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Management of Vascular Risk Factors in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)

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***Background*—**The Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) is a multicenter randomized trial of stenting versus endarterectomy in patients with symptomatic and asymptomatic carotid disease. This study assesses management of vascular risk factors.

***Methods and Results*—**Management was provided by the patient's physician, with biannual monitoring results collected by the local site. Therapeutic targets were low-density lipoprotein, cholesterol <100 mg/dL, systolic blood pressure <140 mm Hg, fasting blood glucose <126 mg/dL, and nonsmoking status. Optimal control was defined as achieving all 4 goals concurrently. Generalized estimating equations were used to compare risk factors at baseline with those observed in scheduled follow-up visits for up to 48 months. In the analysis cohort of 2210, significant improvements in risk-factor control were observed across risk factors for all follow-up visits compared with baseline. At 48 months, achievement of the low-density lipoprotein cholesterol goal improved from 59.1% to 73.6% ($P<0.001$), achievement of the systolic blood pressure goal improved from 51.6% to 65.1% ($P<0.001$), achievement of the glucose goal improved from 74.9% to 80.7% ($P=0.0101$), and nonsmoking improved from 74.4% to 80.9% ($P<0.0001$). The percentage with optimal risk-factor control also improved significantly, from 16.7% to 36.2% ($P<0.001$), but nearly 2 of 3 study participants did not achieve optimal control during the study.

***Conclusions*—**Site-based risk-factor control improved significantly in the first 6 months and over the long term in CREST but was often suboptimal. Intensive medical management should be considered for future trials of carotid revascularization.

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Treatment of hypertension, hyperlipidemia, and diabetes mellitus and assisting patients with cessation of cigarette smoking are efficacious in preventing first-time[1] and recurrent[2] stroke. The opportunities to favorably influence blood pressure, cholesterol, and other vascular risk factors are substantial. The prevalence in the United States of persons with low risk-factor burden has been <11% for decades.[3] Intensive medical therapy has been associated with a low absolute risk of stroke in patients with asymptomatic carotid stenosis.[4] Intensive statin therapy reduced the risk of any stroke by 33% in the >1000 patients with known carotid disease in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial.[5] It is not known how well vascular risk factors are controlled in this population at risk for stroke. The Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) is a multicenter randomized clinical trial of carotid stenting versus endarterectomy in patients with symptomatic and asymptomatic carotid disease.

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The purpose of this study was to assess whether the methods used in CREST to manage vascular risk factors resulted in improvements in risk-factor status.

Methods

This study involves an exploratory analysis. The CREST trial was approved by the local governing institutional review board of each participating center, and all patients provided written informed consent. The trial methods[6] and primary results[7] have been published. The investigational devices, the Acculink/RX Acculink carotid stent system and the Accunet/RX Accunet, were manufactured by Abbott Vascular, Inc. The primary aim of the trial was to compare 2 types of revascularization procedures, carotid endarterectomy and carotid stenting; however, the investigators recognized that monitoring and medical management of vascular risk factors were essential for patient safety and overall stroke risk reduction. Patients underwent twice-yearly assessments of blood pressure, blood glucose, lipids, and cigarette smoking status for the first 48 months of the trial. The medical treatments were provided by the patient's usual-care physician. The principal investigators and study coordinators at CREST participating centers were instructed to inform the patients' primary care physicians regarding the results of the vascular-risk-factor assessments using a standardized letter. Published American Heart Association guideline statements for levels of control of blood pressure, glucose in diabetic patients, and lipids were adopted studywide and were provided to the usual-care physician. The importance of appropriate concomitant medical therapy was emphasized at CREST investigators and annual coordinators meetings throughout the course of the trial. Studywide control of vascular risk factors was reported to and monitored by the independent data and safety monitoring board appointed by the National Institute of Neurological Disorders and Stroke.

For this exploratory analysis, group means and rates for risk factors were calculated using generalized estimating equations (using an unstructured covariance matrix) to account for the differences in sample sizes at each follow-up visit while still accounting for the repeated measures for

Table 1. Vascular Risk Factors for Symptomatic and Asymptomatic Patients Enrolled in CREST*

	Clinic Visit (Months)					
Characteristic	0 (n=2210)	6 (n=1824)	12 (n=1742)	24 (n=1310)	36 (n=822)	48 (n=402)
LDL, mg/L						
n	1961	1483	1495	1099	672	322
Mean (SE)	96.9 (0.8)	92.2 (0.8)	91 (0.8)	89.4 (0.9)	89.4 (1.1)	89.2 (1.4)
P value†		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Systolic BP, mm Hg						
n	2180	1751	1656	1239	778	366
Mean (SE)	142.1 (0.4)	138 (0.5)	138.1 (0.5)	136.9 (0.5)	137.2 (0.7)	136.6 (0.9)
P value†		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diastolic BP, mm Hg						
n	2179	1747	1654	1239	779	367
Mean (SE)	73.9 (0.3)	75 (0.3)	74.3 (0.3)	73.6 (0.3)	73.7 (0.4)	72.6 (0.5)
P value†		0.0015	0.1884	0.4070	0.6593	0.0163
Glucose, mg/dL						
n	2104	1544	1529	1112	667	318
Mean (SE)	116.9 (0.9)	114.8 (1.1)	114.4 (1.1)	114.3 (1.1)	116.3 (1.7)	115.4 (2.2)
P value†		0.0624	0.0264	0.0228	0.7095	0.5317
Current smoker						
n	2169	1816	1740	1296	807	397
%	25.6	21.4	21.9	21.6	19.6	19.0
P value†		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

BP indicates blood pressure; CREST, Carotid Revascularization Endarterectomy vs Stenting Trial; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from a statistical model to account for missing data.
†*P* values test changes from baseline (note that changes from baseline on smoking are provided in Table 5).

the same patient.[8] This approach accounts for data missing completely at random. Results were analyzed overall and stratified by symptomatic status at baseline. In addition, rates were calculated for achieving key benchmarks of blood pressure, cholesterol, and glucose. To have a more sensitive marker of successful risk factor control, an all-or-none measurement was constructed post hoc.[9] Patients were considered to be optimally medically managed if they achieved all of the following therapeutic goals: low-density lipoprotein (LDL) cholesterol <100 mg/dL, glucose <126 mg/dL, systolic blood pressure <140 mm Hg, and no active cigarette smoking. To test for significant changes in control of individual risk factors and achieving optimal medical management, the generalized estimating equations were used to calculate predicted percentages and to test for significant differences from baseline. The analysis cohort consisted of 2210 patients at enrollment; 1824 patients at 6 months; and 1742, 1320, 822, and 402 patients at 12, 24, 36, and 48-month follow-up, respectively. The glucose target of <126 mg/dL was assessed for all patients regardless of diabetic status.

Results

Patients were enrolled in CREST from December 21, 2000, to July 18, 2008. Half of the patients were enrolled by August 15, 2006. The last patient to be followed up to 48 months after randomization was seen January 20, 2010. Table 1 shows that mean LDL cholesterol at baseline was 96.9 mg/dL. Median LDL cholesterol was 91.0 mg/dL (interquartile range 46.0). Mean systolic blood pressure was 142.1 mm Hg. Median systolic blood pressure was 140.0 mm Hg (interquartile range 27.0). Mean diastolic blood pressure was 73.9 mm Hg. Median diastolic blood pressure was 74.0 mm Hg (interquartile range 15.0). Mean glucose concentration was 116.9 mg/dL. Median glucose concentration was 104.0 mg/dL (interquartile range 33.0). Approximately a quarter of the patients reported cigarette smoking.

Table 1 also shows the status of vascular risk factors from randomization to 48 months of follow-up for symptomatic and asymptomatic patients overall. Tables 2 and 3 show the status of these risk factors separately for symptomatic and

Table 2. Vascular Risk Factors for Patients Who Had Symptomatic Carotid Stenosis at Entry Into CREST*

	Clinic Visit (Months)					
Characteristic	0	6	12	24	36	48
LDL, mg/dL						
n	947	689	680	524	363	225
Mean (SE)	102.3 (1.2)	96.1 (1.3)	94.5 (1.2)	92.7 (1.3)	91.7 (1.5)	92.3 (1.8)
P value†		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Systolic BP, mm Hg						
n	1060	822	763	593	418	253
Mean (SE)	142.5 (0.6)	138.5 (0.7)	138.1 (0.7)	136.6 (0.8)	136.1 (0.9)	136.5 (1.1)
P value†		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diastolic BP, mm Hg						
n	1061	822	763	593	419	253
Mean (SE)	74.5 (0.4)	75.4 (0.4)	75 (0.4)	74.4 (0.4)	73.2 (0.5)	72.9 (0.6)
P value†		0.0589	0.3156	0.8368	0.0226	0.0212
Glucose, mg/dL						
n	1029	719	703	538	362	221
Mean (SE)	114.4 (1.3)	113.2 (1.6)	114.9 (1.7)	115.1 (1.6)	117.6 (2.3)	115.9 (3)
P value†		0.4314	0.7903	0.6683	0.1704	0.6248
Current smoker						
n	1053	866	821	632	442	284
%	27.3	21.9	22.8	22.2	21.1	21.0
P value†		<0.0001	<0.0001	0.0001	<0.0001	<0.0001

BP indicates blood pressure; CREST, Carotid Revascularization Endarterectomy versus Stenting Trial; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from statistical model to account for missing data.
†*P* values test changes from baseline (note that changes from baseline on smoking are provided in Table 5).

Table 3. Vascular Risk Factors for Patients Who Had Asymptomatic Carotid Stenosis at Entry*

Characteristic	Clinic Visit (Months)					
	0	6	12	24	36	48
LDL, mg/dL						
n	1014	794	815	575	309	97
Mean (SE)	91.9 (1.1)	88.5 (1.1)	87.8 (1.1)	86.4 (1.2)	87.3 (1.5)	84.1 (2.4)
P value†		0.0028	0.0005	<0.0001	0.0046	0.0020
Systolic BP, mm Hg						
n	1120	929	893	646	360	113
Mean (SE)	141.8 (0.6)	137.5 (0.6)	138.2 (0.6)	137.1 (0.7)	138.3 (1)	136.8 (1.6)
P value†		<0.0001	<0.0001	<0.0001	0.0010	0.0029
Diastolic BP, mm Hg						
n	1118	925	891	646	360	114
Mean (SE)	73.3 (0.3)	74.6 (0.4)	73.8 (0.3)	72.9 (0.4)	74.4 (0.5)	72.2 (0.9)
P value†		0.0088	0.3270	0.3785	0.0822	0.2178
Glucose, mg/dL						
n	1075	825	826	574	305	97
Mean (SE)	119.3 (1.3)	116.2 (1.6)	114.1 (1.3)	113.5 (1.6)	114 (2.3)	114.5 (2.7)
P value†		0.0605	0.0005	0.0005	0.0254	0.1033
Current smoker						
n	1116	950	919	664	365	113
%	24.0%	21.1%	21.1%	21.0%	17.2%	14.5%
P value†		0.0037	0.0051	0.0102	<0.0001	0.0007

BP indicates blood pressure; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from statistical model to account for missing data.
†*P* values test changes from baseline (note that changes from baseline on smoking are provided in Table 5).

Table 4. Rates of Optimal Risk Factor Control at Enrollment by Calendar Year of Enrollment in CREST

Year of Randomization	Number Randomized	Optimally Managed on at Least 3 of 4 Goals* (%)	Optimally Managed on 4 of 4 Goals† (%)
2000–2004	288	48.6	14.2
2005	348	53.7	14.1
2006	519	57.8	17.2
2007	478	60.7	19.3
2008	256	55.5	17.2

CREST indicates Carotid Revascularization Endarterectomy vs Stenting Trial; LDL, low-density lipoprotein.
*Patients were considered to be optimally medically managed if they achieved at least 3 of the following therapeutic goals: LDL cholesterol <100 mg/dL, glucose <126 mg/dL, systolic blood pressure <140 mm Hg, and no active cigarette smoking.
†Patients were considered to be optimally medically managed if they achieved all of the following therapeutic goals: LDL cholesterol <100 mg/dL, glucose <126 mg/dL, systolic blood pressure <140 mm Hg, and no active cigarette smoking.

asymptomatic patients. In the period from December 21, 2000, to January 3, 2006, when the first third of patients were enrolled in the trial, the rate of optimal risk-factor control at enrollment was 14%. Table 4 shows the rates of optimal risk-factor control at enrollment by calendar year of enrollment. The proportion of patients achieving optimal control of the 4 risk-factor goals was 14.2% for the years 2000–2004 and rose to >17% over the years 2005–2008, although the improvements over time were not significant.

Table 5 shows the change in proportion of all patients achieving targets for vascular risk factors from baseline to 6 months, from baseline to 12 months, from baseline to 24 months, from baseline to 36 months, and from baseline to 48 months. The same outcomes are shown separately for symptomatic and asymptomatic patients in Tables 6 and 7, respectively. By 6 months, significant improvements were observed for all therapeutic targets. The majority of patients had achieved therapeutic targets for systolic blood pressure, blood glucose, and cigarette smoking; however, less than two thirds of patients achieved LDL cholesterol levels <100 mg/dL. The rates for achieving a target LDL of <70 mg/dL were 22.9% at baseline, 27.4% at 12 months (*P*=0.0003 versus baseline), and 27.9% at 48 months (*P*=0.0258 versus baseline). Only 16.7% of patients had optimal risk-factor control at enrollment

Table 5. Changes in Goals Attained From Baseline to 6, 12, 24, 36, and 48 Months for Symptomatic and Asymptomatic Patients

Characteristic	Clinic Visit (Months)					
	0 (n=2210)	6 (n=1824)	12 (n=1742)	24 (n=1310)	36 (n=822)	48 (n=402)
LDL cholesterol <100 mg/dL						
n	1160	998	1033	769	469	235
Achieved goal %*	59.1	67.0	68.4	69.1	69.8	73.6
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Systolic BP <140 mm Hg						
n	1124	1079	1003	792	492	237
Achieved goal %*	51.6	61.7	60.7	64.1	64.1	65.1
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Glucose at target						
n	1573	1270	1253	919	559	255
Achieved goal %*	74.9	82.0	81.9	81.8	82.4	80.7
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	0.0101
Nonsmoker						
n	1611	1435	1367	1049	673	328
Achieved goal %*	74.4	78.6	78.1	78.4	80.4	80.9
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Rate of achieving at least 3 of 4 goals						
n	1059	974	983	753	440	218
Achieved goal %*	56.2	69.2	69.4	71.9	71.7	74.6
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Rate of achieving 4 of 4 goals						
n	315	384	381	305	196	104
Achieved goal %*	16.7	27.1	26.8	29.0	32.0	36.2
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

BP indicates blood pressure; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from statistical model to account for missing data.

in the trial, and although the change at 6 months was significant, this rate rose to only 27.1%. Significant benefits in risk-factor control were observed across all risk factors throughout follow-up. The percentage of patients achieving the LDL cholesterol goal improved from 59.1% at baseline to 73.6% at 48 months ($P<0.001$). The percentage achieving the systolic blood pressure goal improved from 51.6% to 65.1% ($P<0.001$), and the percentage achieving the glucose goal improved from 74.9% to 80.7% ($P=0.0101$). Nonsmoking improved from 74.4% to 80.9% ($P<0.0001$). The percentage of optimal risk-factor control improved from 16.7% at baseline to 36.2% at 48 months ($P<0.001$).

Discussion

We observed that the majority of participants had control of blood pressure, glucose, and smoking but not LDL cholesterol at the time of enrollment. Very early in the course of participation in the trial, significant improvements were seen for all 4 tracked risk factors. The improvements seen at 6 months of follow-up were sustained for up to 4 years. The statistically significant improvement in risk factors, however, should not obscure the fact that the absolute levels of control of risk factors were far from ideal. Only 28% had achieved optimal risk-factor control by 6 months, and only 35% had achieved it by 48 months. These rates are comparable to the rates of optimal risk-factor control achieved for patients without diabetes and coronary artery disease enrolled in the COURAGE trial and are substantially better than what was achieved for patients with diabetes and coronary artery disease in the COURAGE, BARI 2D, and FREEDOM trials.[10]

Our results may not reflect the epidemiology of risk-factor control among patients with carotid stenosis. One would anticipate that risk-factor control is poorer among the general

Table 6. Changes in Goals Attained From Baseline to 6, 12, 24, 36 and 48 Months for Symptomatic Patients

Characteristic	Clinic Visit (Months)					
	0	6	12	24	36	48
LDL cholesterol <100 mg/dL						
n	494	422	435	347	244	153
Achieved goal %*	52.0	60.5	63.4	65.0	66.8	68.9
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Systolic BP <140 mm Hg						
n	534	496	463	385	271	162
Achieved goal %*	50.4	60.4	61.1	64.8	65.5	64.1
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Glucose at target						
n	811	603	593	453	299	179
Achieved goal %*	79.0	83.8	84.3	83.0	80.9	81.7
P value for difference from baseline		0.0008	0.0002	0.0157	0.3176	0.3100
Nonsmoker						
n	764	677	637	507	363	233
Achieved goal %*	72.7	78.1	77.2	77.8	78.8	78.9
P value for difference from baseline		<0.0001	<0.0001	0.0001	<0.0001	<0.0001
Rate of achieving at least 3 of 4 goals						
n	479	424	428	365	233	144
Achieved goal %*	52.8	65.4	67.8	72.0	69.8	71.9
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Rate of achieving 4 of 4 goals						
n	138	160	170	142	99	73
Achieved goal %*	15.2	25.1	26.8	27.1	29.4	35.4
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

BP indicates blood pressure; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from statistical model to account for missing data.

population with carotid stenosis because of the healthy-participant bias. Consequently, there may be an even greater opportunity to improve vascular risk factors in the general population of patients with carotid atherosclerosis. For patients with coronary artery disease, there is considerable opportunity to improve vascular risk factors. Among the >3000 patients with self-reported coronary artery disease in the REGARDS study, only 16% met all 3 goals for aspirin, blood pressure, and LDL cholesterol.[11]

CREST had no treatment group that received only medical therapy. Emphasis in the trial was placed on selecting sites with outstanding surgical and interventional teams and ensuring low risk for periprocedure stroke following either carotid endarterectomy or carotid stenting. The medical management was decentralized, even beyond the site level, because it was often provided by the usual-care physician (generally the referring physician). Accordingly, aggressive and timely control of risk factors by the site or by the CREST central leadership was not feasible. The results of the medical monitoring were provided to the usual-care physician, but whether or not the results were acted on when provided (eg, systolic blood pressures ≥140 mm Hg or LDLs ≥100 mg/dL) or how they were acted on could not be determined.

The enrollment period for CREST was 7.5 years from 2000 until midyear 2008. During this time, risk-factor-management guidelines for primary and secondary prevention of stroke were published and widely disseminated.[1,2] Consequently, it is not surprising that control of risk factors at baseline improved in comparisons of the earlier years of enrollment to the later years. In the secondary prevention trial, Vitamin Intervention for Stroke Prevention (VISP), control of several risk factors at baseline also improved significantly during the 4.4-year recruitment period from August 1997 to December 2001.[12] Hypertension and hypercholesterolemia management

Table 7. Changes in Goals Attained From Baseline to 6, 12, 24, 36 and 48 Months for Asymptomatic Patients

Characteristic	Clinic Visit (Months)					
	0	6	12	24	36	48
LDL cholesterol <100 mg/dL						
n	666	576	598	422	225	82
Achieved goal %*	65.7	73.0	73.1	72.7	72.1	82.3
P value for difference from baseline		<0.0001	<0.0001	0.0006	0.0122	0.0002
Systolic BP <140 mm Hg						
n	590	583	540	407	221	75
Achieved goal %*	52.7	63.0	60.4	63.7	62.8	67.2
P value for difference from baseline		<0.0001	0.0002	<0.0001	0.0004	0.0024
Glucose at target						
n	762	667	660	466	260	76
Achieved goal %*	71.0	80.3	79.7	80.7	84.7	82.0
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	0.0118
Nonsmoker						
n	847	758	730	542	310	95
Achieved goal %*	76.0	79.0	79.0	79.0	82.8	85.5
P value for difference from baseline		0.0030	0.0050	0.0098	<0.0001	0.0007
Rate of achieving at least 3 of 4 goals						
n	580	550	555	388	207	74
Achieved goal %*	59.4	72.6	70.9	71.9	73.4	82.0
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Rate of achieving 4 of 4 goals						
n	177	224	211	163	97	31
Achieved goal %*	18.2	29.0	27.0	30.4	34.5	36.0
P value for difference from baseline		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

BP indicates blood pressure; LDL, low-density lipoprotein.
*Values (and SE) are the predicted values from statistical model to account for missing data.

and control improved; there was an increase in use of antiplatelet medications, newer classes of antihypertensive medications, and lipid-lowering drugs.[12] Similar to the CREST recruitment period, during the VISP enrollment period, national guidelines were released in addition to results from other secondary prevention trials. For stroke prevention trials with long recruitment periods, it is important that risk-factor management be standardized and be as stable as possible across all treatment groups so as not to differentially reduce the event rate and thus the ability of the trial to detect treatment effects.[13]

There is growing interest in conducting a randomized trial to compare intensive medical therapy and revascularization, similar to what has been done for stable coronary disease,[14] atherosclerotic renal artery stenosis,[15] and intracranial cerebrovascular disease.[16] In the Stenting Versus Aggressive Medical Management for Intracranial Stenosis (SAMMPRIS) study, a centralized model for treatment of risk factors was used. Management of medications for risk factors was provided by the local-site neurologist but was specified in a step-by-step protocol. Adherence to the protocol was monitored and enforced centrally by a SAMMPRIS medical core; lifestyle coaching was also provided by a national provider under direction of the SAMMPRIS medical core. The control of risk factors was exceptional with these methods. At baseline, 4 months, and 1 year, the mean systolic blood pressure was 146.8±21.8, 134.8±17.0, and 133.8±17.1 mm Hg, respectively. For LDL, the results at baseline, 4 months, and 1 year were 97.7±36.6, 72.8±26.0, and 68.2±27.5 mg/dL, respectively. Consequently, along with the results we report in this paper, SAMMPRIS suggests that achieving intensive therapeutic targets with medical therapy may require a tightly integrated organizational model with close central management of a hands-on local medical management team. The

soon-to-be-initiated CREST-2 trial of intensive medical management with or without revascularization in patients with asymptomatic carotid stenosis will use such an approach to management of vascular risk factors.[17]

The so-called inclusion benefit has not been clearly demonstrated in cancer trials[18]; however, it may be present in trials like CREST-2, in which proven therapies will be given to all patients adjunctive to the interventions to which the patients are being randomized. We do not know how risk factors changed for patients who were eligible for CREST but who refused participation. Nonetheless, we suspect that patients benefited from being included in the trial because favorable effects were observed across key vascular risk factors. In CREST, adherence to evidence-based guidelines was promoted across clinical centers. Such guidelines have been shown to improve clinical practice.[19] It is both surprising and disappointing that the rates of optimal risk-factor control, although relatively improved, remain poor in an absolute sense. One might have anticipated a greater effect on behaviors of the treating physicians; however, reasons for lack of risk-factor control are multifaceted and involve not only the treating physicians but also other healthcare providers, the healthcare system, and the individual patient. Related reasons include medication noncompliance, inadequate therapy, and inappropriate therapy.

A limitation of our study is that data are provided on only 4 metrics for vascular risk factors. Data were not available for other important risk factors such as frequency of exercise or quality of diet. In addition, not every patient enrolled in the study had every follow-up visit, and not every risk factor was assessed at every follow-up visit. Loss to follow-up was more problematic for the later visits than for the earlier visits. Although missing visits did not occur at random, the proportion of missed visits was very low and was unlikely to have altered the basic conclusions that risk factors improved and that optimal risk-factor control was rarely achieved. Cigarette smoking was assessed by self-report and not by objective measures such as the detection of nicotine metabolites in serum; however, smoking status tends to be slightly underestimated by self-report.[20] This implies that the rate of 17% for active smoking at 48 months after randomization conservatively estimates the true active smoking rate.

Conclusion

In conclusion, significant improvements were seen in control of vascular risk factors in patients enrolled in CREST. However, substantial opportunities remained for most patients to further improve upon medical management. Future carotid interventional trials should place increasing emphasis on controlling vascular risk factors.

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Disclosures

None.

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