Chromosome 9p21 Single Nucleotide Polymorphisms Are Not Associated With Recurrent Myocardial Infarction in Patients With Established Coronary Artery Disease

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Background: Chromosome 9p21 single nucleotide polymorphisms (SNPs) have been shown to be associated with coronary heart disease in multiple studies. The aim of the present study was to identify whether these SNPs are associated with recurrent myocardial infarction (MI), revascularization, or death in acute coronary syndrome (ACS) patients or in those undergoing coronary artery bypass grafting (CABG).

Methods and Results: TexGen registry participants with ACS (n=2,067) or CABG (n=1,176) were evaluated, to assess whether 9p21 SNPs (rs1333049, rs2383206, rs10757278, rs10757274) were associated with recurrent MI (primary outcome), recurrent revascularization, or death (secondary outcomes) at approximately 3.2 years of follow-up. Carriers of risk allele (C) for rs1333049 presented at an earlier age (62 vs. 63.5 years in non-carriers, P=0.0004) with more extensive disease (number of vessels with significant stenosis: 1.9 vs. 1.7 in non-carriers, P=0.001) in the ACS group. In adjusted models, the C allele was not associated with recurrent MI (hazard ratio [HR], 1.01; 95% confidence interval [CI]: 0.74–1.38), recurrent revascularization (HR, 0.98; 95%CI: 0.78–1.23), or death (HR, 0.91; 95%CI: 0.69–1.18) in the ACS or CABG groups (recurrent MI: HR, 0.64; 95%CI: 0.40–1.05; recurrent revascularization: HR, 0.98; 95%CI: 0.61–1.55; death: HR, 0.89; 95%CI: 0.61–1.30). Results were similar for the other 3 SNPs.

Conclusions: 9p21 SNPs were not associated with recurrent MI, revascularization, or mortality after ACS or CABG. Individuals with the rs1333049 C allele, however, may present with earlier and more extensive disease. (Circ J. 2012; 76: 950–956)

Key Words: 9p21 locus; Mortality; Recurrent myocardial infarction; Recurrent revascularization
Similarly, the associations between these polymorphisms and the risk of recurrent MI (and revascularization) in those with established CAD remain controversial. In a recent study, 9p21 SNPs were not associated with clinical or angiographic outcomes in patients undergoing placement of drug-eluting stents (DES). Conversely, rs1333049 was marginally associated with an increased risk of recurrent MI or cardiac death following acute coronary syndrome (ACS). In this latter study, the mean follow-up was only 6 months after the index ACS event, the results were only borderline significant for the primary outcome of recurrent MI (P=0.053) after multivariate adjustment, and these findings have not been replicated in other cohorts.

In order to better understand whether variants in 9p21 pathophysiology act as precipitators of MI and of adverse cardiovascular outcomes in patients with established CHD, the aim of the present study was to identify whether SNPs in this region were associated with recurrent MI, revascularization or death at intermediate-term follow-up in patients presenting with ACS or those undergoing coronary artery bypass grafting (CABG).

**Methods**

**Subjects**

TexGen is a collaborative, prospective genetic registry that enrolls patients with any personal history of cardiovascular disease, who attend any of several institutions within the Texas Medical Center including the University of Texas Health Science Center, the University of Texas M.D. Anderson Cancer Center, Baylor College of Medicine and their affiliated hospitals, and the Texas Heart Institute at St Luke’s Episcopal Hospital.

For the current study, we limited our analyses to TexGen patients presenting with ACS and those undergoing CABG surgery (with or without valve surgery procedures) from September 2001 through September 2008, who self-reported their race as Caucasian. Written informed consent was obtained from all study participants.

**Data Collection**

Preoperative, intra-operative and postoperative characteristics of patients were obtained through a clinical research database maintained at the Texas Heart Institute at St Luke’s Episcopal Hospital. This research database prospectively collects information on patients enrolled in the TexGen registry. The variables used for analysis included age, gender, history of hypertension, diabetes mellitus, smoking, presence of renal insufficiency, New York Heart Association (NYHA) functional class, and use of aspirin, β-blockers, or statins.

Prospective follow-up of outcomes included annual follow-up phone calls by the research nurses as well as annual surveys mailed to each patient. In addition, any hospitalization for patients enrolled in the database was also verified using hospitalization records.

**Genotyping**

Genotyping of 4 SNPs on the 9p21 locus (rs1333049, rs2383206, rs10757278, and rs10757274) was performed using TaqMan assays. These SNPs of 9p21 locus were chosen based on their associations with CHD in prior studies. All the SNPs had a call rate of >99%. QC concordance for 37 blind duplicate samples was 100%.

The primary aim was to evaluate a single SNP that tagged a haplotype block containing the most commonly studied variation in this region. rs1333049 was the SNP used in the most recent study evaluating the association between the 9p21 locus and the risk for recurrent MI in ACS patients, as well as in a meta-analysis evaluating associations between 9p21 and CAD. For this reason, along with the fact that all 4 SNPs from our analyses (rs1333049, rs2383206, rs10757278, and rs10757274) have been shown to be in strong linkage disequilibrium (LD), we chose rs1333049 as the tagSNP on an a priori basis to limit the need to correct for multiple testing.

**Outcome Definition**

The primary outcome of interest was the development of recurrent MI at intermediate-term follow-up after the index ACS event or following CABG. Secondary outcomes included mortality or the need for revascularization (need for percutaneous coronary intervention [PCI] or CABG after the index ACS event or CABG). We included all-cause death as one of the secondary outcomes because it is possible that some of the patients experiencing MI could have suffered a sudden arrhythmic death and could possibly be mis-classified if only recurrent MI was used as the outcome measure.

MI was defined as new ST-segment elevation in 2 contiguous leads in the setting of ischemic symptoms, or new horizontal or down-sloping ST depression ≥0.05 mV in 2 contiguous leads; and/or T wave inversions ≥0.1 mV in 2 contiguous leads and serum TnI >99th percentile of the upper normal limit. In-hospital MI following CABG was defined as increased level of creatine kinase-MB isoenzyme with appearance of new Q waves on electrocardiogram, a new regional wall motion abnormality (other than paradoxical septal motion) on echocardiogram, or the presence of MI at autopsy. Recurrent revascularization was defined as the receipt of another PCI or CABG after the index ACS event or CABG. Vital status was ascertained on patients using data from the Texas State Bureau of Vital Statistics.

**Statistical Analysis**

The primary outcome of recurrent MI was used for sample size calculations. With a hazard ratio (HR) of 1.48 for recurrent MI risk in ACS patients carrying the risk allele (C) for rs1333049 (as shown in a recent study of ACS patients), a recurrent MI event rate of 11% in the present ACS group at a median follow-up of approximately 3.2 years, and a 2-sided α of <0.05, we estimated that a sample size of 482 patients would be needed at the end of the study period to have 80% power to show an association between recurrent MI and rs1333049.

To test the association between the 9p21 locus and the risk of recurrent MI (primary outcome), we initially carried out log-rank test to evaluate the univariate association between rs1333049 and the risk of recurrent MI. Cox proportional hazards regression models (adjusting for age, gender, hypertension, diabetes mellitus, current smoking, renal insufficiency, NYHA functional class, and aspirin, β-blocker, and statin use) were subsequently used to determine whether the risk allele (C) for rs1333049 was independently associated with recurrent MI. Cox regression analyses were also performed to study whether the risk allele for rs1333049 was an independent predictor of the need for recurrent revascularization or all-cause mortality (secondary outcomes). We initially used a dominant model of inheritance for analysis because the risk ratios in the prior study followed a dominant genetic model, although results are also presented using an additive genetic model. Analyses were performed separately for TexGen patients presenting with ACS and those who underwent CABG.

Statistical analysis was performed using SAS version 9.1.
Table 1. Baseline Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ACS group (n=2,067)</th>
<th>CABG group (n=1,176)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.95±10.89</td>
<td>64.83±10.04</td>
</tr>
<tr>
<td>Male gender</td>
<td>1,527 (73.88)</td>
<td>1,527 (73.88)</td>
</tr>
<tr>
<td>Family history of premature coronary artery disease</td>
<td>752 (36.38)</td>
<td>974 (46.93)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>625 (30.24)</td>
<td>790 (39.79)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1,575 (76.20)</td>
<td>1,349 (65.26)</td>
</tr>
<tr>
<td>History of transient ischemic attacks or stroke</td>
<td>180 (8.71)</td>
<td>110 (5.36)</td>
</tr>
<tr>
<td>History of renal insufficiency</td>
<td>345 (16.69)</td>
<td>90 (4.30)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>456 (22.06)</td>
<td>50 (2.31)</td>
</tr>
<tr>
<td>NYHA functional class III/IV symptoms</td>
<td>970 (46.93)</td>
<td>640 (30.27)</td>
</tr>
<tr>
<td>Ejection fraction &lt;35%</td>
<td>145 (7.01)</td>
<td>145 (7.01)</td>
</tr>
<tr>
<td>β-blocker use</td>
<td>1,047 (50.65)</td>
<td>1,047 (50.65)</td>
</tr>
<tr>
<td>Statin use</td>
<td>1,075 (52.01)</td>
<td>1,075 (52.01)</td>
</tr>
<tr>
<td>Aspirin use</td>
<td>1,349 (65.26)</td>
<td>1,349 (65.26)</td>
</tr>
<tr>
<td>Received PCI</td>
<td>1,314 (63.57)</td>
<td>1,314 (63.57)</td>
</tr>
<tr>
<td>Received drug-eluting stent</td>
<td>895 (43.30)</td>
<td>895 (43.30)</td>
</tr>
</tbody>
</table>

Data given as mean±SD or n (%).

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

Results

Baseline Characteristics

Among TexGen patients in the ACS group (n=2,944), a total of 2,067 patients self-identified their race as Caucasian and had available genotyping data. These patients were included in the final analyses pertaining to the ACS subgroup. A total of 1,568 patients undergoing CABG were enrolled in the TexGen registry. Out of this group, 1,176 patients self-identified their race as Caucasian and had available genotyping data.

Baseline characteristics are described in Table 1 for the TexGen ACS and CABG subgroups. Both groups had a predominance of male subjects with a mean age of 63 years for the ACS patients and 65 years for the CABG patients. More than 75% of the patients had hypertension and almost one-third had diabetes. Less than half of the patients in the ACS subgroup received DES. The left internal mammary artery was used in two-thirds of the CABG subgroup.

Major and Minor Allele Frequencies

Frequencies of CC, CG, and GG genotypes were 27.48%, 49.68%, and 22.83% in the ACS group and 29.84%, 49.53%, and 20.63% in the CABG group, respectively. Overall, 77% of the patients in the TexGen ACS group and 79% of the patients in the TexGen CABG group were carriers of at least one copy of the risk allele (C) for rs1333049. The observed rs1333049 genotype frequencies did not deviate from Hardy-Weinberg equilibrium (P>0.05 using a chi-squared goodness-of-fit model).

Among the TexGen ACS patients, carriers of the risk allele for rs1333049 (C) had an earlier onset of disease (mean age at presentation, 62 years vs. 63.5 years, P=0.0004). The carriers of the risk allele also had more extensive disease (mean number of vessels with significant stenosis, 1.9 in the carriers vs. 1.7 in the non-carriers, P=0.001). No such associations were seen in the CABG group.

rs1333049 and Future Risk of MI, Revascularization, and Death in the ACS Group

At a median follow-up of 1,168 days (mean±SD, 1,223.43±839.8 days), a total of 231 (11.18%) patients had a recurrent MI. Using a dominant model of inheritance (GG vs. CC/CG), the risk allele of rs1333049 (C) was not associated with recurrent MI in either univariate (HR, 1.05; 95% confidence interval [CI]: 0.76–1.46) or multivariate analysis (HR, 1.01; 95%CI: 0.74–1.38; Table 2). Kaplan-Meier curves pertaining to the primary outcome of recurrent MI in the ACS subgroup are shown in Figure 1.

A total of 419 ACS patients (20.27%) underwent recurrent revascularization over the follow-up period, and 290 patients (14.03%) died. The C allele for rs1333049 was not associated with an increased need for recurrent revascularization or death either in unadjusted analysis (revascularization: HR, 0.99; 95%CI: 0.78–1.26; death: HR, 0.91; 95%CI: 0.68–1.22), or fully adjusted analysis (revascularization: HR, 0.98; 95%CI: 0.78–1.23; death: HR, 0.91; 95%CI: 0.69–1.18).

rs1333049 and Future Risk of MI, Revascularization, and Death in the CABG Group

At a median follow-up of 1,150 days (mean±SD, 1,212±840 days), a total of 78 patients (6.63%) had a recurrent MI. Using a dominant model of inheritance, the risk allele of rs1333049 (C) was not associated with recurrent MI in either univariate analysis (HR, 0.65; 95%CI: 0.38–1.09) or multivariate analysis (HR, 0.64; 95%CI: 0.40–1.05; Table 3). Indeed, the HR tended (albeit non-significantly) in the direction of being protective for the carriers of the risk allele. Kaplan-Meier curves pertaining to the primary outcome of recurrent MI in the CABG subgroup are shown in Figure 2.

(SAS Institute, Cary, NC, USA). All analyses were performed using 2-tailed tests for significance. Because we evaluated a single SNP (rs 1333049) that tagged a haplotype block containing the most commonly studied variation in the 9p21 region with future risk of MI, revascularization, or death on an a priori basis, a 2-sided P<0.05 was considered statistically significant to reject the null hypothesis, and adjustments were not made for multiple testing. The study was supported through a research grant funded by Roderick D. MacDonald Research Fund at St Luke’s Episcopal Hospital, Houston, TX, USA. The authors were solely responsible for the design and conduct of the study, all analyses, the drafting and editing of the paper, and its final contents.
A total of 103 patients (8.76%) in the CABG group had repeat revascularization and 150 patients (12.76%) died. The risk allele (C) for rs1333049 was not associated with an increased need for revascularization or death either in unadjusted analysis (revascularization: HR, 0.98; 95%CI: 0.78–1.26; death: HR, 0.98; 95%CI: 0.78–1.23, 0.88).

Post-hoc analyses did not show an association between recurrent MI and the risk allele for rs2383206, rs10757278, and rs10757274 either in the TexGen ACS (Table S1) or the TexGen CABG group (Table S2). Similarly, no associations were found between the risk allele for rs2383206, rs10757278, rs10757274, and the need for recurrent revascularization (Tables S3.4) or mortality (Tables S5.6).

Analyses performed using the additive genetic model did
not show any associations between the polymorphisms and an increased risk of recurrent MI in either ACS (Table S7) or the CABG subgroups (Table S8). In the CABG subset, the HRs tended to be protective for the heterozygote carriers of the risk allele for rs1333049 and rs10757274, but the number of recurrent MI events was small for these comparisons and no consistent pattern was seen in patients carrying 2 copies of the risk alleles for these SNPs.

Data given as n (%).
†Risk allele=C. ‡Adjusted for age, gender, hypertension, diabetes, current smoking, renal insufficiency, presence of NYHA functional class III/IV symptoms, aspirin use, β-blocker use, and statin use. Abbreviations see in Tables 1,2.

**Table 3.** Association Between rs1333049† and Future Risk of MI, Revascularization and Death in the CABG Group

<table>
<thead>
<tr>
<th></th>
<th>No recurrent MI</th>
<th>Recurrent MI</th>
<th>HR (95%CI), P-value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Fully adjusted model‡</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1,098 (93.37)</td>
<td>78 (6.63)</td>
<td>Ref</td>
</tr>
<tr>
<td>GG</td>
<td>222 (90.61)</td>
<td>23 (9.39)</td>
<td>Ref</td>
</tr>
<tr>
<td>CC+GC</td>
<td>876 (94.09)</td>
<td>55 (5.91)</td>
<td>0.65 (0.38–1.09), 0.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No recurrent revascularization</th>
<th>Recurrent revascularization</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1,073 (91.24)</td>
<td>103 (8.76)</td>
</tr>
<tr>
<td>GG</td>
<td>222 (90.61)</td>
<td>23 (9.39)</td>
</tr>
<tr>
<td>CC+GC</td>
<td>851 (91.41)</td>
<td>80 (8.59)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1,026 (87.24)</td>
<td>150 (12.76)</td>
</tr>
<tr>
<td>GG</td>
<td>209 (85.31)</td>
<td>36 (14.69)</td>
</tr>
<tr>
<td>CC+GC</td>
<td>817 (87.76)</td>
<td>114 (12.24)</td>
</tr>
</tbody>
</table>

Figure 2. Kaplan-Meier curves showing freedom from myocardial infarction between the carriers of the risk allele for rs1333049 (CC/CG) and major allele (GG) in the TexGen coronary artery bypass grafting group. Analysis adjusted for age, gender, hypertension, diabetes, current smoking, renal insufficiency, presence of New York Heart Association functional class III/IV symptoms, aspirin use, β-blocker use, and statin use. CI, confidence interval; HR, hazard ratio.

Discussion

We assessed whether chromosome 9p21 genetic variation predicted recurrent MI, revascularization, or death in patients with established CHD (ie, patients with history of ACS or those undergoing CABG). This study primarily focused on rs10333049, a tagSNP for the LD block containing the most commonly studied variants in this region. We did not find an increased
risk for these outcomes in the carriers of the risk allele for rs10333049, although the carriers of the risk allele had an earlier age at presentation and more extensive angiographic CAD compared with non-carriers in the ACS subgroup. The present findings suggest that, although polymorphisms in 9p21 could play a role in the initiation and possibly progression of coronary atherosclerosis, they have minimal role in precipitation of MI in those with established CHD at a median follow-up of approximately 3.2 years.

Although the present findings are in contrast with the findings of an earlier study by Buysschaert et al,8 they are consistent with other studies showing that, although the presence of the risk allele for 9p21 is associated with the presence of coronary atherosclerosis, it may not be associated with the actual precipitation of MI. It is possible that the association of 9p21 with MI seen in epidemiologic cohorts is a reflection of its association with the presence of coronary atherosclerosis or its severity, because patients with coronary atherosclerosis (or more severe coronary atherosclerosis) are more likely to have MI compared with those who do not have coronary atherosclerosis. In these studies, the control group represents patients without any coronary atherosclerosis. Therefore, the association between the presence of risk allele for 9p21 and MI could be driven by the association between 9p21 and the presence of coronary atherosclerosis. If this assumption is true, then any association between 9p21 and the risk of MI would be lost once this confounding by the presence of coronary atherosclerosis is accounted for. In that respect, prior analyses have shown that, although 9p21 predicts CAD diagnosis, the frequency of the risk allele for 9p21 was not higher among those patients with CAD who sustained MI vs. those who did not.9 Horne et al also showed that the 9p21 locus was not associated with prevalent or incident MI in CAD patients, although it did predict CAD diagnosis.7 It is important to note in the present study that all patients had established atherosclerosis (whether they were 9p21 carriers or not), and therefore, any association with subsequent risk of MI could have been accounted for by the presence of coronary atherosclerosis in both carriers and non-carriers of the risk allele on the 9p21 locus.

We did not find an association between subsequent need for revascularization in carriers of the risk allele of 9p21. Prior studies have yielded varying results, with some studies showing an association between 9p21 status and CAD severity,8 whereas others have not.13-15 It is possible that the progression of atherosclerosis in those with established atherosclerosis (after the receipt of coronary stents or bypass grafts) is different compared with native coronary atherosclerosis. In that respect, the present results are consistent with a recent study that did not show an association between the SNPs on the 9p21 locus with death, MI, or repeat revascularization for up to 3 years of follow-up after DES placement.9 Alternatively, these patients with established atherosclerosis were likely on a good medical regimen with a higher use of evidence-based medical therapies. This might attenuate the association between the 9p21 locus and the risk of recurrent MI or recurrent revascularization in these patients.

The present findings highlight the importance of replication of initial findings in genetic studies. Although Buysschaert et al did find associations between 9p21 and the risk of recurrent MI at 6-month follow-up in patients with ACS,10 we did not find an association either in ACS patients or those undergoing CABG. This could be due to the baseline differences in subjects studied and the duration of follow-up (6 months vs. approx. 3.2 years). Similarly, in the Buysschaert et al study, the association between recurrent MI and the presence of 9p21 was attenuated once multivariate adjustments were made (P=0.053 for the dominant model) indicating a ≥5% probability for a type 1 error leading to positive findings.10 Therefore, we believe that the associations between 9p21 and the risk of recurrent events in patients with established atherosclerosis need to be replicated in other large studies with prospective follow-up of outcomes. Alternatively, the present findings could reflect a limited statistical power to show associations, although it should be noted that there were more recurrent MI events (n=231) in the present ACS subgroup compared with the Buysschaert et al study (n=70).10 Indeed, the present post-hoc calculations showed that if the risk estimates obtained by Buysschaert et al were to be applied to the present cohort, our study would have a >99% power to show an association (ie, the probability of type 2 error was <1%). In addition, the risk estimates for some of the outcomes (Tables 2, 3, S1–S8) were not consistent across various SNPs at the 9p21 locus and were indeed protective (albeit with a small number of events) for some outcomes in carriers of the risk allele in the CABG subgroup (Table S8).

In the present study, 77% of the patients in the ACS subgroup and 79% of the patients in the CABG subgroup were carriers of at least one copy of the risk allele (C) for rs1333049. This frequency for the risk allele is higher than the reported frequency of 70.8% for the risk allele (C) in the Caucasian population in HapMap (CC, 20.4%; CG, 50.4%; and 29.2%, GG) for rs1333049. These results are expected, and likely stem from the fact that the present subjects represent patients with established atherosclerosis and therefore, that these subject groups (ACS, CABG) were enriched for the risk allele (C) for rs1333049.

Study Limitations
We included Caucasian patients with ACS or CABG; therefore, these findings are not applicable to other racial groups/ethnicities. It is also possible that we may not have captured all the events, although patients enrolled in TexGen receive yearly letters and annual phone calls from research nurses to completely capture all the events. In addition, the event rate for MI, revascularization in the present study is comparable to those in some of the contemporary studies.8,16,17 Although patients with non-ST segment elevation MI (STEMI), STEMI, and unstable angina constituted the ACS cohort, these qualifying diagnoses were not separately coded in the TexGen database, precluding any subgroup analysis by ACS type. The strengths of the present analysis include a large number of events especially in the ACS subgroup to confidently evaluate outcomes, and the strict quality checks maintained by the database.

Conclusion
The SNPs on the 9p21 locus were not associated with recurrent MI, need for revascularization, or mortality in patients presenting with ACS or those undergoing CABG during a 3-year follow-up period. Individuals with the risk allele for rs1333049, however, presented with earlier and more extensive disease than non-carriers in the ACS subgroup. The present results indicate that although the 9p21 locus may have a role in the initiation and possibly progression of coronary atherosclerosis, its role in the precipitation of MI, especially in those with established atherosclerosis, needs further investigation. Studies evaluating the mechanism by which the 9p21 locus increases the risk of coronary atherosclerosis should focus more on factors associated with atherosclerosis initiation rather than with actual precipitation of MI.
Acknowledgments

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Disclosures

The authors have no conflicts of interest with the data presented in this study.

References


Supplemental Files

Supplemental File 1

Table S1. Associations Between rs2383206, rs10757278, and Risk of Recurrent MI in the TexGen ACS Group
Table S2. Associations Between rs2383206, rs10757278, and Risk of Recurrent MI in the CABG Group
Table S3. Associations Between rs2383206, rs10757278, and Risk of Recurrent MI in the CABG Group
Table S4. Associations Between rs2383206, rs10757278, and Risk of Recurrent Revascularization in the ACS Group
Table S5. Associations Between rs2383206, rs10757278, and Mortality in the ACS Group
Table S6. Associations Between rs2383206, rs10757278, and Mortality in the CABG Group
Table S7. Associations Between rs1333049, rs2383206, rs10757278, and Risk of Recurrent MI in the CABG Group
Table S8. Associations Between rs1333049, rs2383206, rs10757278, and Risk of Recurrent MI in the CABG Group

Please find supplemental file(s) at http://dx.doi.org/10.1253/circj.CJ-11-1166