**Long-Term Mortality Follow-up of Radial Artery vs Saphenous Vein in Coronary Artery Bypass Grafting; A Multicenter, Randomized Trial**

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**Running Title:** Long-Term Follow-up Radial Artery Grafting CABG

There is debate about whether radial artery (RA) grafts are better conduits than saphenous vein grafts (SVG) for patients undergoing coronary artery bypass grafting (CABG). Our Department of Veterans Affairs multicenter, randomized controlled trial (RCT) (NCT00054847*) showed no difference in graft patency up to one year[1]. Here we report a post-hoc analysis of long-term all-cause mortality in the 726 of 733 participants who consented to follow-up via VA health care databases. The study was approved by each site's institutional review board; written informed consent was obtained from each patient before screening.[1] As in the source trial, baseline, operative, and surgical characteristics were balanced between the groups (data not shown). The only difference was longer time in the intensive care unit for patients with RA grafts. Survival was measured from randomization to death or February 15, 2021 (when mortality was extracted from the VA database), whichever was earlier. The median survival was 14.6 years for SVG and 14.2 years for RA grafts (log rank test P=0.89) (Figure 1). After adjustment for pre-specified covariates including age, Canadian Cardiovascular Society Angina Class, smoking status, total cholesterol, high-density lipoprotein, triglycerides, diabetes, hypertension, and heart failure, there was no difference in mortality between the two graft types (adjusted hazard ratio 1.12, 95%CI 0.91 to 1.38). We conducted post-hoc subgroup analyses using Cox proportional hazards models baseline variables that were included in the model associated with survival <0.05. The subgroups included: age (<65 vs. ≥65 years), smoking status (never, past, current), diabetes, hypertension, and triglycerides (<150 vs. ≥150 mg/dL). Survival did not differ significantly between graft types for any of the subgroups examined. None of the graft type by subgroup interactions were statistically significant.

Some observational data have associated radial artery use with reduced all-cause mortality.[2] Those outcomes are likely influenced by surgeon expertise and imperfect risk-adjustment. The latter cannot account for residual confounding due to unmeasured variables including patient frailty, target vessel and conduit size and quality, and target vessel stenosis. Therefore, there is a risk of bias introduced by healthier patients with better targets receiving radial grafts. No RCT has demonstrated a survival advantage of radial artery versus SVG. Most RCTs have focused on short to mid-term graft patency or clinical outcomes. However, longer follow-up is critical to determining whether radial artery grafting is more effective than SVG, because failure of SVG typically occurs 5 to 10 years after CABG. Only the Radial Artery Patency and Clinical Outcomes (RAPCO) Trial was designed to look at long-term clinical outcomes and reported for RA vs SVG 10-year patency of 85% vs 71%, and 10-year patient survival of 72.6% vs 65.2%. The RAPCO trial was limited by small patient numbers (n=225) and excluded patients younger than 70 years old. Our trial had no adult age restriction and almost 18 years of follow-up.

An individual participant data meta-analysis with a median follow-up of 10 years showed a reduction in the composite of death, myocardial infarction, or repeat revascularization with RA vs SVG.[3] This study incorporated six small studies (1036 patients), mainly at non-United States centers with established expertise in radial artery grafting. Among those trials, strict patient and target selection criteria were universal and included surgeons with extensive experience in radial artery grafting. Thus, their outcomes may not be generalizable to the average surgical practice. In our study there were no

requirements for radial artery grafting experience at the 11 centers. Critics may explain the non-superiority of the radial artery graft in our study based on lower quality of radial grafting. However, our perioperative mortality (0.5% in SVG and 0.8% in RA), graft patency rates at one week (97%) and one year (89%) across the two groups and internal thoracic artery ITA graft patency at one year (96%)[5] compare favorably with other studies. Our findings are consistent with no incremental benefit towards survival beyond that achieved by a patent left ITA (LITA) to the LAD. Data sharing is available from the VA Cooperative Studies Program (see Funding Source).

The choice of the second-best conduit to supplement the LITA to LAD is unsettled. The 2016 Society of Thoracic Surgeons (STS) arterial conduits guidelines encouraged (Class IIa recommendation) the use of radial arteries in selected patients as a supplement to LITA to the LAD. The 2021 ACC/AHA/SCAI Coronary Revascularization guidelines assigned radial artery use a class I (standard of care) recommendation[4], but this was challenged and not endorsed by the AATS and STS or the European Association of Cardio-Thoracic Surgery because of lack of robust supporting evidence. Importantly, the lack of support for using the radial artery as a preferred conduit during CABG has resulted in it being used <10% of the time in the United States.[5] Our findings do not support the use of the radial artery as a class 1 recommendation.

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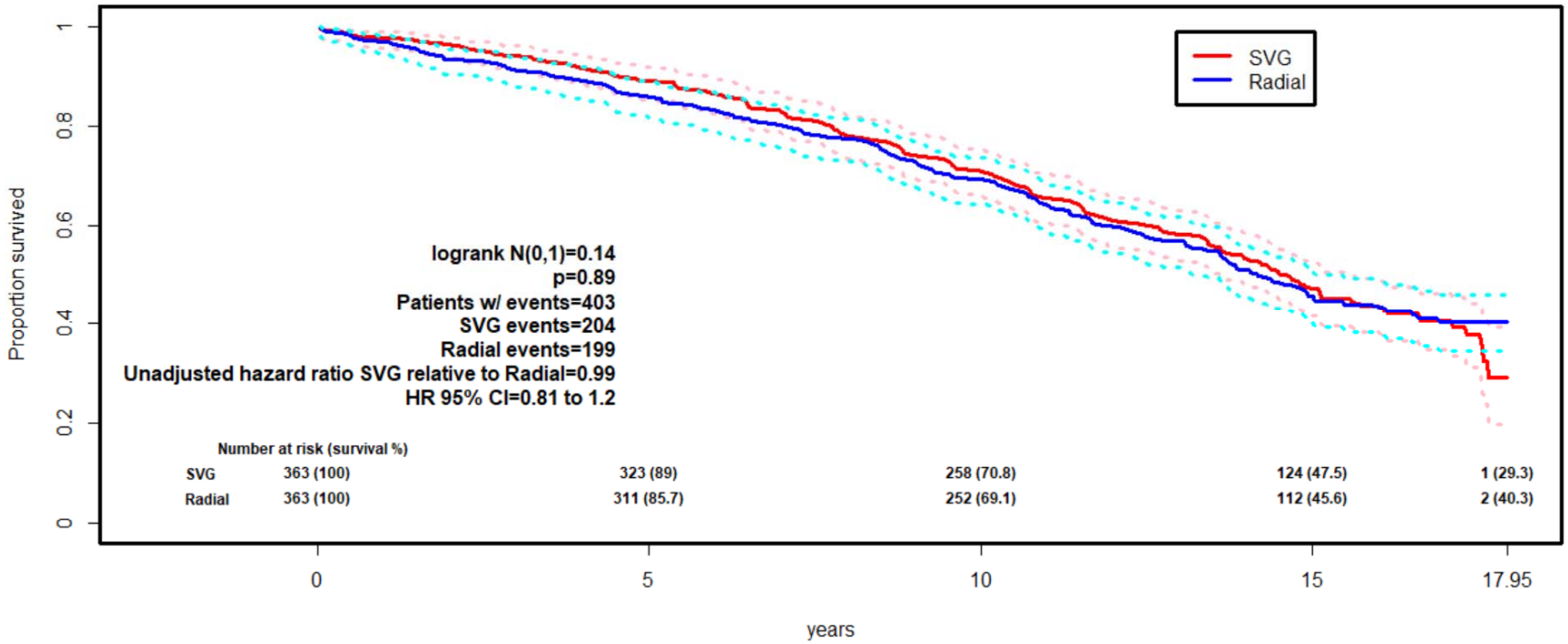
**Figure 1.**

Kaplan Meier survival curve in patients entered into the study. Patients who received saphenous vein grafts (SVG) are shown in red and patients who received radial artery grafts (RA) are shown in blue (95% confidence intervals are in pink for SVG group and in cyan for RA group). There is no difference in survival up to 17.95 years after Coronary Artery Bypass Grafting (CABG). The number of patients at risk at each 5-year interval is shown on the X-axis.


SVG
Radial
logrank N(0,1)=0.14
p=0.89
Patients w/ events=403
SVG events=204
Radial events=199
Unadjusted hazard ratio SVG relative to Radial=0.99
HR 95% CI=0.81 to 1.2
Number at risk (survival %)
SVG 363 (100) 323 (89) 258 (70.8) 124 (47.5) 1 (29.3)
Radial 363 (100) 311 (85.7) 252 (69.1) 112 (45.6) 2 (40.3)
Proportion survived
0
0.2
0.4
0.6
0.8
1
0
5
10
15
17.95
years

## Article Information

https://clinicaltrials.gov (Trial Registration clinicaltrials.gov Identifier: NCT00054847)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