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Letters

TO THE EDITOR

Temporal Changes in Outcomes After Stenting or Bypass Surgery for Unprotected Left Main Coronary Artery Disease According to Diabetes Status

Diabetes mellitus (DM) is associated with poor outcomes after coronary revascularization (1-3). Over the last several decades, a remarkable evolution in stent technology, procedures, and adjunctive pharmacology has reduced the treatment gap between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for unprotected left main coronary artery (ULMCA) disease (4). However, it is still unclear whether there are differences in secular changes over time in the treatment effects between PCI and CABG according to DM status.

The IRIS-MAIN (the Interventional Research Incorporation Society-Left MAIN Revascularization) registry is an observational study involving consecutive patients with ULMCA disease who were treated with PCI, CABG, or medication alone (4). We analyzed 5,217 patients who underwent coronary revascularization and compared the relative outcomes after PCI and CABG according to DM status. To evaluate the secular trend of outcomes over time, 3 time periods were chosen according to the availability of the specific stent types: wave 1 (bare-metal stents) for 1995 to 2002; wave 2 (first-generation drug-eluting stents [DES]) for 2003 to 2006; and wave 3 (second-generation DES) for 2007 to 2013. The primary outcome was a major adverse cardiac or cerebrovascular event (MACCE), defined as composite of death, myocardial infarction (MI), stroke, or repeat revascularization. Secondary outcomes included all-cause death, serious composite outcome (death, MI, or stroke), or repeat revascularization.

After overall outcomes between disease groups (DM vs. non-DM) were initially assessed, the adjusted risks for outcomes after PCI versus CABG were evaluated stratified by the presence of DM. We fit weighted Cox proportional hazards models using the propensity scoring that incorporates all the variables regarding baseline characteristics of the patients, with inverse probability of treatment weighting. Interaction terms were used to test for the statistical significance of 2 treatment effects by the time-waves on outcomes (for the time-by-treatment interaction). All statistical analyses were performed using R software version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

Of the 5,217 patients with coronary revascularization, 2,866 were treated with PCI, and 2,351 were treated with CABG. Overall, patients with DM had higher risk profiles of baseline characteristics than patients without DM. In both the DM and non-DM populations, the CABG group had higher clinical and angiographic risk profiles than the PCI group. The median follow-up times were 9.7 years (interquartile range [IQR]: 7.0 to 12.4 years), 5.6 years (IQR: 4.1 to 8.0 years), and 3.0 years (IQR: 1.9 to 4.1 years) for patients treated in waves 1, 2, and 3, respectively. Overall, the 3-year rates of MACCE, death, and composite of death, MI, or stroke, but not repeat revascularization, were significantly greater in patients with DM than those without DM (**Table 1**). The adjusted risks of MACCE, death, and serious composite outcomes were also significantly higher in patients with versus without DM (**Table 2**). Among the non-DM population, patients receiving PCI rather than CABG had higher 3-year rates of MACCE; however, this treatment gap markedly declined over time, with improving outcomes of PCI (**Table 1**). Among the DM population, the 3-year rates of MACCE were higher in the PCI than in the CABG group; however, this treatment gap was persistent over time. In analyses of fitted weighted Cox proportional hazards models using propensity scoring, as compared with crude analyses, the hazard ratio of PCI over CABG for clinical outcomes uniformly increased, which justified the relative benefit of CABG (**Table 2**). In adjusted analyses, overall trends were also consistent. Over time, the adjusted hazard ratio for MACCE after PCI relative to CABG has progressively declined from wave 1 to 3 among patients without DM (p for the wave-by-treatment interaction <0.001), but not among those with DM ($p = 0.75$ for the wave-by-treatment interaction). A similar pattern was observed for death and serious composite outcome.

TABLE 1 Observed 3-Year Event Rate and Crude HRs for the Overall Impact of the Presence of DM and the Effect of Revascularization Type on Outcomes by DM Status*

	Overall Patients (N = 5,217)				Patients Without DM (n = 3,408)				Patients With DM (n = 1,809)			
Outcomes	Non-DM (n = 3,408)	DM (n = 1,809)	HR (95% CI)†	p Value	PCI (n = 1,941)	CABG (n = 1,467)	HR (95% CI)‡	p Value	PCI (n = 925)	CABG (n = 884)	HR (95% CI)‡	p Value
Overall period (1995–2013)												
MACCE	15.4 (495)	20.0 (342)	1.31 (0.77–1.14)	<0.001	17.3 (309)	13.4 (192)	1.33 (1.11–1.59)	0.002	23.5 (200)	16.5 (142)	1.51 (1.22–1.87)	<0.001
Death	7.3 (232)	11.2 (190)	1.52 (1.26–1.85)	<0.001	6.6 (113)	8.7 (125)	0.73 (0.56–0.94)	0.015	10.3 (85)	12.2 (105)	0.83 (0.62–1.10)	0.195
Death, MI, or stroke	8.9 (283)	13.5 (229)	1.52 (1.28–1.81)	<0.001	7.9 (139)	10.4 (150)	0.74 (0.59–0.94)	0.011	12.5 (104)	14.5 (125)	0.85 (0.65–1.10)	0.218
Repeat revascularization	7.7 (241)	8.0 (131)	1.03 (0.84–1.28)	0.76	11.0 (195)	3.4 (46)	3.48 (2.52–4.80)	<0.001	13.2 (109)	2.7 (22)	5.24 (3.31–8.29)	<0.001
Wave 1 (1995–2002)§					(n = 211)	(n = 461)			(n = 58)	(n = 214)		
MACCE	–	–	–	–	30.5 (64)	14.3 (66)	2.37 (1.68–3.35)	<0.001	25.9 (15)	16.4 (35)	1.71 (0.93–3.13)	0.083
Death	–	–	–	–	6.7 (14)	8.0 (37)	0.82 (0.44–1.52)	0.534	6.9 (4)	10.3 (22)	0.66 (0.23–1.91)	0.440
Death, MI, or stroke	–	–	–	–	8.6 (18)	10.9 (50)	0.78 (0.45–1.33)	0.363	12.1 (7)	12.7 (27)	0.95 (0.41–2.19)	0.909
Repeat revascularization	–	–	–	–	26.5 (54)	4.3 (19)	7.10 (4.21–11.98)	<0.001	17.7 (10)	4.0 (8)	4.92 (1.94–12.47)	0.001
Wave 2 (2003–2006)			–	–	(n = 640)	(n = 586)			(n = 296)	(n = 366)		
MACCE	–	–	–	–	20.7 (132)	13.4 (78)	1.62 (1.22–2.14)	0.001	23.4 (69)	16.2 (59)	1.51 (1.07–2.14)	0.020
Death	–	–	–	–	9.2 (59)	8.4 (49)	1.10 (0.75–1.61)	0.619	9.5 (28)	14.0 (51)	0.66 (0.42–1.05)	0.082
Death, MI, or stroke	–	–	–	–	9.8 (62)	9.8 (57)	0.99 (0.69–1.42)	0.955	10.8 (32)	15.3 (56)	0.69 (0.45–1.07)	0.095
Repeat revascularization	–	–	–	–	13.0 (80)	4.0 (22)	3.49 (2.18–5.60)	<0.001	13.8 (39)	1.8 (6)	8.42 (3.57–19.9)	<0.001
Wave 3 (2007–2013)					(n = 1,090)	(n = 420)			(n = 571)	(n = 304)		
MACCE	–	–	–	–	12.1 (113)	12.2 (48)	0.99 (0.71–1.39)	0.973	23.5 (116)	17.0 (48)	1.47 (1.05–2.06)	0.025
Death	–	–	–	–	4.5 (40)	9.9 (39)	0.43 (0.27–0.66)	<0.001	11.3 (53)	11.4 (32)	0.98 (0.63–1.52)	0.933
Death, MI, or stroke	–	–	–	–	6.5 (59)	10.9 (43)	0.57 (0.38–0.84)	0.005	13.8 (65)	15.0 (42)	0.91 (0.62–1.34)	0.635
Repeat revascularization	–	–	–	–	6.5 (61)	1.4 (5)	5.08 (2.04–12.65)	<0.001	12.3 (60)	2.8 (8)	4.49 (2.15–9.4)	<0.001

Values are n (%) unless otherwise indicated. *Event rates are shown as Kaplan-Meier estimates (percentage and number of events). †Hazard ratios are for the DM group, as compared with the non-DM group. ‡Hazard ratios are for the PCI group, as compared with CABG group. §Three historical time waves were chosen according to the availability of the specific stent types: wave 1 (bare-metal stents) for 1995–2002; wave 2 (first-generation DES) for 2003–2006; and wave 3 (second-generation DES) for 2007–2013.

CABG = coronary artery bypass grafting; CI = confidence interval; DES = drug-eluting stent(s); DM = diabetes mellitus; HR = hazard ratio; MACCE = major adverse cardiovascular events (death, MI, stroke or repeat revascularization); MI = myocardial infarction; PCI = percutaneous coronary intervention.

TABLE 2 Adjusted HRs for the Overall Impact of the Presence of DM and the Effect of Revascularization Type on Outcomes by DM Status*

	Overall Patients		Patients Without DM		Patients With DM	
Outcomes	HR (95% CI)† DM vs. Non-DM	p Value	HR (95% CI)‡ PCI vs. CABG	p Value	HR (95% CI)‡ PCI vs. CABG	p Value
Overall period (1995–2013)						
MACCE	1.65 (1.51–1.79)	<0.001	1.66 (1.46–1.89)	<0.001	1.89 (1.62–2.20)	<0.001
Death	2.29 (2.04–2.57)	<0.001	0.88 (0.73–1.06)	0.18	0.94 (0.76–1.15)	0.52
Death, MI, or stroke	2.20 (1.98–2.45)	<0.001	0.88 (0.75–1.05)	0.15	1.03 (0.86–1.24)	0.76
Repeat revascularization	1.01 (0.88–1.17)	0.87	4.61 (3.67–5.79)	<0.001	6.73 (4.87–9.31)	<0.001
Wave 1 (1995–2002)§						
MACCE	–	–	3.05 (2.36–3.94)	<0.001	2.58 (1.74–3.84)	<0.001
Death	–	–	1.06 (0.65–1.72)	0.83	0.68 (0.31–1.49)	0.33
Death, MI, or stroke	–	–	0.95 (0.62–1.46)	0.83	1.25 (0.71–2.22)	0.44
Repeat revascularization	–	–	8.27 (5.75–11.91)	<0.001	6.50 (3.65–11.59)	<0.001
Wave 2 (2003–2006)						
MACCE	–	–	2.16 (1.77–2.64)	<0.001	1.94 (1.51–2.50)	<0.001
Death	–	–	1.30 (0.99–1.71)	0.06	0.79 (0.57–1.10)	0.17
Death, MI, or stroke	–	–	1.18 (0.91–1.53)	0.22	0.88 (0.65–1.20)	0.42
Repeat revascularization	–	–	5.47 (3.85–7.76)	<0.001	11.30 (5.91–21.48)	<0.001
Wave 3 (2007–2013)						
MACCE	–	–	1.13 (0.89–1.42)	0.33	1.72 (1.36–2.18)	<0.001
Death	–	–	0.49 (0.36–0.67)	<0.001	1.04 (0.76–1.41)	0.83
Death, MI, or stroke	–	–	0.64 (0.49–0.84)	0.002	1.00 (0.76–1.30)	0.98
Repeat revascularization	–	–	6.47 (3.43–12.18)	<0.001	6.88 (3.91–12.11)	<0.001
p value for interaction‖						
MACCE	–	–	–	<0.001	–	0.75
Death	–	–	–	0.002	–	0.66
Death, MI, or stroke	–	–	–	0.006	–	0.75
Repeat revascularization	–	–	–	0.12	–	0.45

*Adjusted hazard ratios were derived from the weighted Cox proportional hazards regression models with the inverse-probability-of-treatment weighting (IPTW). In the IPTW method, weights for patients receiving CABG were the inverse of (1 − propensity score), and weights for patients receiving PCI were the inverse of propensity score. The propensity scores were estimated with multiple logistic-regression analysis, which included baseline covariates (age, sex, body mass index, clinical diagnosis, cardiogenic shock on presentation, left ventricular ejection fraction, atrial fibrillation, hypertension, current smoking, hyperlipidemia, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass grafting, previous stroke, previous congestive heart failure, chronic lung disease, chronic kidney disease, peripheral vascular disease, disease extent, presence of right coronary artery disease, left main bifurcation involvement). †Hazard ratios are for the DM group, as compared with the non-DM group. ‡Hazard ratios are for the PCI group, as compared with CABG group. §Three historical time waves were chosen according to the availability of the specific stent types: wave 1 (BMS) for 1995–2002; wave 2 (first-generation DES) for 2003–2006; and wave 3 (second-generation DES) for 2007–2013. ‖p-for-interaction: the interaction terms in the weighted Cox model using the IPTW method were used to test for the statistical significance of 2 treatment effects (PCI vs. CABG) by the time (waves) on clinical outcomes (for the waves-by-treatment interaction).

MACCE = major cardiac and cerebrovascular adverse event(s); other abbreviations as in Table 1.

Our study findings suggested that there were differential trends in the relative treatment effects between PCI and CABG for ULMCA disease according to DM status over time. In patients without DM, the adjusted risk for MACCE between PCI and CABG significantly decreased over time, and a substantial interaction between revascularization type and time waves on MACCE was present. By contrast, in patients with DM, there was no significant temporal change in the adjusted risk for MACCE between PCI and CABG. Remarkable advancements in stent technology, procedural techniques, increased experience in complex LMCA stenting, antithrombotic agents, and background medical therapy during the last 2 decades might improve interventional device-related outcomes and lead to comparable outcomes of stenting relative to CABG (4). In addition, the technical aspect of CABG has significantly improved over time, including wide use of off-pump CABG, minimally invasive approach, or more use of arterial grafts. With such medical improvements, the temporal changes in the relative effect of PCI versus CABG was prominent among patients without DM, but was not remarkable in those with DM. Previously, differential clinical responses to coronary revascularization according to the presence of DM have been reported in several studies (5,6). Although the exact mechanism to fully explain the loss of benefit of PCI among the DM population is still unclear, the higher chance of incomplete revascularization, higher risk of restenosis, and rapid progression of atherosclerosis in the nonstented segment among patients with DM compared with those without DM might partly explain differential revascularization outcomes (7–10).

In conclusion, in patients without DM with ULMCA disease, treatment effect of stenting has been much improved over time and comparable to CABG in the era of second-generation DES. However, in the DM population, CABG was consistently better than stenting.

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Is Multislice Computed Tomography a Feasible Option for Follow-Up of Complex Coronary Lesions Treated With Bioresorbable Scaffolds?

Over the past 5 years bioresorbable vascular scaffolds (BVS) have become an attractive option for percutaneous coronary intervention because of the complete reabsorption process that occurs post-implantation (1), but the ideal follow-up technique after BVS implantation remains a challenge.

In fact, in recent years, multislice computed tomography (MSCT) has emerged both as a possible intermediate test to better select patients referred for coronary angiography and as an alternative or complementary test for monitoring revascularized patients, with the limitation of blooming artifacts that originate from metallic stents (2).

The use of this technique after BVS implantation has been evaluated in a cohort of the ABSORB trial (3). The study showed that MSCT could be an alternative to invasive imaging, ensuring good visualization of the treated segment and allowing a functional assessment of the vessel. It must be stressed, however, that the cited study enrolled patients with simple lesions, treated with a single short scaffold. A slightly more clinically complex population was enrolled in the PRAGUE-19 (Primary Angioplasty in Patients Transferred From General Community Hospitals to Specialized PTCA Units With or Without Emergency Thrombolysis) study (4), which evaluated the usefulness of MSCT after BVS implantation in patients with ST-segment elevation myocardial infarction.

We therefore decided to evaluate the feasibility of a detailed multislice computed tomographic analysis of BVS (not limited to assessment of scaffold patency but extended to evaluation of scaffold luminal area and quantification of percentage of restenosis) in an anatomically complex population treated with the Absorb BVS (Abbott Vascular, Santa Clara, California) at 2 high-volume centers in Milan, Italy, between May