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Authors

Gebhard, Catherine
Fuchs, Tobias A
Stehli, Julia
et al.

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Coronary Dominance and Prognosis in Patients Undergoing Coronary Computed Tomographic Angiography: Results from CONFIRM (Coronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry)

Catherine Gebhard, MD *; Tobias A. Fuchs, MD *; Julia Stehli, MD *; Heidi Gransar, MS †, Daniel S. Berman, MD †; Matthew J. Budoff, MD §; Stephan Achenbach, MD ‖; Mouaz Al-Mallah, MD ¶; Daniele Andreini, MD #; Filippo Cademartiri, MD, PhD **; Tracy Q. Callister, MD ††; Hyuk-Jae Chang, MD ‡‡; Kavitha Chinnaiyan, MD §§; Benjamin J. W. Chow, MD ‖‖; Ricardo Cury, MD ¶¶; Augustin Delago, MD ##; Millie Gomez, MD ***, Martin Hadamitzky, MD †††; Joerg Hausleiter, MD ‡‡‡; Niree Hindoyan, BS ***; Gudrun Feuchtner, MD §§§; Yong-Jin Kim MD ‖‖‖; Jonathon Leipsic, MD ¶¶¶, Fay Y. Lin, MD †, Erica Maffei, MD ****, Gianluca Pontone, MD #, Gilbert Raff, MD §§; Leslee J. Shaw, PhD ††††; Todd C. Villines, MD ‡‡‡‡; Allison Dunning, MS §§§§, ; James K. Min, MD ***; Philipp A. Kaufmann, MD *

* Department of Nuclear Cardiology, Cardiovascular Center, University Hospital Zurich, Zurich, Switzerland † Department of Radiology, Dalio Institute of Cardiovascular Imaging, NewYork-Presbyterian Hospital and Weill Cornell Medical College, New York, NY; † Department of Imaging and Division of Cardiology, Department of Medicine, Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA; § Department of Medicine, Harbor UCLA Medical Center, Los Angeles, CA, USA; ‖ Department of Medicine, University of Erlangen, Erlangen, Germany; ¶ Department of Medicine, Wayne State University, Henry Ford Hospital, Detroit, MI, USA; # Department of Clinical Sciences and Community Health,

University of Milan, Centro Cardiologico Monzino, IRCCS Milan, Italy; ** Cardio Vascular Imaging Unit, Giovanni XXIII Hospital, Monastier, Italy and Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands; †† Tennessee Heart and Vascular Institute, Hendersonville, TN, USA; ‡‡ Division of Cardiology, Severance Cardiovascular Hospital, Seoul, South Korea; §§ William Beaumont Hospital, Royal Oaks, MI, USA; ‖‖ Department of Medicine and Radiology, University of Ottawa Heart Institute, Ontario, Canada; ¶¶ Baptist Cardiac and Vascular Institute, Miami, FL, USA; ## Capitol Cardiology Associates, Albany, NY, USA; *** Dalio Institute of Cardiovascular Imaging, Department of Radiology, NewYork-Presbyterian Hospital and Weill Cornell Medical College, New York, NY ††† Division of Cardiology, Deutsches Herzzentrum München, Munich, Germany; ‡‡‡ Medizinische Klinik I der Ludwig-Maximilians-Universität München, Munich, Germany; §§§ Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria; ‖‖‖ Department of Medicine and Radiology, Seoul National University Hospital, Seoul, South Korea; ¶¶¶ Department of Medical Imaging and Division of Cardiology, St. Paul's Hospital, University of British Columbia, Vancouver, BC; ### Department of Medicine, NewYork-Presbyterian Hospital, New York, NY; **** Cardio Vascular Imaging Unit, Giovanni XXIII Hospital, Monastier, Italy; †††† Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA; ‡‡‡‡ Department of Medicine, Walter Reed National Medical Center, Bethesda, MD, USA; §§§§ Duke Clinical Research Institute, Durham, NC, USA

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Corresponding author:
†††Philipp A. Kaufmann, MD
Professor and Director of Cardiac Imaging
University Hospital Zurich
Ramistrasse 100, NUK C 42
CH-8091 Zurich, Switzerland
Phone: +41-44 255 41 96, Fax: +41-44 255 44 14
Email: pak@usz.ch

Abstract

Aim: Coronary computed tomography angiography (CCTA) has become an important tool for non-invasive diagnosis of coronary artery disease (CAD). Recently, small studies in various patient populations have indicated that left coronary dominance (LCD) over right coronary dominance (RCD) appears to be independently associated with increased long-term mortality. However, conflicting data exist on whether coronary artery dominance may have a prognostic value or not.

Methods and results: The study population consisted of 6382 patients with or without coronary artery disease (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. A Kaplan Meier proportional hazards analysis was used to compare all-cause mortality, nonfatal myocardial infarction and revascularization by dominance. 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 to patients with left dominance (hazard ratio 0.46, 95% CI 0.16-1.32, p=0.15). Further, no differences were observed for the type of coronary dominance in patients with non-obstructive CAD (hazard ratio 0.95, 95% CI 0.41-2.21, p=0.8962) or normal coronary arteries (hazard ratio 1.04, 95% CI 0.68-1.59, p=0.9).

Conclusion Coronary dominance does not predict outcomes (non-fatal myocardial infarction, all-cause mortality and late revascularisation) in patients with normal as well as diseased coronary arteries as assessed by CCTA. Therefore, assessment of coronary vessel dominance by CCTA may not contribute to risk stratification.

Introduction

Coronary computed tomographic angiography (CCTA) has recently been introduced as a highly accurate (1-4) and prognostically robust (5-8) non-invasive imaging modality for the assessment of coronary artery disease (CAD). Novel advances in computerized tomographic technology allow to see the origin and course of coronary arteries by a 3D display of anatomy thereby permitting the determination of coronary artery variations (9, 10). The CONFIRM registry enrolled ≥20000 patients from 12 centres across North America, Europe, and Asia with suspected CAD who underwent a ≥64-detector-row CCTA and is the first prospective database evaluating the prognostic role of CCTA (11). Coronary artery dominance is determined according to the coronary artery that emits the posterior descending artery. Right dominance is the most prevalent pattern observed in normal humans and is found in 72%–90% of individuals, while prevalence of left dominance is reported to be 8-33%, whereas codominance has about 7% population prevalence (12). 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 biologic 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 (13). Indeed, a previous post-mortem study in 75 patients has indicated that left coronary dominance seems to be independently associated with increased long-term mortality in patients with an acute coronary syndrome and may predispose individuals to mechanical complications following an acute coronary syndrome (ACS) in the event of occlusion of the LCA (14). Further, a prior study in 27 289 patients,

who underwent cardiac catheterization for ACS, demonstrated that left dominance was associated with an increased hazard of death during a 3.5-year follow-up (15) and data from a U.S. registry showed that left and co-dominance were associated with increased in hospital mortality in 207,926 patients undergoing percutaneous coronary intervention (PCI) for ACS (16). However, this work has been done on 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 multislice CCTA which not only provides information about the presence and degree of coronary stenosis, it also allows the evaluation of cardiac anatomy including coronary vessel dominance (17, 18). Although coronary vessel dominance is easily assessed on CCTA, there is sparse information about the prognostic value of coronary vessel dominance in patients referred for CCTA. a recent prospective study of 1425 patients referred for CCTA, nonfatal myocardial infarction and all-cause mortality were increased in patients with left dominance during a 2-year follow-up period (19). However, due to the small study population and limited follow-up time, the relationship between coronary vessel dominance and the prognostic importance of a significant stenosis and its location remains unclear. Therefore, the goal of the present study was to assess the prevalence and prognosis of coronary dominance in a large prospective, international multicentre cohort of patients undergoing CCTA.

Methods

Study design, patients and outcome measures

This study represents 6382 patients from the CONFIRM Registry (Coronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry). Briefly, CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) enrolled consecutive adults >18 years of age between 2005 and 2009 who underwent ≥64-detector row CCTA for suspected CAD at 12 centers in 6 countries (Canada, Germany, Italy, Korea, Switzerland, and the United States). Details of the CONFIRM registry design and data elements have been published (11, 20-22). Patients with normal coronary arteries, with non-obstructive, obstructive and severe obstructive CAD where coronary dominance had been assessed were included in the present analysis. Patients with 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 analyses, therefore, 6382 remaining individuals with and without CAD were included for the final analyses of the composite end point all-cause mortality, nonfatal MI, and coronary revascularizations. Patient consent or a waiver of informed consent (as per recommendations of each institutional review board) was obtained at each site in keeping with sites-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 (11). Image interpretation was uniformly

performed at each site according to Society of Cardiovascular Computed Tomography guidelines (23) by highly experienced imagers who were 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 right dominant if the right coronary artery or as left dominant if the left circumflex coronary artery gave rise to the posterior descending artery, respectively. Each site performed per-segment analysis for individual coronary artery segments by using a 16-segment model. 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% to 49%), moderate (50% to 69%), or severe (>70%). A coronary lesion compromising the lumen by more than 50% was defined as obstructive. Vessels were classified into 4 arterial territories: left main artery (LM), left anterior descending artery (LAD), left circumflex coronary artery (LCx), and right coronary artery (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 1-, 2-, and 3-vessel disease or left main disease.

Statistical analysis

SPSS version 12.0 and 17.0 (SPSS Inc., Chicago, Illinois) and SAS version 9.2 (SAS Institute, Cary, North Carolina) were used for all statistical analyses. Categorical variables are presented as frequencies and continuous variables as mean ± SD.

Variables were compared with x2 statistic for categorical variables and by Student's unpaired t-test or Wilcoxon/Mann-Whitney non-parametric 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 patients with significant CAD on CCTA. The primary outcome variable was a composite endpoint of all-cause mortality, nonfatal MI and revascularisation. Multivariable analyses were calculated with the multivariabe Cox regression model for prediction of the combined end-point (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  ght 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 6 countries. Patients were followed for a median of 2.1 years (interquartile range 1.5-3.1 years). 956 (3.5%) patients were lost to follow-up, for 20743 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 6,382 patients (47% females, 53% males, mean age 56.9±12.3 years) with or without CAD remained for the present analysis and were included in the study. Table 1 depicts baseline characteristics of the patient population, categorized by coronary vessel dominance. LCD patients tend to have a higher BMI (27.8±5.4 versus 27.2±5.3, p=0.0288), were more often male (62% versus 38%, p<0.0001) and asymptomatic (24% versus 37%, p=0.0003) than patients with 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 patients (53%), non-obstructive CAD in 1787 (28%), obstructive CAD in 457 patients (7%) and severe obstructive in 776 patients (12%) (Table 2). Mean Agatston calcium score was 420.0 in right dominance and 363.0 in left dominance (p=0.8675) (Table 2). Of those patients with significant (>50% stenosis) CAD, 648 patients (10%) had one-vessel disease, 351 patients (10%) had two-vessel disease, and 222 patients (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% versus 27%, p<0.0001), significant stenosis in left anterior descending or circumflex artery (19% versus 14%, p=0.0067 and 10% versus 7%, p=0.0203, respectively), while patients with right dominance tend to have more often normal coronary arteries (54% versus 43%, p<00001) or obstructive CAD in RCA (10% versus 5%, p<0.0001) (Table 2).

Event and survival rate

During a follow-up time 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%) patients and 120 patients (1.9%) underwent revascularisation. 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 late revascularisation did not differ significantly between patients with left or right coronary dominance (log-rank p=0.14, Figure 1B) with low cumulative event rates of 1.7% and 0.9% respectively. Results remained the same when a separate analysis for each endpoint in patients with normal coronary arteries was conducted (logrank p=0.41 for all-cause mortality, logrank p=0.13 for myocardial infarction, and p=0.73 for late revascularisation, data not shown). Similarly, in patients with significant coronary artery disease (>50% stenosis), no significant difference was observed in event-free survival between left dominant and right dominant coronary artery systems, with cumulative event rates of 18.8% and 19.1% after 5 years of follow-up for a right and left dominant coronary artery system, respectively (log-rank p=0.84, Figure 1A).

These results remained the same when a separate analysis for each endpoint in patients with significant coronary artery disease was conducted (logrank p=0.069 for all-cause mortality, logrank p=0.63 for myocardial infarction, and p=0.76 for late revascularisation, data not shown) or when patients with obstructive CAD (stenosis 50-70%) (logrank p=0.60, data not shown) or severe obstructive CAD (stenosis >70%) (logrank 0.92, data not shown) were analysed separately. When stratified for gender, patients with left coronary dominance and right coronary dominance showed similar survival rates for the incidence of all-cause mortality, non-fatal MI and late revascularisation (log rank p=0.72 for males and log-rank p=0.3842 for females) (Figure 2A and 2B).

Prognostic value

Univariable and multivariable proportional hazards models confirmed that obstructive and severe obstructive CAD [illegible] coronary variations were predictors of all-cause mortality, non-fatal myocardial infarction and revascularisation and had incremental value over clinical variables (Table 3). In patients with non-obstructive coronary artery disease, right dominance system was identified as a significant predictor of the combined endpoint when compared with patients with normal coronary arteries, 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), while left dominance did not predict any events in this subpopulation (HR 2.79, 95% CI: 0.77-10.1, p=0.1172, Table 3). When female and male patients were analysed separately, results remained the same (p<0.0001 for females with right coronary dominance patients and non-obstructive CAD, p<0.0001 for males with right coronary dominance patients and non-obstructive CAD, data not shown).

We further assessed the difference in 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 late revascularisation: Cox regression model analysis showed that the difference in the risk estimate of obstructive CAD between patients with a right dominant and patients 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 coronary artery disease no difference in 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).

Further, 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 left dominant system and a HR of 24.43 (95% CI: 15.9-37.5, p<0.0001 vs. normal coronary arteries) in right dominant system. Consequently, in both univariable and multivariable models accounting for individual Framingham risk factors, the risk was dose-dependently increased when more vessels were affected with a HR of 10.53 (left dominance) and 31.9 (right dominance) in 2-vessel disease and a HR of 29.07 (left dominance) and 51.56 (right dominance) in 3-vessel disease (p<0.0001 vs. normal coronary arteries) (Table 5, upper panel).

Prognostic value of significant stenosis location

After stratification according to stenosis location, cumulative event rate for left coronary dominance patients with significant LAD stenosis was 8% for non-fatal MI,

9% for late revascularisation, and 8% for all-cause mortality (Figure 3A), while in patients with right dominance and significant RCA stenosis event rates for non-fatal MI, late revascularisation, 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 late revascularisation for left dominance (HR 7.01 for LAD, HR 3.83 for LCx) as well as for right dominance (HR 10.12 for LAD and HR 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 hazard ratio 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; Table 5 lower panel). A significant lesion in the right system was associated with an increased risk of the composite 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 according to coronary vessel dominance, survival rates for the cumulative incidence of all-cause mortality, non-fatal MI and late revascularisation after 5 years of follow up did not differ significantly between patients with left or right coronary dominance with low cumulative event rates of 1.7% and 0.9%, respectively. Similarly, in patients with coronary artery disease (>50% stenosis), no significant difference was observed in event-free survival between right dominant and left dominant coronary artery systems.

In our study, right dominance was present in 91% and left dominance in 9%, which is not significantly different from [illegible] given in the literature, varying from 8.2% to 15% for left dominance and from 72% - 90% for right dominance (12-15, 24). The variation may be related to the ethnic diversity of the populations under study. Further, left dominance was observed more often in males (62%) compared to females (38%), while previous retrospective studies indicate that there is no difference in coronary dominance with regard to gender (24-27). 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 (15, 16). Nevertheless, those studies were retrospective analyses done on angiograms and the study population consisting of high risk ACS patients and patients with prior coronary artery bypass graft differed substantially from our study population. In a recent prospective study of 1425 patients referred for CCTA, nonfatal myocardial infarction and all-cause mortality were increased (HR 3.15) in patients with left dominance during a 2-year follow-up period (19). However, follow-up time in this study was limited to 2 years, a potential selection bias due to smaller patient numbers cannot be excluded, and no differences in prognosis for different coronary dominance pattern were observed when late revascularisation was included in the combined primary endpoint. Taken together with these previous findings, it seems that left dominance may have different prognostic values regarding short and long-term mortality in patients with acute coronary syndrome compared to patients with stable coronary artery disease. However, underlining the importance of angiographic interventions in left dominance patients with ACS. However, prospective studies in patients with acute coronary syndromes are needed to confirm this.

At present, little is known about the prognostic value of stenosis location in relation to coronary vessel dominance and only one recent study in 1425 patients referred for CCTA demonstrated that a stenosis in the left coronary system was associated with an increased risk of events while a stenosis in the RCA did not statistically significant predict events (19). Our analysis among subgroups with left main disease showed an elevated hazard of the combined endpoint for left dominance (HR 6.45) that was statistically significant while a stenosis in the left main did not statistically significant predict events in right dominance (HR 1.35; 0.73-2.51). This finding is consistent with previous observations in patients undergoing PCI for

ACS. In these patients the odds of death given left dominance was highest in those with left main disease or LCx culprit lesions as compared with RCA or LAD lesions (16). Coronary vessel dominance has influence on the relative contribution of the different coronary arteries to the total left ventricular blood flow (28) and In most individuals with left coronary dominance, 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 ischemia 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 (29). However, to date, the underlying pathophysiology has not been investigated and further research is needed to investigate the effect modification by culprit lesion site 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 left coronary dominance was associated with a higher incidence of arteriosclerosis (30) while others showed more extensive CAD in patients with a right dominant coronary artery system (15, 24) or did not detect differences in the extent of CAD between left and right coronary dominance (19, 26). However, this discrepancy can most likely be explained by a potential selection bias due to small patient numbers in these studies. In the present study we observed a higher incidence of coronary artery disease (obstructive and non-obstructive) in left dominance patients, while the prevalence of normal coronary arteries was more frequent in right dominance. However, no difference in predisposition to three-vessel

disease was seen between left and right coronary dominance, which strongly supports the hypothesis that dominance pattern does not predict outcomes in patients with CAD.

Interestingly, in patients with non-obstructive coronary artery disease right dominance system was identified as a significant predictor of the combined endpoint, and remained a significant predictor after correction for baseline risk factors, while left dominance did not predict any events in this subpopulation. When female and male patients were analysed separately, results remained the same. 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 dominan  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. First, we did not include patients with co-dominant circulation in our analysis, since our study was likely underpowered to detect statistical effect modification in this subgroup, due to the very low prevalence of coronary co-dominane in the general population. Second, because of the relatively low event rate in the subgroup analysis, larger studies are needed to evaluate the effect of coronary vessel dominance in patients with left main disease or non-obstructive lesions. Coronary dominance is a non-modifiable risk factor, and as such, our study findings are of prognostic relevance but, for now, do not have accompanying therapeutic implications.

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

Figure legends

Figure 1: A. Event free survival (Kaplan Meier curve) from major adverse events (all-cause mortality, non-fatal myocardial infarction, coronary revascularisation) with follow-up extending to 5 years in patients with right and left coronary dominance stratified for the presence of obstructive coronary artery disease (>50%) on coronary computed tomography angiography. Patients with 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 myocardial infarction, coronary revascularisation) in patients with right and left coronary dominance stratified for normal coronary arteries. Patients with 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 myocardial infarction, coronary revascularisation) with follow-up extending to 5 years stratified by coronary dominance in patients with obstructive coronary artery disease (>50%) on coronary computed tomography angiography. **B.** Females: Event free survival (Kaplan Meier curve) from major adverse events (all-cause mortality, non-fatal myocardial infarction, coronary revascularisation) with follow-up extending to 5 years stratified by coronary dominance in patients with obstructive coronary artery disease (>50%) on coronary computed tomography angiography. Patients with a balanced coronary artery system were excluded from the analysis.

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

Table 1: Baseline characteristics of the study population by dominance. BMI, body mass index; CAD, coronary artery disease, data are presented as n (%).Patients with a balanced coronary artery system were excluded from the analysis.

Table 2: CCTA results. Prevalence of coronary dominance in study population. CAD, coronary artery disease, LCX=left circumflex artery, RCA=right coronary artery; LM=left main artery; LAD=left anterior descending artery. Data are presented as mean or n (%).Patients with a balanced coronary artery system were excluded from the analysis.

Table 3: Univariate and multivariate analysis adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking and dyslipidemia. Hazard ratios of coronary artery disease (non-obstructive:<50% stenosis, obstructive:>50%stenosis, severe obstructive:>70%stenosis) for the composite outcome of all-cause mortality, non-fatal myocardial infarction and late revascularisation in left and right coronary dominance compared with normal coronary arteries on coronary computed tomography angiography. CAD, coronary artery disease, RF risk factor. HR, hazard ratio, CI, confidence interval. Patients with a balanced coronary artery system were excluded from the analysis.

Table 4: Univariate and multivariate analysis adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking and dyslipidemia. Hazard ratios of right versus left coronary dominance for the composite outcome of all-cause mortality, non-fatal myocardial infarction and late revascularisation according to extend of coronary artery disease (non-obstructive:<50% stenosis, obstructive:>50%stenosis, severe obstructive:>70%stenosis) on coronary computed tomography angiography. CAD, coronary artery disease, RF risk factor. HR, hazard ratio, CI, confidence interval. Patients with a balanced coronary artery system were excluded from the analysis.

Table 5: Upper panel: Univariate and multivariate analysis adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking and dyslipidemia. Hazard ratios of coronary artery disease according to the amount of diseased vessels (1-vessel disease, 2-vessel disease, and 3-vessel disease) for the composite outcome of all-cause mortality, non-fatal myocardial infarction and late revascularisation in left and right coronary dominance compared with normal coronary arteries on coronary computed tomography angiography. **Lower panel:** Univariate and multivariate analysis adjusted by Framingham risk factors including age, sex, hypertension, diabetes mellitus, current smoking and dyslipidemia. Hazard ratios of coronary artery disease according to the stenosis location for the composite outcome of all-cause mortality, non-fatal myocardial infarction and late revascularisation in left and right coronary dominance compared with normal coronary arteries on coronary computed tomography angiography. LM=left main artery; LAD=left anterior descending artery, LCx=left circumflex artery, RCA=right coronary artery, CAD, coronary artery disease, RF risk factor. HR, hazard ratio, CI,

confidence interval. Patients with a balanced coronary artery system were excluded from the analysis.

Disclosures

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here are those of the investigators only and are not to be construed as those of the United States Department of the Army or Department of Defense.

Conflicts of interest

Dr. Min received modest speakers' bureau and medical advisory board compensation and significant research support from GE Healthcare. Dr. Achenbach received grant support from Siemens and Bayer Schering Pharma and has served as a consultant for Servier. Dr. Al-Mallah received support from the American Heart Association, BCBS Foundation of Michigan, and Astellas. Dr. Cademartiri received grant support from GE Healthcare and has served on the Speakers' Bureau of Bracco and as a consultant for Servier; Dr. Maffei received grant support from GE Healthcare. Dr. Chinnaiyan received grant support from Bayer Pharma and Blue Cross Blue Shield Blue Care MI. Dr. Chow received research and fellowship support from GE Healthcare, research support from Pfizer, AstraZeneca, and educational support from TeraRecon. Dr. Hausleiter received a research grant from Siemens Medical Systems. Dr. Kaufmann received institutional research support from GE Healthcare and grant support from Swiss National Science Foundation. Dr. Maffei received grant support from GE Healthcare Dr. Raff received grant support from Siemens, Blue Cross Blue Shield Blue Care MI, and Bayer Pharma. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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