Complete Coronary Revascularization and Outcomes in Patients Who Underwent Coronary Artery Bypass Grafting: Insights from The REGROUP Trial

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There is growing evidence in support of coronary complete revascularization (CR). Nonetheless, there is no universally accepted definition of CR in patients who undergo coronary bypass grafting surgery (CABG). We sought to investigate the outcomes of CR, defined as surgical revascularization of any territory supplied by a suitable coronary artery with ≥50% stenosis. We performed a preplanned subanalysis in the Randomized Trial of Endoscopic or Open Saphenous Vein Graft Harvesting (REGROUP) clinical trial cohort. Of 1,147 patients who underwent CABG, 810 (70.6%) received CR. The primary outcome was a composite of major adverse cardiac events (MACEs), including death from any cause, nonfatal myocardial infarction, or repeat revascularization over a median 4.7 years of follow-up. MACE occurred in 175 patients (21.6%) in the CR group and 86 patients (25.5%) in the incomplete revascularization (IR) group (hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.67 to 1.13, p = 0.29). A total of 97 patients (12.0%) in the CR group and 48 patients (14.2%) in the IR group died (HR 0.93, 95% CI 0.65 to 1.32, p = 0.67); nonfatal myocardial infarction occurred in 49 patients (6.0%) in the CR group and 30 patients (8.9%) in the IR group (HR 0.76, 95% CI 0.48 to 1.2, p = 0.24), and repeat revascularization occurred in 62 patients (7.7%) in the CR group and 39 patients (11.6%) in the IR group (HR 0.64; 95% CI 0.42 to 0.95, p = 0.027). In conclusion, in patients with a great burden of co-morbidities who underwent CABG in the REGROUP trial over a median follow-up period of a median 4.7 years, CR was associated with similar MACE rates but a reduced risk of repeat revascularization. Longer-term follow-up is warranted. **(Am J Cardiol 2024;217:127−135)**

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The guiding principle of coronary revascularization, whether through percutaneous catheter intervention (PCI) or coronary bypass grafting surgery (CABG), is to provide improved blood flow to areas affected by ischemic heart disease and supplied by a suitable (≥1.5 mm in diameter) coronary artery.[1−4] Controversy, however, exists as to the optimal way to achieve that goal, the correct way to define coronary complete revascularization (CR), and whether it makes a clinically significant difference in CABG. At 1 end of the spectrum, when examined in the setting of ST elevation myocardial infarction (MI) without cardiogenic shock, the best available data from randomized controlled trials involving PCI indicate an improvement in major adverse cardiac events (MACEs) comprising all-cause mortality, nonfatal MI, and need for repeat revascularization when patients achieve CR, as defined as treatment of not only the culprit lesion but any lesion in a suitable coronary artery that is angiographically >70% stenosed, or lesions stenosed between 50% and 69% with a reduction of fractional flow reserve (FFR) <0.8.[5] This difference exists in stable ischemic heart disease but to a less profound degree. In the ISCHEMIA trial, CR through both anatomic and functional definitions involving PCI, CABG, and hybrid revascularization showed no statistically significant difference in cardiovascular death or

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MI compared with incomplete revascularization (IR) after adjustment.[6] Although no randomized controlled trials exist exclusively for CABG, some retrospective reviews, such as that by Bianco et al, showed a significant reduction in MACEs and major adverse cerebrovascular events (hazard ratio [HR] 0.82; 95% confidence interval [CI] 0.7 to 0.95, p = 0.01).[7]

Conceptually, this paves the way for an anatomic definition of CR that defines territories at risk as those with an angiographic definition of significant obstruction.[2] Although a functional definition also exists, no substantial differences between anatomic and functional CR have been indicated. Given the paucity of evidence available and the lack of randomized studies prospectively comparing planned CR with IR, no formal recommendation for CR in CABG was made in the most recent guidelines.[8] This was mirrored in the European guidelines published in 2018, which acknowledged published variable outcomes and a trend toward favorability for CR but failed to offer a commitment statement.[1] Additional alternative adjuncts to angiography such as FFR and instantaneous wave/free ratio (iFR) have been evaluated as guides to a more "functional" revascularization but thus far have not shown a clear benefit in terms of graft patency and MACE. In a 2018 study, Thuesen et al revealed, in a randomized controlled trial, that patients randomly allocated to FFR versus angiography-guided revascularization had fewer grafts (2.6 vs 3) but similar graft failure rates (11 [28%] vs 11 [33%], p = 0.64 for FFR vs angiography-guided revascularization plan).[9] Although we do not have randomized controlled trial data regarding iFR-guided CABG, an inverse relation between graft patency and iFR values has been shown in retrospective studies[10]; whether this translates into a clinical benefit remains not known. This contrasts with PCI in which a functional component to revascularization has previously been shown to improve MACE outcomes, with fairly similar results, both in the short term and up to 5 years, in iFR and FFR.[11−13]

We hypothesized that the greatest clinical benefit would be observable with the broadest definition seen in a population with high rates of cardiovascular disease risk factors, such as those with diabetes, tobacco use, and cerebral and peripheral vascular disease. Our primary outcome was focused on MACEs, with secondary outcomes of the components of MACE that included death from any cause, nonfatal MI, or repeat revascularization.

The REGROUP[14−16] trial was a randomized controlled trial performed in the unique population of the Veterans Affairs healthcare system that compared endoscopic with open saphenous vein harvesting in patients who underwent CABG for primarily elective or urgent indications. Its major findings showed no significant difference in outcomes between the endoscopic group and open saphenous vein harvest, including the rate of revascularization. Patients in the REGROUP trial were older (average age 66 ± 7 years) and more likely to be diabetic (51.8%), active smokers (47%), hypertensive (90%), and dyslipidemic (85%) and to have a history of stroke (8.4%). This presented an opportunity to retrospectively review a substantially co-morbid cohort to better understand whether we would see a dampened or amplified effect of CR versus IR.

Methods

We performed a post hoc analysis of the REGROUP trial cohort comparing the composite and individual outcomes of MACE in patients with CR, defined as surgical revascularization of any territory supplied by a suitable coronary artery with ≥50% stenosis, with the outcomes of those with IR over the active and passive follow-up phases (median of 4.7 years). The determination of complete versus incomplete revascularization was performed retrospectively with review of the preoperative angiography and angiography report, and this was compared with the operative notes and vessels bypassed. The trial enrolled patients from March 2014 to April 2017 at 16 Veterans Affairs cardiac surgery centers in the United States. The institutional review board (IRB) or equivalent ethics committee of each participating center approved the study protocol and publication of data (Cooperative Studies Program 588 IRB 2694 approved August 14, 2013). The patients provided informed written consent for the publication of the study data. The demographics of the patients are listed in Table 1. The definition of CR used was a surgical bypass for any lesion with >50% stenosis in a suitable coronary artery (≥1.5 mm in diameter). From the original population of 1,147 patients who underwent surgery, 810 patients (70.6%) received CR, and 337 patients had IR (29.4%). The primary outcome was MACE as defined as all-cause death, nonfatal MI, or the need for repeat revascularization intervention (redo CABG or PCI).

Table 1
Assessment of outcomes of CR vs IR

	Complete Revascularization (n=810) n (%)	Incomplete Revascularization (n=337) n (%)	Hazard Ratio	95% Confidence Interval	P-value*
Death from any cause	97 (12.0)	48 (14.2)	0.91	0.64 to 1.3	0.6
Composite of death, myocardial infarction and revascularization	175 (21.6)	86 (25.5)	0.85	0.65 to 1.11	0.23
Acute myocardial infarction	49 (6.0)	30 (8.9)	0.729	0.46 to 1.17	0.19
Repeat revascularization	62 (7.7)	39 (11.6)	0.630	0.42 to 0.94	0.025

* p Values from Cox proportional hazards model adjusted for chronic renal disease, peripheral vascular disease, cerebral vascular disease, smoking status, STS risk of mortality, previous MI, graft types (arterial, venous), SYNTAX score, age, NYHA class, diabetes, and angina.

Table 2
Demographics of the complete and incomplete revascularization subgroups

	Statistic	Complete (N= 810)	Incomplete (N= 337)	Total (N=1147)	P-value
Age	n	810	337	1147	0.67
	Mean (SD)	66.5 (7.00)	66.2 (6.65)	66.4 (6.90)	
Biological Sex	n	810	337	1147	0.68
Male	n (%)	805 (99.4)	336 (99.7)	1141 (99.5)	
Female	n (%)	5 (0.6)	1 (0.3)	6 (0.5)	
Race or ethnic group	n	810	337	1147	0.23
American Indian or Alaskan Native	n (%)	4 (0.5)	2 (0.6)	6 (0.5)	
Asian or Pacific Islander	n (%)	9 (1.1)	1 (0.3)	10 (0.9)	
Black, not of Hispanic origin	n (%)	66 (8.1)	25 (7.4)	91 (7.9)	
Hispanic	n (%)	49 (6.0)	13 (3.9)	62 (5.4)	
White, not of Hispanic origin	n (%)	676 (83.5)	296 (87.8)	972 (84.7)	
Other	n (%)	6 (0.7)	0 (0.0)	6 (0.5)	
Body Mass Index	n	809	337	1146	0.99
	Mean (SD)	30.4 (5.14)	30.5 (5.24)	30.4 (5.17)	
Hypertension	n	810	337	1147	0.54
No	n (%)	77 (9.5)	36 (10.7)	113 (9.9)	
Yes	n (%)	733 (90.5)	301 (89.3)	1034 (90.1)	
Hyperlipidemia	n	810	337	1147	0.73
No	n (%)	112 (13.8)	44 (13.1)	156 (13.6)	
Yes	n (%)	698 (86.2)	293 (86.9)	991 (86.4)	
Diabetes	n	810	337	1147	0.3
No	n (%)	412 (50.9)	160 (47.5)	572 (49.9)	
Yes	n (%)	398 (49.1)	177 (52.5)	575 (50.1)	
Insulin Dependent	n	398	177	575	0.43
Yes	n (%)	177 (44.5)	85 (48.0)	262 (45.6)	
No	n (%)	221 (55.5)	92 (52.0)	313 (54.4)	
Chronic Renal Disease	n	810	337	1147	0.021*
No	n (%)	712 (87.9)	279 (82.8)	991 (86.4)	
Yes	n (%)	98 (12.1)	58 (17.2)	156 (13.6)	
Peripheral Vascular Disease	n	810	337	1147	0.093
No	n (%)	706 (87.2)	281 (83.4)	987 (86.1)	
Yes	n (%)	104 (12.8)	56 (16.6)	160 (13.9)	
Cerebral Vascular Disease	n	810	337	1147	0.051
No	n (%)	723 (89.3)	287 (85.2)	1010 (88.1)	
Yes	n (%)	87 (10.7)	50 (14.8)	137 (11.9)	
Smoking Status	n	807	336	1143	0.004*
Never smoked	n (%)	191 (23.7)	68 (20.2)	259 (22.7)	
Current smoker (last use < 1 year)	n (%)	199 (24.7)	115 (34.2)	314 (27.5)	
Former smoker (last use ≥ 1 year)	n (%)	417 (51.7)	153 (45.5)	570 (49.9)	
Chronic Lung Disease	n	810	337	1147	0.44
No	n (%)	660 (81.5)	268 (79.5)	928 (80.9)	
Yes	n (%)	150 (18.5)	69 (20.5)	219 (19.1)	
Previous CABG	n	810	337	1147	
No	n (%)	810 (100.0)	337 (100.0)	1147 (100.0)	
Yes	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Previous MI	n	809	337	1146	0.017*
No	n (%)	526 (65.0)	194 (57.6)	720 (62.8)	
Yes	n (%)	283 (35.0)	143 (42.4)	426 (37.2)	
Previous PCI	n	810	337	1147	0.95
No	n (%)	585 (72.2)	244 (72.4)	829 (72.3)	
Yes	n (%)	225 (27.8)	93 (27.6)	318 (27.7)	
Ejection fraction	n	808	333	1141	0.69
	Mean (SD)	54.1 (9.77)	54.0 (10.10)	54.1 (9.86)	
History of Atrial Fibrillation/Atrial Flutter	n	574	218	792	0.49
No	n (%)	526 (91.6)	203 (93.1)	729 (92.0)	
Yes	n (%)	48 (8.4)	15 (6.9)	63 (8.0)	
Cardiogenic Shock	n	810	337	1147	>0.99
No	n (%)	808 (99.8)	336 (99.7)	1144 (99.7)	
Yes	n (%)	2 (0.2)	1 (0.3)	3 (0.3)	

(*continued*)

Table 2 (***Continued***)

	Statistic	Complete (N= 810)	Incomplete (N= 337)	Total (N=1147)	P-value
Presentation on Admission	n	810	337	1147	0.12
No symptoms or angina	n (%)	81 (10.0)	33 (9.8)	114 (9.9)	
Symptoms, non-ischemic	n (%)	24 (3.0)	13 (3.9)	37 (3.2)	
Stable angina	n (%)	443 (54.7)	167 (49.6)	610 (53.2)	
Unstable angina	n (%)	170 (21.0)	66 (19.6)	236 (20.6)	
Non-ST elevation MI	n (%)	83 (10.2)	54 (16.0)	137 (11.9)	
ST elevation MI	n (%)	9 (1.1)	4 (1.2)	13 (1.1)	
Angina Class by CCCS	n	785	315	1100	0.73
No angina present on admission	n (%)	81 (10.3)	33 (10.5)	114 (10.4)	
Class I	n (%)	120 (15.3)	53 (16.8)	173 (15.7)	
Class II	n (%)	330 (42.0)	131 (41.6)	461 (41.9)	
Class III	n (%)	200 (25.5)	71 (22.5)	271 (24.6)	
Class IV	n (%)	54 (6.9)	27 (8.6)	81 (7.4)	
Congestive Heart Failure	n	810	333	1143	0.22
No	n (%)	412 (50.9)	156 (46.8)	568 (49.7)	
Yes	n (%)	398 (49.1)	177 (53.2)	575 (50.3)	
Functional Class by NYHA	n	807	333	1140	0.42
No Congestive Heart Failure	n (%)	412 (51.1)	156 (46.8)	568 (49.8)	
Class I	n (%)	93 (11.5)	35 (10.5)	128 (11.2)	
Class II	n (%)	220 (27.3)	97 (29.1)	317 (27.8)	
Class III	n (%)	77 (9.5)	42 (12.6)	119 (10.4)	
Class IV	n (%)	5 (0.6)	3 (0.9)	8 (0.7)	

* Statistically significant to p = 0.05

Patients who underwent CABG using cardiopulmonary bypass and cardioplegic arrest were randomized to either endoscopic or open greater saphenous vein harvesting. Only expert Endoscopic vein harvesting harvesters (i.e., those who had performed >100 Endoscopic vein harvesting with <5% conversions to OVH) were allowed to perform the procedures. The REGROUP trial was approved by the IRB at each participating center. These patients were aged ≥18 years and underwent elective or urgent intervention through a full median sternotomy, with ≥1 saphenous vein graft planned. The demographics of the CR and IR cohorts were similar in most characteristics (Table 1) except for a higher rate of chronic renal disease (17.2% vs 12.1% for IR vs CR), current smoking (34.2% vs 24.7% for IR vs CR), and previous MI (42.4 vs 35% for IR vs CR) (Table 2). Patients who needed a concomitant valve operation, had severe valvulopathy, were in cardiogenic shock, had a life expectancy of less than a year, or did not have suitable venous conduit were excluded. SYNTAX score was similarly recorded and observed for this patient population (Table 3). Postintervention assessments were collected by research personnel using a combination of in-clinic interviews, phone calls, or chart review. These assessments were repeated before, intraoperatively, at discharge or 30 days after surgery, at 6 weeks, and every 3 months for the first year. Subsequent follow-up was passive through medical record review.

A preplanned, post hoc analysis of the REGROUP trial sought to investigate the outcome of MACE and its subcomponents in patients with CR, defined as surgical revascularization of any territory supplied by a coronary artery with ≥50% stenosis, compared with those with IR over the active and passive follow-up phases (median of 4.7 years). The follow-up was complete. All statistical analyses were conducted with SAS statistical software (version 9.4; SAS Institute, Inc., Cary, North Carolina).

Results

Over a median follow-up period of 4.7 years, MACE occurred in 175 patients (21.6%) in the CR group and 86 patients (25.5%) in the IR group (HR 0.85, 95% CI 0.65 to 1.11, p = 0.23). A total of 97 patients (12.0%) in the CR group and 48 patients (14.2%) in the IR group died (HR 0.91, 95% CI 0.64 to 1.3, p = 0.60); nonfatal MI occurred in 49 patients (6.0%) in the CR group and 30 patients (8.9%) in the IR group (HR 0.73, 95% CI 0.46 to 1.17, p = 0.19), and repeat revascularization occurred in 62 patients (7.7%) in the CR group and 39 patients (11.6%) in the IR group (HR 0.63, 95% CI 0.42 to 0.94, p = 0.025). Repeat revascularization was the only statistically significant different finding between groups. To obtain more information between groups, we also analyzed the timing of repeat revascularization retrospectively (Table 4). We found that when separated to reintervention within 3 months, >3 months but within 1 year, or >1 year, most of those who had an IR required intervention within a year, whereas the converse was true for those who underwent CR. In those who had CR, 7 (11.3%) required revascularization within 3 months; 12 (19.4%) required it within 1 year but >3 months, and 43 (69.4%) required it at >1 year. For the IR group, 8 (20.5%) needed it within 3 months, 14 (35.9%) at 3 months to 1 year, and 17 (43.6%) at >1 year (Figure 1).

Table 3
Anatomical details of complete and incomplete revascularization subgroups

	Statistic	Complete (N= 810)	Incomplete (N= 337)	Total (N=1147)	P-value
Syntax Score	n	809	336	1145	0.46
	Mean (SD)	28.3 (11.51)	28.9 (11.57)	28.5 (11.53)	
STS Risk of Mortality	n	809	337	1146	0.018*
	Mean (SD)	0.9 (0.81)	1.0 (0.96)	0.9 (0.86)	
VASQIP Patient Risk	n	809	336	1145	0.16
	Mean (SD)	1.0 (0.93)	1.0 (0.98)	1.0 (0.95)	
No of grafts/pt	n	810	335	1145	0.003*
	Mean (SD)	3.2 (0.79)	3.0 (0.83)	3.1 (0.80)	
Graft Type					
IMA	n (%)	792 (97.8)	328 (97.9)	1120 (97.8)	0.89
Radial Artery	n (%)	9 (1.1)	4 (1.2)	13 (1.1)	>0.99
Venous	n (%)	809 (99.9)	329 (98.2)	1138 (99.4)	0.003*
Number of CTOs	n	810	337	1147	0.099
None	n (%)	499 (61.6)	195 (57.9)	694 (60.5)	
One	n (%)	244 (30.1)	102 (30.3)	346 (30.2)	
Two	n (%)	49 (6.0)	33 (9.8)	82 (7.1)	
Three	n (%)	17 (2.1)	5 (1.5)	22 (1.9)	
Four	n (%)	1 (0.1)	2 (0.6)	3 (0.3)	
Location of CTO					
Proximal Major Branch	n (%)	168 (20.7)	65 (19.3)	233 (20.3)	0.58
LAD	n (%)	87 (10.7)	26 (7.7)	113 (9.9)	0.12
Proximal LAD	n (%)	45 (5.6)	11 (3.3)	56 (4.9)	0.1
LAD System	n (%)	93 (11.5)	35 (10.4)	128 (11.2)	0.59
Non-LAD	n (%)	253 (31.2)	123 (36.5)	376 (32.8)	0.084
Proximal RCA (a)	n (%)	106 (13.1)	47 (13.9)	153 (13.3)	0.7
Proximal RCA (b)	n (%)	156 (19.3)	72 (21.4)	228 (19.9)	0.42
RCA System	n (%)	186 (23.0)	98 (29.1)	284 (24.8)	0.029*
Left Circumflex	n (%)	97 (12.0)	45 (13.4)	142 (12.4)	0.52
Proximal Circumflex	n (%)	25 (3.1)	7 (2.1)	32 (2.8)	0.34
LMCA	n (%)	0 (0.0)	1 (0.3)	1 (0.1)	0.29
Graft Type to CTO Segment					
IMA	n (%)	100 (12.3)	29 (8.6)	129 (11.2)	0.068
Radial Artery	n (%)	2 (0.2)	0 (0.0)	2 (0.2)	>0.99
Venous	n (%)	247 (30.5)	68 (20.2)	315 (27.5)	<0.001*
Percentage of CTO lesions that were bypassed	n	311	142	453	<0.001*
	Mean (SD)	100.0 (0.00)	52.9 (45.66)	85.2 (33.59)	
Proximal Major Branch	n	168	65	233	<0.001*
	Mean (SD)	100.0 (0.00)	56.2 (47.28)	87.8 (31.70)	
LAD	n	87	26	113	<0.001*
	Mean (SD)	100.0 (0.00)	84.9 (21.86)	96.5 (12.13)	
Proximal LAD	n	45	11	56	<0.001*
	Mean (SD)	100.0 (0.00)	86.4 (23.35)	97.3 (11.36)	
LAD System	n	93	35	128	<0.001*
	Mean (SD)	100.0 (0.00)	76.0 (32.13)	93.4 (19.80)	
Non-LAD	n	253	123	376	<0.001*
	Mean (SD)	100.0 (0.00)	45.6 (46.74)	82.2 (36.93)	
Proximal RCA (a)	n	106	47	153	<0.001*
	Mean (SD)	100.0 (0.00)	48.6 (49.49)	84.2 (36.16)	
Proximal RCA (b)	n	156	72	228	<0.001*
	Mean (SD)	100.0 (0.00)	50.6 (48.74)	84.4 (35.68)	
RCA System	n	186	98	284	<0.001*
	Mean (SD)	100.0 (0.00)	46.9 (48.72)	81.7 (38.13)	
Left Circumflex	n	97	45	142	<0.001*
	Mean (SD)	100.0 (0.00)	47.0 (44.56)	83.2 (35.09)	
Proximal Circumflex	n	25	7	32	<0.001*
	Mean (SD)	100.0 (0.00)	42.9 (53.45)	87.5 (33.60)	
LMCA	n	0	1	1	
	Mean (SD)		66.7	66.7	
Location of Disease					
LAD System	n (%)	738 (91.1)	320 (95.0)	1058 (92.2)	0.027*
RCA System	n (%)	601 (74.2)	293 (86.9)	894 (77.9)	<0.001*
Left Circumflex	n (%)	625 (77.2)	286 (84.9)	911 (79.4)	0.003*

(continued)

Table 3 (***Continued***)

	Statistic	Complete (N= 810)	Incomplete (N= 337)	Total (N=1147)	P-value
Percent of Lesions Bypassed					
LAD System	n	738	320	1058	<0.001*
	Mean (SD)	100.0 (0.00)	67.8 (17.99)	90.3 (17.80)	
RCA System	n	601	293	894	<0.001*
	Mean (SD)	100.0 (0.00)	55.3 (40.77)	85.3 (31.39)	
Left Circumflex	n	625	286	911	<0.001*
	Mean (SD)	100.0 (0.00)	58.4 (30.18)	86.9 (25.67)	

* Statistically significant to p = 0.05

Table 4
Timing of repeat revascularization

	Total	Complete Revascularization (n=810)	Incomplete Revascularization (n=337)	P-value
In patients who had a repeat revascularization	101	62	39	0.037
Within 3 months	15 (14.9%)	7 (11.3%)	8 (20.5%)	
Greater than 3 Months, but within 1 year	26 (25.7%)	12 (19.4%)	14 (35.9%)	
Greater than 1 Year	60 (59.4%)	43 (69.4%)	17 (43.6%)	

When we reviewed the anatomical differences in the groups, we observed similar SYNTAX scores, Society of Thoracic Surgeons risk, and median number of grafts—with most cases involving a mammary graft (97.8% vs 97.9% for CR vs IR) and saphenous vein grafts (Table 3). Most of the patients did not have complete total occlusion (CTO) (no CTO 61.6% vs 57.9% for CR vs IR); however, the group with IR were more likely to have a CTO in the right coronary artery system (23% vs 29.1% for CR vs IR, p = 0.029). This was also reflected in the location of disease, which showed a greater percentage of disease within the right coronary artery system for the IR group (74.2% vs 86.9% CR vs IR, p <0.001). Other anatomical factors in groups were comparable.

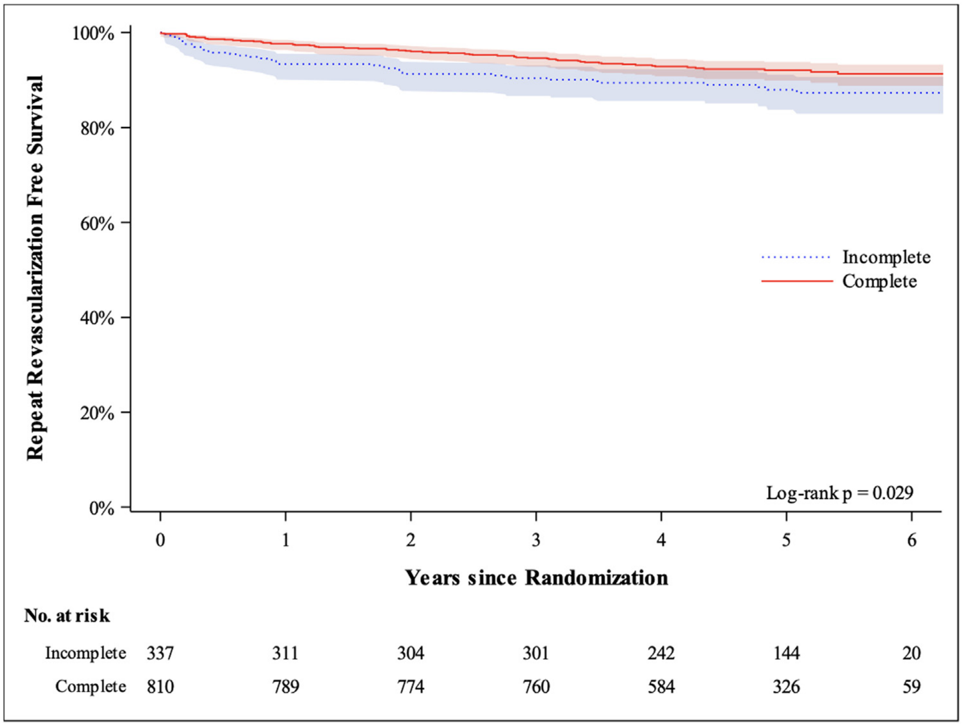

Figure 1. Kaplan-Meier plot of CR versus IR and need for subsequent revascularization.

Discussion

Durable results in freedom from reintervention, MACEs, and low (i.e., <1%) perioperative morbidity and mortality are the cornerstone of a successful CABG surgery. In our retrospective review in the REGROUP patient cohort, we observed, over an intermediate-term follow-up of a median 4.7 years, no difference in our primary outcome of MACE but did note a positive secondary outcome of fewer repeat revascularizations in those with CR. We used a more stringent definition of CR down to 50% angiographic stenosis to parse whether the effect would persist, given variability in bypass and intervention practice exists nationally.[5] Previous studies comparing such a definition with a less stringent CR definition of bypasses to all major arterial territories >50% did not identify a difference between groups but did identify an advantage over IR for a period of 10 years.[17] The duration of follow-up was the maximal available because previous studies such as the 1-year assessment of the ARTS trial by van den Brand et al showed no difference between CR and IR when limited to just the first year in its CABG cohort.[18] The applicability of a CR strategy remains nebulous in clinical practice for surgeons, given identifying reliable data that mirror one's patient population can be difficult. Our group of veterans displayed higher rates of cardiovascular co-morbidities than those in many national trials, and substantially higher than those in the general population (Figure 2).

Repeat revascularization affects long-term morbidity and overall survival. In a 5-year update on the SYNTAX trial, Parasca et al examined the impact of repeat revascularization on MACE and mortality.[19,20] They found that although repeat revascularization was more common after initial PCI than initial CABG (33.3 vs 13.4%, p <0.001), both were at increased risk for the composite safety end point of death, stroke, and MI (HR 2.2, 95% CI 1.6 to 3.0, p <0.001 for PCI; and HR 1.8, 95% CI 1.2 to 2.9, p = 0.011 for CABG). Although we did not observe a statistical difference in MACE, in examining the timing of reintervention, we did find an interesting dichotomy, with most events occurring early in those with IR compared with beyond 1 year for those with CR. A similar observation was visible in the COMPLETE trial, with patients with culprit-only lesion PCI experiencing their second coprimary outcome of death from cardiovascular causes, new MI, or ischemia-driven revascularization occurring in >10% of the total 16.7% incidence for the study period within the first year.[5]

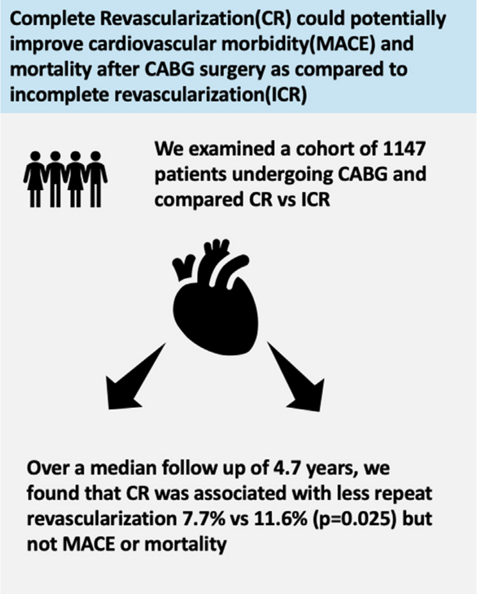

Figure 2. Central Illustration of the report highlighting a smaller chance of repeat revascularization after CR than after IR.

The degree and impact of CR versus IR continue to be of interest in the cardiovascular community. Patients with CABG who have IR are more likely to have higher rates of co-morbidities (e.g., older age, medically treated diabetes, renal failure, previous MI, poor left ventricular function, higher SYNTAX score), and therefore, non-randomized studies comparing patients who receive CR or IR are ill-equipped to identify situations in which a surgeon might choose to revascularize only a limited area. In 1 retrospective review, Kieser et al did find an overall advantage to CR in octogenarians who underwent CABG with arterial grafts because on their adjusted retrospective analysis, IR, higher logistical EuroSCORE, and male gender were predictors of decreased long-term survival.[21]

Multiple definitions of completeness of revascularizations exist, with no universal agreement. Oliveira et al[22] studied the impact of 4 different definitions of CR in the same group of 162 patients with CABG: numerical (number of stenotic vessels with a luminal reduction of ≥50% equal to the number of distal anastomoses), functional (all viable myocardial territories are reperfused), anatomical conditional (all stenotic main branch vessels with a diameter ≥1.5 mm are revascularized), and anatomical unconditional (all stenotic vessels are revascularized irrespective of the size and territory supplied). At 5.5 years of follow-up, they concluded that only complete functional revascularization was a predictor of survival (HR 0.47, 95% CI 0.23 to 0.97, p = 0.041); The definition of CR did not affect MACE or the need for repeat revascularization. The authors did, however, cite the limitations of only being able to recruit a small cohort of patients because of the rigors of their definitions, desire to use the same cohort of patients for all definitions, and availability of preoperative myocardial perfusion imaging.

The major limitations of this study stem from its retrospective design, the predominantly male population of veterans, and the intermediate-term duration of follow-up. It is also worth noting that there was heterogeneity between our patients with CR and those with IR in terms of worse chronic renal disease, greater incidence of MI, and greater likelihood of persistent smoking in the incompletely revascularized group. Another limitation comes from the follow-up not being prespecified, and occurring passively through review of medical records. CABG was carried out by different surgeons, and the extent of revascularization was dependent on their clinical assessment; hence, it was not possible to evaluate the reasons for IR. As pointed out in the 10-year follow-up of the STICH trial,[23,24] surgery is a long-term intervention, and the persistence of any 1 treatment effect can require years to parse. As the armamentarium of techniques for assessing the functional significance of coronary lesions continues to expand, identifying whether anatomic or functional definitions of CR are optimal will become necessary. Some studies including subgroup analyses of the STICH trial cohort indicated no impact of functional assessment of myocardium when it comes to revascularization.[25] Others, however, found differences only in those receiving functional revascularization—such as the 2021 study by Veiga Oliveira et al, which directly compared definitions and outcomes in the same cohort of patients and saw only an advantage to functional revascularization (HR 0.47, 95% CI 0.23 to 0.97, p = 0.041).[22] Although certain groups have reported using noninvasive methods for assessing severity of coronary disease, most surgeons still rely on quality angiography to guide their surgical revascularization plan.[26,27] A randomized trial to determine the optimal method of defining CR, whether anatomic or functional, and prospective assessments within these groups of the effects of CR versus IR are needed.

Declaration of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Leonid Belyayev: Data curation, Writing − original draft, Writing − review & editing. **Eileen M. Stock:** Formal analysis. **Brack Hattler:** Writing − review & editing. **Faisal G. Bakaeen:** Writing − review & editing. **Scott Kinlay:** Writing − review & editing. **Jacqueline A. Quin:** Writing − review & editing. **Miguel Haime:** Writing − review & editing. **Kousick Biswas:** Writing − review & editing. **Marco A. Zenati:** Conceptualization, Writing − review & editing.

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