Influence of coronary vessel dominance on short- and long-term outcome in patients after ST-segment elevation myocardial infarction

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Aims
Prognostic importance of coronary vessel dominance in patients with ST-elevation myocardial infarction (STEMI) remains uncertain. The aim of this study was to assess influence of coronary vessel dominance on the short- and long-term outcome after STEMI.

Methods and results
Coronary angiographic images of consecutive patients presenting with first STEMI were retrospectively reviewed to assess coronary vessel dominance. Patients were followed after STEMI during a median period of 48 (IQR 38–61) months for the occurrence of all-cause mortality and the composite of reinfarction and cardiac death. The population comprised 1131 patients of which 971 (86%) patients had a right dominant, 102 (9%) a left dominant, and 58 (5%) a balanced system. After 5 years of follow-up, the cumulative incidence of all-cause mortality was significantly higher in patients with a left dominant system, compared with a right dominant and balanced system (log-rank $P = 0.013$). Moreover, a left dominant system was an independent predictor for 30-day mortality (OR 2.51, 95% CI 1.11–5.67, $P = 0.027$) and the composite of reinfarction and cardiac death within 30-days after STEMI (OR 2.25, 95% CI 1.09–4.61, $P = 0.028$).

In patients surviving first 30-days post-STEMI, coronary vessel dominance had no influence on long-term outcome.

Conclusions
A left dominant coronary artery system is associated with a significantly increased risk of 30-day mortality and early reinfarction after STEMI. After surviving the first 30-days post-STEMI, coronary vessel dominance had no influence on long-term outcome.

Keywords
Myocardial infarction • Prognosis • Coronary circulation • Vessel dominance

Introduction
Coronary vessel dominance, defined by the coronary artery that supplies the posterior descending artery (PDA) and posterolateral branches, influences the relative contribution of the different coronary arteries to the total left ventricular blood flow.1 A right dominant system has a reported prevalence of 82–89%.2–5 In patients with a left dominant system, ~60% of the left ventricular myocardium is supplied by the posterolateral branches and PDA originating from the LCx.6 This less well-balanced coronary circulation might have a negative influence on prognosis of patients with coronary artery disease (CAD). Currently, the prognostic importance of coronary vessel dominance in patients presenting with first ST-segment elevation myocardial infarction (STEMI) remains uncertain. The aim of this study was to assess the influence of coronary vessel dominance on the 30-day mortality and long-term outcome after STEMI.

Methods
Patients
The population consisted of consecutive patients presenting with first STEMI at the Leiden University Medical Center between 2004 and 2008. Patients with previous myocardial infarction, previous...
percutaneous coronary intervention (PCI), and/or previous coronary artery bypass grafting were excluded. The diagnosis of STEMI was defined based on criteria of typical chest pain, elevated cardiac enzyme levels, and typical changes on the electrocardiogram. All patients were treated according to the institutional MISSION protocol, based on the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines. The protocol includes primary PCI, optimal medical therapy initiated early during hospitalization, and two-dimensional echocardiography performed within 48 h of admission to assess residual left ventricular function.

Demographic, clinical, angiographic, and echocardiographic data were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analysed. Patients with uninterpretable coronary angiographic images for coronary vessel dominance were excluded from analysis.

Primary percutaneous coronary intervention and angiographic data analysis
Images of the coronary angiography and PCI were obtained using standardized angiographic projections according to the guidelines of the American College of Cardiology/American Heart Association, and stored digitally. All images were retrospectively reviewed by two experienced observers. During the analysis coronary vessel dominance, the culprit vessel and culprit lesion and severity of CAD were recorded. A coronary artery system was classified as right dominant if the RCA originated from the LCx artery, and balanced if the PDA and the artery system was classified as right dominant if the PDA and posterolateral branch originated from the LCx artery, left dominant if the PDA and the artery system was classified as right dominant if the PDA and posterolateral branch originated from the LCx artery, and balanced if the PDA originated from the RCA, left dominant if the PDA and the artery system was classified as right dominant if the RCA, left dominant if the PDA and the PDA and posterolateral branch originated from the LCx artery, and balanced if the PDA and posterolateral branch originated from the LCx artery.

The culprit vessel was determined on the coronary artery territory subtended by the regions of acute electrocardiographic changes. If the culprit vessel had more than two lesions, the most severe proximal stenosis or a stenosis identified with thrombus was considered the culprit lesion. The extent of CAD was expressed as the presence of one-, two- or three-vessel disease (stenosis causing ≥50% luminal narrowing). Complete revascularization was defined as treating all present significant coronary artery stenosis (≥70% luminal narrowing) during primary PCI or during secondary revascularization before discharge.

Follow-up and endpoint definitions
After discharge, patients were followed according to the institutional STEMI protocol. By reviewing medical records, retrieval of survival status through municipal civil registries and telephone interviews, data on the occurrence of adverse events after discharge were collected. The adverse events included non-fatal reinfarction and all-cause mortality during follow-up. Non-fatal reinfarction was defined based on criteria of typical chest pain, elevated cardiac enzyme levels, and typical changes on the electrocardiogram. The primary cause of death was recorded on the electrocardiogram. The primary endpoint was the composite of reinfarction and cardiac death. Short- and long-term outcome after STEMI were investigated using these endpoints. Short-term outcome was defined as within the first 30 days post-STEMI.

Follow-up was updated regularly until 2012. Patients with <2 years of follow-up after STEMI, but who were alive according to the municipal civil registries, were considered lost to follow-up. Data of these patients were included up to the last date of follow-up.

Statistical analysis
Continuous variables are presented as mean ± standard deviation or as median and interquartile range. Categorical variables are presented as number and percentages. Differences in baseline characteristics between the three coronary vessel dominance groups were evaluated with one-way analysis of variance and Chi-squared tests, where appropriate. To estimate the cumulative incidences of the primary and secondary endpoints during long-term follow-up, Kaplan–Meier analyses stratified for coronary vessel dominance were performed. In addition, to investigate the difference in short-term outcome between the different coronary vessel dominance groups, multivariate binary logistic regression analysis was performed with the endpoints 30-day mortality and the occurrence of reinfarction within 30 days post-STEMI. The number of covariables included in the analysis was adjusted to the number of events and complete availability, resulting in inclusion of the clinical risk factors: age, gender, diabetes, hypertension, and smoking. The results of the binary logistic regression analysis were reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Subsequently, the influence of coronary vessel dominance on long-term outcome was evaluated using the Cox regression analysis in a subgroup of patients surviving the first 30 days after STEMI. In the multivariate Cox regression model, the covariables were selected based upon univariate significance of P-value ≤0.20 and/or significant difference in baseline distribution among the vessel dominance groups, resulting in inclusion of age, gender, diabetes, hypertension, smoking, Killip class during STEMI, three-vessel disease, peak cardiac troponin T, glomerular filtration rate, left-ventricular ejection fraction, and finally reinfarction within the first 30 days post-STEMI was corrected for to adjust for its effect on long-term outcome in the survivors of the 30 days post-STEMI. The results of the Cox regression analysis were reported as adjusted hazard ratios (HRs) with 95% CIs. In addition, Bootstrap validation for model optimism was performed to test whether the parameter estimates were stable in the Cox regression analysis. Statistical analysis was performed using SPSS software (version 20.0, SPSS, Inc., Chicago, IL, USA). A P-value of <0.05, by a two-sided test, was considered statistically significant.

Results

Patient and angiographic characteristics
A total of 1156 consecutive patients were included. Twenty-five patients (2%) were excluded from the analysis due to uninterpretable coronary vessel dominance. The final population comprised 1131 patients of which 971 (86%) patients had a right dominant system, 102 (9%) patients had a left dominant system, and 58 (5%) patients had a balanced system. The patients’ characteristics and angiographic data are presented in Table 1. Overall baseline characteristics were similar between coronary vessel dominance groups. However, patients with a balanced system tended to be younger (P = 0.026) and patients with a left dominant system more frequently had hypertension (P = 0.036). The RCA was most often the culprit vessel in patients with a right dominant system, whereas in patients with a left dominant or balanced system, the LAD artery was most often the culprit vessel. Moreover, a relatively high incidence of the LCx as culprit vessel was observed in patients with a left dominant system (P < 0.001). Importantly, the majority of patients presented with single vessel disease. Complete revascularization was achieved in 789 patients (70%). A trend towards a slightly lower left ventricular ejection fraction at discharge was observed in patients with a left dominant system.
Follow-up
Follow-up was completed in 1076 patients (95%), with 55 patients (5%) lost to follow-up. The median follow-up was 48 months (IQR 38–61). The primary endpoint occurred in 119 patients (11%): 77 patients (7%) died from cardiac death and 42 patients (4%) died from non-cardiac causes. Furthermore, 92 patients (8%) had reinfarction, of which 9 were fatal. The secondary endpoint occurred in 154 patients (14%).

The cumulative incidence of both the primary and secondary endpoints after 5 years post-STEMI was higher in patients with a left dominant system (Table 1).

Coronary vessel dominance and 30-day adverse outcome
Among 119 patients who died, 45 patients (4%) died within the first 30 days after STEMI of which 25 patients (56%) died within 24 h after STEMI. The majority was classified as cardiac death (43 of the 45 patients): cardiogenic shock (20 patients), ventricular fibrillation (3 patients), left ventricular free wall rupture (4 patients), heart failure (9 patients), reinfarction due to in-stent restenosis (4 patients), and undetermined (3 patients). Two patients were classified as non-cardiac death as they died due to an infection after coronary bypass surgery and a gastro-intestinal bleeding after PCI. Furthermore, 24 patients (2%) had reinfarction within the first 30 days after STEMI. The secondary endpoint was reached in 63 patients (5.5%) at 30-days post-STEMI.

Patients who died within 30 days post-STEMI were more likely to be female, of advanced age and less likely to smoke (Table 2). Furthermore, these patients presented with a higher Killip class during STEMI and were more likely to have three-vessel disease. Importantly, the culprit lesion was more frequently located in the left main (LM) artery or the dominant LCx artery compared with patients who survived the first 30 days post-STEMI. Finally, a higher prevalence of a left dominant system was observed in patients who died within the first 30 days post-STEMI (Table 2).

Multivariate logistic regression analyses demonstrated that coronary vessel dominance and age were independent predictors of both the primary and secondary endpoints within 30 days post-STEMI (Table 3). A left dominant system was associated with an OR of 2.51 (95% CI 1.11–5.67) for 30-day mortality and with an OR of
2.25 (95% CI 1.09–4.61) for reinfarction or cardiac death within 30 days post-STEMI.

Coronary vessel dominance and long-term outcome in survivors of the first 30 days post-STEMI

A total of 1086 patients survived the first 30 days post-STEMI. The primary endpoint was reached in 74 patients (7%) and the secondary endpoint was reached in 98 patients (9%) during long-term follow-up. No differences in the cumulative incidence of the primary endpoint were observed between patients during 5 years of follow-up with 31 days post-STEMI as start of follow-up (log-rank \( P = 0.259 \); Figure 2A). Moreover, no differences in cumulative incidences for the secondary endpoint were observed (log-rank \( P = 0.117 \); Figure 2B). Multivariate Cox regression analysis showed that coronary vessel dominance was not associated with the occurrence of either the primary or secondary endpoint during long-term follow-up in patients who survived the first 30 days post-STEMI (Table 4).

Discussion

The main finding of this study is that a left dominant system is associated with an increased risk of all-cause mortality and reinfarction or cardiac death post-STEMI. Importantly, patients with a left dominant system had a more than two-fold increased risk of mortality within the first 30 days post-STEMI, whereas in patients surviving the first 30 days post-STEMI cumulative incidences of the primary and secondary endpoints were comparable to a right dominant or balanced system at 5 years of follow-up after STEMI.

Prognostic value of coronary vessel dominance

Variations in coronary circulation are common, particularly with regard to the supply of the posterior wall of the left ventricle. While a right dominant coronary artery is most commonly observed, a left dominant system is considered to be a normal variant of the coronary anatomy with reported prevalence of 7–10%. In line with previous literature, the presence of a left dominant coronary artery system was noted in 9% of patients in the current evaluation. At present, little is known about the clinical relevance of this anatomical variation. A study screening 1620 postmortem angiograms showed that the prevalence of a left dominant system decreased with age, suggesting a higher death rate among patients with a left dominant coronary artery system. An explanation could be that a larger amount of myocardium is at risk in these patients, resulting in more extensive myocardial infarction in case of a left coronary artery occlusion.

Data describing the prognostic value of coronary vessel dominance in patients with STEMI are scarce. Previously, Goldberg et al. \cite{16} showed that the presence of a left dominant system was associated with an increased mortality (HR: 1.13, 95% CI 1.00–1.28) in 27,289 patients presenting with acute coronary syndrome (ACS). Accordingly, a more recent registry (the Cath PCI registry) observed a higher in-hospital mortality after PCI in patients with a left dominant system (OR 1.29, 95% CI 1.17–1.42). \cite{17} However, both registries represent a heterogeneous patient populations, including patients with STEMI as well as non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina, having varying risks. In the study by Goldberg et al., \cite{16} the increased risk of mortality in the presence of a left dominant system was more pronounced in patients presenting with STEMI. In contrast, in the subanalysis of the CathPCI registry, the increased risk in patients with a left dominant system only remained significant in patients presenting with NSTEMI. \cite{17}

Our study is the first to include only patients with STEMI, demonstrating significantly worse outcome in patients with a left dominant system compared with a right dominant or balanced system.
Moreover, a primary endpoint of all-cause mortality and secondary endpoint of reinfarction or cardiac death were studied at both short- and long-term follow-up, extending the earlier findings.\textsuperscript{16,17} Differences in outcome compared with the CathPCI registry can be explained by differences in patient population and type of PCI used.
Coronary vessel dominance and 30-day outcome

In this study, a more than two-fold increased risk for 30-day mortality was found in patients with a left dominant system compared with a right dominant system. This can be explained by the impact coronary anatomy has on the extent of the infarcted area and recovery of left ventricular function post-STEMI. Ilia et al.\textsuperscript{6} showed that acute occlusion of a proximal dominant LCx artery resulted in a higher proportion of patients presenting with cardiogenic shock and higher in-hospital mortality rate when compared with patients with a proximal LAD artery occlusion, underlining the importance of a dominant LCx artery which supplies \(\approx 60\%\) of the left ventricular myocardium.

Another factor contributing to the poor outcome of patients with a left dominant system could be lack of collateral circulation in patients with a left dominant system.\textsuperscript{20,21} Additionally, this study showed a higher risk of early reinfarction in patients with a left dominant system. Yip et al.\textsuperscript{22} showed that a left dominant system was independently predictive of failed reperfusion in patients with LCx artery infarction. Furthermore, Lam et al.\textsuperscript{23} lately reported a higher incidence of periprocedural myocardial infarction in patients with left coronary dominance undergoing PCI. Subsequently, a recent Japanese multicentre study showed inferior outcome in patients with a left dominant system, including a significantly higher number of intra-aortic balloon pump insertions during and after PCI.\textsuperscript{24}

**Coronary vessel dominance and long-term outcome after surviving the first month after ST-elevation myocardial infarction**

Coronary vessel dominance had impact on outcome during the first 30 days post-STEMI, but had no prognostic significance during long-term follow-up. At 30 days post-STEMI, a natural selection of patients has taken place, leaving those patients with less severe myocardial infarctions. This mechanism of selection might be influenced by coronary dominance, since the presence of left coronary dominance is hypothesized to lead to a bigger area of jeopardized myocardium in case of left coronary occlusion. Subsequently, the influence of coronary vessel dominance on long-term outcome may be less prominent once surviving the first 30 days post-STEMI. This explanation is strengthened by the fact that the proportion of patients with left dominance is significantly higher in the deceased compared with the survivors (20 vs. 9\% respectively, \(P = 0.009\)).

Still, while this is the first study providing information about the relation between long-term outcome and coronary dominance after STEMI, future research is needed to confirm these findings.

**Clinical implication**

The present study showed that coronary dominance affects outcome after STEMI. Up till present, the awareness of the prognostic relevance of coronary dominance seemed limited. In risks scores estimating the risk of adverse events after ACS, many known risk factors such as age, systolic blood pressure, ECG changes, heart rate, and cardiac enzymes are incorporated.\textsuperscript{25,26} However, coronary anatomy is not taken into account in these risk scores. The present evaluation provides novel information on the relation between coronary circulation and clinical outcome after STEMI, showing an inferior 30-day survival in patients with a left dominant system. The incorporation of coronary anatomy in clinical risk scores and future prognostic analyses in patients with STEMI could improve risk estimation of adverse events during follow-up post-STEMI.

Moreover, the increased risk of reinfarction during the first month post-STEMI as observed in the present study and the previously reported increased risk of periprocedural myocardial infarction\textsuperscript{23} underscores that caution is needed in case of significant coronary lesions in a left dominant system and additional measures such as aggressive antiplatelet or anticoagulation therapy could be considered.

**Limitations**

This is a retrospective analysis with all inherent limitations. Second, although we adjusted for a wide range of potential confounders in the multivariate analysis, the possibility of unmeasured confounding remains. In patients who died within the first 30 days post-STEMI, covariates such as peak cardiac troponin T level and left ventricular ejection fraction at discharge were incomplete or unavailable.
Table 4  Multivariate Cox regression analysis in survivors of the first 30 days post- ST-segment elevation myocardial infarction

<table>
<thead>
<tr>
<th>Coronary vessel dominance</th>
<th>All-cause mortality</th>
<th>Reinfarction or cardiac death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>1.05</td>
<td>(1.02–1.09)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.95</td>
<td>(1.02–3.70)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.70</td>
<td>(0.84–3.45)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.96</td>
<td>(0.56–1.63)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.68</td>
<td>(0.99–2.87)</td>
</tr>
<tr>
<td>Killip class during STEMI</td>
<td>1.37</td>
<td>(0.96–1.95)</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>1.93</td>
<td>(1.12–3.33)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>0.99</td>
<td>(0.98–1.00)</td>
</tr>
<tr>
<td>Peak cardiac troponin T level (µg/L)</td>
<td>1.06</td>
<td>(1.03–1.10)</td>
</tr>
<tr>
<td>LV ejection fraction at discharge (%)</td>
<td>0.97</td>
<td>(0.95–1.00)</td>
</tr>
<tr>
<td>Reinfarction within 30 days post-STEMI</td>
<td>1.99</td>
<td>(0.58–6.82)</td>
</tr>
</tbody>
</table>

Hence, these factors could not be corrected for in the multivariate analysis on 30-day outcome. Finally, hospitalization for heart failure has been used as clinical endpoint in patients after STEMI, but was not assessed in the current study.

Conclusions

This study demonstrated that patients with a left dominant system have worse outcome after STEMI, with a two-fold increased risk of 30-day mortality and an increased risk of reinfarction during the first month post-STEMI. In patients surviving the first 30 days post-STEMI, coronary vessel dominance had no influence on long-term outcome. Awareness of the prognostic relevance of coronary dominance is important, recognizing a left dominant system as one of the risk factors for future adverse events post-STEMI.

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Conflict of interest: none declared.

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