Repeat Coronary Revascularization after Coronary Artery Bypass Surgery in Older Adults: The Society of Thoracic Surgeons’ National Experience 1991-2007

Running title: Fosbol et al.; Revascularization after CABG

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Abstract:

**Background**—A major advantage of coronary artery bypass graft surgery (CABG) relative to percutaneous coronary intervention (PCI) is its durability, yet there is a paucity of information on rates and predictors of repeat coronary revascularization following CABG in the modern era.

**Methods and Results**—We included STS National Adult Cardiac Surgery Database patients ≥65 years undergoing first-time isolated CABG from 1991–2007 (n=723,134, median age 73 years). After linking to Medicare claims data, long-term outcomes of CABG (up to 18 years post-surgery) were examined using cumulative incidence curves. Multivariable Cox proportional hazard analysis was used to identify factors associated with 1-year and 5-year repeat revascularization trends and variability. We found that the overall 18-year survival rate was 20%.

Cumulative incidences of any repeat revascularization (PCI or CABG, yet most often PCI) were 2%, 7%, 13%, and 16% at 1, 5, 10, and 18 years post-surgery, respectively. The rates of repeat CABG procedures were quite low for all time points (0.1%, 0.6%, 1.3%, and 1.7%, respectively). Female gender, disease severity represented by a history of PCI, pre-operative dialysis, and partial revascularization were strongly associated with a higher revascularization rate; whereas advanced age, left main disease, and smoking were associated with a lower rate. There was approximately a two-fold variation in repeat revascularization rates across centers at 1 year (IQR 1.7%–3.6%) and at 5 years (IQR 6.7%–12.0%).

**Conclusions**—Repeat revascularization is infrequently performed among older patients who undergo CABG; however, these rates vary substantially by patient subgroups and among providers.

**Key words:** repeat coronary revascularization, older adults, coronary artery bypass surgery, revascularization
As the acute morbidity and mortality of coronary artery bypass graft (CABG) surgery progressively declines, long-term outcomes have become an increasingly more important consideration in decisions regarding revascularization. While patients undergoing CABG are generally thought to require fewer repeat revascularization procedures than those receiving percutaneous coronary intervention (PCI), information on contemporary rates of repeat revascularization following CABG is sparse. Although most previous studies have demonstrated finite longevity of saphenous vein grafts, there have been modern improvements in conduit harvesting techniques, greater use of arterial grafts (which have higher long-term patency), and secondary prevention—all of which may reduce the need for repeat revascularization. Conversely, the ability to treat saphenous vein graft disease using percutaneous interventional techniques has also evolved, which may have prompted more interventions over time.

There is currently limited information on contemporary rates of repeat revascularization following CABG surgery, and there is a clear need to establish national benchmarks for reference. Having access to this information is particularly important given that studies comparing CABG to PCI often examine revascularization rates. Using linked data from the Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database and the Centers for Medicare & Medicaid Services (CMS), we sought to: (1) determine long-term rates of repeat coronary revascularization (PCI and reoperative CABG) after initial CABG; (2) describe temporal trends in repeat revascularization; (3) identify patient-level factors associated with early and late repeat revascularization; and (4) determine whether these rates vary among hospital providers.
Methods

Data Sources/Study Population

Data Sources and Linkages

We identified isolated CABG procedures from the STS database (which includes detailed clinical information), and linked these records to Medicare Part A claims data from CMS. Though the STS database is limited to short-term follow-up, we have previously shown that STS data can be linked with CMS claims data to obtain longitudinal, long-term follow-up.3

Study Patients

We identified all patients in STS who underwent isolated CABG at STS-participating sites and who were discharged between January 1, 1991 and December 31, 2007; therefore, 18 years of outcomes data are available for this cohort. Patients were excluded from the cohort if they had a concomitant valve procedure or other cardiac procedure (other than the placement of pacemaker or ablation procedure for atrial fibrillation) or if the CABG status was emergent or salvage. Patients who underwent previous CABG (as defined in the STS database) were likewise excluded, but we included patients who had a prior PCI. We included only patients enrolled in fee-for-service Medicare parts A and B (Figure 1).

A subset of CABG patients who underwent surgery between 2001 and 2003 was used to analyze contemporary factors associated with 1 year and 1 to 5 year rates of repeat revascularization (Table 1).

Outcomes

The primary outcome for this study was repeat revascularization, identified as either CABG (International Classification of Diseases, Ninth Revision [ICD-9] procedure codes 36.10-36.19 in any claims procedure field) or PCI (ICD-9 procedure codes 00.66, 36.00, 36.06, 36.07, or 36.09
in any claims procedure field). Since Medicare data were used to assess outcomes and revascularizations, follow-up assessment was complete and independent of STS participation. To assess the competing risk of death, we also examined the association with all-cause mortality. Mortality was obtained through the Medicare beneficiary summary file and was available for analyses.

**Covariates**

In addition to the covariates used in prior CABG risk models, repeat revascularization might also be associated with partial revascularization during the index procedure. As a crude proxy for the latter, which is not specifically documented in the STS database, we created a covariate for anatomical revascularization completeness by subtracting the number of diseased vessels found preoperatively from the number of grafts placed, and categorized into the following groups: <0, 0, 1-2, and >2. To examine variation in repeat revascularization across sites, we selected all centers with more than 100 CABG cases per year in the database from 2001-2003.

**Statistical Analysis**

To identify statistical differences between groups, we used the Kruskal-Wallis test for continuous variables and \( \chi^2 \) tests for categorical variables. Longitudinal non-fatal outcomes after CABG were described using the cumulative incidence function and also by the Kaplan-Meier estimator, censoring patients at the time of death for sensitivity purposes. Similarly, we performed analyses for mortality in order to assess the degree of competing risk by death. For each surgical year, the revascularization rate at the end of the first year of follow-up was estimated by Kaplan-Meier estimator to show temporal trends in revascularization after CABG. Comparative temporal trends were also summarized using an averaged hazard ratio for revascularization over the first year following CABG, with year 1999 as the reference. Modeling
the cause-specific hazard function up to the end of the first year of follow-up, unadjusted and adjusted Cox regression was performed to obtain the hazard ratios for surgical years. A non-parsimonious Cox regression model included the following variables: age, gender, race (white, black, Asian, and other), body surface area, left ventricular ejection fraction, past or present smoker, hypertension, hypercholesterolemia, chronic lung disease, cerebrovascular disease, cerebrovascular accident, peripheral vascular disease, immunosuppressive treatment, diabetes (insulin, non-insulin, none), renal failure (dialysis-dependent, not dialysis-dependent, no renal failure), arrhythmia, angina (stable, unstable, none), history of myocardial infarction (<21 days, \( \geq 21 \) days, none), cardiogenic shock, pre-operative intra-aortic balloon pump or administration of inotropes, congestive heart failure (New York Heart Association [NYHA] class IV, NYHA class I-III, no heart failure), left main disease, number diseased coronary vessels (0, 1, 2, 3), previous percutaneous transluminal coronary angioplasty, number of previous cardiovascular interventions (0, 1, 2 or more), and acuity status (urgent, elective).

Missing data in the baseline characteristics (used for the adjusted temporal trend analysis) were estimated using multiple imputations, assuming they were missing at random. The multiple imputation procedure was performed using R software (www.R-project.org) with the add-on library package Multivariate Imputation by Chained Equations, which generates multiple imputations for incomplete multivariate data by Gibbs sampling.\(^4\) Imputation was performed separately for each calendar year using the covariates from the multivariate Cox model plus logarithms of the survival time, the time-to-CABG, the time-to-PCI, and the corresponding censor indicators. Ten complete imputed datasets were created, risk adjusted analyses were performed separately for each of these datasets, and the ten sets of results were then combined using the method of Rubin.\(^5\)
Finally, a subset of the population (procedures performed during 2001-2003) was used to examine factors significantly associated with both early (≤1 year) and late (1-5 years) revascularization. Previously reported patient-level predictors for long-term survival following CABG, year of surgery, and relevant hospital characteristic variables were included in the multivariate Cox regression model with time-dependent coefficients (for two time periods: ≤1 year and 1-5 years). This can be viewed as two separate Cox regressions: (1) predictor inference for ≤1 year revascularization was obtained by modeling the cause-specific hazard function up to the end of the first year of follow-up; and (2) predictor inference for 1-5 year revascularization was obtained by a similar regression conditional on patients who are event-free and survived to 1 year, with maximal 4-year follow-up (i.e., censoring alive, event-free patients at the end of 4-years of follow-up). The second Cox regression is comparable to a landmark analysis.

In order to assess variability in revascularization at the hospital-level, we calculated the crude revascularization rates at 1 year and at 5 years and illustrated these using box plots. The cohort was further stratified according to pre-defined subgroups of interest: gender, pre-operative dialysis, age groups (65-69, 70-74, 75-79, and 80+ years), prior PCI, diabetes, and completeness of revascularization. The results are shown in Supplemental Figure 1.

A P value <0.05 was considered statistically significant. All analyses were performed using the SAS software package (SAS 9.2, SAS Institute, Cary, North Carolina, USA).

Results

A total of 723,134 patients undergoing first-time isolated CABG between 1991 and 2007 were included in this study after applying inclusion/exclusion criteria (Figure 1). Overall, 15.4% of patients were excluded due to prior CABG or emergent/salvage status and an additional 26.9% were excluded because of unsuccessful linkage or Medicare Part A eligibility only. Baseline
characteristics are shown in the Table for the overall cohort (1991-2007) and for the subset (2001-2003) used for identifying factors associated with 1- and 1- to 5-year repeat revascularization. The overall cohort had a median age of 73 years (interquartile range [IQR] 69-77 years) and the majority of patients were men (75.8%). Maximum duration of follow-up was 18 years with a median of 8.0 years (IQR 4.4-11.8 years). For the subset of patients operated on between 2000 and 2003, the median follow-up was 6.9 years (IQR 5.9-7.9 years).

Figure 2 shows the long-term longitudinal mortality and repeat revascularization outcomes over the 18 years of follow-up (cumulative incidence). By 18 years, only 20% of this elderly original sample was still alive. Cumulative incidences of repeat revascularization were 2%, 7%, 13%, and 16% at 1, 5, 10, and 18 years post-surgery, respectively. The mode of revascularization was almost always PCI (93% of patients who underwent repeat revascularization). The cumulative incidence rates of repeat CABG were quite low at all investigated time points (0.1%, 0.6%, 1.3%, and 1.7% at 1, 5, 10, and 18 years post-surgery, respectively). Conditional on patients having survived, the overall rate of repeat revascularization at 1, 5, 10, and 18 years post-surgery were 2%, 8%, 16%, and 25%, respectively (Supplemental Figure 2). Supplemental Figure 1 illustrates that older patients were less likely than younger patients to be revascularized. For the youngest age group of patients (65-69 years old), the repeat revascularization rate at 18 years post-surgery was 30%, and the age-group curves separated very clearly after approximately 6 years. In contrast, the 80+ age group had an 18-year revascularization rate of 11%. Moreover, the young age group had a higher repeat CABG rate at 18 years (4.5% vs. 0.5% for those 80 years of age and older, P<0.001). Other factors associated with a higher rate of repeat revascularization included female sex, diabetes, prior PCI, dialysis, and suboptimal revascularization.
Figures 3A and B show the temporal trends in short- and long-term revascularization rates. There was an increasing repeat revascularization rate from 1991 to 2004, after which the rate decreased slightly. This trend was still evident after comprehensive adjustment for confounders (data not shown).

Factors Associated with Repeat Revascularization

Figure 4 illustrates factors statistically significantly associated with 1- and 5-year repeat revascularization as determined by landmark Cox regression analysis. After multivariate adjustment, younger age at baseline and female sex were associated with higher rates of repeat revascularization both at 1-year and between 1 and 5 years. Obesity was associated with a lower likelihood of repeat revascularization at 1-year, but a higher rate between 1 and 5 years postsurgery. Atrial fibrillation showed a similar inverse relationship as a function of time. Relative to “complete revascularization” (grafts placed minus diseased vessels = 0), partial revascularization was associated with a higher short- and long-term likelihood of repeat revascularization.

We used the subset of patients from 2001-2003 to examine variability in repeat revascularization at 1 and between 1 and 5 years at the hospital-level (Figure 5). Overall, variability in repeat revascularization rates was approximately two-fold between sites (IQR 1.7% to 3.6% for 1 year revascularization rates, and 6.7-12.0% for 1-5 years post-surgery).

Discussion

Our study examined repeat revascularization among older Medicare adults who had undergone CABG. We had four major findings. First, repeat revascularization rates after CABG in older individuals are generally low and are almost always PCI, with very low rates of repeat CABG. Second, the overall rates of repeat revascularization after CABG have risen slightly over time,
with an increasing use of PCI and declining use of repeat CABG. Third, rates of repeat revascularization following CABG varies among patient subgroups, and the factors associated with early (≤1 year) and late (1-5 years) repeat revascularization sometimes differ. Finally, there is two-fold variation in repeat revascularization rates across centers.

Historically, the need for repeat revascularization after CABG was driven both by the progression of native vessel disease and by relatively low rates of vein graft patency.\textsuperscript{1,7-10} Clinical registry and trials data have shown a repeat revascularization rate of about 5% at 5 years post-surgery,\textsuperscript{10} but these prior studies were limited in size, types of centers, and duration of follow-up.\textsuperscript{1,7,8,10,11} Over an 18-year time frame, our study was able to document a low rate of repeat revascularization after CABG among patients aged 65 years and older. Less than 10% of CABG patients required a repeat revascularization procedure within 5 years, 13% within 10 years, and only one in six patients who survive 18 years underwent a repeat procedure. By 10 years, this rate is only approximately 13%. By 18 years, less than one in 25 will require a repeat CABG procedure. The observed lower rate of repeat revascularization may reflect differences in the rate of progression of atherosclerosis in the elderly, higher contemporary usage of arterial grafting for CABG, and the near universal use of statin drugs, which have mitigated the development of both native vessel and vein graft disease. Importantly, we were only able to study patients over the age of 65 years; therefore, rates of repeat revascularization could be substantially higher in younger post-CABG patients. Supporting that hypothesis, we did see a substantial decline in repeat revascularization rates as a function of age, and rates of repeat CABG were also higher among the youngest group of patients. For patients older than 70 years, the need for repeat revascularization is minimal. In contrast, our results suggest that among CABG patients aged 65-69 years, almost one-third will be revascularized at least one more time.
during the subsequent 18 years. Nevertheless, among those 65-69 years, the rate of repeat CABG remained under 5% during this long term follow-up. Our results also show that revascularization rates have varied over time. Repeat CABG rates have been steadily declining from 1991 to 2007, though the absolute changes are small. Conversely, the use of PCI steadily increased from 1991 to 2004, after which it declined for unclear reasons.

Numerous factors were associated with short- and long-term repeat revascularization. Age, left main disease, smoking, and complete revascularization were associated with lower short- and long-term revascularization rates, whereas female gender, cardiovascular risk factors, left ventricular ejection fraction, unstable angina, and dialysis were associated with higher rates of repeat revascularization. Interestingly, the association between body mass index and repeat revascularization rates completely reversed over time. Obese patients had lower rates of repeat revascularization at 1 year relative to those with normal body mass index at surgery; however, between 1 and 5 years, the obese patients had a higher likelihood of being revascularized compared with those who had a normal weight at the time of their initial surgery.

Prior studies have shown that standard cardiovascular risk factors are closely related to subsequent CABG graft failure.2,12-15 Our results suggest further opportunities for identifying categories of patients with higher odds of requiring repeat revascularization, due to graft failure or progression of native vessel disease (Supplemental Figure 1).

Our study showed two-fold variation between centers for repeat revascularization with 10, 90 percentiles of 1.1% and 5.1% at 1 year and 5.1% and 14.5% from 1 to 5 years post-surgery. Rates of repeat revascularization are a potential measure of hospital performance after CABG, and the variability in these rates across STS sites in the current study lends support to this strategy.
Limitations

Our study has several limitations. First, the STS database gathers information from a large sample of hospitals in the United States, but the registry is voluntary. Nevertheless, the STS database now encompasses about 95% of all United States cardiac surgery programs, and results derived from it should at least be generalizable within this country. This being said, our selection criteria excluded a substantial number of CABG patients in order to create a homogenous and meaningful cohort; therefore, interpretation of the present study is only applicable to the selected cohort, and consequent extrapolation should be done cautiously. Second, this study was limited to patients aged 65 and older who could be followed through Medicare part A claims files; therefore, we cannot necessarily extrapolate our results regarding repeat revascularization following CABG to younger patients. However, given that the median age of isolated CABG patients in the United States was 65 years (IQR 58-73) in 2011, our study population should be quite representative.16 Third, we did not have any information regarding the indication for repeat revascularization, nor about subsequent studies such as stress testing and echocardiography. Fourth, our models used repeat revascularization as the outcome, and death will be a natural competing outcome for this nonfatal event. We analyzed the data using cause-specific Cox proportional hazard models and censored patients at death, acknowledging that this may result in an underestimation of repeat revascularization rates. In addition, cumulative incidence rates were also reported for revascularization and these results are methodologically influenced by mortality; revascularization rates are naturally low if mortality is high and the measure represents the actual observed rate in the baseline cohort. Finally, all observed results for our metric of revascularization completeness should be interpreted cautiously. Our findings are interesting and should be further examined in a database with further angiographic detail.
Conclusions

The rate of repeat revascularization after CABG in older individuals is low during nearly two decades of follow-up, and the vast majority of procedures during this time are PCIs. Repeat revascularization rates have increased slightly over time, but remain low—approximately 2-3% of patients will be revascularized annually. Important factors associated with higher rates of repeat revascularization at 1 and 5 years post-surgery included younger age and female sex, traditional cardiovascular risk factors for atherosclerosis, and incomplete revascularization. We observed modest variation in rates of repeat revascularization among centers in the STS database. The information provided in this report provides national benchmarks that should be useful in future studies dealing with revascularization.

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Conflict of Interest Disclosures: Dr. Peterson reports research funding from Eli Lilly & Company, Ortho-McNeil-Janssen Pharmaceuticals, Inc., Society of Thoracic Surgeons, American Heart Association, and the American College of Cardiology (all significant); consulting for AstraZeneca, Boehringer Ingelheim, Genentech, Johnson & Johnson, Ortho-McNeil-Janssen Pharmaceuticals, Inc., Pfizer, Sanofi-Aventis, and WebMD (all modest). All of Dr. Peterson’s disclosures can be found at: www.dcri.org. The remaining authors have no disclosures to report.
References:


Table 1. Baseline Characteristics for Overall Cohort and those Done between 2001 and 2003.

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<tr>
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<td>73 (69-78)</td>
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<td>Race, %</td>
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<td><strong>Surgery characteristics</strong></td>
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<td>Renal failure, %</td>
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BMI indicates body mass index; IQR, interquartile range
Figure Legends:

**Figure 1.** Patient Selection. Flow chart displaying patient selection.

**Figure 2.** Long-term Revascularization Rates after CABG. Cumulative incidence for long-term revascularization rates after CABG according to mode of revascularization. CABG indicates coronary artery bypass graft surgery; PCI, percutaneous coronary intervention

**Figure 3.** Revascularization Rates by Calendar Year. Annual (Figure 3A) and 5-year (Figure 3B) revascularization rates according to calendar year. CABG indicates coronary artery bypass graft surgery; PCI, percutaneous coronary intervention

**Figure 4.** Factors Associated with Revascularization. Factors associated with 1 years and 5 years revascularization after CABG. BMI indicates body mass index; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention

**Figure 5.** Revascularization Rates across Centers. Box plot illustration of the variability in 1 and 5 year revascularization rates across centers.
Patients in the STS adult database with Isolated CABG surviving to discharge (1991-2007) and age ≥ 65 years
N=1,304,008

Excluded:
Prior CABG or emergent/salvage status (N=201,050)
Unsuccessful linkage or Medicare part A only patients (N=350,221)

Patients with isolated CABG. STS linked to Medicare claims
N=752,737

Excluded:
Medicare Part A only patients (N=29,603)

Patients with complete data and follow-up (1991-2007)
N=723,134 (1036 STS sites)

Excluded:
Patients operated before 2001 or after 2003 (N=527,836)

N=195,298 (588 STS sites)
Figure 2

Cumulative incidence rate (in %) vs. Time since surgery (in years)

- CABG
- Revasc. (PCI or CAGB)
- PCI
- Death
Figure 3A
Figure 3B

Kaplan-Meier probability (%)

Rate of revascularization 5 years after surgery

Surgical year


CABG  PCI
Figure 4

Demographics:
- Age, per 10 year increment
- Female vs. Male
- Race: Black vs. white
- Race: Hispanic vs. white
- Race: Asian vs. white
- Race: Other vs. white

History of:
- PCI
- Atrial fibrillation
- Hypertension
- Insulin dependent diabetes
- Non-insulin dependent diabetes
- Peripheral vascular disease

Preoperative characteristics:
- BMI <=20 vs. 21-30
- BMI 21-35 vs. 21-30
- BMI >35 vs. 21-30
- LVEF, per 10% increment
- Unstable angina
- Left main disease
- Current smoker
- Aortic gradient, by 10 mmHg
- No of diseased vessels: 3
- Dialysis
- Grafts minus diseased vessels
  - <0 vs. 0
  - 1-2 vs. 0
  - >2 vs. 0
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SUPPLEMENTAL MATERIAL
Supplemental Figure 1. Revascularization Rates Per Subgroups, Kaplan-Meier Probability (%)

Long-term revascularization rates according to: (A) gender, (B) age groups, (C) diabetes, (D) prior PCI, (E) pre-operative dialysis, and (F) completeness of revascularization.
Supplemental Figure 2. Long-term Revascularization Rates after CABG

Kaplan-Meier estimation of long-term revascularization rates after CABG according to mode of revascularization.

CABG indicates coronary artery bypass graft surgery; PCI, percutaneous coronary intervention.