**Statistical Analysis**

Continuous variables are reported as mean along with SD and compared using the ANOVA test, whereas categorial variables are reported as frequency and percentage and compared using the \( \chi^2 \) test. Analyses were performed with SAS version 9.4 software (SAS Institute, Cary, NC). Cox proportional hazards models were performed using Medina 1.0.0 as the reference category to assess the hazard ratio (HR) of 1-year outcomes across different Medina subtypes, adjusting for PCI indication (chronic coronary syndrome, unstable angina, non–ST-segment–elevation myocardial infarction, and ST-segment–elevation myocardial infarction), CBL vessel location (right coronary artery, left main stem, left anterior descending artery, and left circumflex artery), radial access, stenting strategy (1 versus 2 stents), and use of intracoronary imaging and/or proximal optimization technique.

**RESULTS**

A total of 4003 patients undergoing PCI for CBLs at the index procedure were included in the analysis. The most prevalent lesion subtypes were Medina 1.1.1 (n=1420, 35.5%) and Medina 1.1.0 (n=1064, 26.8%), whereas the least prevalent subtype was Medina 0.0.1 (n=137, 3.5%) (Figure 1).

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Table 1. Continued

| Characteristic | True bifurcation | Nontrue bifurcation | P value |
|---------------|------------------|----------------------|--------|
|               | Medina 1.0.1     | Medina 1.1.1         |        |
|               | n=1420           | n=1364               |        |
| Bifurcation main vessel, % [n] | 34.8 [492/1420] | 34.8 [479/1364] | <0.001 |
| Left main     | 61.2 [878/1420]  | 61.2 [857/1364]      | <0.001 |
| Left anterior descending | 34.8 [492/1420] | 34.8 [479/1364] | <0.001 |
| Left circumflex | 35.4 [492/1420] | 35.4 [479/1364] | <0.001 |
| Right coronary artery | 35.4 [492/1420] | 35.4 [479/1364] | <0.001 |
| Bilateral technique, % [n] | 35.4 [492/1420] | 35.4 [479/1364] | <0.001 |
| 1 stent       | 35.5 [415/1183]  | 35.5 [411/1162]      | <0.001 |
| PVT           | 29.8 [343/1143]  | 29.8 [341/1162]      | <0.001 |

CABG indicates coronary artery bypass graft surgery; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; POT, proximal optimization technique; PTCA, percutaneous transluminal coronary angioplasty; and STEMI, ST-segment–elevation myocardial infarction.
Patient and Procedural Characteristics

The median age for the entire cohort was ≈65 years, with the majority being men (70.8%–77.5%), undergoing PCI for chronic coronary syndrome (48.0%–55.9%) (Table 1). However, no differences were observed between Medina subtypes for characteristics such as age, sex, diabetes, hypertension, hypercholesterolemia, and previous MI, coronary artery bypass graft surgery, and percutaneous transluminal coronary angioplasty. Acute coronary syndrome was the most frequent indication for Medina 1.0.1 (52.0%) and the least frequent for Medina 0.1.1 (44.1%).

In terms of procedural characteristics, the rate of use of intracoronary imaging was highest in the Medina 1.1.0 subtype (14.5%) and lowest in the Medina 1.0.0 subtype (7.6%) (Table 1). Although there was no difference in the mean number of total lesions treated among Medina subtypes, the greatest number of stents implanted were in Medina 0.1.1 (2.1±1.1), whereas the lowest was in Medina 0.0.1 (1.5±0.8 each). Overall, the left anterior descending artery was the most treated vessel, and this was most frequent in Medina 0.1.1 (69.1%) and least frequent in Medina 0.0.1 (47.5%). The majority of CBLs were treated by a

| Table 2. One-Year Clinical Outcomes According to Medina Classification Subtype |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | True bifurcation | Nontrue bifurcation |                |                |                |                |                |
|                                | 1.0.1 | 1.1.1 | 0.1.1 | 0.0.1 | 0.1.0 | 1.0.0 | 1.1.0 |                |
| Outcome                        | n=337 | n=1368 | n=276 | n=136 | n=385 | n=320 | n=1033 | P value          |
| TLF, % [n]                    | 4.5% [15] | 6.1% [83] | 2.9% [8] | 8.1% [11] | 3.4% [13] | 2.5% [8] | 4.7% [49] | 0.016          |
| TVF, % [n]                    | 5.3% [18] | 7.4% [101] | 2.9% [8] | 8.8% [12] | 3.9% [15] | 4.1% [13] | 5.8% [60] | 0.009          |
| POCE, % [n]                   | 9.8% [33] | 10.8% [148] | 6.2% [17] | 9.6% [13] | 7.0% [27] | 6.3% [20] | 9.7% [100] | 0.040          |
| All-cause death, % [n]        | 3.6% [12] | 3.6% [49] | 0.7% [2] | 2.9% [4] | 2.9% [11] | 1.9% [8] | 1.9% [20] | 0.056          |
| Cardiac death, % [n]          | 1.2% [4] | 2.4% [33] | 0.4% [1] | 2.9% [4] | 2.1% [8] | 0.9% [3] | 1.5% [15] | 0.115          |
| TV-MI, % [n]                  | 1.5% [5] | 1.8% [25] | 0.4% [1] | 0.7% [1] | 0.3% [1] | 0.9% [3] | 1.4% [14] | 0.179          |
| CD-TVR, % [n]                 | 3.9% [13] | 4.9% [67] | 2.5% [7] | 6.6% [9] | 1.6% [6] | 2.8% [9] | 4.1% [42] | 0.028          |
| CD-TLR, % [n]                 | 3.0% [10] | 3.4% [46] | 2.5% [7] | 5.2% [7] | 1.0% [4] | 1.3% [4] | 2.8% [29] | 0.068          |
| Definite/probable ST, % [n]   | 1.2% [4] | 1.1% [15] | 0.0% [0] | 0.0% [0] | 0.3% [1] | 0.9% [3] | 0.7% [7] | 0.290          |

CD-TLR indicates clinically driven target lesion revascularization; CD-TVR, clinically driven target vessel revascularization; POCE, patient-oriented composite end point (composite of all-cause death, any myocardial infarction, and any revascularization); ST, stent thrombosis; TLF, target lesion failure (composite of cardiac death, target vessel myocardial infarction, and clinically driven target lesion revascularization); TVF, target vessel failure (composite of cardiac death, target vessel myocardial infarction, and clinically driven target vessel revascularization); and TV-MI, target vessel myocardial infarction.

*P<0.05 vs Medina 1.0.0.
†P<0.01 vs Medina 1.0.0.
1-stent technique, especially the nontrue bifurcation subtypes Medina 0.1.0 (97.4%), Medina 1.0.0 (96.3%), and Medina 1.1.0 (94.3%), whereas the use of a 2-stent technique was highest in true bifurcations (34.8%–47.8%) as well as Medina 0.0.1 (43.2%). The proximal optimization technique was more frequently used in the Medina 1.1 subtype (41.1%) and least commonly in Medina 0.0.1 (15.3%). Furthermore, the overall use of the proximal optimization technique and poststenting kissing balloon was higher in 2-stent than 1-stent techniques (77.4% versus 31.1% and 49.4% versus 36.8%, respectively). Several 2-stent techniques were used for true and nontrue bifurcations (Tables S1 and S2, respectively), T-stenting (23.8%) being the most used, followed by the Crush technique (17.0%) and TAP (16.1%) in true bifurcation lesions. There was a variation depending on the type of the true bifurcation. For nontrue bifurcations, another technique that was not specified was the most used (29.6%), whereas for true bifurcations, T-stenting was the common strategy (23.8%).

Clinical Outcomes

Overall, TLF and TVF rates were highest in Medina 1.1.1 (6.1% and 7.4%, respectively) and Medina 0.0.1 (8.1% and 8.8%, respectively) subtypes, whereas the lowest TLF and target vessel revascularization rates were in the Medina 1.0.0 and Medina 0.1.0 subtypes, respectively (TLF: 2.5%, TVF: 2.9%) (Table 2, Figure 2). The high TLF and TVF rates were primarily driven by high rates of clinically driven TLR and target vessel revascularization, respectively. Patient-oriented composite end point rates were highest among Medina 1.1.1 (10.8%), Medina 0.0.1 (9.6%), and Medina 1.1.0 (9.7%) subtypes compared with all other bifurcation distributions. No statistically significant differences between Medina subtypes were observed for other outcomes including all-cause and cardiac death, target vessel MI, and definite/probable stent thrombosis.

Using Medina 1.0.0 as the reference category, the risk of 1-year TLF was only increased in Medina 1.1.1 (HR, 2.6 [95% CI, 1.3–5.5]) and Medina 0.0.1 (HR, 4.0 [95% CI, 1.6–9.9]) subtypes, driven by an increased risk of clinically driven TLR in either subtype (Medina 1.1.1: HR, 3.1 [95% CI, 1.1–8.6]; Medina 0.0.1: HR, 4.6 [95% CI, 1.3–16.0]) and cardiac death in the Medina 0.0.1 subtype (HR, 4.7 [95% CI, 1.0–21.6]) (Table 3, Figure 3). No other differences in risk of adverse clinical outcomes (target vessel MI, cardiac death, and stent thrombosis) were observed between Medina 1.0.0 and other Medina subtypes.

Subgroup Analysis

Comparison by Medina subtype found no difference between stenting techniques (1 versus 2 stents) except...
in the Medina 1.0.0 group, where a 2-stent strategy was associated with higher rates of clinically driven TLR (8.3% versus 1.0%, \(P<0.05\)) (Table S3). Furthermore, there were no differences in clinical outcomes at 1 year per type of 2-stent technique except for all-cause death, with the lowest rate observed with V-stenting (0.0%, 0/48) and the highest with the Culotte technique (9.2%, 8/87). (Table S4).

Tables S5 and S6 summarize 1-year clinical outcomes for bifurcation lesions involving the left main and left anterior descending arteries, respectively, as per the Medina classification. No differences in clinical outcomes were observed between Medina subtypes, except for patient-oriented composite end point for lesions involving the left main artery for which the highest rate was observed in Medina 1.1.1 (21.9%) and the lowest in Medina 0.0.1 (0.0%).

**DISCUSSION**

The present study is the first to outline the impact of lesion distribution according to Medina classification on 1-year clinical outcomes among >4000 patients undergoing CBL PCI using the same contemporary stent platform. Our findings can be summarized as follows (Figure 4). First, we found that Medina 1.1.1 (35.5%) and Medina 1.1.0 (26.8%) were the most prevalent CBL distributions, whereas Medina 0.0.1 (3.5%) was the least prevalent. Second, no clinically meaningful differences in patient characteristics were observed following stratification for Medina subtypes. Despite this, PCI of Medina 1.1.1 and 0.0.1 subtypes was associated with significantly higher crude rates of TLF compared with all other bifurcation distributions and were independently associated with an increased hazard of TLF (2.6- and 4-fold, respectively) at 1 year.

Although previous studies have examined differences in procedural outcomes between true and non-true CBLs, there are limited data on the prognostic impact of disease distribution in CBLs.\textsuperscript{10–12} Our findings highlight differences in 1-year outcomes between CBL distributions, with the greatest hazard for TLF and TVF observed among Medina 1.1.1 and Medina 0.0.1, even after adjustment for baseline differences between Medina subtypes. Given the limited previous literature comparing outcomes between CBL lesion
distributions, it is difficult to place our findings within the context of other studies. A study of 2897 patients undergoing CBL PCI reported higher crude rates of Major acute cardiovascular events and cardiac death/MI among specific Medina subtypes (Medina 1.1.1: 12.4% and 4.5%, respectively; Medina 0.1.1: 13.9% and 3.7%, respectively). However, the authors did not compare outcomes between different Medina subtypes except within true CBL groups (Medina 1.1.1 and Medina 0.1.1 versus Medina 1.0.1) and reported no differences between these groups. Furthermore, their findings were derived from an old procedural cohort (enrolled between 2003 and 2009), managed with older (first and second) generation drug-eluting stents. In contrast, Todara et al reported no difference in in-hospital and 12-month cardiac death, TLR, and reinfarction between Medina 1.1.1 and all other subtypes combined. However, their analysis was based on a small sample size (n=120, including n=25 with Medina 1.1.1) from an old procedural cohort (2005–2006), where 25% of patient were not managed with a drug-eluting stent.

The finding that 0.0.1 isolated SB disease has the highest hazard of TLF is interesting and deserves further comment. Our subgroup analysis suggests that the worse outcomes associated with 0.0.1 are observed irrespective of whether a single- or 2-stent approach is used. Isolated SB disease is complex to treat, because lesions are often fibrocalcific with significant recoil, which makes achieving good minimal luminal area challenging, particularly if the lesions are not adequately prepared. Furthermore, isolated SB lesions often supply a limited myocardial territory (<10%), with only 1 in 5 non–left main artery SB lesions shown to supply >10% fractional myocardial mass in a multicenter registry analysis of 482 patients undergoing computed tomography coronary angiography. Isolated SB lesions are also difficult to treat, because identification of the ostium may be challenging, resulting in geographical or ostial miss, or compromise of the main vessel, which may account for 27% of isolated SB lesions treated with a 2-stent approach. Furthermore, stent underexpansion or recoil, smaller SB vessel size in relation to the MB, and SB length may all contribute to the worse outcomes observed in this group. The mean stent diameter for SB 0.0.1 lesions in our study was 2.79 mm compared with >3 mm used to treat MB lesions. Consequently, many operators may choose to treat these lesions conservatively or use alternative interventional strategies such as drug-eluting balloons, although there is limited evidence to support the latter.

Figure 4. Summary of study findings.
CBL indicates coronary bifurcation lesion; CD-TLR, target lesion revascularization; PCI, percutaneous coronary intervention; and TLF, target lesion failure.
An observational study of 49 patients of Medina 0.0.1 lesions with associated ischemia showed that careful predilatation with a cutting balloon followed by a drug-eluting balloon use was sufficient in the majority of cases, with only 14% requiring stent implantation for acute recoil/coronary dissection. Nevertheless, their reported rate of TLF was still high at 14%, 1-year after the procedure. The present findings highlight the complexity of this lesion subset, for which there are limited evidence-based therapies, and emphasize the need for prospective work around alternative management strategies for isolated SB lesions.

Limitations

There are several limitations to the present study. First, the outcomes that we report are only in patients treated with PCI; our data do not inform on outcomes of lesions treated medically, which is particularly relevant for isolated SB lesions. Second, although the events in our study were independently adjudicated, it is possible that some events were underreported. However, measures to preserve the quality of data reporting, including on-site and remote monitoring, and close communication with the participating sites were in place. Furthermore, the Medina classification was identified based on data submitted in the electronic case report form and not assessed from a core laboratory. Third, some of the CIs in our results are wide because of the relatively small sample size for individual Medina subgroups. Finally, our findings are based on 1-year outcomes, and it is possible that further prognostic differences are observed between Medina subtypes on longer follow-up.

CONCLUSIONS

Within prospective multicenter data collection with independent event adjudication, we demonstrated significant prognostic differences among 4000 bifurcation PCI procedures according to coronary bifurcation distribution patterns, with Medina 1.1.1 and Medina 0.0.1 associated with worse clinical outcomes at 1 year, including clinically driven TLR and consequently TLF, compared with other Medina subtypes. The present findings should prompt greater caution among operators when managing these higher-risk lesions.

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Table S1. Type of 2-stent techniques used for patients with a true bifurcation lesion.

| True | Missing | Crush | Culotte | Kissing stents | Other | T-stenting | TAP | V-stenting |
|------|---------|-------|---------|----------------|-------|------------|-----|------------|
| 0.1.1 | 1.5% (2/133) | 13.5% (18/133) | 12.8% (17/133) | 9.8% (13/133) | 6.0% (8/133) | 21.1% (28/133) | 15.0% (20/133) | 20.3% (27/133) |
| 1.0.1 | 0.9% (1/116) | 12.9% (15/116) | 6.0% (7/116) | 6.9% (8/116) | 40.0% (46/116) | 24.1% (28/116) | 5.2% (6/116) | 4.3% (5/116) |
| 1.1.1 | 1.0% (5/479) | 19.0% (91/479) | 13.8% (66/479) | 7.9% (38/479) | 10.4% (50/479) | 24.4% (117/479) | 19.0% (91/479) | 4.4% (21/479) |
| All  | 1.1% (8/728) | 17.0% (124/728) | 12.4% (90/728) | 8.1% (59/728) | 14.3% (104/728) | 23.8% (173/728) | 16.1% (117/728) | 7.3% (53/728) |
Table S2. Type of 2-stent techniques used for patients with a non-true bifurcation lesion.

| Non-true | Missing | Crush | Culotte | Kissing stents | Other | T-stenting | TAP | V-stenting |
|----------|---------|-------|---------|--------------|-------|------------|-----|------------|
| 0.0.1    | 0.0% (0/16) | 6.3% (1/16) | 18.8% (3/16) | 6.3% (1/16) | 18.8% (3/16) | 37.5% (6/16) | 6.3% (1/16) | 6.3% (1/16) |
| 0.1.0    | 0.0% (0/10)  | 0.0% (0/10)  | 40.0% (4/10)  | 0.0% (0/10)  | 30.0% (3/10)  | 10.0% (1/10)  | 10.0% (1/10)  | 10.0% (1/10)  |
| 1.0.0    | 0.0% (0/12)  | 8.3% (1/12)  | 0.0% (0/12)  | 25.0% (3/12) | 0.0% (0/12)  | 58.3% (7/12) | 0.0% (0/12)  | 8.3% (1/12)  |
| 1.1.0    | 5.0% (3/60)  | 5.0% (3/60)  | 8.3% (5/60)  | 6.7% (4/60)  | 38.3% (23/60) | 20.0% (12/60) | 11.7% (7/60) | 5.0% (3/60)  |
| All      | 3.1% (3/98)  | 5.1% (5/98)  | 12.2% (12/98) | 8.2% (8/98)  | 29.6% (29/98) | 26.5% (26/98) | 9.2% (9/98)  | 6.2% (6/98)  |
Table S3. Clinical outcomes at 1-year for true and non-true bifurcations according to stent strategy (1 vs. 2 stents) and Medina classification subtype.

| True bifurcation | Non-true bifurcation |
|-------------------|-----------------------|
|                    | 0.1.1 | 0.1.1 | 1.0.1 | 1.0.1 | 1.1.1 | 1.1.1 | 0.0.1 | 0.0.1 | 0.1.0 | 0.1.0 | 1.0.0 | 1.0.0 | 1.1.0 | 1.1.0 |
| 1-stent           | 141   | 2-stent| 129   | 1-stent| 211   | 2-stent| 108   | 2-stent| 879   | 2-stent| 463   | 2-stent| 16    | 2-stent| 367   | 2-stent| 10  | 2-stent| 302   | 2-stent| 12  | 2-stent| 962   | 2-stent| 60  |
| TLF, % [n]        | 2.8 [4]| 2.3 [3]| 4.3 [9]| 5.6 [6]| 5.5 [48]| 6.7 [31]| 11.9 [5]| 12.5 [2]| 3.5 [13]| 0.0 [0]| 2.3 [7]| 8.3 [1]| 4.9 [47]| 3.3 [2]|
| POCE, % [n]       | 6.4 [9]| 5.4 [7]| 9.0 [19]| 12.0 [13]| 9.8 [86]| 12.3 [57]| 14.3 [6]| 12.5 [2]| 7.4 [27]| 0.0 [0]| 6.3 [19]| 8.3 [1]| 10.0 [96]| 3.3 [2]|
| Cardiac death, % [n] | 0.7 [1]| 0.0 [0]| 0.5 [1]| 2.8 [3]| 2.3 [20]| 2.4 [11]| 4.8 [2]| 6.3 [1]| 2.2 [8]| 0.0 [0]| 1.0 [3]| 0.0 [0]| 1.6 [15]| 0.0 [0]|
| TV-MI, % [n]      | 0.0 [0]| 0.0 [0]| 1.4 [3]| 1.9 [2]| 1.6 [14]| 1.9 [9]| 2.4 [1]| 0.0 [0]| 0.3 [1]| 0.0 [0]| 1.0 [3]| 0.0 [0]| 1.4 [13]| 1.7 [1]|
| CD-TLR, % [n]     | 2.1 [3]| 2.3 [3]| 3.8 [8]| 1.9 [2]| 3.1 [27]| 3.7 [17]| 7.1 [3]| 6.3 [1]| 1.1 [4]| 0.0 [0]| 1.0 [3]| 8.3 [1]*| 2.9 [28]| 1.7 [1]|
| ST [def/prob], % [n] | 0.0 [0]| 0.0 [0]| 0.5 [1]| 2.8 [3]| 0.8 [7]| 1.3 [6]| 0.0 [0]| 0.0 [0]| 0.3 [1]| 0.0 [0]| 1.0 [3]| 0.0 [0]| 0.7 [7]| 0.0 [0]|

*p-value for 1 vs. 2-stent strategy: <0.05, non-significant for all other outcomes.
Table S4. Clinical outcomes at 1-year per type of 2-stent technique.

| 2-stents  | Crush | Culotte stents | Kissing stents | Other | T-stenting | TAP | V-stenting | p-value |
|-----------|-------|---------------|---------------|-------|------------|-----|------------|---------|
| TLF       | 8.6%  | 9.2%          | 1.7%          | 4.0%  | 5.4%       | 5.3%| 2.1%       | 0.29    |
|           | (10/117) | (8/87) | (1/58) | (4/101) | (9/167) | (6/114) | (1/48) |
| POCE      | 11.1% | 20.7%         | 8.6%          | 10.9% | 7.8%       | 10.5%| 6.3%       | 0.07    |
|           | (13/117) | (18/87) | (5/58) | (11/101) | (13/167) | (12/114) | (3/48) |
| All death | 2.6%  | 9.2%          | 3.5%          | 7.9%  | 1.2%       | 0.9% | 0.0%       | <0.01   |
|           | (3/117) | (8/87) | (2/58) | (8/101) | (2/167) | (1/114) | (0/48) |
| Cardiac death | 2.6%  | 4.6%          | 1.7%          | 4.0%  | 0.6%       | 0.9% | 0.0%       | 0.21    |
|           | (3/117) | (4/87) | (1/58) | (4/101) | (1/167) | (1/114) | (0/48) |
| All MI    | 3.4%  | 3.5%          | 0.0%          | 1.0%  | 2.4%       | 0.9% | 2.1%       | 0.59    |
|           | (4/117) | (3/87) | (0/58) | (1/101) | (4/167) | (1/114) | (1/48) |
| CD-TLR    | 6.0%  | 3.5%          | 0.0%          | 0.0%  | 3.6%       | 4.4% | 2.1%       | 0.17    |
|           | (7/117) | (3/87) | (0/58) | (0/101) | (6/167) | (5/114) | (1/48) |
| Stent thrombosis (def/prob) | 1.7%  | 2.3%          | 0.0%          | 1.0%  | 1.2%       | 1.8% | 0.0%       | 0.87    |
|           | (2/117) | (2/87) | (0/58) | (1/101) | (2/167) | (2/114) | (0/48) |
Table S5. Clinical outcomes at 1-year for bifurcation lesions involving the left main per Medina classifications.

| Left main | 0.0.1 | 0.1.0 | 0.1.1 | 1.0.0 | 1.0.1 | 1.1.0 | 1.1.1 | P-value |
|-----------|-------|-------|-------|-------|-------|-------|-------|---------|
| TLF       | 0.0%  | 9.4%  | 4.2%  | 2.8%  | 5.3%  | 7.1%  | 13.5% | 0.25    |
|           | (0/3) | (3/32) | (1/24) | (1/36) | (1/19) | (11/154) | (24/178) |         |
| POCE      | 0.0%  | 18.8% | 4.2%  | 2.8%  | 15.8% | 13.6% | 21.9% | 0.04    |
|           | (0/3) | (6/32) | (1/24) | (1/36) | (3/19) | (21/154) | (39/178) |         |
| All death | 0.0%  | 9.4%  | 4.2%  | 0.0%  | 15.8% | 4.6%  | 9.6%  | 0.17    |
|           | (0/3) | (3/32) | (1/24) | (0/36) | (3/19) | (7/154) | (17/178) |         |
| Cardiac death | 0.0% | 6.3% | 4.2% | 0.0% | 5.3% | 3.3% | 6.2% | 0.70 |
|           | (0/3) | (2/32) | (1/24) | (0/36) | (1/19) | (5/154) | (11/178) |         |
| All MI    | 0.0%  | 3.1%  | 0.0%  | 0.0%  | 0.0%  | 0.7%  | 2.8%  | 0.62    |
|           | (0/3) | (1/32) | (0/24) | (0/36) | (0/19) | (1/154) | (5/178) |         |
| CD-TLR    | 0.0%  | 0.0%  | 0.0%  | 2.8%  | 0.0%  | 3.9%  | 7.3%  | 0.29    |
|           | (0/3) | (0/32) | (0/24) | (1/36) | (0/19) | (6/154) | (13/178) |         |
| Stent thrombosis (def/prob) | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.7% | 1.1% | 0.97 |
|           | (0/3) | (0/32) | (0/24) | (0/36) | (0/19) | (1/154) | (2/178) |         |
Table S6. Clinical outcomes at 1-year for bifurcation lesions involving the LAD per Medina classifications.

| LAD    | 0.0.1 | 0.1.0 | 0.1.1 | 1.0.0 | 1.0.1 | 1.1.0 | 1.1.1 | p-value |
|--------|-------|-------|-------|-------|-------|-------|-------|---------|
| TLF    | 7.7%  | 2.8%  | 2.6%  | 3.5%  | 6.0%  | 3.3%  | 5.5%  | 0.11    |
|        | (5/65)| (7/252)| (5/193)| (6/171)| (11/183)| (20/599)| (47/858)|         |
| POCE   | 9.2%  | 5.2%  | 5.7%  | 8.2%  | 12.6% | 7.5%  | 8.9%  | 0.11    |
|        | (6/65)| (13/252)| (11/193)| (14/171)| (23/183)| (45/599)| (76/858)|         |
| All death | 3.1%  | 2.4%  | 0.5%  | 2.9%  | 1.6%  | 1.2%  | 3.2%  | 0.12    |
|        | (2/65)| (6/252)| (1/193)| (5/171)| (3/183)| (7/599)| (27/858)|         |
| Cardiac death | 3.1%  | 1.6%  | 0.0%  | 1.8%  | 0.0%  | 0.8%  | 2.1%  | 0.08    |
|        | (2/65)| (4/252)| (0/193)| (3/171)| (0/183)| (5/599)| (18/858)|         |
| All MI | 0.0%  | 0.8%  | 0.0%  | 1.2%  | 3.8%  | 1.8%  | 2.2%  | 0.07    |
|        | (0/65)| (2/252)| (0/193)| (2/171)| (7/183)| (11/599)| (19/858)|         |
| CD-TLR | 4.6%  | 1.2%  | 2.6%  | 1.8%  | 5.5%  | 2.3%  | 2.8%  | 0.15    |
|        | (3/65)| (3/252)| (5/193)| (3/171)| (10/183)| (14/599)| (24/858)|         |
| Stent thrombosis (def/prob) | 0.0% | 0.4%  | 0.0%  | 1.2%  | 1.6%  | 0.7%  | 1.1%  | 0.52    |
|        | (0/65)| (1/252)| (0/193)| (2/171)| (3/183)| (4/599)| (9/858)|         |
Figure S1. Bifurcation subtypes as per the Medina classification.