Coronary dominance and prognosis in patients undergoing coronary computed tomographic angiography: results from the CONFIRM (COronary CT Angiography Evaluation For Clinical Outcomes: An InteRnational Multicenter) registry

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Coronary dominance and prognosis in patients undergoing coronary computed tomographic angiography: results from the CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry


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Aims

Coronary computed tomographic angiography (CCTA) has become an important tool for non-invasive diagnosis of coronary artery disease (CAD). Coronary dominance can be assessed by CCTA; however, the predictive value of coronary dominance is controversially discussed. The aim of this study was to evaluate the prevalence and prognosis of coronary dominance in a large prospective, international multicentre cohort of patients undergoing CCTA.

Methods and results

The study population consisted of 6382 patients with or without CAD (47% females, 53% males, mean age 56.9 ± 12.3 years) who underwent CCTA and were followed over a period of 60 months. Right or left coronary dominance was determined. Right dominance was present in 91% (n = 5817) and left in 9% (n = 565) of the study population. At the end of follow-up, outcome in patients with obstructive CAD (>50% luminal stenosis) and right dominance was similar compared with patients with left dominance [hazard ratio (HR) 0.46, 95% CI 0.16–1.32, P = 0.15]. Furthermore, no differences were observed for the type of coronary dominance in patients with non-obstructive CAD (HR 0.95, 95% CI 0.83–1.09, P = 0.4).
Coronary dominance and co-dominance were associated with increased mortality in 207,926 patients undergoing percutaneous coronary intervention (PCI) for ACS demonstrated that left dominance was associated with an increased hazard of death across North America, Europe, and Asia with suspected CAD who underwent ≥64-detector row CCTA, and is the first prospective database evaluating the prognostic role of CCTA. Coronary artery dominance is determined according to the coronary artery that emits the posterior descending artery. Right dominance is the most prevalent pattern of coronary circulation and is found in 72–90% of individuals, while prevalence of left dominance is reported to be 8–33%, whereas co-dominance has ~3–7% of population prevalence. The relatively low prevalence of left dominance in the general population and the decreasing prevalence of a left dominant or co-dominant coronary system with age have raised the question whether this variant may reflect a biological disadvantage relative to right dominance, and recent studies have hypothesized that left dominance may represent less well-balanced circulation with more myocardium at risk in acute coronary syndromes (ACSs). Indeed, a previous study of 27,289 patients undergoing cardiac catheterization for ACS demonstrated that left dominance was associated with an increased hazard of death during a 3.5-year follow-up, and a US registry reported that left dominance and co-dominance were associated with increased in-hospital mortality in 207,926 patients undergoing percutaneous coronary intervention (PCI) for ACS. However, this work has been based on conventional angiograms. Since it is often difficult to delineate the course of coronary arteries by angiography because it only provides a two-dimensional view of a three-dimensional structure, the present study analysed coronary dominance and outcome by multidetector coronary CTA that not only provides information about the presence and degree of coronary stenosis, but also allows to see the origin and course of coronary arteries by a three-dimensional display of anatomy thereby permitting the determination of coronary artery variations. Although coronary vessel dominance is easily assessed on coronary CTA, there is sparse information about the prognostic value of coronary vessel dominance in patients referred for PCI. Therefore, the goal of the present study was to assess the prevalence and prognosis of coronary dominance in a large prospective, international multi-centre cohort of patients undergoing PCI.

**Methods**

**Study design, patients, and outcome measures**

This study represents 63,822 patients from the CONFIRM registry. Briefly, CONFIRM enrolled consecutive adults >18 years of age between 2005 and 2009 who underwent ≥64-detector row CCTA for suspected CAD at 12 centres in six countries (Canada, Germany, Italy, Korea, Switzerland, and the USA). Details of the CONFIRM registry design and data elements have been published. Patients with no CAD, non-obstructive, obstructive, and severe obstructive CAD where coronary dominance had been assessed were included in the present analysis. Patients with a balanced coronary artery system were excluded from the analysis, because of the low number of patients in this group. Cases with missing data on dominance were excluded from analysis; therefore, 63,822 remaining individuals with and without CAD were included for the final analyses. The primary clinical endpoint of the study was a composite of all-cause mortality, non-fatal myocardial infarction (MI), and early and late coronary revascularizations. Non-fatal MI was defined as evidence of myocardial necrosis consistent with myocardial ischaemia, as detected by changes in cardiac biomarkers together with symptoms of ischaemia, ECG changes, or imaging evidence, according to the ESC/ACCF/AHA/WHF consensus document on the universal definition of non-fatal MI. Notably, in the CONFIRM registry, post-CCTA treatment regimens were not mandated and our database did not include information on previous or post-CCTA functional testing results. The study complies with the Declaration of Helsinki, and patient consent or a waiver of informed consent (as per recommendations of each institutional review board) was obtained at each site in keeping with site-specific regulations.

**Data acquisition, image reconstruction, and CCTA analysis**

CCTA scanners used in the CONFIRM registry and data acquisition for CCTA have been described in detail previously. Image interpretation was uniformly performed at each site according to the Society of Cardiovascular Computed Tomography guidelines by at least one highly experienced imager who was level III equivalent and/or board certified in cardiovascular computed tomography. Dominance was determined independently at each participating site. The coronary artery system was classified as a right dominant if the right coronary artery (RCA), as a left dominant if the left circumflex coronary artery (LCx), or as a co-dominant if RCA and LCx gave rise to the posterior descending artery. Each site performed per-segment analysis for individual coronary artery segments by using a 16-segment model. A CAD was defined as the presence of any plaque. Coronary atherosclerotic lesions were quantified for lumen diameter stenosis by visual estimation and graded as none (0% luminal stenosis), mild (1–49%), moderate (50–69%), or severe (>70%). A coronary lesion compromising the lumen by ≥50%
was defined as obstructive. Vessels were classified into four arterial territories: left main artery (LM), left anterior descending artery (LAD), LCx, and RCA. Obstructive CAD in the diagonal branches, obtuse marginal branches, and posterolateral branches was considered as part of the LAD, LCx, and RCA system, respectively. The posterior descending artery was considered as part of the RCA or LCx system, depending on the coronary artery dominance. A >50% stenosis in the LM was considered obstructive in all models. Individuals manifesting obstructive CAD were further categorized as having one-, two-, and three-vessel disease or left main disease. For the purposes of the study analysis, a left main coronary stenosis of ≥50% was considered equivalent to three-vessel CAD.

Statistical analysis

SPSS version 12.0 and 17.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.2 (SAS Institute, Cary, NC, USA) were used for all statistical analyses. Categorical variables are presented as frequencies and continuous variables as mean ± SD. Variables were compared with χ² statistic for categorical variables and by Student’s unpaired t-test, Wilcoxon/ Mann–Whitney non-parametric test, or median comparison test where appropriate for continuous variables. The Kaplan–Meier method and the log-rank A Cox proportional hazards analysis were used to compare cumulative event-free survival by dominance in patients without significant CAD on CCTA and in those with significant CAD on CCTA. The primary outcome variable was a composite endpoint of all-cause mortality, non-fatal MI, and revascularization. Multivariable analyses were calculated with the multivariable Cox regression model for prediction of the combined endpoint (with 95% confidence intervals). According to univariate significance and baseline differences between groups, risk factors such as age, male gender, hypertension, dyslipidaemia, diabetes, and smoking were included in the multivariate model. Furthermore, the prognostic value of severity of stenosis and significant stenosis location were determined for patients with a right dominant coronary artery system and patients with a left dominant coronary artery system. A two-tailed P-value of 0.05 was considered statistically significant.

Results

Study cohort

The CONFIRM registry screened 27 125 CCTA patients at 12 participating centres in six countries. Patients were followed for a median of 2.1 years (interquartile range 1.5–3.1 years). A total of 956 (3.5%) patients were lost to follow-up; for 20 743 patients, coronary artery dominance pattern had not been evaluated due to different reasons including technical reasons, extensive atherosclerosis, presence of occluding thrombi with large filling defects distally, or prior CABG. Thus, the final study population comprised 6382 patients (47% females, 53% males, mean age 56.9 ± 12.3 years) with or without CAD remained for the present analysis and was included in the study. Table 1 depicts baseline characteristics of the patient population, categorized by coronary vessel dominance. Left coronary dominance (LCD) patients tend to have a higher BMI (27.8 ± 5.4 vs. 27.2 ± 5.3, P = 0.0288), and were more often male (62 vs. 38%, P < 0.0001) and asymptomatic (24 vs. 37%, P = 0.0003) than patients with right coronary dominance (RCD).

CCTA findings

Right dominance was present in 91% (n = 5817) and left dominance in 9% (n = 565) of the study population. Normal coronary arteries were found by CCTA in 3361 (53%) patients, non-obstructive CAD in 1787 (28%), obstructive CAD in 457 (7%), and severe obstructive in 776 (12%; Table 2). Patients with left dominance tend to have a lower Agatston score than those with right dominance.

### Table 1  Baseline characteristics of the study population by dominance

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total (n = 6382)</th>
<th>Right dominant (n = 5817)</th>
<th>Left dominant (n = 565)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>3343 (53%)</td>
<td>2995 (51%)</td>
<td>348 (62%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI</td>
<td>27.3 ± 5.3</td>
<td>27.2 ± 5.3</td>
<td>27.8 ± 5.4</td>
<td>0.0288</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.9 ± 12.3</td>
<td>56.9 ± 12.2</td>
<td>56.6 ± 13.0</td>
<td>0.1726</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3287 (52%)</td>
<td>2970 (52%)</td>
<td>317 (56%)</td>
<td>0.0453</td>
</tr>
<tr>
<td>Diabetes</td>
<td>757 (12%)</td>
<td>680 (12%)</td>
<td>77 (14%)</td>
<td>0.1799</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>3373 (54%)</td>
<td>3093 (54%)</td>
<td>280 (50%)</td>
<td>0.0742</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1231 (19%)</td>
<td>1111 (19%)</td>
<td>120 (21%)</td>
<td>0.246</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>2036 (33%)</td>
<td>1839 (33%)</td>
<td>197 (36%)</td>
<td>0.2314</td>
</tr>
<tr>
<td>Symptons</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>2114 (34%)</td>
<td>1913 (24%)</td>
<td>201 (37%)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Non-Cardiac</td>
<td>977 (16%)</td>
<td>868 (15%)</td>
<td>109 (20%)</td>
<td></td>
</tr>
<tr>
<td>Atypical</td>
<td>2230 (36%)</td>
<td>2077 (37%)</td>
<td>153 (28%)</td>
<td></td>
</tr>
<tr>
<td>Typical</td>
<td>825 (13%)</td>
<td>747 (13%)</td>
<td>78 (14%)</td>
<td></td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>1793 (31%)</td>
<td>1611 (31%)</td>
<td>182 (35%)</td>
<td>0.0383</td>
</tr>
<tr>
<td>Diamond and Forrester pre-test probability</td>
<td>32.9 ± 29.2</td>
<td>33.0 ± 29.1</td>
<td>32.5 ± 29.8</td>
<td>0.69</td>
</tr>
<tr>
<td>Morise score</td>
<td>11.9 ± 4.3</td>
<td>11.8 ± 4.3</td>
<td>12.0 ± 4.2</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Data are presented as n (%) and mean ± SD. Patients with a balanced coronary artery system were excluded from the analysis.

BMI, body mass index; CAD, coronary artery disease.
(420.0 in the right dominance and 363.0 in the left dominance, P < 0.0001, median comparison test; Table 2). In our study cohort, 648 (10%) patients had one-vessel disease, 351 (10%) had two-vessel disease, and 222 (3%) were diagnosed with three-vessel disease. The severity of CAD and stenosis location on CCTA differed significantly among patients with a left dominant and right dominant coronary artery system: patients with left dominance tend to have more non-obstructive CAD (35 vs. 27%, P < 0.0001) and significant stenosis in the left anterior descending or circumflex artery (19 vs. 14%, P = 0.0067 and 10 vs. 7%, P = 0.0203, respectively), whereas patients with right dominance tend to have more often normal coronary arteries (54 vs. 43%, P < 0.0001) or obstructive CAD in the RCA (10 vs. 5%, P < 0.0001; Table 2).

**Event and survival rate**

During a follow-up of 60 months, the composite endpoint occurred in 321 (5.0%) patients. All-cause mortality was reported in 100 (1.6%) patients, non-fatal MI occurred in 131 (2.1%), and 120 patients (1.9%) underwent revascularization. When comparing event-free survival during 5 years of follow-up in patients with normal coronary arteries according to coronary vessel dominance, survival rates for the cumulative incidence of all-cause mortality, non-fatal MI, and coronary revascularization did not significantly differ between patients with LCD or RCD (log-rank P = 0.14, Figure 1B), with low cumulative event rates of 1.7 and 0.9%, respectively. Similar results were obtained when a separate analysis for each endpoint in patients with significant CAD was conducted (log-rank P = 0.069 for all-cause mortality, log-rank P = 0.63 for MI, and P = 0.76 for coronary revascularization, data not shown) or when patients with obstructive CAD (stenosis 50–70%; log-rank P = 0.60, data not shown) or severe obstructive CAD (stenosis >70%; log-rank 0.92, data not shown) were analysed separately. When stratified for sex, patients with LCD and RCD showed similar survival rates for the incidence of all-cause mortality, non-fatal MI, and coronary revascularization (log-rank P = 0.72 for males and log-rank P = 0.3842 for females; Figure 2A and B).

**Prognostic value of coronary dominance**

Uni- and multivariable proportional hazards models confirmed that obstructive and severe obstructive CAD in both coronary variations were predictors of all-cause mortality, non-fatal MI, and revascularization, and had an incremental value over clinical variables (Table 3). In patients with non-obstructive CAD, a right dominant system was identified as a significant predictor of the combined endpoint when compared with patients without coronary artery atherosclerosis [hazard ratio (HR) 4.78, 95% CI 3.01–7.59, P < 0.0001, Table 3] and remained a significant predictor after correction for baseline risk factors (P < 0.0001), whereas left dominance did not predict any events in this subpopulation (HR 2.79, 95% CI 0.77–10.1.

### Table 2  CCTA results: prevalence of coronary dominance in the study population

<table>
<thead>
<tr>
<th>CCTA findings</th>
<th>Total (N = 6382)</th>
<th>Right dominant (n = 5817)</th>
<th>Left dominant (n = 565)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agatston score (mean ± SD)*</td>
<td>141.3 ± 415</td>
<td>141.1 ± 420.0</td>
<td>144.2 ± 363.0</td>
<td>&lt;0.001b</td>
</tr>
<tr>
<td>Number of obstructive vessels</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None/normal</td>
<td>3361 (53%)</td>
<td>3119 (54%)</td>
<td>242 (43%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-obstructive</td>
<td>1788 (28%)</td>
<td>1591 (27%)</td>
<td>197 (35%)</td>
<td></td>
</tr>
<tr>
<td>One-vessel CAD</td>
<td>636 (10%)</td>
<td>563 (10%)</td>
<td>73 (13%)</td>
<td></td>
</tr>
<tr>
<td>Two-vessel CAD</td>
<td>325 (5%)</td>
<td>289 (5%)</td>
<td>36 (6%)</td>
<td></td>
</tr>
<tr>
<td>Three-vessel/LM CAD</td>
<td>272 (4%)</td>
<td>255 (4%)</td>
<td>17 (3%)</td>
<td></td>
</tr>
<tr>
<td>Level of obstructive CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3361 (53%)</td>
<td>3119 (54%)</td>
<td>242 (43%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-obstructive (1–49%)</td>
<td>1788 (28%)</td>
<td>1591 (27%)</td>
<td>197 (35%)</td>
<td></td>
</tr>
<tr>
<td>Obstructive CAD (50–70%)</td>
<td>457 (7%)</td>
<td>408 (7%)</td>
<td>49 (9%)</td>
<td></td>
</tr>
<tr>
<td>Severe obstructive CAD (&gt;70%)</td>
<td>776 (12%)</td>
<td>699 (12%)</td>
<td>77 (14%)</td>
<td></td>
</tr>
<tr>
<td>Left main &gt; 50%</td>
<td>85 (1%)</td>
<td>76 (1%)</td>
<td>9 (2%)</td>
<td>0.5423</td>
</tr>
<tr>
<td>LAD &gt; 50%</td>
<td>939 (15%)</td>
<td>834 (14%)</td>
<td>105 (19%)</td>
<td>0.0067</td>
</tr>
<tr>
<td>LCx &gt; 50%</td>
<td>465 (7%)</td>
<td>410 (7%)</td>
<td>55 (10%)</td>
<td>0.0203</td>
</tr>
<tr>
<td>RCA &gt; 50%</td>
<td>602 (9%)</td>
<td>576 (10%)</td>
<td>26 (5%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are presented as mean (± SD) or n (%). Patients with a balanced coronary artery system were excluded from the analysis.

CCTA, coronary computed tomographic angiography; CAD, coronary artery disease; LCx, left circumflex artery; RCA, right coronary artery; LM, left main artery; LAD, left anterior descending artery.

*Missing in 1309 patients.

P value given for median Agatston score (non-normal distribution of data).
Figure 1 (A) Event-free survival (Kaplan–Meier curve) from major adverse events (all-cause mortality, non-fatal MI, and coronary revascularization) with follow-up extending to 5 years in patients with RCD and LCD stratified for the presence of obstructive CAD (>50%) on CCTA. Patients with a balanced coronary artery system were excluded from the analysis, because of the low number of patients in this group. (B) Event-free survival (Kaplan–Meier curve) from major adverse events (all-cause mortality, non-fatal MI, and coronary revascularization) in patients with RCD and LCD stratified for normal coronary arteries. Patients with a balanced coronary artery system were excluded from the analysis, because of the low number of patients in this group.

Figure 2 (A) Males: event-free survival (Kaplan–Meier curve) from major adverse events (all-cause mortality, non-fatal MI, and coronary revascularization) with follow-up extending to 5 years stratified by coronary dominance in patients with obstructive CAD (>50%) on CCTA. (B) Females: event-free survival (Kaplan–Meier curve) from major adverse events (all-cause mortality, non-fatal MI, and coronary revascularization) with follow-up extending to 5 years stratified by coronary dominance in patients with obstructive CAD (>50%) on CCTA. Patients with a balanced coronary artery system were excluded from the analysis.
When female and male patients were analyzed separately, results remained the same (P = 0.0001 for females with RCD patients and non-obstructive CAD and P = 0.0001 for males with RCD patients and non-obstructive CAD, data not shown).

We further assessed the difference in a prognostic value between left and right coronary vessel dominance in patients with obstructive CAD for the composite endpoint of all-cause mortality, non-fatal MI, and coronary revascularization: Cox regression model analysis showed that the difference in the risk estimate of obstructive CAD between patients with a right dominant and those with a left dominant coronary artery system was statistically not significant (HR 1.04, 95% CI 0.68–1.59, P = 0.8461, right vs. left dominant, Table 4). Similarly, in patients with normal coronary arteries or non-obstructive CAD, no difference in the predictive value between the two coronary dominance pattern was found (HR 0.46, 95% CI 0.16–1.32, P = 0.1496 and HR 0.95, 95% CI 0.41–2.21, P = 0.8962, right vs. left dominant, respectively, Table 4).

Furthermore, significant CAD in one vessel was also identified as a predictor for the combined endpoint with a HR of 16.92 (95% CI 5.5–52.1, P < 0.0001 vs. normal coronary arteries) in the left dominant system and a HR of 24.43 (95% CI 15.9–37.5, P < 0.0001 vs. normal coronary arteries) in the right dominant system. Consequently, in both uni- and multivariable models accounting for individual Framingham risk factors, the risk was dose-dependently increased when more vessels were affected (data not shown).

### Prognostic value of significant stenosis location

After stratification according to stenosis location, the rate of cumulative event for LCD patients with significant LAD stenosis was 8% for non-fatal MI, 9% for coronary revascularization, and 8% for all-cause mortality (Figure 3A), whereas in patients with right dominance and significant RCA stenosis event rates for non-fatal MI, non-obstructive CAD

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Uni- and multivariate analyses adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking, and dyslipidaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Univariate</strong></td>
</tr>
<tr>
<td></td>
<td><strong>HR</strong></td>
</tr>
<tr>
<td>Left dominant</td>
<td></td>
</tr>
<tr>
<td>None/normal</td>
<td>1</td>
</tr>
<tr>
<td>Non-obstructive</td>
<td>2.79</td>
</tr>
<tr>
<td>Obstructive (50–70%)</td>
<td>10.31</td>
</tr>
<tr>
<td>Severe obstructive (&gt;70%)</td>
<td>20.67</td>
</tr>
<tr>
<td>Right dominant</td>
<td></td>
</tr>
<tr>
<td>None/normal</td>
<td>1</td>
</tr>
<tr>
<td>Non-obstructive</td>
<td>4.78</td>
</tr>
<tr>
<td>Obstructive (50–70%)</td>
<td>23.38</td>
</tr>
<tr>
<td>Severe obstructive (&gt;70%)</td>
<td>35.58</td>
</tr>
</tbody>
</table>

**HRs of CAD (non-obstructive: <50% stenosis, obstructive: >50% stenosis, severe obstructive: >70% stenosis) for the composite outcome of all-cause mortality, non-fatal MI, and coronary revascularization in LCD and RCD compared with normal coronary arteries on CCTA. Patients with a balanced coronary artery system were excluded from the analysis.**

**CAD,** coronary artery disease; **RF,** risk factor; **HR,** hazard ratio; **CI,** confidence interval.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Uni- and multivariate analyses adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking, and dyslipidaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Univariate</strong></td>
</tr>
<tr>
<td></td>
<td><strong>HR</strong></td>
</tr>
<tr>
<td>Normal coronary artery</td>
<td></td>
</tr>
<tr>
<td>Right dominant (vs. left dominant)</td>
<td>0.46</td>
</tr>
<tr>
<td>Non-obstructive CAD</td>
<td></td>
</tr>
<tr>
<td>Right dominant (vs. left dominant)</td>
<td>0.95</td>
</tr>
<tr>
<td>Obstructive CAD</td>
<td></td>
</tr>
<tr>
<td>Right dominant (vs. left dominant)</td>
<td>1.04</td>
</tr>
</tbody>
</table>

**HRs of RCD vs. LCD for the composite outcome of all-cause mortality, non-fatal MI, and coronary revascularization according to the extend of CAD (non-obstructive: <50% stenosis, obstructive: >50% stenosis, severe obstructive: >70% stenosis) on CCTA. Patients with a balanced coronary artery system were excluded from the analysis.**

**CAD,** coronary artery disease; **RF,** risk factor; **HR,** hazard ratio; **CI,** confidence interval.
coronary revascularization, and all-cause mortality were 10, 12, and 4%, respectively (Figure 3B). A significant stenosis in the left coronary system (LAD and LCx) was observed in 1489 patients and was associated with an increased risk of the combined endpoint all-cause mortality, non-fatal MI, and coronary revascularization for left dominance (HR 7.01 for LAD and 3.83 for LCx) as well as for right dominance (HR 10.12 for LAD and 8.29 for LCx, Table 5, lower panel).

However, significant left main disease was observed in 85 patients and the presence of LM disease conferred an increased HR for the combined adverse event by 6.45 after multivariable adjustment (95% CI 1.66–25.0, \( P = 0.007 \)) in patients with left dominance. In right dominance, however, LM disease was not significantly associated with the composite prognosis endpoint (HR 1.35, 95% CI 0.73–2.51, \( P = 0.3456 \) after adjustment for CAD and risk factors).

**Figure 3** (A) Risk estimates for all-cause mortality, non-fatal MI, and coronary revascularization in patients with significant LAD stenosis and a left dominant system. Patients with a balanced coronary artery system were excluded from the analysis. (B) Risk estimates for all-cause mortality, non-fatal MI, and coronary revascularization in patients with significant RCA stenosis and a right dominant system.

**Table 5** Upper and lower panels: Uni- and multivariate analyses adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking, and dyslipidaemia

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate (CAD RF adjusted)</th>
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<tr>
<td></td>
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<tr>
<td>Upper panel</td>
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<tr>
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<tr>
<td>Right dominant</td>
<td></td>
<td></td>
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<tr>
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<td>10.33</td>
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HRs of CAD according to (upper panel) the amount of diseased vessels (one-, two-, and three-vessel disease) and (lower panel) the stenosis location for the composite outcome of all-cause mortality, non-fatal MI, and coronary revascularization in LCD or RCD compared with normal coronary arteries on CCTA. LM, left main artery; RCA, right coronary artery; CAD, coronary artery disease; RF, risk factor; HR, hazard ratio; CI, confidence interval.
Table 5, lower panel). A significant lesion in the right system was associated with an increased risk of the combined endpoint in left dominance (HR 3.49, 95% CI 1.29–9.47, P = 0.0141) as well as in right dominance (HR 5.7, 95% CI 4.27–7.59, P < 0.0001, Table 5, lower panel).

Discussion

In this prospective multicentre study, we systematically evaluated the prognostic value of coronary dominance assessed by CCTA in a large cohort of patients. When comparing event-free survival in patients with normal coronary arteries or obstructive CAD according to coronary vessel dominance, survival rates for the cumulative incidence of all-cause mortality, non-fatal MI, and coronary revascularization after 5 years of follow-up did not differ significantly between patients with LCD or RCD.

In our study, right dominance was present in 91% and left dominance in 9%, which is not significantly different from values given in the literature, varying from 8.2 to 15% for left dominance and from 72 to 90% for right dominance.10–12,23,24 Left dominance was observed more often in males (62%) compared with females (38%), while previous retrospective studies indicate that there is no difference in coronary dominance with regard to gender.23,25–27 However, these differences may arise due to different selection of patients, e.g. the inclusion of low-to-intermediate risk patients at an advanced age in the present study.

In contrast to our findings, two previous retrospective angiographic studies using cardiac catheterization databases in patients with ACS have shown that left dominance was associated with modestly increased odds of death during a 3.5-year follow-up (HR 1.13; 1.00–1.28) or in-hospital mortality (HR 1.19; 1.06–1.34) following PCI, respectively.12,13 Left dominance was observed more often in males (62%) compared with females (38%), while previous retrospective studies indicate that there is no difference in coronary dominance with regard to gender.23,25–27 However, these differences may arise due to different selection of patients, e.g. the inclusion of low-to-intermediate risk patients at an advanced age in the present study.

Interestingly, in patients with non-obstructive CAD, a right dominance system was identified as a significant predictor of the combined endpoint, whereas left dominance did not predict any events in this subpopulation. The possibility that intermediate lesions may carry an increased risk in right dominant circulations is of particular importance since it would challenge the current paradigm of non-intervention for these non-obstructive lesions. However, there was no statistically significant difference in univariate analysis in this subgroup when right dominance was compared with left dominance. Yet, our study was likely statistically underpowered to detect effect modification between left and right dominance in this subgroup with non-obstructive CAD.

As with any study, certain design limitations are inherent. Of note is the low prevalence of left and co-dominant coronary circulation in the general population. While our study was sufficiently powered to detect an effect size in LCD, we did not include patients with co-dominant circulation in our analysis, since our study was underpowered to detect statistical effect modification in this subgroup. Secondly, as with any observational, open-label registry, potential heterogeneity between sites, interobserver and intersite variability in CCTA diagnosis, and different post-CCTA treatment patterns cannot be excluded. Thirdly, in the CONFIRM registry, CAD was defined using CCTA and not using invasive coronary angiography or other imaging modalities; therefore, the possibility of false-positive or false-negative CCTA findings exists despite the finding is consistent with previous observations in patients undergoing PCI for ACS.13 Coronary vessel dominance has influence on the relative contribution of the different coronary arteries to the total left ventricular blood flow29 and in most individuals with LCD, the RCA is usually small and often fails to reach the acute margin of the heart. Thus, a proximal stenosis of the left coronary artery may result in more extensive ischaemia and worse consequences in a left dominant system than in a right dominant system. In addition, the potential to rapidly form collaterals might be diminished in patients with a left dominant coronary artery system due to the fact that the RCA is not sufficient to perfuse the myocardium.30 However, to date, the underlying pathophysiology has not been investigated and further research is needed to assess the effect modification by culprit lesion site or coronary collateral formation in patients with left main disease and left coronary system.

The relationship between coronary vessel dominance and the extent of CAD remains uncertain as different studies showed opposing results. Indeed, one previous study has shown that LCD was associated with a higher incidence of atherosclerosis,31 whereas others showed more extensive CAD in patients with a right dominant coronary artery system12,23 or did not detect differences in the extent of CAD between LCD or RCD.26,28 However, this discrepancy may most likely be explained by a potential selection bias due to small study populations, and the differences in modalities used for the assessment of CAD in these studies. In the present study, we observed a higher incidence of CAD (obstructive and non-obstructive) in left dominance patients, whereas the prevalence of normal coronary arteries was more frequent in right dominance. However, no difference in predisposition to three-vascular disease was seen between LCD or RCD which strongly supports the hypothesis that dominance pattern does not predict outcomes in patients with CAD.
performance of CCTA by international experts. Finally, information regarding the coronary dominance pattern was not uniformly available for our study cohort, since not all CONFIRM sites collected this information. Thus, the final study comprised only 23.5% of the entire CONFIRM population and, as such, may have the potential for selection bias which may limit the generalizability of the data. However, our study population is the largest, presently available prospective CCTA cohort evaluating the predictive value of coronary dominance and may therefore provide solid data and good evidence regarding the prognostic information of coronary dominance.

In conclusion, our findings suggest that the assessment of coronary vessel dominance by CCTA may not enhance the risk stratification beyond the assessment of the degree of stenosis in patients with normal coronary arteries or obstructive CAD referred for CCTA, but may add prognostic information for specific subpopulations such as patients with left main disease or non-obstructive CAD.

Conflict of interest: J.K.M. received modest speakers' bureau and medical advisory board compensation, and significant research support from GE Healthcare. M.A.-M. received support from the American Heart Association, BCBS Foundation of Michigan, and Astellas. B.J.W.C. received research and fellowship support from GE Healthcare, research support from Pfizer and AstraZeneca, and educational support from TeraRecon. J.H. received a research grant from Siemens Medical Systems. J.L. has received research support and serves on the speakers bureau for GE Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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References
Transthoracic three-dimensional echocardiography visualization of functional anatomy of double-orifice mitral valve

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A 14-year-old boy was referred to our echocardiography laboratory because of a recent history of palpitations. Both physical examination and ECG were unremarkable. An ambulatory ECG recording detected only rare supraventricular ectopic beats. A two-dimensional transthoracic echocardiogram (2DE, Panel A, see Supplementary data online, Video S1) raised the suspect of a double-orifice mitral valve (DOMV), without either stenosis or regurgitation at colour and spectral Doppler analyses (Panel B). Three-dimensional transthoracic echocardiography (3DE) visualization of the valve from both ventricular and atrial perspectives (Panels C and D, see Supplementary data online, Videos S2 and S3) clearly showed the double orifices (white * ) with a central bridge of abnormal tissue connecting the anterior with the posterior leaflet. The two orifices were asymmetric, being the medial orifice slightly larger than the lateral one. Valvular leaflets were thin and normally sized. There were two papillary muscles that showed normal morphology and position. No other combined congenital abnormalities were detected. The patient was discharged without performing additional tests and no prescription.

* mitral valve orifice; AML, anterior mitral leaflet; AV, aortic valve; IAS, interatrial septal defect; LAA, left atrial appendage; PML, posterior mitral leaflet; RV, right ventricle.

Supplementary data are available at European Heart Journal — Cardiovascular Imaging online.

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