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ORIGINAL RESEARCH

Perioperative Cardiometabolic Targets and Coronary Artery Bypass Surgery Mortality in Patients With Diabetes

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BACKGROUND: Coronary artery bypass graft (CABG) surgery represents the preferred revascularization strategy for most patients with diabetes and multivessel disease. We aimed to evaluate the role of optimized, perioperative cardiometabolic targets on long-term survival in patients who underwent CABG.

METHODS AND RESULTS: Single-institution retrospective study was conducted in patients with diabetes who underwent CABG between January 2010 and June 2018. Demographic, surgical, and cardiometabolic determinants were identified during the perioperative period. Clinical characteristics and longitudinal survival outcomes data were obtained. A total of 1534 patients with CABG were considered for analysis and 1273 met inclusion criteria. The mean age of patients was 63.3 years (95% CI, 62.7–63.8 years), and most were men (65%) and Hispanic or Latino (47%). Comorbidities included hypertension (95%) and dyslipidemia (88%). In total, 490 patients (52%) had a low-density lipoprotein cholesterol level >70 mg/dL. Furthermore, 390 patients (31%) had uncontrolled systolic blood pressure >130 mm Hg. Last, only 386 patients (29%) had a hemoglobin A_{1c} level between 6% and 7%. At 5 years, 121 patients (10%) died. Failure to achieve goal systolic blood pressure was associated with all-cause (hazard ratio [HR], 1.573; 95% CI, 1.048–2.362 [*P*=0.029]) and cardiovascular (HR, 2.023; 95% CI, 1.196–3.422 [*P*=0.009]) mortality at 5 years post-CABG. In contrast, prescription of a statin during the perioperative interval demonstrated a protective effect for all-cause (HR, 0.484; 95% CI, 0.286–0.819 [*P*=0.007]) and cardiovascular (HR, 0.459; 95% CI, 0.229–0.920 [*P*=0.028]) mortality. There was no association between achievement of low-density lipoprotein cholesterol, triglycerides, non–high-density lipoprotein cholesterol, or hemoglobin A_{1c} level goals and mortality risk at 5 years.

CONCLUSIONS: Among patients with diabetes, blood pressure control and statin therapy were the most important perioperative cardiometabolic survival determinants 5 years after CABG.

Key Words: CABG ■ coronary artery disease ■ cardiometabolic ■ diabetes ■ hypertension ■ lipids ■ mortality

The incidence of diabetes continues to increase in the Unites States, with a prevalence of 1 in 10, and even 1 in 3 for prediabetes.[1,2] New diabetes cases are the highest in Hispanic and non-Hispanic Black patients. Patients with diabetes have accelerated atherothrombosis with earlier, more extensive and rapidly progressive coronary artery disease.[3] Moreover, cardiovascular disease is the principal cause of death among patients with diabetes.[4] Coronary artery bypass graft (CABG) surgery is particularly utilized in patients with diabetes who have a high SYNTAX score and/or decreased left ventricular (LV) systolic function. Even after appropriate revascularization, patients with CABG remain at significantly increased risk for subsequent cardiovascular events.[5] Hypertension, diabetes, and dyslipidemia represent the strongest modifiable independent cardiovascular risk factors associated

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CLINICAL PERSPECTIVE

What Is New?

- Defining appropriate postoperative management and/or deciding to delay surgery for medical optimization of patients with diabetes remains a significant challenge for cardiologists and cardiac surgeons.
- We found that among patients with diabetes, systolic blood pressure control <130 mm Hg and statin therapy are independent perioperative cardiometabolic survival determinants 5 years after coronary artery bypass graft surgery.

What Are the Clinical Implications?

- Assessment of appropriate medical management and definition of perioperative cardiometabolic targets is essential to improve survival after coronary artery bypass graft surgery.

Nonstandard Abbreviations and Acronyms

NDI	National Death Index
SBP	systolic blood pressure
SYNTAX	Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery

with adverse cardiovascular outcomes, and medical therapy has demonstrated important survival effects after CABG.[5] Combined optimization of these variables has shown survival benefit in primary prevention[6] and represent guideline-identified targets for secondary prevention after CABG.[7] Despite this knowledge, studies have revealed that less than one third of patients with diabetes reach target control for these variables,[8] and a high percentage of these patients with cardiovascular disease may not receive statin therapy.[9] Nonetheless, data on the effect of cardiometabolic control in patients with CABG who have diabetes remain scant.

The aim of this study was to characterize the relationship between optimized cardiometabolic targets during the perioperative period surrounding CABG with long-term postoperative survival.

METHODS

Study Population

We performed a retrospective ad hoc analysis derived from an institutional cardiac surgery registry. All patients who underwent an isolated CABG procedure between January 2010 and June 2018 at a large tertiary institution were considered. Patients without a documented preoperative diagnosis of diabetes were excluded. Demographics, perioperative features, and hospital outcomes were obtained from the institutional registry. Cardiometabolic determinants including hemoglobin A_{1c} (HbA_{1c}), triglycerides, and low-density lipoprotein cholesterol (LDL-C) were obtained by retrospective review of the electronic medical record. Patients who died during the 3-month postoperative period were similarly excluded from analysis. Given the lack of statin benefit in randomized controlled trials[10–13] and differences in markers accuracy and/or medical and surgical management we labeled as high-risk and analyzed separately the group of patients with re-do CABG, severely decreased ejection fraction (LV ejection fraction <25%), and glomerular filtration rate <30 mL/min per m^2 (Figure S1). These exclusion criteria parallel institutional risk stratification schemes as determined by the Society of Thoracic Surgeons Perioperative Risk Calculator as determined by our institution. The study is presented according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. Deidentified data will be made available for independent review.

Study Design

Demographic features including age, sex, and patient-reported race were reviewed. A perioperative period defined as 3 months before and 3 months after surgery was utilized for analysis of serum markers. Optimized control of cardiometabolic determinants was defined by the lowest HbA_{1c} and triglyceride counts during this period. Concurrent LDL-C and non–high-density lipoprotein cholesterol (HDL-C) measurements were obtained based on same-day measurements as the triglyceride count, aiming to decrease the influence of triglycerides on LDL-C. During the perioperative interval, mean systolic blood pressure (SBP) was calculated for all patients. This included an average of combined inpatient and outpatient measurements during the perioperative period. A comprehensive report of SBP readings over time are provided in Table S4 and S11. Target control was defined as a mean SBP <130 mm Hg, any HbA_{1c} between 6.0% and 7.0%, LDL-C <70 mg/dL, triglycerides <150 mg/dL, and non–HDL-C <100 mg/dL. HbA_{1c} between 6.0% and 7.0% was chosen to reflect a tightly controlled cohort, independent of age or other covariates. Patients missing data on two thirds of the aforementioned cardiometabolic determinants (triglyceride count, HbA_{1c}, or mean SBP) were excluded from analysis. Low-intermediate–risk patients with CABG who had missing triglyceride or LDL-C values were described and analyzed separately (Table S9).

A request was made to the National Death Index (NDI) through the Centers for Disease Control and Prevention for access to long-term mortality data (NDI search number 2019-X116#00). All available demographic data were obtained for the patient cohort and submitted to the NDI for review for years 2010 through 2018 and 2019 using an early access report. These reports reflected the most up-to-date information at the time of the data request. All NDI data were manually reviewed for accuracy. Patient death and date of death were included for all matches with a probabilistic score consistent with NDI status code 1 ("assumed dead"). All included patients were considered at least NDI class 3, associated with a predicted mortality accuracy of 87% to 97.1%.[14]

Patients without defined mortality per the NDI report but known mortality within the hospital electronic medical record were included. High probabilistic matches for mortality per NDI review were not corroborated with the electronic medical record. In the case of discrepancy between date of death in both the 2010 to 2018 and early access 2019 data, the mortality result from the 2010 to 2018 data was utilized to account for the reliability of this report.

Statistical Analysis

All categorical and continuous variables are presented as counts with percentages and means with 95% CIs, respectively. Univariate analysis was conducted using chi-square tests for categorical variables and Wilcoxon rank sum tests for continuous variables. All univariate analyses are presented in Table S5. Where relevant, poorly populated variables with limited statistical association on univariate analyses were excluded from models to optimize power and patient inclusion. Multivariate models were constructed using stepwise backward elimination using the same comprehensive list of covariates listed in the table unless otherwise noted. Multicollinearity was assessed by examining a correlation matrix with removal of variables with a correlation >0.40. The proportional hazards assumption was assessed for LDL-C, SBP, and HbA_{1c}. This was done both by visual inspection and by a formal test of proportionality. In all cases, no evidence indicated a violation of this assumption.

Cardiovascular mortality was defined by a composite of death attributable to acute coronary syndrome, heart failure, arrhythmia, stroke, and pulmonary embolism. Causes of death were reviewed based on provided *International Statistical Classification of Diseases, Tenth Revision* (*ICD-10*), coding available, per patient, through the NDI.

All statistical tests were 2-sided and all *P* values <0.05 were considered statistically significant. All statistical analyses were performed in consultation with a departmental biostatistician and were completed using SPSS Statistics (version 2.27.00; IBM) and Statistical Analysis System (SAS version 9.4; SAS Institute Inc). Approval for this study was provided by the Albert Einstein College of Medicine's internal review board (#2018-9273) before data collection and analysis. Because of its retrospective nature, informed consent was waived for this study.

RESULTS

In total, 1534 patients met inclusion criteria for the study after removal of 16 patients with insufficient cardiometabolic data (Figure 1). Forty-four patients (3%) who died within 3 months after CABG were excluded. Demographics and perioperative outcomes are summarized for low-intermediate–risk patients in Table 1.

Low-Intermediate Risk

Low-intermediate–risk patients had a mean age of 63.3 years (95% CI, 62.7–63.8 years) and were most commonly men (65%) and non-White (79%), with 47% self-reported Hispanic or Latino. Detail conduit data are summarized in Table S1. Almost one half of the patients underwent a CABG procedure electively (48%), while the remainder underwent urgent or emergent surgical revascularization. The majority (66%) underwent surgery for stable coronary artery disease. Among all low-intermediate–risk patients, 13 of 1273 (1%) died within 3 months of surgery.

A high percentage of patients had a preoperative diagnosis of dyslipidemia (88%) and hypertension (95%) and 18% had heart failure. As described in Table 2, elevated LDL-C, >70 mg/dL, was observed in 490 patients (52%). Similarly, elevated non–HDL-C and triglyceride levels were observed in 470 (49%) and 240 (26%) patients, respectively. The mean SBP was 124.7 mm Hg (95% CI, 124.1–125.3 mm Hg) with 390 patients (31%) uncontrolled. The majority of lower-intermediate–risk patients were prescribed statin (91%) and insulin (55%) therapy during the perioperative period. Almost half of these patients (61%) were considered uncontrolled with an HbA_{1c} >7%.

Analysis of patient medications showed that most patients received aspirin (89%), but a small percentage received a second antiplatelet (29%) and 12% received anticoagulation. Most patients received β-blockers (94%), but only 60% received angiotensin receptor blockers/angiotensin-converting enzyme inhibitors. While statins were frequently prescribed, only a small percentage of patients received ezetimibe (3%) and no patients received proprotein convertase subtilisin/kexin type 9 inhibitors. Similarly, sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide 1 agonists were rarely prescribed (Table S2).

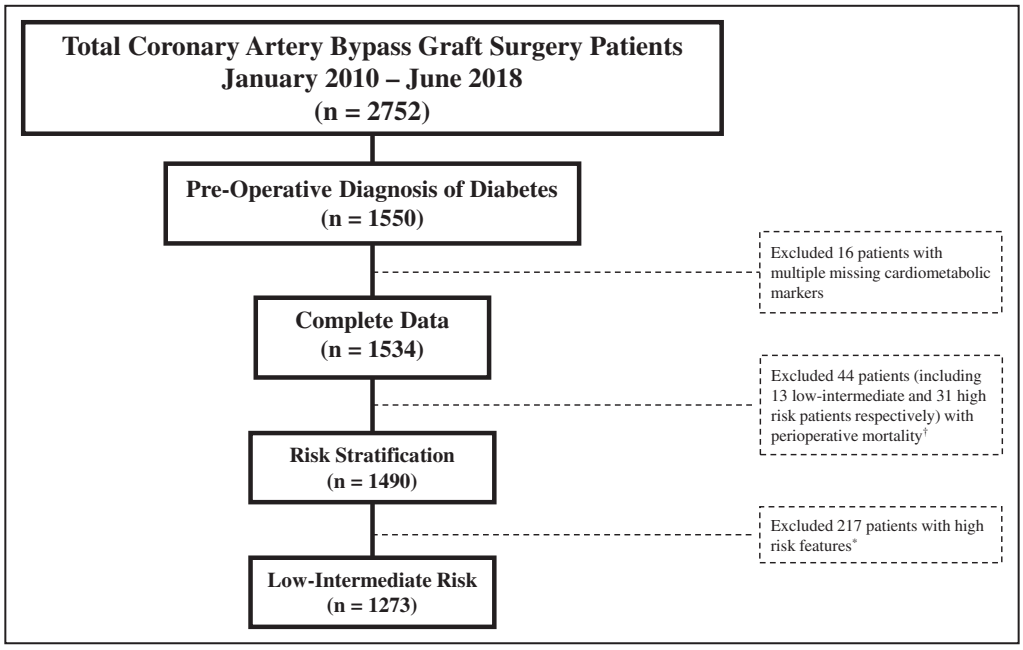

Figure 1. Flow diagram.
Flow diagram for inclusion and exclusion criteria. High-risk (*) patients included those with an ejection fraction <25%, glomerular filtration rate <30 mL/min, or redo coronary artery bypass graft (CABG) surgery. Perioperative mortality (†) was defined by death from any cause within 3 months of surgery.

High-Risk Patients

For context, the high-risk patient subgroup is described for cardiometabolic targets in Tables S3 and S4.

No comparative statistical tests were performed on survival because of known differences in LV and renal function. In brief, high-risk patients were more likely to be men (67% versus 65%) and of non-White race (88% versus 79%). There was a higher preoperative diagnosis of heart failure (39% versus 18%) and fewer patients underwent CABG electively (39% versus 48%).

Survival Analyses

In total, 121 of 1273 (10%) and 57 of 1273 (5%) low-intermediate–risk patients died from all or cardiovascular causes, respectively, at 5 years. Survival outcomes were also described for high-risk patients at 5 years (Figure S1). Kaplan-Meier survival curves for overall and cardiovascular survival are shown in Figure 2. Comparative analyses using cardiometabolic determinants were performed for unadjusted overall and cardiovascular survival. Kaplan-Meier survival curves for uncontrolled LDL-C and triglyceride counts are shown in Figure 3. Survival curves for SBP and uncontrolled HbA_{1c} are also shown. Mean SBP ≥130 mm Hg was associated with worse overall and cardiovascular survival (log-rank, P=0.035). Statin prescription during the perioperative interval was associated with improved overall and cardiovascular survival. No association between LDL-C, triglycerides, or HbA_{1c} was observed for overall or cardiovascular survival.

Univariate Cox proportional hazards for each demographic, perioperative, and cardiometabolic factor for all-cause and cardiovascular mortality are summarized in Table S5. In brief, perioperative LDL-C, triglyceride, and non–HDL-C counts by continuous or stratified measurement demonstrated no statistically significant association with all-cause or cardiovascular mortality. Similarly, HbA_{1c} by continuous or stratified measurement demonstrated no association with either end outcome. Failure to meet the mean SBP target of 130 mm Hg was associated with worse all-cause (hazard ratio [HR], 1.853; 95% CI, 1.295–2.652 [P<0.001]) and cardiovascular (HR, 2.220; 95% CI, 1.321–3.732 [P=0.003]) mortality in the low-intermediate–risk population. Furthermore, this association was maintained when mean SBP was analyzed continuously. In contrast, perioperative statin (HR, 0.445; 95% CI, 0.276–0.720 [P<0.001]) and β-blocker (HR, 0.547; 95% CI, 0.307–0.972 [P=0.040]) prescriptions were associated with improved all-cause mortality. This effect was maintained with statin prescriptions for cardiovascular mortality (HR, 0.404; 95% CI, 0.204–0.801 [P=0.009]) but not for β-blockers (HR, 0.570; 95% CI, 0.245–1.328 [P=0.193]).

A multivariate Cox proportional hazards model for all-cause mortality was constructed to estimate the

Table 1. Demographics and Perioperative Outcomes

Demographics	Patients with low-intermediate risk (n=1273)
Age, y	63.3 (62.7–63.8)
Age >65 y, n (%)	582 (45.7)
Sex, n (%)	
Men	828 (65.0)
Women	445 (35.0)
Race or ethnicity, n (%)	
White	266 (20.9)
Black	217 (17.0)
Hispanic/Latino	595 (46.7)
Asian	175 (13.7)
Unknown	20 (1.6)
Comorbidities, n (%)	
Heart failure	224 (17.6)
Dyslipidemia	1118 (87.8)
Hypertension	1211 (95.1)
Body mass index, kg/m^2	29.3 (29.0–29.6)
Ejection fraction, %	52.5 (51.8–53.2)
Ejection fraction between 25% and 40%, n (%)	281 (22.1)
Glomerular filtration rate, mL/min	75.5 (73.6–77.4)
Glomerular filtration rate <90 mL/min, n (%)	934 (73.4)
Operative features	
Indication for procedure, n (%)	
ST-segment–elevation myocardial infarction	79 (6.2)
Non–ST-segment–elevation myocardial infarction or unstable angina	356 (28.0)
Stable coronary artery disease	838 (65.8)
Elective procedure, n (%)	612 (48.1)
Perfusion time, min	97.9 (96.2–99.5)
Cross clamp time, min	79.7 (78.3–81.1)
Intraoperative blood products administered, n (%)	313 (24.6)
Redo CABG surgery, n (%)	0 (0.0)
Length of stay, d	7.4 (7.0–7.7)
Discharged home, n (%)	993 (78.0)
Hospital readmission within 30 d, n (%)	169 (13.3)
Outcome at 5 y, n (%)	
Alive	1152 (90.5)
Death, all-cause	121 (9.5)
Death, cardiovascular	57 (4.5)

CABG indicates coronary artery bypass graft. Values are expressed as means (95% CI) unless otherwise indicated.

Table 2. Pharmacologic Management and Optimized Cardiometabolic Targets Within the Perioperative Period

Cardiometabolic factors	Patients with low-intermediate risk (n=1273)
Medications, n (%)	
Statin, any	1155 (90.7)
Insulin	705 (55.4)
LDL-C, mg/dL*	78.7 (76.0–81.4)
LDL-C ≥70 mg/dL, n (% of complete)	490 (52.3)
Triglycerides, mg/dL†	128.1 (122.8–133.4)
Triglycerides ≥150 mg/dL, n (% of complete)	240 (25.6)
Non–HDL-C, mg/dL‡	105.0 (101.9–108.1)
Non-HDL-C ≥100 mg/dL, n (% of complete)	470 (49.3)
Systolic blood pressure, mean, mm Hg	124.7 (124.1–125.3)
Systolic blood pressure ≥130 mm Hg, n (% of complete)	390 (30.6)
HbA_{1c}, %§	
Between 6% and 7%, n (% of complete)	368 (29.0)
≤6%, n (% of complete)	133 (10.5)
≥7%, n (% of complete)	766 (60.5)

HbA_{1c} indicates hemoglobin A_{1c}; HDL, high-density lipoprotein cholesterol; and LDL-C, low-density lipoprotein cholesterol. Values are expressed as means (95% CI) unless otherwise indicated.

*Missing n=336 (26.4%).
†Missing n=317 (24.9%).
‡Missing n=319 (25.1%).
§Missing n=6 (0.5%).

HR for cardiometabolic variables for all-cause survival after adjusting for age. The final model is summarized in Table 3. Failure to meet target SBP was independently associated with all-cause mortality (HR, 1.573; 95% CI, 1.048–2.362 [*P*=0.029]) after adjustment for age (HR, 1.050; 95% CI, 1.027–1.074 [*P*<0.001]). Statin prescription during the perioperative interval was independently associated with a protective effect (HR, 0.484; 95% CI, 0.286–0.819 [*P*=0.007]). The remaining cardiometabolic determinants were not associated with all-cause mortality. Statistical interactions among predictors in Table 3 are provided in Table 4. Analysis for multivariate predictors of cardiovascular mortality is shown in Table 5, with similar findings to the previous model. Again, failure to meet SBP target was independently associated with higher mortality (*P*=0.009) when adjusted for age (*P*=0.020), and perioperative statin prescription had a protective effect (*P*=0.028).

Subgroup Analyses

Several additional analyses were performed to fully characterize the role of cardiometabolic determinants in various low-intermediate–risk patient populations. Unadjusted overall and cardiovascular survival analysis are shown for patients aged >65 years (Figure S2), patients with chronic kidney disease (glomerular filtration rate <90 mL/min; Figure S3), and patients with depressed LV ejection fraction (25%–40%; Figure S4). Multivariate Cox proportional

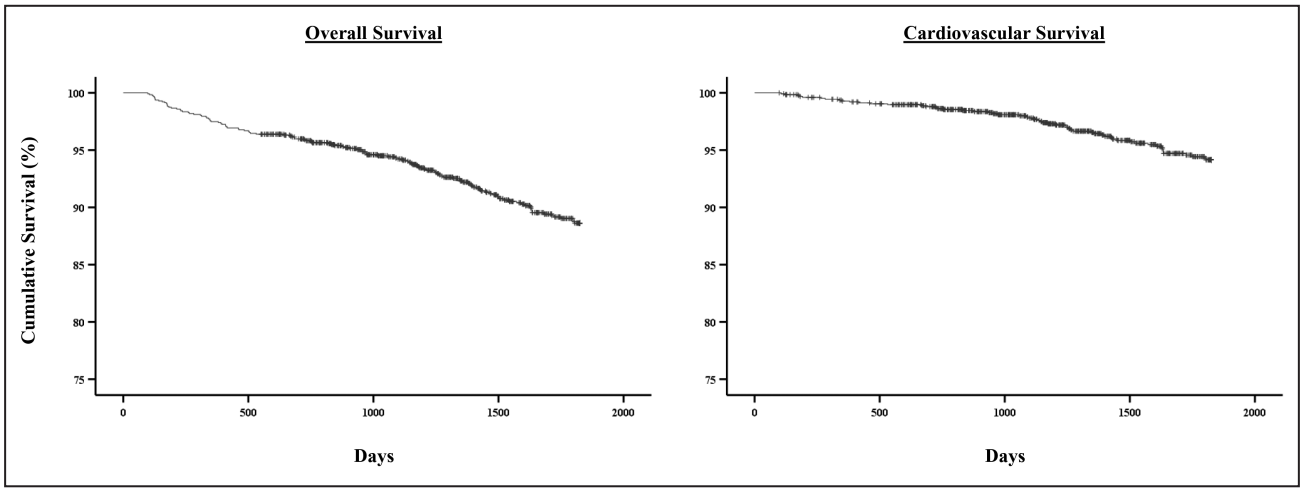

Figure 2. Unadjusted overall and cardiovascular survival for low-intermediate patients with coronary artery bypass graft surgery at 5 years.
Cardiovascular mortality was defined by a composite of death caused by acute coronary syndrome, heart failure, arrhythmia, stroke, and pulmonary embolism; all other events were censored at the time of outcome or at 5 years.

hazards models for all-cause and cardiovascular mortality were constructed for each subgroup and under each condition. In all cases, failure to meet SBP target and perioperative statin prescription were included in each model. Failure to meet SBP target was associated with increased all-cause mortality in patients aged <65 years (Tables S6A and S6B), with and without chronic kidney disease (Tables S7A and S7B), and those without depressed LV function (Tables S8A and S8B). Furthermore, statin prescriptions were independently associated with a protective effect in patients aged >65 years, with chronic kidney disease, and patients with depressed LV function.

Because of the lack of triglyceride and LDL-C data among the low-intermediate–risk group, additional subgroup analyses were performed to compare patients with complete (n=937) and incomplete (n=336) data. Demographics, perioperative outcomes, and available cardiometabolic markers are described in Table S9. There were few differences in demographic features; however, patients with incomplete data had higher rates of HbA_{1c} >7% (68.5 versus 57.6%). This subgroup also demonstrated superior overall survival (log-rank, *P*=0.02) but not cardiovascular survival (log-rank, *P*=0.177; Figure S5). When adjusted for similar covariates in a multivariate model of 5-year overall and cardiovascular survival, failure to reach SBP target was associated with cardiovascular survival (HR, 4.248; 95% CI, 1.270–14.205 [*P*=0.019]) but did not reach statistical significance for overall survival (HR, 2.210; 95% CI, 0.967–5.051 [*P*=0.060]). No association between HbA_{1c} and statin use were identified (Table S10).

DISCUSSION

This study analyzed a large single-center database of patients with diabetes, including a high representation of self-identified Black and Hispanic patients, to identify whether the achievement of perioperative cardiometabolic targets was associated with long-term survival following isolated CABG surgery. Our main finding was the association between perioperative hypertension control and statin prescription with all-cause and cardiovascular mortality up to 5 years after CABG. On the contrary, there was no association with other perioperative cardiometabolic determinants including LDL-C, triglycerides, non–HDL-C, or HbA_{1c} on all-cause or cardiovascular mortality.

Several studies have confirmed the association between individual treatment levels and cardiovascular events; however, the effects of a combined cardiometabolic profile in secondary prevention have received less attention. The importance of optimal medical therapy after CABG in a mostly nondiabetic group of patients with de novo lesions without myocardial infarction and mostly stable coronary artery disease has been suggested by a subanalysis of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) study.[5] However, the identification and effects of reaching appropriate cardiometabolic targets after CABG remains unknown, with current guidelines being extrapolated from nonsurgical populations. In addition, treatment remains suboptimal[15] and there has been an ongoing debate defining the optimal blood pressure (BP) target for patients after CABG. No prior trials have assessed the effect of targets on cardiovascular events and

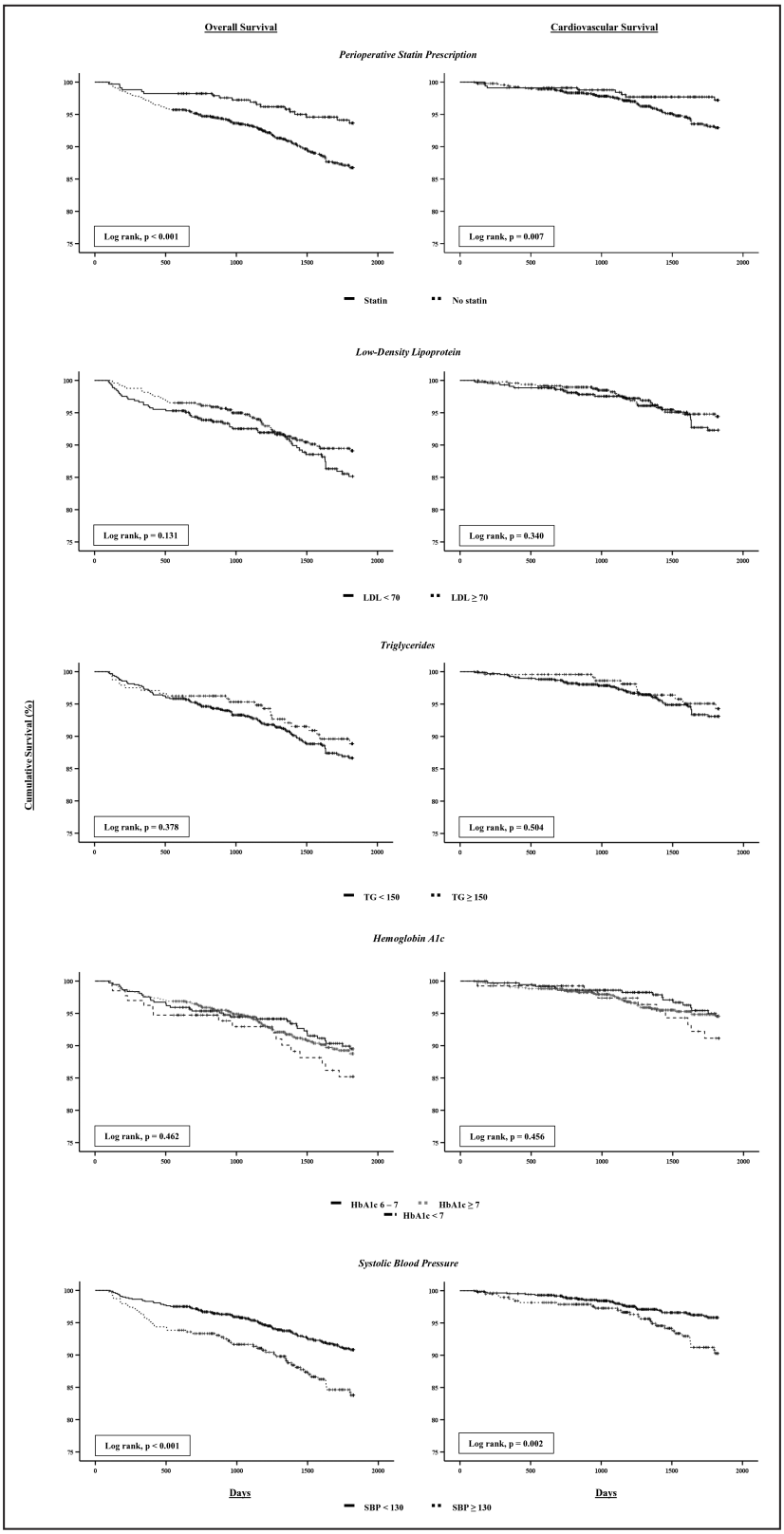

Figure 3. Unadjusted overall and cardiovascular analyses at 5 years for optimized cardiometabolic targets in low-intermediate–risk patients.
Overall survival is shown in the left column, and cardiovascular survival is shown in the right column; log-rank, $P<0.05$ for statin use and systolic blood pressure (SBP).

Table 3. Multivariate Proportional Hazards for All-Cause Mortality at 5 Years: Low-Intermediate–Risk Analysis*

Predictors	HR (95% CI)	*P* value
Age, y (continuous)	1.050 (1.027–1.074)	<0.001
LDL-C ≥70 mg/dL	0.793 (0.522–1.207)	0.280
SBP ≥130 mm Hg	1.573 (1.048–2.362)	0.029
HbA_{1c}		
Between 6% and 7%	Reference	…
≤6%	1.419 (0.732–2.751)	0.301
≥7%	1.512 (0.947–2.413)	0.083
Statin use	0.484 (0.286–0.819)	0.007

HbA_{1c} indicates hemoglobin A_{1c}; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; and SBP, systolic blood pressure.

*A total of 931 (73.1%) low-intermediate–risk patients were included in the final model, with analysis of 98 all-cause mortality events (10.5%). All cardiometabolic determinants were considered in the model. Target triglyceride counts were not associated with the end outcome and were excluded from the model. The complete correlation matrix is shown in Table 4.

Table 5. Multivariate Proportional Hazards for Cardiovascular Mortality at 5 Years: Low-Intermediate–Risk Analysis

Predictors	HR (95% CI)*	*P* value
Age, y (continuous)	1.035 (1.005–1.065)	0.020
LDL-C ≥70 mg/dL†	0.802 (0.443–1.451)	0.466
SBP ≥130 mm Hg	2.023 (1.196–3.422)	0.009
HbA_{1c}		
Between 6% and 7%	Reference	…
≤6%	1.690 (0.738–3.867)	0.214
≥7%	1.303 (0.698–2.431)	0.405
Statin use	0.459 (0.229–0.920)	0.028

HR indicates hazard ratio.

*A total of 1266 low-intermediate–risk patients (99.4% of total) were included in the final model, with analysis of 57 cardiovascular mortality events (4.5%). All cardiometabolic determinants were considered in the model. The correlation matrix was previously shown (Table 3).

†A total of 930 low-intermediate–risk patients (73.1% of total) had complete low-density lipoprotein cholesterol (LDL-C) data for analysis and were analyzed after adjusted for age, systolic blood pressure (SBP), hemoglobin A_{1c} (HbA_{1c}), and statin use. The correlation matrix was previously shown in Table 3.

mortality after CABG and it is not known whether the J curve for BP and outcomes occurs at a higher level of BP after CABG.[7] In our study, 31% and 48% of low-intermediate– and high-risk patients, respectively, did not have appropriate BP control (defined as a mean SBP <130 mm Hg). Low-intermediate–risk patients with appropriately controlled BP demonstrated superior overall and cardiovascular survival at 5 years. This effect was independently observed after adjustment with age and statin prescription in multivariate analysis. Although the specific association varied by subgroup analysis, these effects remained robust and persistent.

Elevated LDL-C has a strong influence in the development and progression of native and graft atherosclerosis. Statins have been shown to inhibit development and progression in both native arteries and venous grafts and reduce the risk of myocardial infarction during the perioperative period and the first year after CABG.[7] The beneficial effects of statins go beyond cholesterol lowering. Statins have pleiotropic effects including improvement of endothelial function, increased nitric oxide bioavailability, antioxidant properties, and reduction of inflammation and thrombosis.[16]

Moreover, statins have been shown to decrease cardiovascular and all-cause mortality after CABG in a >90% White cohort of patients aged >65 years with <50% of those with diabetes and a low percentage of statin use (31.8%).[17] On the contrary, our low-intermediate cohort was younger (63.3 years [62.7–63.8 years]), contained only patients with diabetes, and was 79% non-White. The protective effect of statins was also demonstrated in our subgroup analysis of patients aged >65 years, but was not observed in younger patients. Taken together, these findings suggest that non-White patients with diabetes develop severe coronary artery disease earlier than White patients with diabetes. Moreover, statin use was present in a higher percentage of patients. Importantly, 52% and 26% of patients had an LDL-C ≥70 mg/dL and triglycerides ≥130 mg/dL, respectively. Moreover, 9% of low-intermediate–risk patients did not receive statin therapy. In these cases, there was a great potential for expanding lipid-lowering therapy in our CABG population. Our findings are consistent with

Table 4. Interactions Between Multivariate Proportional Hazards for All-Cause Mortality at 5 Years: Low-Intermediate–Risk Analysis*

Factors	Age	LDL-C	SBP	HbA_{1c}	Statin use
Age	…	−0.051 (*P*=0.119)	0.136 (*P*<0.001)	−0.181 (*P*<0.001)	−0.120 (*P*<0.001)
LDL-C		…	0.051 (*P*=0.119)	0.014 (*P*=0.661)	0.091 (*P*=0.005)
SBP			…	−0.004 (*P*=0.881)	−0.005 (*P*=0.859)
HbA_{1c}				…	0.055 (*P*=0.050)
Statin use					…

HbA_{1c} indicates hemoglobin A_{1c}; LDL-C, low-density lipoprotein cholesterol; and SBP, systolic blood pressure.

*A total of 931 (73.1%) low-intermediate–risk patients were included in the final model, with analysis of 98 all-cause mortality events (10.5%). All cardiometabolic determinants were considered in the model. Target triglyceride counts were not associated with the end outcome and were excluded from the model.

prior studies demonstrating that, despite a decrease in cardiovascular and all-cause mortality with statin therapy, a significant number of patients do not receive any statins.[18] Compliance with evidence-based medical therapies is a complex construct of patient and physician behavior.[19] In addition, elevated perioperative lipid markers were not associated with either all-cause or cardiovascular mortality. In spite of extensive evidence that reduction of LDL-C with statin use has a clear survival benefit, interpretation of LDL-C measurements and mortality have proven to be more complex with a possible U-shaped relationship[20] and medication nonadherence possibly playing a role.[21]

Poorly controlled diabetes as per preoperative HbA_{1c} has been related to higher all-cause mortality in retrospective studies.[22,23] In our study, we did not find any difference in mortality for patients that met the HbA_{1c} target during the perioperative period and those who did not. Further, prospective studies are clearly needed.

Defining appropriate postoperative management and/or deciding to delay surgery for medical optimization of patients with diabetes and other comorbidities remains an incredible challenge for cardiologists and cardiac surgeons. Further investigation is required to characterize the effects of hypertension management target and concurrent pharmacologic management to improve long-term survival outcomes.

Study Limitations

There were several limitations involved in this study. Because of its retrospective design, there was bias involved in the definition of the perioperative period and selection of the cardiometabolic targets. Moreover, it is likely that the effects on mortality are influenced by the adherence to prolonged medical therapy and not just during the perioperative period. Our study did not explicitly evaluate adherence or duration of therapy over time. Only 13 patients were entirely excluded as a result of missing or incomplete data availability; however, 342 patients (26.9%) were not included in the multivariate analysis for all-cause mortality because of incomplete data. However, these patients were separately described in Tables S9 and S10 and Figure S5. There were few obvious demographic differences between these populations. It is unclear whether LDL-C or triglyceride data were missing or never monitored by physicians at the time. Nevertheless, patients with incomplete data demonstrated improved survival at 5 years, and failure to reach SBP target was similarly associated with worse survival outcome. We hypothesize that these patients reflect a less sick patient population that is incompletely described by our analyses.

Moreover, the use of a preoperative diagnosis of diabetes excluded patients with newly diagnosed or inaccurately recorded diabetes. Also, the accuracy of HbA_{1c} during the perioperative interval may change as a result of intraoperative blood loss and blood product transfusion. Last, the use of NDI data may underestimate patient deaths in the studied cohort.

CONCLUSIONS

Hypertension control and statin utilization may decrease cardiovascular and all-cause mortality after CABG in an ethnically diverse cohort of patients with diabetes.

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Supplemental Material

Tables S1–S11
Figures S1–S5

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SUPPLEMENTAL MATERIAL

Table S1. Conduit Analysis for Low-Intermediate and High Risk Patients

	Low-Intermediate Risk (n = 1273)	High Risk* (n = 217)
Total arterial conduits – no. (%)		
Zero	7 (0.5)	4 (1.8)
One	963 (75.6)	180 (82.9)
Two	292 (22.9)	31 (14.3)
Three	11 (0.9)	2 (0.9)
Total venous conduits – no. (%)		
Zero	91 (7.1)	14 (6.5)
One	354 (27.8)	74 (34.1)
Two	597 (46.9)	94 (43.3)
Three	206 (16.2)	33 (15.2)
Four	24 (1.9)	2 (0.9)
Five	1 (0.1)	0 (0.0)
Total distal anastomoses – no. (%)		
One	40 (3.1)	12 (5.5)
Two	260 (20.4)	58 (26.7)
Three	653 (51.3)	103 (47.5)
Four	277 (21.8)	40 (18.4)
Five	40 (3.1)	4 (1.8)
Six	3 (0.2)	0 (0.0)

*Defined by re-do coronary artery bypass graft surgery, ejection fraction less than 25%, or glomerular filtration rate less than 30 mL/min.

Table S2. Medications Prescribed during Perioperative Period for Low-Intermediate and High Risk Patients

	Low-Intermediate Risk (n = 1,273)	High-Risk* (n = 217)
Cardiovascular – no. (%)		
Aspirin	1135 (89.2)	180 (82.9)
Anti-platelet*	369 (29.0)	65 (30.0)
Anti-coagulant	155 (12.2)	40 (18.4)
Triple therapy†	39 (3.1)	7 (3.2)
Hypertension – no. (%)		
ACE inhibitor or ARB	769 (60.4)	115 (53.0)
Beta blocker	1196 (94.0)	197 (90.8)
Calcium channel blocker	416 (32.7)	110 (50.7)
Potassium-sparing diuretic	48 (3.8)	18 (8.3)
Nitrate	197 (15.5)	57 (26.3)
Dyslipidemia – no. (%)		
Statin, any	1155 (90.7)	188 (86.6)
Ezetimibe	41 (3.2)	8 (3.7)
Fibrate	45 (3.5)	7 (3.2)
Niacin	20 (1.6)	5 (2.3)
Diabetes – no. (%)		
Insulin	705 (55.4)	139 (64.1)
Metformin	638 (50.1)	31 (14.3)
Glitazone	8 (3.7)	60 (4.7)
GLP-1 agonist	41 (3.2)	6 (2.8)
DPP-4 inhibitor	317 (24.9)	35 (16.1)
SGLT-2 inhibitor	28 (2.2)	2 (0.9)
Sulfonylurea	295 (23.2)	42 (19.4)

ACE – angiotensin-converting enzyme; ARB – angiotensin II receptor blocker; GLP – glucagon-like peptide; DPP – dipeptidyl-peptidase; SGLT – sodium-glucose co-transporter

*Composite of clopidogrel, prasugrel, and ticagrelor

†Concurrent aspirin, anti-platelet, and anti-coagulant

Table S3. Comparison of Demographics and Perioperative Outcomes for Low-Intermediate and High Risk Patients

	Low-Intermediate Risk (n = 1,273)	High Risk* (n = 217)	p-value
Age – years	63.3 [62.7 – 63.8]	62.6 [61.2 – 64.0]	0.482
Age greater than 65 years – no. (%)	582 (45.7)	99 (45.6)	1.000
Sex – no. (%)			0.644
Male	828 (65.0)	145 (66.8)	
Female	445 (35.0)	72 (33.2)	
Race – no. (%)			**< 0.001**
White/Caucasian	266 (20.9)	26 (12.0)	
Black/African American	217 (17.0)	63 (29.0)	
Hispanic/Latino	595 (46.7)	99 (45.6)	
Asian	175 (13.7)	27 (12.4)	
Unknown	20 (1.6)	2 (0.9)	
Comorbidities – no. (%)			
Heart failure	224 (17.6)	84 (38.7)	**< 0.001**
Dyslipidemia	1118 (87.8)	181 (83.4)	0.079
Hypertension	1211 (95.1)	215 (99.1)	**0.029**
Body mass index – kg/m^2	29.3 [29.0 – 29.6]	28.4 [27.7 – 29.1]	**0.027**
Ejection fraction – %	52.5 [51.8 – 53.2]	43.2 [41.1 – 45.3]	**< 0.001**
Ejection fraction between 25 and 40 % – no. (%)	281 (22.1)	91 (41.9)	**< 0.001**
Glomerular filtration rate – mL/min	75.5 [73.6 – 77.4]	26.5 [22.8 – 30.3]	**< 0.001**
Glomerular filtration rate less than 90 mL/min – no. (%)	934 (73.4)	209 (96.3)	**< 0.001**
Operative features			
Indication for procedure – no. (%)			**< 0.001**
ST-segment myocardial infarction	79 (6.2)	18 (8.3)	
Non-ST-segment myocardial infarction or unstable angina	356 (28.0)	91 (41.9)	
Stable coronary artery disease	838 (65.8)	108 (49.8)	
Elective procedure – no. (%)	612 (48.1)	84 (38.7)	**0.024**
Perfusion time – min	97.9 [96.2 – 99.5]	102.2 [97.7 – 106.7]	0.072
Cross clamp time – min	79.7 [78.3 – 81.1]	79.2 [75.6 – 82.8]	0.879
Intraoperative blood products administered– no. (%)	313 (24.6)	111 (51.2)	**< 0.001**
Redo coronary artery bypass graft surgery – no. (%)	0 (0.0)	19 (30.0)	---
Length of stay – days	7.4 [7.0 – 7.7]	10.1 [9.0 – 11.1]	**< 0.001**
Discharged home – no. (%)	993 (78.0)	132 (60.8)	**< 0.001**
Hospital readmission within 30 days – no. (%)	169 (13.3)	48 (22.1)	**< 0.001**
Outcome at 5 years – no. (%)			---
Alive	1152 (90.5)	138 (63.6)	
Dead, all-cause	121 (9.5)	79 (36.4)	
Dead, cardiovascular	57 (4.5)	47 (21.7)	

*Defined by re-do coronary artery bypass graft surgery, ejection fraction less than 25%, or glomerular filtration rate less than 30 mL/min

Table S4. Pharmacologic Management and Optimized Cardiometabolic Targets within Perioperative Period for Low-Intermediate and High Risk Patients

	Low-Intermediate Risk (n = 1273)	High Risk* (n = 217)
LDL-C – mg/dL †	78.7 [76.0 – 81.4]	67.9 [60.6 – 75.1]
LDL-C ≥70 mg/dL – no. (%)	490 (52.3)	61 (37.0)
Triglyceride – mg/dL ‡	128.1 [122.8 – 133.4]	111.0 [99.0 – 123.0]
Triglyceride ≥150 mg/dL – no. (%)	240 (25.6)	25 (15.2)
Non-HDL-C – mg/dL§	105.0 [101.9 – 108.1]	90.5 [82.4 – 98.6]
Non-HDL-C ≥100 mg/dL – no. (%)	470 (49.3)	57 (33.9)
Systolic blood pressure, overall mean – mmHg	124.7 [124.1 – 125.3]	128.5 [126.7 – 130.2]
Systolic blood pressure ≥130 mmHg – no. (%)	390 (30.6)	103 (47.5)
Total measurements count – no.	117.7 [110.8 – 124.6]	191.1 [167.4 – 214.8]
Systolic blood pressure, between 30 to 90 days before surgery		
Systolic blood pressure, mean – mmHg	135.3 [133.6 – 137.0]	139.0 [135.1 – 142.9]
Total count – no.	4.2 [3.2 – 5.2]	9.8 [6.3 – 13.3]
Systolic blood pressure between 30 days before and 30 days after surgery		
Systolic blood pressure, mean – mmHg	124.3 [123.7 – 124.9]	128.0 [126.2 – 129.8]
Total count – no.	99.1 [94.8 – 103.4]	143.9 [129.2 – 158.5]
Systolic blood pressure, between 30 to 90 days after surgery		
Systolic blood pressure, mean – mmHg	130.0 [128.8 – 131.3]	135.1 [131.6 – 138.6]
Total count – no.	14.9 [11.2 – 18.6]	37.4 [25.1 – 49.8]
Hemoglobin A1C – %II		
Between 6 and 7 % – no. (%)	368 (29.0)	77 (35.6)
Less or equal than 6 % – no. (%)	133 (10.5)	60 (27.8)
Greater or equal than 7 % – no. (%)	766 (60.5)	79 (36.6)

LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol

*Defined by re-do coronary artery bypass graft surgery, ejection fraction less than 25%, or glomerular filtration rate less than 30 mL/min

†Missing n=336 (26.4%) and n=52 (24.0) for low-intermediate risk and high risk groups respectively

‡Missing n=317 (24.9%) and n=47 (21.7%) for low-intermediate risk and high risk groups respectively

§Missing n=319 (25.1%) and n=49 (22.6%) for low-intermediate risk and high risk groups respectively

IIMissing n=6 (0.5%) and n=1 (0.5%) for low-intermediate risk and high risk groups respectively

Table S5. Univariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Low-Intermediate Risk Analysis

	All-Cause Mortality		Cardiovascular Mortality	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
Demographics				
Age – years (continuous)	1.053 [1.033 – 1.073]	**< 0.001**	1.043 [1.014 – 1.072]	**0.003**
Age greater than 65 years	2.154 [1.490 – 3.115]	**< 0.001**	1.543 [0.916 – 2.598]	0.103
Male sex	0.982 [0.677 – 1.425]	0.942	0.862 [0.506 – 1.470]	0.587
Race				
White or Caucasian	Reference	---	Reference	---
Black or African American	0.825 [0.478 – 1.425]	0.491	0.936 [0.450 – 1.945]	0.859
Hispanic or Latino	0.756 [0.486 – 1.176]	0.214	0.540 [0.280 – 1.042]	0.066
Asian or Native	0.556 [0.286 – 1.083]	0.084	0.536 [0.210 – 1.369]	0.192
Unknown or missing	0.870 [0.208 – 3.634]	0.848	1.725 [0.396 – 7.503]	0.468
Comorbidities				
Heart failure	2.132 [1.448 – 3.139]	**< 0.001**	2.430 [1.401 – 4.215]	**0.002**
Dyslipidemia	1.371 [0.756 – 2.490]	0.299	1.311 [0.562 – 3.055]	0.531
Hypertension	3.269 [0.808 – 13.225]	0.097	1.536 [0.375 – 6.297]	0.551
Indication for procedure				
Stable coronary artery disease	**Reference**	**---**	**Reference**	**---**
Non-ST-segment myocardial infarction or unstable angina	**1.365 [0.913 – 2.040]**	**0.130**	**1.150 [0.622 – 2.124]**	**0.656**
ST-segment myocardial infarction	**1.202 [0.580 – 2.489]**	**0.621**	**0.902 [0.279 – 2.917]**	**0.863**
Body mass index (continuous)	1.001 [0.970 – 1.033]	0.950	1.003 [0.958 – 1.050]	0.898
Ejection fraction (continuous)	0.967 [0.953 – 0.980]	**< 0.001**	0.973 [0.954 – 0.993]	**0.008**
Ejection fraction between 25 and 40 %	1.984 [1.364 – 2.885]	**< 0.001**	1.733 [0.991 – 3.029]	0.054
Glomerular filtration rate – mL/min (continuous)	0.984 [0.976 – 0.992]	**< 0.001**	0.984 [0.972 – 0.995]	**0.005**
Glomerular filtration rate less than 90 mL/min	2.200 [1.334 – 3.631]	**0.002**	2.391 [1.132 – 5.048]	**0.022**
Discharged to rehabilitation or nursing care facility	3.290 [2.301 – 4.706]	**< 0.001**	2.496 [1.464 – 4.255]	**< 0.001**
Cardiometabolic				
LDL-C – mg/dL (continuous)	0.737 [0.495 – 1.097]	0.132	0.996 [0.989 – 1.004]	0.338
LDL-C ≥70 mg/dL	0.823 [0.523 – 1.297]	0.401	0.753 [0.419 – 1.352]	0.342
Triglyceride – mg/dL (continuous)	0.997 [0.994 – 1.000]	**0.048**	0.997 [0.992 – 1.002]	0.197
Triglyceride ≥150 mg/dL	0.808 [0.503 – 1.299]	0.379	0.787 [0.390 – 1.590]	0.505
Non-HDL – mg/dL (continuous)	0.997 [0.993 – 1.001]	0.147	0.996 [0.989 – 1.002]	0.170
Non-HDL ≥100 mg/dL	0.731 [0.491 – 1.089]	0.124	0.788 [0.438 – 1.419]	0.428
Systolic blood pressure, mean – mmHg (continuous)	1.034 [1.019 – 1.050]	**< 0.001**	1.039 [1.016 – 1.062]	**< 0.001**
Systolic blood pressure ≥130 mmHg	1.853 [1.295 – 2.652]	**< 0.001**	2.220 [1.321 – 3.732]	**0.003**
Hemoglobin A1C (continuous)	1.030 [0.932 – 1.138]	0.561	1.037 [0.897 – 1.199]	0.619
Between 6 and 7 %	Reference	---	Reference	---

Less or equal than 6 % – no. (%)	1.435 [0.799 – 2.577]	0.226	1.664 [0.728 – 3.803]	0.227
Greater or equal than 7 % – no. (%)	1.078 [0.713 – 1.630]	0.721	1.118 [0.607 – 2.059]	0.720
Medications				
Statin	0.445 [0.276 – 0.720]	**< 0.001**	0.404 [0.204 – 0.801]	**0.009**
Insulin	1.613 [1.104 – 2.355]	**0.013**	1.473 [0.855 – 2.538]	0.163
Beta blocker	0.547 [0.307 – 0.972]	**0.040**	0.570 [0.245 – 1.328]	0.193
Calcium channel blocker	1.647 [1.151 – 2.357]	**0.006**	1.972 [1.173 – 3.314]	**0.010**

CI – confidence interval; LDL-C – low-density lipoprotein; HDL-C – high-density lipoprotein

Table S6A. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients with Age ≥ 65 Years

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
LDL-C ≥70 mg/dL	0.763 [0.459 – 1.268]	0.296	0.539 [0.236 – 1.232]	0.143
Systolic blood pressure ≥130 mmHg	1.656 [0.994 – 2.761]	0.053	1.938 [0.869 – 4.322]	0.106
Hemoglobin A1C				
Between 6 and 7 %	Reference	---	---	---
Less or equal than 6 % – no. (%)	1.898 [0.881 – 4.086]	0.102	---	---
Greater or equal than 7 % – no. (%)	1.457 [0.828 – 2.564]	0.192	---	---
Statin use	0.503 [0.269 – 0.941]	**0.032**	0.422 [0.165 – 1.081]	0.072

LDL-C – low-density lipoprotein cholesterol

*A total of 432 low-intermediate risk patients (74.2% of eligible total) were included in the final model with analysis of 62 overall mortality events (14.4%).
†A total of 435 low-intermediate risk patients (74.7% of eligible total) were included in the final model with analysis of 25 cardiovascular mortality events (5.7%). All cardiometabolic determinants were considered for each model. Target TG count was not associated with either end-outcome and was excluded from the model. Target hemoglobin A1c ranges were not associated with cardiovascular mortality and were excluded from the model. There was no significant correlation between included covariates.

Table S6B. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients with Age < 65 Years

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
Systolic blood pressure ≥130 mmHg	2.059 [1.136 – 3.735]	**0.017**	2.405 [1.106 – 5.227]	**0.027**
Statin use	0.461 [0.181 – 1.177]	0.105	0.439 [0.131 – 1.475]	0.183

*A total of 691 low-intermediate risk patients (100% of eligible total) were included in the final model with analysis of 45 overall mortality events (6.5%).
†A total of 691 low-intermediate risk patients (100% of eligible total) were included in the final model with analysis of 26 cardiovascular mortality events (3.8%). All cardiometabolic determinants were considered for each model. Target hemoglobin A1C ranges, and target TG and LDL-C counts were not associated with either end-outcome and were excluded from the model. There was no significant correlation between included covariates.

Table S7A. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients with Chronic Kidney Disease (GFR < 90 mL/min)

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
LDL ≥70 mg/dL	0.779 [0.505 – 1.203]	0.261	---	---
Systolic blood pressure ≥130 mmHg	1.598 [1.037 – 2.463]	**0.034**	2.020 [1.153 – 3.539]	**0.014**
Statin use	0.462 [0.266 – 0.801]	**0.006**	0.432 [0.210 – 0.892]	**0.023**

LDL-C – low-density lipoprotein cholesterol

*A total of 689 low-intermediate risk patients (73.8% of eligible total) were included in the final model with analysis of 84 overall mortality events (12.2%).
†A total of 934 low-intermediate risk patients (100% of eligible total) were included in the final model with analysis of 49 cardiovascular mortality events (5.2%). All cardiometabolic determinants were considered for each model. Target hemoglobin A1C ranges, and target TG count were not associated with either end-outcome and were excluded from the model. Target LDL-C count was not associated with cardiovascular mortality and was excluded from that model. There was no significant correlation between included covariates.

Table S7B. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients without Chronic Kidney Disease (GFR ≥ 90 mL/min)

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
Systolic blood pressure ≥130 mmHg	3.958 [1.569 – 9.981]	**0.004**	---	---
Statin use	0.417 [0.095 – 1.824]	0.417	---	---

*A total of 339 low-intermediate risk patients (100% of eligible total) were included in the final model with analysis of 18 overall mortality events (5.3%). All cardiometabolic determinants were considered for each model. Target hemoglobin A1c ranges, and target TG and LDL-C counts were not associated with the end-outcome and were excluded from the model. There was no significant correlation between included covariates.
†Only 5 cardiovascular mortality events were encountered in this subgroup. There were insufficient data to report this analysis.

Table S8A. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients with Reduced Left Ventricular Function (EF between 25 – 40 %)

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
Systolic blood pressure ≥130 mmHg	1.776 [0.952 – 3.314]	0.071	---	---
Statin use	0.320 [0.157 – 0.651]	**0.002**	---	---

*A total of 281 low-intermediate risk patients (100% of eligible total) were included in the final model with analysis of 42 overall mortality events (14.9%). All cardiometabolic determinants were considered for each model. Target hemoglobin A1C ranges, and target TG and LDL-C counts were not associated with either end-outcome and were excluded from the model. There was no significant correlation between included covariates.
†Only 13 cardiovascular mortality events were encountered in this subgroup. There were insufficient data to report this analysis.

Table S8B. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Low-Intermediate Risk Patients with Preserved Left Ventricular Function (EF > 40 %)

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
LDL-C ≥70 mg/dL	0.706 [0.431 – 1.158]	0.168	0.521 [0.253 – 1.074]	0.077
Systolic blood pressure ≥130 mmHg	2.094 [1.286 – 3.410]	**0.003**	2.352 [1.175 – 4.709]	**0.016**
Statin use	0.521 [0.264 – 1.030]	0.061	0.524 [0.200 – 1.374]	0.189

LDL-C – low-density lipoprotein cholesterol

*A total of 718 low-intermediate risk patients (72.4% of eligible total) were included in the final model with analysis of 65 overall mortality events (9.1%).
†A total of 718 low-intermediate risk patients (72.4% of eligible total) were included in the final model with analysis of 32 cardiovascular mortality events (4.5%). All cardiometabolic determinants were considered for each model. Target hemoglobin A1C ranges, and target TG count were not associated with either end-outcome and were excluded from the models. There was no significant correlation between included covariates.

Table S9. Comparison of Select Demographics, Perioperative Outcomes, and Cardiometabolic Markers for Patient with Complete and Missing Lipid Markers

	Complete Lipid Profile (n = 937)	Missing* (n = 336)	p-value
Demographics and Perioperative Outcomes			
Age – years	63.2 [62.6 – 63.9]	63.4 [62.3 – 64.4]	0.892
Age ≥65 years – no. (%)	435 (46.4)	147 (43.8)	0.407
Sex – no. (%)			0.083
Male	596 (63.6)	232 (69.0)	
Female	341 (36.4)	104 (31.0)	
Race – no. (%)			0.858
White/Caucasian	194 (20.7)	72 (21.4)	
Black/African American	162 (17.3)	55 (16.4)	
Hispanic/Latino	442 (47.2)	153 (45.5)	
Asian	126 (13.4)	49 (14.6)	
Unknown	13 (1.4)	7 (2.1)	
Comorbidities – no. (%)			
Heart failure	173 (18.5)	51 (15.2)	0.183
Dyslipidemia	817 (87.2)	301 (89.6)	0.285
Hypertension	894 (95.4)	317 (94.3)	0.630
Body mass index – kg/m^2	29.2 [28.9 – 29.6]	29.5 [28.9 – 30.1]	0.460
Ejection fraction – %	52.2 [51.4 – 53.0]	53.4 [52.1 – 54.7]	0.250
Ejection fraction between 25 and 40 % – no. (%)	219 (23.4)	62 (18.5)	0.066
Glomerular filtration rate – mL/min	75.7 [73.3 – 78.0]	74.9 [72.1 – 77.7]	0.958
Glomerular filtration rate less than 90 mL/min – no. (%)	689 (73.5)	245 (72.9)	0.829
Operative features			
Elective procedure – no. (%)	430 (45.9)	182 (54.2)	**0.010**
Perfusion time – min	97.3 [95.4 – 99.3]	99.3 [96.2 – 102.5]	0.096
Cross clamp time – min	79.1 [77.4 – 80.7]	81.4 [78.8 – 84.1]	0.055
Intraoperative blood products administered– no. (%)	235 (25.1)	78 (23.2)	0.507
Length of stay – days	7.6 [7.1 – 8.0]	6.8 [6.2 – 7.4]	0.116
Discharged home – no. (%)	216 (23.1)	54 (16.1)	**0.023**
Hospital readmission within 30 days – no. (%)	129 (13.8)	40 (11.9)	0.453
Outcome at 5 years – no. (%)			---
Alive	839 (89.5)	313 (93.2)	
Dead, all-cause	23 (6.8)	98 (10.5)	
Dead, cardiovascular	45 (4.8)	12 (3.6)	
Cardiometabolic Targets			
Systolic blood pressure, mean – mmHg	124.7 [124.0 – 125.4]	124.5 [123.4 – 125.7]	0.918
Systolic blood pressure g≥130 mmHg – no. (%)	285 (30.4)	105 (31.3)	0.783
Hemoglobin A1C – %‡	7.7 [7.6 – 7.8]	8.0 [7.8 – 8.2]	**< 0.001**
Between 6 and 7 % – no. (%)	290 (31.1)	78 (23.2)	**0.002**
Less or equal than 6 % – no. (%)	105 (11.3)	28 (8.3)	---
Greater or equal than 7 % – no. (%)	536 (57.6)	230 (68.5)	---

*Missing triglyceride count or low-density lipoprotein-C count

Table S10. Multivariate Proportional Hazards for All-Cause and Cardiovascular Mortality at 5 Years: Subgroup Analysis of Patients with Missing Cardiometabolic Profile

	All-Cause Mortality*		Cardiovascular Mortality†	
	Hazard Ratio [95% CI]	**P-value**	**Hazard Ratio [95% CI]**	**P-value**
Age, years (continuous)	1.039 [0.993 – 1.086]	0.904	1.025 [0.963 – 1.090	0.441
Systolic blood pressure ≥130 mmHg	2.210 [0.967 – 5.051]	0.060	4.248 [1.270 – 14.205]	**0.019**
Hemoglobin A1c				
Between 6 and 7 %	Reference	---	Reference	---
Less or equal than 6 % – no. (%)	2.324 [0.623 – 8.670]	0.209	2.997 [0.604 – 14.867]	0.179
Greater or equal than 7 % – no. (%)	1.106 [0.395 – 3.097]	0.848	0.753 [0.186 – 3.044]	0.691

*A total of 336 patients (100% of eligible total) were included in the final model with analysis of 23 mortality events (6.8%).

†A total of 336 patients (100% of eligible total) were included in the final model with analysis of 12 mortality events (3.6%). Statin use was not associated with overall or cardiovascular mortality and was excluded from the model. There was no significant correlation between included covariates.

Table S11. Expanded Analysis for Systolic Blood Pressure Targets.

	Total Cohort (n=1550)	p-value	Low-Intermediate (n=1273)	p-value	High Risk (n=217)	p-value
Pre-Operative (30 to 90 days before surgery)						
Total measurements, mean	5.1 [4.1-6.0]		4.2 [3.2-5.2]		9.8 [6.3-13.3]	
Systolic blood pressure – no. (%)						
≥ 130 mmHg	303 (19.5)		227 (17.8)		28 (12.9)	
< 130 mmHg	190 (12.3)		156 (12.3)		68 (31.3)	
Unavailable	1057 (68.2)		890 (69.9)		121 (55.8)	
Univariate HR all-cause mortality						
SBP < 130 mmHg	Reference		Reference		Reference	
SBP ≥ 130 mmHg	1.293 [0.843-1.983]	0.240	1.513 [0.822-2.785]	0.184	0.742 [0.363-1.516]	0.413
Unavailable	0.779 [0.529-1.147]	0.206	0.759 [0.435-1.323]	0.331	0.725 [0.374-1.406]	0.342
Univariate HR CV-mortality						
SBP < 130 mmHg	Reference	0.471	Reference	0.991	Reference	0.722
SBP ≥ 130 mmHg	1.484 [0.758-2.909]	0.250	1.027 [0.366-2.885]	0.960	1.461 [0.491-4.344]	0.495
Unavailable	1.221 [0.669-2.229]	0.516	1.055 [0.448-2.483]	0.902	1.198 [0.418-3.435]	0.737
Peri-Operative (30 days before to 30 days after surgery)						
Total measurements, mean	107.5 [102.8-112.2]		99.1 [94.8-103.4]		128.0 [126.2-129.8]	
Systolic blood pressure – no. (%)						
≥ 130 mmHg	492 (31.7)		372 (29.2)		103 (47.5)	
< 130 mmHg	1054 (68.0)		900 (70.7)		114 (52.5)	
Unavailable	4 (0.3)		1 (0.1)		0 (0)	
Univariate HR all-cause mortality						
SBP < 130 mmHg	Reference		Reference		Reference	
SBP ≥ 130 mmHg	1.557 [1.207-2.008]	**<0.001**	1.766 [1.231-2.533]	**0.002**	0.907 [0.583-1.412]	0.667
Unavailable	16.648 [5.302-52.276]	**<0.001**	---	---	---	---
Univariate HR CV-mortality						
SBP < 130 mmHg	Reference		Reference		Reference	
SBP ≥ 130 mmHg	2.117 [1.503-2.981]	**<0.001**	2.331 [1.387-3.918]	**0.001**	1.180 [0.665-2.094]	0.571
Unavailable	22.724 [5.559-92.896]	**<0.001**	---	---	---	---

Post-Operative (30 to 90 days after surgery)						
Total measurements, mean	18.4 [14.8-22.0]		14.9 [11.2-18.6]		37.4 [25.1-49.8]	
Systolic blood pressure – no. (%)						
≥ 130 mmHg	454 (29.3)		353 (27.7)		454 (29.3)	
< 130 mmHg	467 (30.1)		394 (31.0)		467 (30.1)	
Unavailable	629 (40.6)		526 (41.3)		629 (40.6)	
Univariate HR all-cause mortality						
SBP < 130 mmHg	Reference		Reference		Reference	
SBP ≥ 130 mmHg	0.998 [0.732-1.359]	0.988	1.079 [0.709-1.643]	0.722	0.824 [0.490-1.385]	0.213
Unavailable	0.670 [0.494 0.909]	**0.010**	0.473 [0.302-0.740]	**0.001**	0.595 [0.333-1.065]	0.465
Univariate HR CV-mortality						
SBP < 130 mmHg	Reference		Reference		Reference	
SBP ≥ 130 mmHg	1.328 [0.856-2.061]	0.206	0.993 [0.525-1.876]	0.982	1.551 [0.745-3.229]	0.241
Unavailable	0.935 [0.608-1.436]	0.758	0.551 [0.293-1.033]	0.063	0.859 [0.370-1.991]	0.723

Figure S1. Unadjusted survival analyses between low-intermediate and high-risk patient coronary artery bypass graft patients at 5 years. Log rank, $p < 0.001$ for overall (*left*) and cardiovascular (*right*) survival analyses.

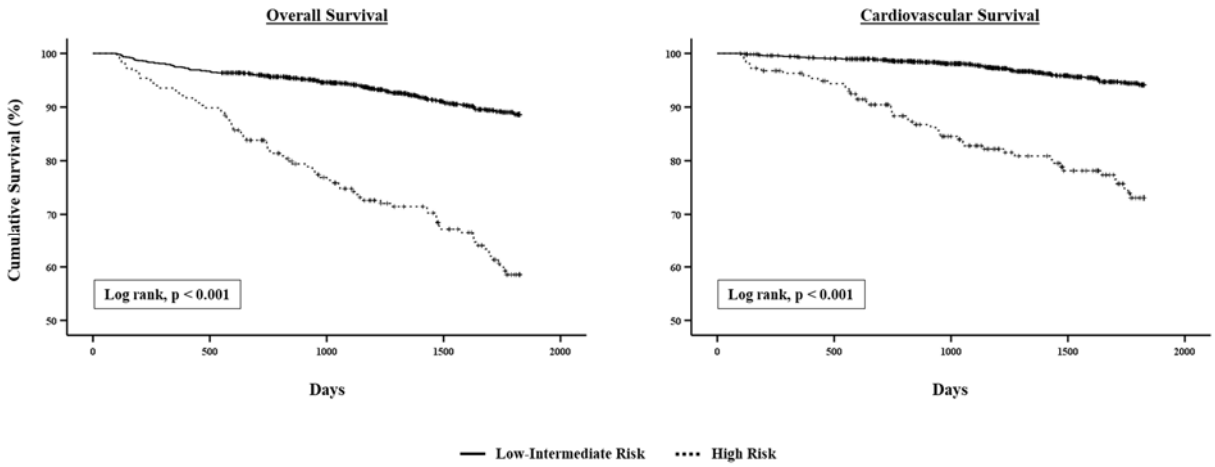

Figure S2. Unadjusted subgroup five year overall (left, $p < 0.001$) and cardiovascular (right, $p = 0.100$) survival analysis of low-intermediate risk patients with age greater or less than 65 years.

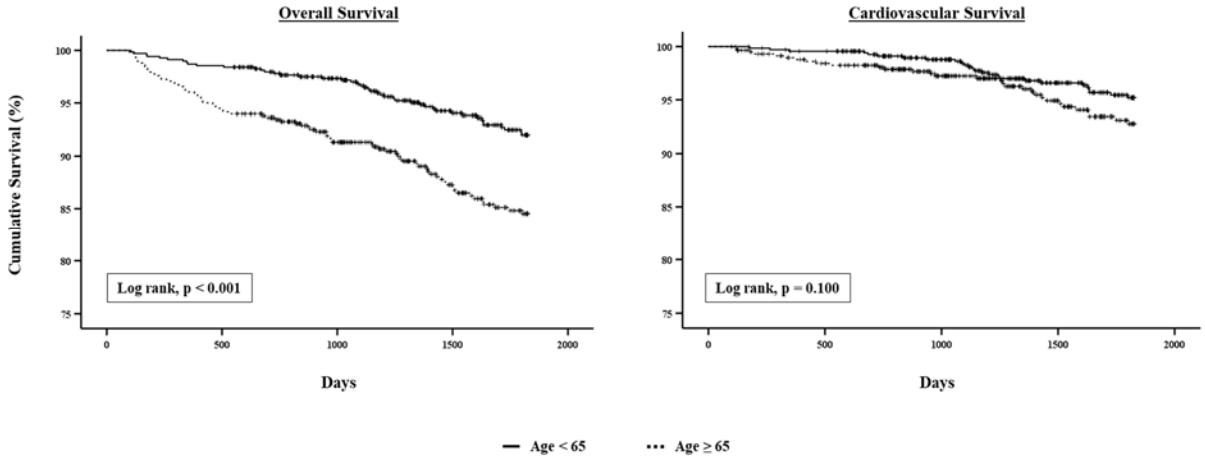

Figure S3. Unadjusted subgroup survival analysis of low-intermediate risk patients with (GFR < 90 mL/min) and without (GFR ≥ 90 mL/min) chronic kidney disease at 5 years. Overall (left) and cardiovascular (right) survival shown.

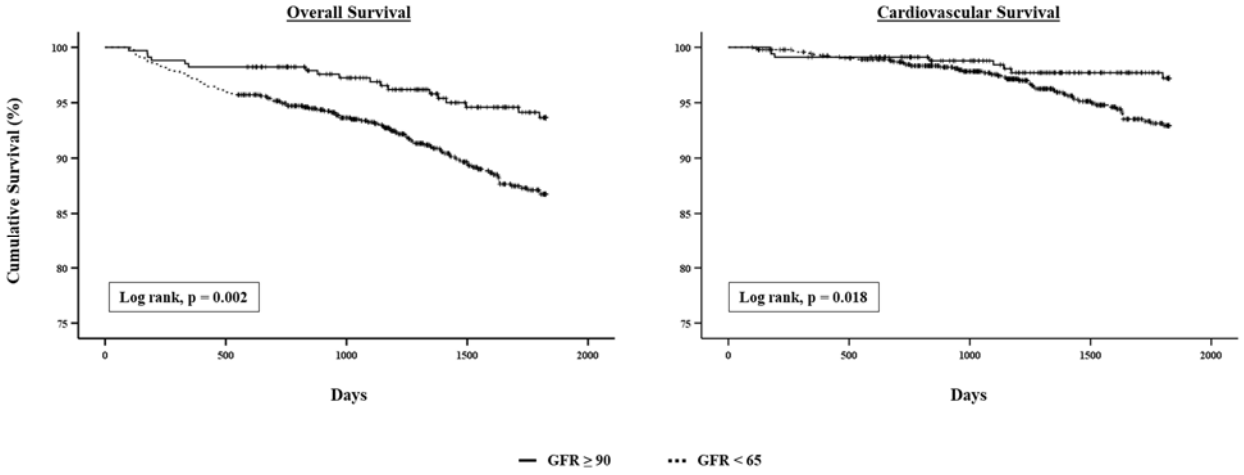

Figure S4. Unadjusted subgroup survival analysis of low-intermediate risk patients with preserved (EF ≥ 40 %) and reduced left ventricular ejection fraction (EF 25 – 40%) at 5 years. Overall (left) and cardiovascular (right) shown.

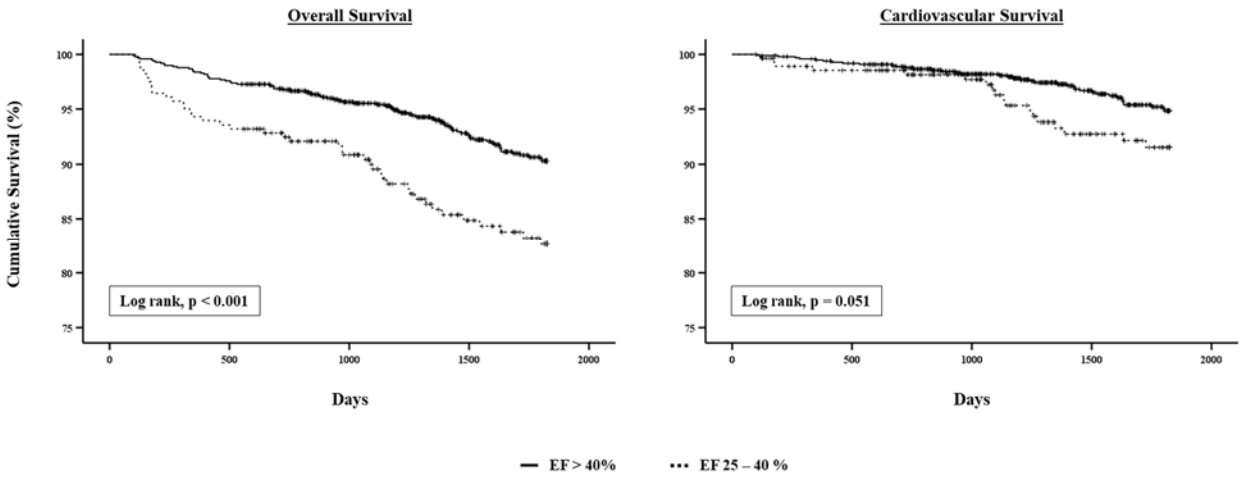

Figure S5. Unadjusted overall and cardiovascular survival analyses between patients with complete (n=937) and missing (n=336) triglyceride or LDL-C counts.