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Renal Artery Stent Outcomes

Effect of Baseline Blood Pressure, Stenosis Severity, and Translesion Pressure Gradient

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ABSTRACT

BACKGROUND Multiple randomized clinical trials comparing renal artery stent placement plus medical therapy with medical therapy alone have not shown any benefit of stent placement. However, debate continues whether patients with extreme pressure gradients, stenosis severity, or baseline blood pressure benefit from stent revascularization.

OBJECTIVES The study sought to test the hypothesis that pressure gradients, stenosis severity, and/or baseline blood pressure affects outcomes after renal artery stent placement.

METHODS Using data from 947 patients with a history of hypertension or chronic kidney disease from the largest randomized trial of renal artery stent placement, the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) study, we performed exploratory analyses to determine if subsets of patients experienced better outcomes after stent placement than the overall cohort. We examined baseline stenosis severity, systolic blood pressure, and translesion pressure gradient (peak systolic and mean) and performed interaction tests and Cox proportional hazards analyses for the occurrence of the primary endpoint through all follow-up, to examine the effect of these variables on outcomes by treatment group.

RESULTS There were no statistically significant differences in outcomes based on the examined variables nor were there any consistent nonsignificant trends.

CONCLUSIONS Based on data from the CORAL randomized trial, there is no evidence of a significant treatment effect of the renal artery stent procedure compared with medical therapy alone based on stenosis severity, level of systolic blood pressure elevation, or according to the magnitude of the trans-stenotic pressure gradient. (Benefits of Medical Therapy Plus Stenting for Renal Atherosclerotic Lesions [CORAL]; NCT00081731) (J Am Coll Cardiol 2015;66:2487–94)

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ABBREVIATIONS AND ACRONYMS

CORAL = Cardiovascular Outcomes in Renal Atherosclerotic Lesions

RAS = renal artery stenosis

SBP = systolic blood pressure

Multiple uncontrolled trials of renal artery angioplasty and stent placement report improved patient outcomes (1-4). However, in the past 15 years there have been at least 5 randomized clinical trials investigating both surrogate endpoints and hard clinical endpoints and none have shown any significant benefit of renal artery intervention plus medical management compared with medical management alone (5-9). Nonetheless, critics claim that the randomized clinical trials are flawed (10,11), and that with appropriate patient selection renal artery intervention improves patient outcomes. The most frequent criticisms are that prior randomized trials enrolled subjects with renal artery stenoses (RAS) that were not hemodynamically or clinically significant or excluded patients with uncontrolled hypertension (12), or alternatively that patient selection should have been done using translesional arterial pressure gradients (13).

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The CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) study was published in 2014 and included data from 947 patients with RAS who were randomized to stent placement and medical therapy or medical therapy alone (9). The CORAL study showed no difference across a range of outcomes by treatment group. We use data from the CORAL study to examine the hypotheses that certain patients with RAS in high-risk subgroups were more likely to benefit from stent placement.

METHODS

The CORAL study randomized 947 patients with either refractory hypertension or chronic kidney disease to optimal medical therapy versus optimal medical therapy plus renal artery stent (9). The primary endpoint was event free survival, with the "event" comprising a composite endpoint of heart attack, stroke, hospitalization for congestive heart failure, progressive renal insufficiency or end-stage renal disease, and cardiovascular or renal-related death (9). A number of preplanned secondary analyses were also reported (9).

In the CORAL study, interaction tests were done to assess whether the primary endpoint was affected by selected physiologic variables in addition to treatment group (9). Variables that were tested included the presence or absence of bilateral RAS or RAS with a single functioning kidney, baseline systolic blood pressure, and maximal renal artery percent diameter stenosis (9). As an unplanned post-hoc analysis, we examined these subgroups for treatment group effect on clinical outcomes in more detail by selecting specific thresholds to be examined. Three hypotheses were tested: 1) patients with higher percent stenosis at baseline would have better outcomes after stent placement than with medical therapy alone; 2) patients with higher intra-arterial pressure gradients would have better outcomes after stent placement compared with medical therapy alone; and 3) patients with higher baseline blood pressure would have better outcomes after stent placement than with medical therapy alone. This was an exploratory analysis done without adjustments for multiple comparisons, an approach that entails a relatively high risk of type I error. Furthermore, since quartile subgroups are smaller populations than the original sample statistical power for these analyses is lower than for the study primary endpoint examined in the original cohort.

For each of the variables examined (baseline percent stenosis, baseline translesional pressure gradient, and baseline systolic blood pressure), we grouped participants according to historic thresholds and also into quartiles as dictated by the data. For baseline angiographic percent stenosis, we used both the investigator-reported as well as the core lab measured percent stenosis. For translesion pressure gradients both peak mean and peak systolic pressure gradients were examined. Cox proportional hazards regression was applied to test treatment-by-subgroup interaction for the composite primary endpoint. Kaplan-Meier event-free survival rates between treatment groups for all examined subgroups were compared using log-rank tests.

RESULTS

The CORAL intention-to-treat population included 931 participants, 459 randomized to stent plus medical therapy and 472 to medical therapy alone.

support from Medtronic and Boston Scientific. Dr. Jamerson is a member of the data safety and monitoring board for Pfizer; and has received research support from Chantix. Dr. Tuttle has served as consultant for therapeutics for diabetic kidney disease for Eli Lilly and Company, Amgen, and Noxxon Pharma; and has received research support from Eli Lilly and Company. Dr. D'Agostino is a member of the data safety and monitoring board and executive committee for Merck, Johnson & Johnson, GlaxoSmithKline, and the Medicines Company. Dr. Massaro has served as a consultant for the Harvard Clinical Research Institute. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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There were 4,375 potential participants screened with a total of 4,672 exclusions. Most (54%) of the reasons for nonenrollment were that participants did not meet study eligibility criteria. Other reasons included patient preference (17%), physician preference (4%), and other unspecified reasons (23%). The baseline characteristics of this population have been previously described (9). The distribution of participants for each of the variables (baseline percent stenosis, baseline systolic blood pressure, baseline peak systolic pressure gradient, baseline mean pressure gradient) by quartile is described in Table 1, and the distribution using conventional clinical thresholds of these variables is given in Table 2. Tests of interaction for these variables did not reveal any consistent treatment effect from stent treatment group, using either quartiles or clinically significant thresholds for each of the variables (Figures 1A and 1B, Central Illustration). Log-rank tests used to compare Kaplan-Meier survival free rates of the primary endpoint for both treatment groups by stenosis category revealed no statistically significant differences (Figures 2A to 2D). Log-rank tests for differences in Kaplan-Meier event-free survival rates for categories of baseline systolic blood pressure, baseline peak systolic pressure gradient, and baseline mean pressure gradient were also not statistically significant (not shown).

TABLE 1 Number of Patients in Each Baseline Quartile Subgroup (by Treatment Group): Randomized Patients

Subgroup	Stent (n = 459)	Medical Therapy (n = 472)	Difference	p Value
% Stenosis (core lab)				
<60.22	23.1 (100/433)	27.3 (83/304)	-4.2 [-10.6 to 2.2]	0.193
60.22 to <68.46	24.7 (107/433)	25.7 (78/304)	-0.9 [-7.3 to 5.4]	0.770
68.46 to <77.05	27.3 (118/433)	22.0 (67/304)	5.2 [-1.1 to 11.5]	0.108
≥77.05	24.9 (108/433)	25.0 (76/304)	-0.1 [-6.4 to 6.3]	0.986
% Stenosis (investigator)				
<69.7	24.9 (107/429)	25.7 (96/374)	-0.7 [-6.8 to 5.3]	0.813
69.7 to <76	26.8 (115/429)	27.5 (103/374)	-0.7 [-6.9 to 5.4]	0.816
76 to <85	19.8 (85/429)	25.9 (97/374)	-6.1 [-11.9 to -0.3]	0.039
>85	28.4 (122/429)	20.9 (78/374)	7.6 [1.7 to 13.5]	0.013
Systolic blood pressure				
<133.83 mm Hg	24.5 (112/457)	25.5 (119/467)	-1.0 [-6.6 to 4.6]	0.732
133.83 to <149.34 mm Hg	25.6 (117/457)	24.8 (116/467)	0.8 [-4.8 to 6.4]	0.790
149.34 to <164.34 mm Hg	24.9 (114/457)	25.1 (117/467)	-0.1 [-5.7 to 5.5]	0.970
≥164.34 mm Hg	24.9 (114/457)	24.6 (115/467)	0.3 [-5.2 to 5.9]	0.910
Peak systolic pressure gradient				
<26 mm Hg	21.5 (26/121)	30.8 (24/78)	-9.3 [-21.9 to 3.3]	0.141
26 to <43 mm Hg	24.8 (30/121)	24.4 (19/78)	0.4 [-11.8 to 12.7]	0.945
43 to <65 mm Hg	28.1 (34/121)	19.2 (15/78)	8.9 [-3.0 to 20.7]	0.156
≥65 mm Hg	25.6 (31/121)	25.6 (20/78)	-0.0 [-12.4 to 12.4]	0.997
Mean systolic pressure gradient				
<10 mm Hg	15.0 (17/113)	34.3 (24/70)	-19.2 [-32.2 to -6.3]	0.002
10 to <19 mm Hg	30.1 (34/113)	21.4 (15/70)	8.7 [-4.1 to 21.5]	0.199
19 to <33 mm Hg	28.3 (32/113)	18.6 (13/70)	9.7 [-2.6 to 22.1]	0.137
≥33 mm Hg	26.5 (30/113)	25.7 (18/70)	0.8 [-12.2 to 13.9]	0.901

Values are % (n/N) or % [95% confidence interval].

DISCUSSION

We performed an analysis of a prospective randomized clinical study designed to identify associations or correlations that were not part of the original pre-planned analysis. Such post-hoc analyses with multiple comparisons pose a considerable risk of type I error. Nevertheless, no significant results were observed that would suggest a benefit for any of the subgroups that have been regarded as important for patient selection in the past (12,13). Each component of the primary endpoint was also examined for relationships with baseline blood pressure, stenosis severity, and translesion pressure gradient, and all were similarly negative (data not shown).

The CORAL study had a requirement for ≥60% stenosis in a dominant renal artery for inclusion (14). When the CORAL study was designed, it was felt that this threshold was similar to those used clinically, and therefore was essential for generalizability of study results. Although a higher percent stenosis for eligibility might have improved detection of a treatment effect for stent placement, it would have been applicable to a smaller subset than those treated in clinical practice. These analyses demonstrate no

TABLE 2 Number of Patients in Each Baseline Subgroup Categorized by Clinically Significant Thresholds (by Treatment Group): Randomized Patients

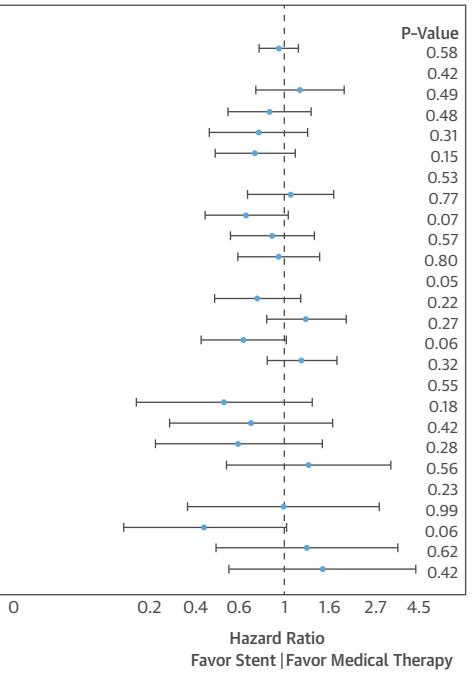
Subgroup	Stent (n = 459)	Medical Therapy (n = 472)	Difference	p Value
% Stenosis (core lab)				
<60	23.1 (100/433)	26.3 (80/304)	-3.2 [-9.6 to 3.1]	0.316
60 to <80	57.3 (248/433)	54.6 (166/304)	2.7 [-4.6 to 10.0]	0.472
≥80	19.6 (85/433)	19.1 (58/304)	0.6 [-5.2 to 6.3]	0.852
% Stenosis (investigator)				
<60	0.2 (1/429)	0.0 (0/374)	0.2 [-0.2 to 0.7]	0.350
60-<80	53.6 (230/429)	55.6 (208/374)	-2.0 [-8.9 to 4.9]	0.570
≥80	46.2 (198/429)	44.4 (166/374)	1.8 [-5.1 to 8.7]	0.615
Systolic blood pressure				
<140 mm Hg	35.0 (160/457)	35.8 (167/467)	-0.7 [-6.9 to 5.4]	0.812
140 to <160 mm Hg	31.9 (146/457)	33.8 (158/467)	-1.9 [-7.9 to 4.2]	0.542
160 to <180 mm Hg	22.5 (103/457)	21.0 (98/467)	1.6 [-3.8 to 6.9]	0.567
≥180 mm Hg	10.5 (48/457)	9.4 (44/467)	1.1 [-2.8 to 4.9]	0.583
Peak systolic pressure gradient				
<20 mm Hg	9.1 (11/121)	7.7 (6/78)	1.4 [-6.4 to 9.2]	0.730
20 to <40 mm Hg	34.7 (42/121)	46.2 (36/78)	-11.4 [-25.4 to 2.5]	0.106
≥40 mm Hg	56.2 (68/121)	46.2 (36/78)	10.0 [-4.1 to 24.2]	0.166
Mean systolic pressure gradient				
<10 mm Hg	15.0 (17/113)	34.3 (24/70)	-19.2 [-32.2 to -6.3]	0.002
10 to <20 mm Hg	33.6 (38/113)	25.7 (18/70)	7.9 [-5.5 to 21.4]	0.259
≥20 mm Hg	51.3 (58/113)	40.0 (28/70)	11.3 [-3.4 to 26.0]	0.136

Values are % (n/N) or % [95% confidence interval].

FIGURE 1 Freedom From the Primary Composite Endpoint Over Time in the CORAL Study Subgroups

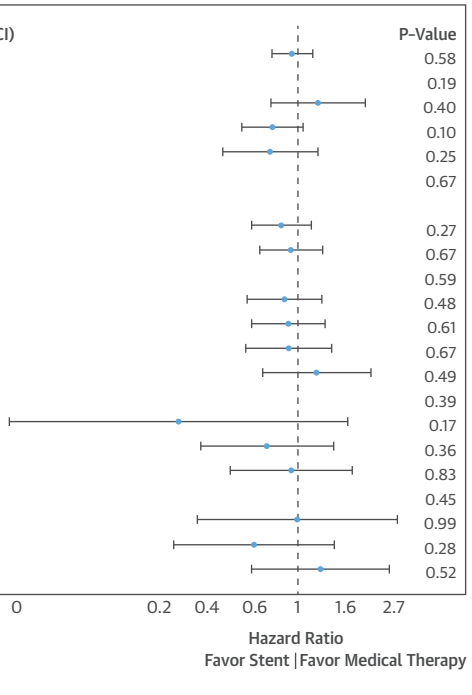
A

Subgroup	Stent	Medical Therapy	Hazard Ratio (95% CI)	P-Value
Overall	35.1% (161/459)	35.8% (169/472)	0.94 (0.76,1.17)	0.58
Percent Stenosis [Core Lab]				0.42
<60.22	40.0% (40/100)	33.7% (28/83)	1.19 (0.73,1.94)	0.49
60.22–<68.46	38.3% (41/107)	42.3% (33/78)	0.85 (0.54,1.34)	0.48
68.46–<77.05	27.1% (32/118)	32.8% (22/67)	0.75 (0.44,1.30)	0.31
>=77.05	39.8% (43/108)	50.0% (38/76)	0.72 (0.47,1.12)	0.15
Percent Stenosis [Investigator]				0.53
<69.7	35.5% (38/107)	33.3% (32/96)	1.07 (0.67,1.73)	0.77
69.7–<76	29.6% (34/115)	39.8% (41/103)	0.66 (0.42,1.04)	0.07
76–<85	40.0% (34/85)	40.2% (39/97)	0.88 (0.55,1.39)	0.57
>=85	39.3% (48/122)	39.7% (31/78)	0.94 (0.60,1.48)	0.80
Baseline SBP				0.05
<133.83	26.8% (30/112)	32.8% (39/119)	0.74 (0.46,1.20)	0.22
133.83–<149.34	37.6% (44/117)	31.9% (37/116)	1.28 (0.83,1.99)	0.27
149.34–<164.34	26.3% (30/114)	35.9% (42/117)	0.64 (0.40,1.02)	0.06
>=164.34	50.0% (57/114)	41.7% (48/115)	1.21 (0.83,1.78)	0.32
Peak Systolic Pressure Gradient				0.55
<26	30.8% (8/26)	41.7% (10/24)	0.51 (0.19,1.36)	0.18
26–<43	33.3% (10/30)	47.4% (9/19)	0.69 (0.28,1.70)	0.42
43–<65	38.2% (13/34)	46.7% (7/15)	0.60 (0.24,1.52)	0.28
>=65	45.2% (14/31)	35.0% (7/20)	1.31 (0.53,3.24)	0.56
Mean Systolic Pressure Gradient				0.23
<10	35.3% (6/17)	33.3% (8/24)	0.99 (0.34,2.87)	0.99
10–<19	32.4% (11/34)	60.0% (9/15)	0.42 (0.17,1.03)	0.06
19–<33	46.9% (15/32)	38.5% (5/13)	1.29 (0.47,3.56)	0.62
>=33	43.3% (13/30)	27.8% (5/18)	1.53 (0.54,4.30)	0.42



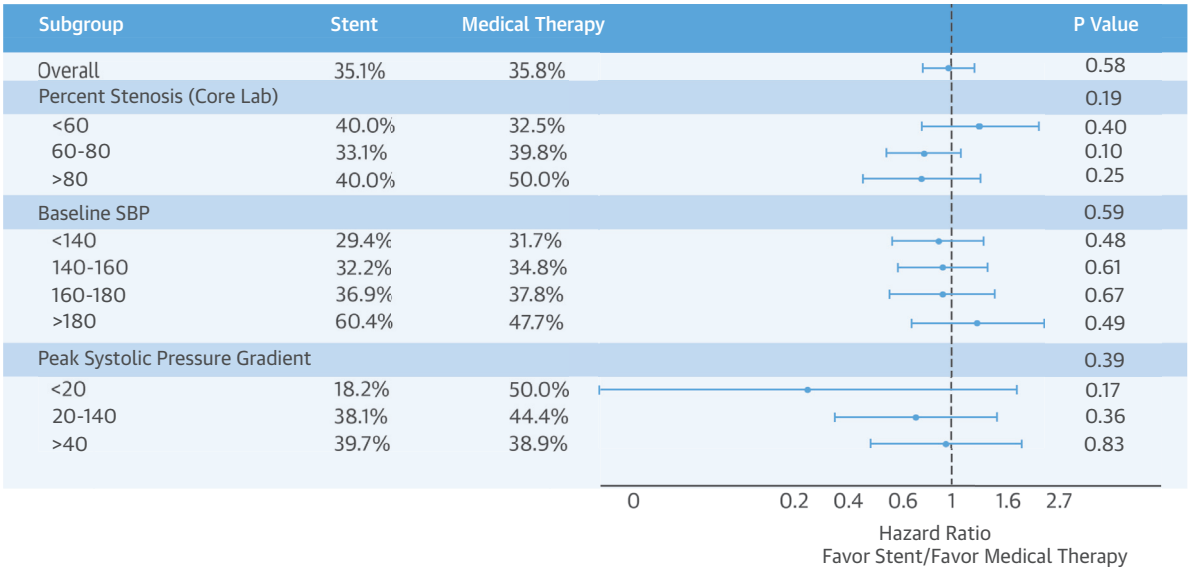
B

Subgroup	Stent	Medical Therapy	Hazard Ratio (95% CI)	P-Value
Overall	35.1% (161/459)	35.8% (169/472)	0.94 (0.76,1.17)	0.58
Percent Stenosis [Core Lab]				0.19
<60	40.0% (40/100)	32.5% (26/80)	1.24 (0.75,2.04)	0.40
60–<80	33.1% (82/248)	39.8% (66/166)	0.76 (0.55,1.06)	0.10
>=80	40.0% (34/85)	50.0% (29/58)	0.74 (0.45,1.23)	0.25
Percent Stenosis [Investigator]				0.67
<60	0% (0/1)	N/A		
60–<80	33.5% (77/230)	38.0% (79/208)	0.84 (0.61,1.15)	0.27
>=80	38.9% (77/198)	38.6% (64/166)	0.93 (0.67,1.30)	0.67
Baseline SBP				0.59
<140	29.4% (47/160)	31.7% (53/167)	0.87 (0.58,1.29)	0.48
140–<160	32.2% (47/146)	34.8% (55/158)	0.90 (0.61,1.34)	0.61
160–<180	36.9% (38/103)	37.8% (37/98)	0.91 (0.58,1.43)	0.67
>=180	60.4% (29/48)	47.7% (21/44)	1.22 (0.69,2.17)	0.49
Peak Systolic Pressure Gradient				0.39
<20	18.2% (2/11)	50.0% (3/6)	0.28 (0.05,1.69)	0.17
20–<40	38.1% (16/42)	44.4% (16/36)	0.72 (0.36,1.46)	0.36
>=40	39.7% (27/68)	38.9% (14/36)	0.93 (0.49,1.78)	0.83
Mean Systolic Pressure Gradient				0.45
<10	35.3% (6/17)	33.3% (8/24)	0.99 (0.34,2.87)	0.99
10–<20	34.2% (13/38)	50.0% (9/18)	0.63 (0.27,1.47)	0.28
>=20	44.8% (26/58)	35.7% (10/28)	1.27 (0.61,2.63)	0.52



Forest plots displaying treatment effects within subgroups by quartiles **(A)** and by historic clinical thresholds **(B)**: baseline percent stenosis (core lab), baseline percent stenosis (investigator), baseline systolic blood pressure (SBP), baseline peak systolic pressure gradient, baseline mean systolic pressure gradient (rates of primary endpoint composite through all available follow-up). The p values for rows labeled as percent stenosis, peak systolic pressure gradient, mean systolic pressure gradient, and baseline SBP are treatment-by-subgroup interaction p values. The rest of the p values are for remaining subgroups. CI = confidence interval; CORAL = Cardiovascular Outcomes in Renal Atherosclerotic Lesions.

CENTRAL ILLUSTRATION **Renal Artery Stent Outcomes: Subgroups Analysis From the CORAL Study**



Murphy, T.P. et al. J Am Coll Cardiol. 2015; 66(22):2487–94.

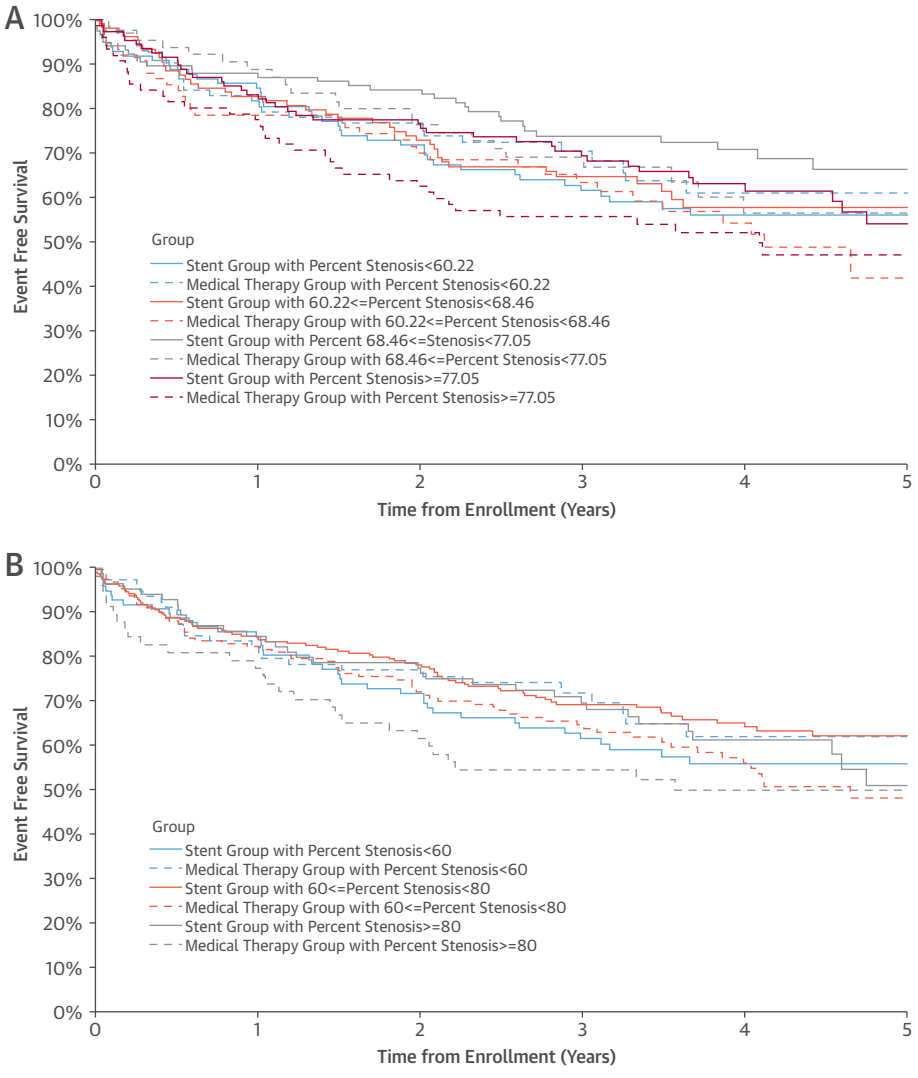
Forest plot displaying treatment effects within clinical-threshold subgroups: baseline percent stenosis (core lab), baseline systolic blood pressure (SBP), and baseline peak systolic pressure gradient. The p values for rows labeled as percent stenosis, peak systolic pressure gradient, and baseline SBP are treatment-by-subgroup interaction p values. The rest of the p values are for remaining subgroups. CORAL = Cardiovascular Outcomes in Renal Atherosclerotic Lesions.

statistically significant difference between stent placement and medical therapy outcomes in CORAL despite a number of thresholds for stenosis severity examined, including for those with >80% stenosis by core lab reading, where the hazard ratio for the primary endpoint by treatment group falls almost squarely on 1.0 (9).

One of the criticisms of the CORAL study and the other clinical trials has been the inclusion of patients with milder degrees of hypertension, for whom it might be difficult to see a benefit of stenting (12). However, the manuscript that was used to support this contention was a meta-analysis of 5 clinical trials, none of which had a medical control group (12). The meta-analysis excluded almost one-half of the patients, and reported a mean reduction in systolic blood pressure of 18 mm Hg at 9 months (12). However, it is known that physiologic variables that are out of range often regress to the mean simply by repeating the measure, as was observed in 1 clinical trial of similar patients that had a run-in period before interventional treatment was implemented and found that systolic blood pressure was on average 8 mm Hg lower after 4 weeks (5). In fact that reduction in systolic blood pressure reported by Weinberg et al. (12) for renal artery stenting in those with extreme blood pressure elevation is similar to that observed in CORAL study in participants who were treated in the medical therapy group (9). Blood pressure improved in both the medical and stent groups of CORAL, with the stent treated patients having a greater reduction in blood pressure by approximately 2.3 mm Hg (14). Finally, an interaction test using a blood pressure threshold of 160 mm Hg systolic in the CORAL study (9) showed no statistically significant difference by treatment groups in the primary endpoint. This post-hoc analysis confirms absence of statistically significant treatment effect of stenting in any of the categories of baseline blood pressure examined. However, this study is not definitive and lacks the power of the original study due to parsing the population into smaller subgroups.

It has also been postulated that a benefit of stent placement compared with medical therapy alone could have been shown for those patients with the most

FIGURE 2 Freedom From the Primary Endpoint by Subgroup in the CORAL Study



(A) Event-free Kaplan-Meier curves for primary endpoint composite through 5 years of follow-up by treatment group for each baseline percent stenosis as reported by the core lab quartile category (<60.22, 60.22 to <68.46, 68.46 to <77.05, ≥77.05 mm Hg). Log-rank test between groups for first quartile (<60.22) = 0.4895. Log-rank test between groups for second quartile = 0.4780. Log-rank test between groups for third quartile = 0.3065. Log-rank test between groups for fourth quartile = 0.1487. The p value is for all available follow-up (not limited to 5 years). **(B)** Event-free Kaplan-Meier curves for primary endpoint composite through 5 years of follow-up by treatment group for each baseline percent stenosis as determined by the core lab by clinically significant category (<60, 60 to <80, ≥80 mm Hg). Log-rank test between groups for first category (<60) = 0.3992. Log-rank test between groups for second category = 0.1023. Log-rank test between groups for third category = 0.2487. The p value is for all available follow-up (not limited to 5 years). **(C)** Event-free Kaplan-Meier curves for primary endpoint composite through 5 years of follow-up by treatment group for each baseline percent stenosis as reported by the investigator quartile category (<69.7, 69.7 to <76, 76 to <85, ≥85 mm Hg). Log-rank test between groups for first quartile (<69.7) = 0.7703. Log-rank test between groups for second quartile = 0.0710. Log-rank test between groups for third quartile = 0.5734. Log-rank test between groups for fourth quartile = 0.8009. The p value is for all available follow-up (not limited to 5 years). **(D)** Event-free Kaplan-Meier curves for primary endpoint composite through 5 years of follow-up by treatment group for each baseline percent stenosis as reported by the investigator category (60 to <80, ≥80 mm Hg). Log-rank test between groups for first category (<60) = N/A (there was no patient in Med Rx group, so the p value is not available). Log-rank test between groups for second category = 0.2736. Log-rank test between groups for third category = 0.6663. The p value is for all available follow-up (not limited to 5 years). CORAL = Cardiovascular Outcomes in Renal Atherosclerotic Lesions.

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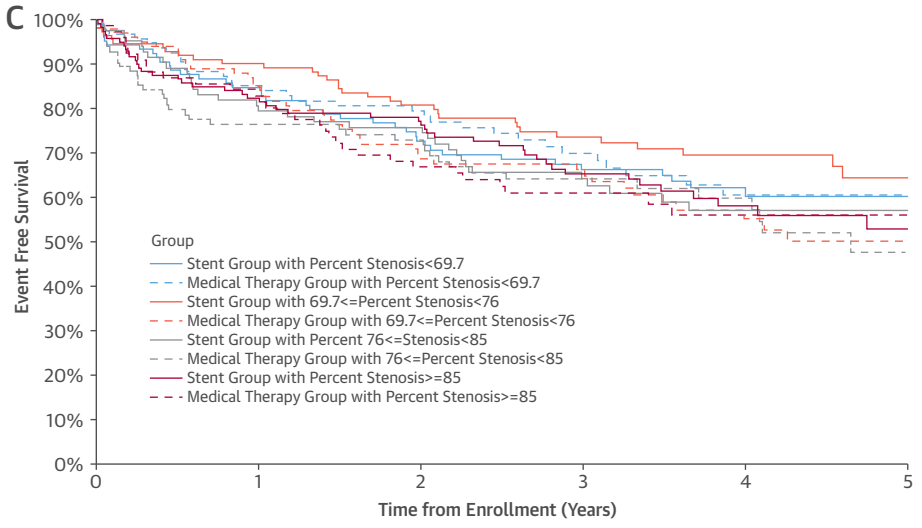
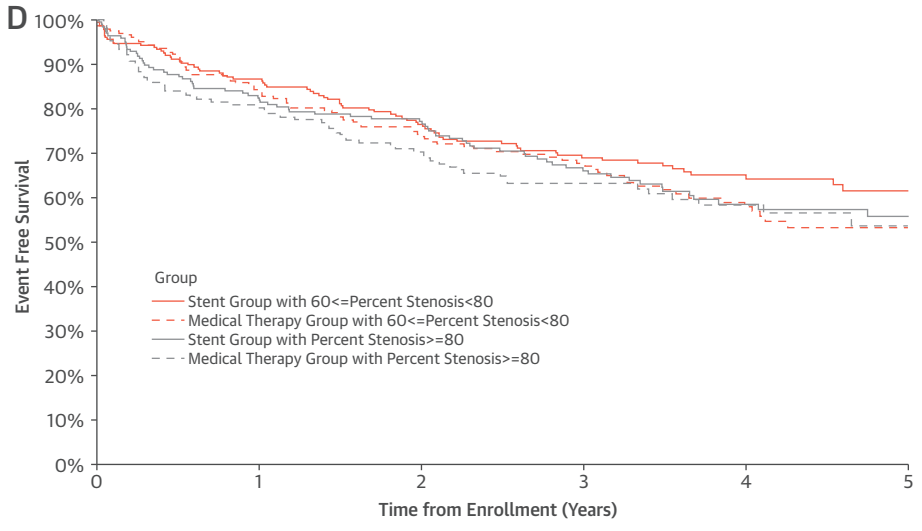
FIGURE 2 Continued





severe translesional pressure gradients measured intra-arterially (13). The CORAL study represents 1 of the largest databases of patients with RAS and intra-arterial translesion pressure gradients measured prospectively, and the only study that measured gradients that had a group treated without revascularization. Tests for interaction on various thresholds of intra-arterial pressure gradients showed no difference in outcomes for those with high versus lower translesional pressure gradients by treatment group. Pressure gradients, obtained mostly at operator discretion, were measured in a small fraction of total participants (n = 199), but still represents the largest database of renal artery pressure gradients in any clinical trial. Another often-quoted manuscript that is the foundation for many of the claims about the importance of renal artery pressure gradients was non-randomized and included data from only 15 patients (15). Furthermore, although the pressure gradient cohort was a small fraction of the total, the centers of the hazard ratios move toward medical therapy and away from stenting as pressure gradients increase (**Figure 1**). Tests for interaction on various thresholds of intra-arterial pressure gradients showed no difference in outcomes for those with high versus lower translesional pressure gradients by treatment group.

STUDY LIMITATIONS. These detailed analyses were not planned in the original study, and therefore in addition to a risk of type I error, these analyses are

underpowered and entail a risk of type II error. However, there were no trends, and as noted in the discussion and seen in the Forest plot (**Figure 1**), for some variables, like pressure gradients, hazard ratios moved further to the medical therapy side as the values moved to the higher values.

CONCLUSIONS

The CORAL study is the largest randomized clinical trial comparing the effects of stenting and optimal medical therapy alone in patients with RAS and hypertension and/or chronic kidney disease, and successfully recruited a broad range of patients reflective of those often treated with renal artery stent placement in clinical practice. A substantial proportion of subjects in the CORAL study had high-grade stenoses, severe systolic hypertension at entry, and significant translesional systolic pressure gradients. These variables have previously been felt to be important, but a positive treatment effect of stenting in these subgroups was not observed. Specifically, the CORAL study data does not support a benefit of stenting based on degree of stenosis, hemodynamic significance of the lesion, or higher pre-treatment blood pressure.

Despite eligibility criteria that included high-risk patients in CORAL, it is impossible to exclude selection bias among physicians referring patients for entry into an intervention trial. But because the CORAL study's population was similar in terms of risk to those in uncontrolled studies that reported a benefit of stent placement (12,13), that potential criticism is suspect. There were patients that were intentionally excluded in CORAL, such as those with advanced chronic kidney disease, a population that was under represented in the CORAL study generally and for whom inferences from these data are not appropriate.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Clinical outcomes in patients with RAS are not improved by renal artery stenting regardless of the severity of baseline hypertension or translesional pressure gradient.

TRANSLATIONAL OUTLOOK: More research is needed to determine whether specific patient features such as impaired kidney function identify individuals who might benefit from renal revascularization.

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