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Ultrasound criteria for severe in-stent restenosis following carotid artery stenting

Wei Zhou, MD,[a] Deborah D. Felkai, RN, RVT,[c] Mark Evans, RVT,[c] Sally A. McCoy, RN,[c] Peter H. Lin, MD,[b,c] Panagiotos Kougias, MD,[b,c] Hosam F. El-Sayed, MD,[b,c] and Alan B. Lumsden, MD,[b] *Stanford, Calif; and Houston, Tex*

Purpose: **In-stent restenosis (ISR) is a known complication following carotid artery stenting (CAS). However, ultrasound criteria determining ISR are not well established. We evaluated alternative ultrasound velocity criteria for >70% ISR in our institution.**

Methods: **Clinical records of 256 patients undergoing 282 consecutive CAS procedures over a 42-month period were reviewed. Follow-up ultrasounds were available for analysis in 237 patients. Selective angiograms and repeat interventions were performed for >70% ISR. Ultrasound criteria including peak systolic velocity (PSV), end diastolic velocity (EDV), and internal carotid to common carotid artery ratios (ICA/CCA) were examined. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for PSV (200, 250, 300, 350, and 400 cm/s), EDV (70, 80, 90, 100 cm/s), and CCA/ICA (3, 3.5, 4, 4.5, 5).**

Results: **Twenty-two carotid angiograms were performed and 18 lesions had confirmations of >70% ISR in 11 patients including prior CEA in five patients and neck irradiation in two patients. Receiver operator characteristics (ROC) was analyzed for PSV, EDV, and CCA/ICA ratio. For 70% or greater angiographic ISR, PSV > 300 cm/s correlated to a 94% sensitivity, 50% specificity, 90% positive predictive value (PPV), and 67% negative predictive value (NPV); EDV > 90 cm/s correlated to an 89% sensitivity, 100% specificity, 100% PPV, and 67% NPV; and ICA/CCA > 4 had a 94.4% sensitivity, 75% specificity, 94% PPV, and 75% NPV. A significant color flow disturbance was detected in one patient who did not meet the aforementioned ultrasound velocity criteria. Further statistical analysis showed that an EDV of 90 cm/s provided the best discriminant value.**

Conclusion: **Our study demonstrated that PSV > 300 cm/s, EDV > 90 cm/s, and ICA/CCA > 4 correlated well with >70% ISR. Although still rudimentary, these velocity criteria combined with color flow patterns can reliably predict severe ISR in our vascular laboratory. However, due to the relatively infrequent cases of severe ISR following CAS, a multicentered study is warranted to establish standard post-CAS ultrasound surveillance criteria for severe ISR. (J Vasc Surg 2008;47:74-80.)**

Several large prospective trials have demonstrated that carotid artery stenting (CAS) is a safe alternative to carotid endarterectomy (CEA), particularly for high risk-patients including those with severe cardiopulmonary comorbidities, recurrent stenosis following endarterectomy, prior neck irradiation, and inaccessible lesions above the C2 level.[1-4] Over the last decade, CAS has become increasingly adopted in the medical community. As the result, The Centers for Medicare and Medicaid Services (CMS) has expanded Medicare coverage for carotid artery stenting in high-risk patients with >70% symptomatic carotid artery stenoses. Additionally, high-risk patients who have symptomatic carotid artery stenosis between 50% and 70% and those who are asymptomatic with an 80% or greater stenosis will be covered if enrolled in investigational device exemption (IDE) clinical trials or FDA required post-approval studies.

Despite the promising results of CAS, questions remain regarding the long-term durability of this endovascular treatment modality.[5-8] Our study and others has demonstrated that CAS-related in-stent restenosis (ISR) is not uncommon, but severe ISR is relatively rare.[5-11] Therefore, it is essential to identify those patients with clinically significant ISR who warrant further interventions. Current ultrasound criteria for classifying the severity of carotid artery stenosis are deemed unreliable for stented arteries due in part to the change of arterial wall compliance following stenting.[12-14] Several studies have evaluated ultrasound criteria for moderate ISR.[12,15] Studies on ultrasound criteria for clinically significant high-grade ISR is limited due to the relatively low incidences of severe ISR following CAS.[16] The purpose of this study is to examine our experience of post-CAS ultrasound surveillance and to evaluate ultrasound criteria for clinically significant >70% ISR following CAS.

MATERIAL AND METHODS

Patient selections and stenting procedures. Hospital charts and clinical records were reviewed on all patients who underwent CAS over a 42-month period

From the Division of Vascular and Endovascular Surgery, Department of Surgery, Stanford University,[a] the Division of Vascular Surgery and Endovascular Therapy, Michael E. DeBakey Department of Surgery, Baylor College of Medicine,[b] and the Division of Vascular Surgery, Michael E. DeBakey VA Medical Center.[c]

Competition of interest: none.

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Correspondence: Wei Zhou, MD, Department of Surgery, Stanford University, 300 Pasteur Dr #H3640, Stanford, CA 94305-5642 (e-mail: weizhou@stanford.edu).

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between January 2003 and July 2006. A total of 282 consecutive CAS procedures were performed on 256 patients at Baylor College of Medicine-affiliated hospitals, primarily at Michael E. DeBakey VA Medical Center. Carotid duplex scans were performed prior to the stenting procedures, and high-grade carotid stenoses were documented on all patients. Follow-up ultrasounds were available for analysis in 237 patients (93%). High-risk patients with symptomatic carotid stenosis of 70% or greater and asymptomatic carotid stenoses of 80% or greater were considered for stenting protocol as described in our previous studies.[9,17] Nonetheless, selected symptomatic patients with 60% or greater ulcerative lesions were also treated.

Carotid stenting procedures were performed using a standard protocol. All CAS procedures were performed in the operating room with the routine use of embolization protection devices (EPD) including FilterWire system (Boston Scientific, Natick, Mass), ACCUNET embolization protection device (Guidant Co, Santa Clara, Calif), and Emboshield embolic protection system (Abbott Vascular, Redwood City, Calif). Either an endovascular operative suite (Siemens, Siemens Medical Systems Inc, Iselin, NJ) or a mobile fluoroscopic unit (OEC 9800 model, GE Medical Systems, Salt Lake City, UT) was used for the procedure. The technical details of CAS has been described previously.[9,17] The stents implanted include Wallstent (Boston Scientific, Natick, Mass), ACCULINK (Guidant Co, Santa Clara, Calif), and Xact (Abbott Vascular Devices, Redwood City, Calif). Post-stenting balloon angioplasty was performed for over 20% residual stenoses. Completion angiogram including biplanar carotid and cerebral views was performed prior to the capture of the EPD to document the vascular anatomy and to exclude cerebral thromboembolism. The groin puncture site was routinely closed with a closure device (Perclose or StarClose, Abbott Vascular Devices, Redwood City, Calif).

Ultrasound surveillance. Patients were routinely kept in the hospital overnight and discharged home the following day. Follow-up visits with carotid duplex ultrasounds were performed at 1, 6, and 12 months following the interventions and each year thereafter. Patients who required interventions for clinically significant ISR following CAS were evaluated with Duplex ultrasounds at 3-month intervals. Follow-up ultrasounds were available for analysis in 237 patients. All Duplex ultrasounds were performed by experienced registered vascular technologists using Phillips/ATL HDL 5000 SonoCT or Phillips IU 22 ultrasound imaging system (Bothell, Wash) in two vascular laboratories. Velocities of the common carotid artery (CCA) were measured proximal to the stent. Velocities of internal carotid artery (ICA) were measured within the stent and distal to the stent when feasible. Peak systolic velocity (PSV) and end diastolic velocity (EDV) of ICA were obtained at the narrowest portion of ICA within the stent. The ICA/CCA ratio was calculated based on the PSV of ICA and CCA. The velocity criteria used to evaluate carotid artery stenosis in non-stented arteries were modified from the University of Washington criteria and were validated in our laboratories.[18] Briefly, peak systolic velocity (PSV) > 125 cm/s, end diastolic velocity (EDV) < 140 cm/s, and ICA/CCA > 4 correlates to 70% to 79% stenosis; and EDV > 140 cm/s correlates to >80% stenosis. A clinically significant stenosis was defined as a luminal reduction of 70% or higher.

Studies have shown that stented arteries have marked increased ultrasound velocity.[12-14] However, for the purpose of this study, patients with PSV > 200 cm/s, EDV > 80 cm/s, or ICA/CCA > 3 were identified as potentially having significant >70% ISR. These preliminary velocity criteria were chosen to include the patients with potentially moderate to severe ISR based on our clinical experiences and were intentionally lower than we anticipated. By doing so, we increased the sensitivity of ultrasound criteria and, therefore, achieved an adequate sample size of patients who underwent angiography. The criteria were also selected to avoid unnecessary exposure of angiography-related risks for the majority of the patients. Patients who met any single criteria were invited for angiographic confirmation. Each velocity criteria was individually considered and examined using receiver operator characteristics (ROC) analysis. Additionally, luminal reductions on gray-scale images as well as color flow disturbances were also considered, which are particularly important for post-stent surveillance.

Angiographic measurement. Patients with potentially >70% ISR as identified on ultrasounds were contacted and subsequently underwent biplanar carotid angiography to verify the severity of the stenosis. Typically, two views of cervical angiography including cross-table lateral and oblique views were obtained to define the lesion. Occasionally, an anterior-posterior view was required to illuminate the lesion. The stenosis was measured geometrically based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criterion using an electronic caliber and a software package provided by Siemens Medical Solution. Specifically, the degree of stenosis was calculated from the ratio of the linear luminal diameter of the narrowest segment of the stented artery to the diameter of the internal carotid artery beyond any poststenotic dilatation. Carotid angioplasty and possible stenting were subsequently performed following the standard protocol upon confirmation of the lesions.

Statistical analysis. The ultrasound velocities for stented arteries with suspected severe ISR were reviewed. The total number of stented arteries that had both angiographic and sonographic data formed the base of the analysis. Continuous variables were expressed as mean ± SEM. Clinical variables that may be associated with ISR following CAS were analyzed. Wilcoxon rank sum tests, χ^2 analyses, or paired Student *t* tests were performed where appropriate. ROC curves were used to compare angiographic data with velocity measurements to determine optimal velocity criteria for >70% ISR. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated to determine the optimal threshold for PSV, EDV, and ICA/CCA ratio in determining >70% ISR. The test results were considered significant at a *P* value of less than .05. All statistical analyses were performed using the StatView software program (SAS Institute, Cary, NC).

RESULTS

Clinical outcomes. Two hundred fifty-six patients successfully underwent 282 consecutive CAS procedures during the study period. Among them, 117 (46%) patients were asymptomatic, and 26 patients had bilateral lesions. Among the 282 successful CAS procedures, the mean carotid artery stenosis decreased from 85% ± 12% prior to the stent placement to a post-stenting mean residual stenosis of 10% ± 5%. Monorail Wallstents (Boston Scientific) were placed in 224 (79%) carotid arteries. ACCULINK stents (Guidant) were used in 28 (10%) procedures and Xact stents (Abbott Vascular) in 30 (11%) procedures. The mean in-hospital length of stay was 1.7 ± 1.4 days. The overall 30-day stroke and death rate was 2.5% (n = 7). There are no significant differences in perioperative mortality and morbidities among three stent systems.

Follow-up ultrasound evaluation. In addition to four perioperative deaths, 15 patients were lost to follow-up. A total of 237 patients were available for ultrasound evaluation during a mean follow-up of 32 months (range, 6 months to 48 months). These patients underwent ultrasound surveillance at 1 month, 6 months, 1 year, and yearly thereafter. Patients with increased flow velocities or suspected ISR were evaluated at 3-month intervals. During the follow-up period, 34 patients died of various causes that were unrelated to the procedures. A total of 22 carotid angiograms were performed on patients with suspected severe ISR based on ultrasound velocity criteria (Table I).

Eighteen angiograms (7.6%) confirmed >70% ISR on 11 patients including prior CEA in five patients, neck irradiation in two, and neck dissection in one. Three patients presented with recurrent ISR. Among them, one patient had multiple bilateral recurrences (patient 2, Table I) that required repetitive interventions on six different occasions. Clinical characteristics of these patients are listed in Table II. Among the significant ISR, four lesions were symptomatic (22.2%) including two lesions that caused strokes, one associated with transient ischemic attack, and one that led to amaurosis fugax. Specificity, sensitivity, PPV, and NPV of various ultrasound measurements were analyzed including multiple potential thresholds for PSV, EDV, and ICA/CCA ratio. The results are shown in Table III. Data derived from the ROC curves were used to calculate the parameters of accuracy for PSV (Fig 1, *a*), EDV (Fig 1, *b*), and ICA/CCA ratio (Fig 1, *c*) through a wide range of values to determine the optimal threshold for >70% ISR. A larger area under the ROC curve measures improved discrimination. Based on these criteria, the area under the curve (area ± SE) and significance (*P*) were calculated for various ultrasound velocity values. Our analysis showed that EDV provided the best discriminative power (Fig 2). Further analyses showed ICA PSV of 293 cm/s on ROC curve corresponded to a 94.4% sensitivity and 50% specificity. We decided PSV of 300 cm/s as the cutoff point, which yielded 89.5% PPV, 66.7% NPV, and an overall accuracy of 86.4%. Additionally, EDV of 89.5 cm/s corresponded to an 89% sensitivity and 100% specificity on ROC curve analysis. We chose EDV of 90 cm/s as a cutoff

Table I. Ultrasound evaluations and angiographic results on patients with suspected ISR

Patients No (n)	*Angiogram No (n)*	*ICA PSV (cm/s)*	*ICA EDV (cm/s)*	*ICA/CCA*	*Angiogram >70% ISR*
1	1	320	116	5.2	Yes
2	2	482	199	5.7	Yes
	3	414	188	3.9	Yes
	4	434	212	5.1	Yes
	5	601	306	28.6	Yes
	6	355	162	4.0	Yes
	7	377	96	5.2	Yes
3	8	322	90	14.0	Yes
	9	431	104	9.0	Yes
4	10	422	90	7.3	Yes
5	11	266	75	5.9	Yes
6	12	509	173	8.1	Yes
	13	488	175	8.4	Yes
7	14	475	170	5.1	Yes
8	15	420	90	5.7	Yes
9	16	420	89	5.6	Yes
10	17	581	159	9.8	Yes
11	18	360	114	5.4	Yes
12	19	387	63	1.3	No
13	20	350	88	6.3	No
14	21	232	76	3.0	No
15	22	247	67	3.5	No

ICA, Internal carotid artery; *PSV,* peak systolic velocity; *EDV,* end diastolic velocity; *ICA/CCA ratio*, internal carotid artery to common carotid artery peak systolic velocity ratio.

Table II. Clinical characteristics of patients with angiographic evident ISR (>70%)

	Number, %
Total number of patients	11
Total number of carotid artery with >70% ISR	18
Male gender	10 (90.9%)
Age (y)	77 (55-87)
Severe ISR carotid lesions (total n = 18)	
Asymptomatic	14 (77.8%)
Stroke	2 (11.1%)
Transient ischemic attack	1 (5.6%)
Amaurosis fugax	1 (5.6%)
Patient comorbidities (total n = 11)	
Coronary artery disease	7 (63.4%)
Congestive heart failure	3 (27.3%)
Hypertension	10 (90.9%)
Diabetes	5 (45.5%)
Chronic obstructive pulmonary disease	4 (36.4%)
Renal insufficiency (creatinine >1.5 mg/dl)	1 (9.1%)
Anatomical limitations (total n = 11)	
History of neck radiation	2 (18.2%)
Post-CEA restenosis	5 (45.4%)
s/p radical neck dissection	1 (9.1%)
High-carotid bifurcation	1 (9.1%)

ISR, In-stent restenosis; *CEA,* carotid endarterectomy.

Table III. Parameters of ICA PSV, EDV, and ICA/CCA ratio for >70% ISR

ICA PSV (cm/s)	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Accuracy (%)*
400	67	100	100	40	73
350	83	50	88	40	77
300	94	50	90	67	86
250	100	50	90	100	91
200	100	0	82		82
ICA EDV (cm/s)					
100	67	100	100	40	73
90	89	100	100	67	91
80	94	75	94	75	91
70	100	50	90	100	91
ICA/CCA ratio					
>5	89	75	94	60	86
>4.5	89	75	94	60	86
>4	94	75	94	75	91
>3.5	100	50	90	100	91
>3	100	25	86	100	91

ICA, Internal carotid artery; *PSV,* peak systolic velocity; *EDV,* end diastolic velocity; *ICA/CCA ratio*, internal carotid artery to common carotid artery peak systolic velocity ratio; *PPV,* positive predictive value; *NPV,* negative predictive value.

point, which yielded 100.0% PPV, 66.7% NPV, and an overall accuracy of 90.9%. Furthermore, various thresholds of ICA/CCA ratios were also examined and revealed an ICA/CCA of 3.95 correlated to a 94.4% sensitivity, 75.0% specificity. A cutoff point of 4.0 yielded 94.4% PPV, 75.0% NPV, and an overall accuracy of 90.9%. Several combinations of PSV, EDV, and ICA/CCA ratio were also evaluated. However, combinations of various ultrasound velocity criteria did not improve the accuracy of predicting >70% ISR.

Management for significant ISR. All patients underwent endovascular interventions, and the average time interval of reintervention from the initial CAS procedure was 11 months (range, 1 month to 24 months). Technical successes as defined by the resolution of the stenosis after treatment were achieved in all patients. The mean carotid artery stenosis decreased from 88% to 16% after reintervention. No procedural-related complications were noted following ISR intervention. All patients received baseline ultrasound evaluations at 1 month following the procedure. Significant velocity decreases in ultrasound parameters were observed including a PSV decrease by 55.2% ($P = .03$) and EDV by 67.9% ($P = .02$). However, a decrease in ICA/CCA ratio did not reach statistical significance ($P = .17$) (Table IV). During a median follow-up period of 18 months following ISR intervention, three patients developed recurrent stenoses including one patient with multiple recurrences. Additional interventions using a cutting balloon angioplasty were successfully performed and one patient required an additional stent placement.

DISCUSSION

We, along with several other investigators, have demonstrated that moderate ISR following carotid stenting is not uncommon and post-procedural follow-ups are essential in identifying those patients with hemodynamically significant ISR that require interventions.[8-10,16] The duplex ultrasound, a sensitive and widely available image modality, is an ideal screening tool for de novo stenosis of carotid artery and post-CEA restenosis. However, carotid ultrasound is deemed unreliable for post-stent surveillance in early studies largely due to lack of well-established ultrasound criteria and falsely elevated velocities associated with increased stiffness of the stented ICA. Although several recent studies have reported ultrasound criteria for mild and moderate ISR, studies investigating severe ISR are limited due in part to the low incidences of severe ISR and relatively short follow-up in most centers.[8,16,19] In this study, we identified a relatively larger number of significant ISR (>70%) that required interventions in our high-volume center and performed systemic analyses to categorize the optimal threshold for ultrasound criteria.

Several studies have shown that ISR is a well-documented late complication following carotid artery stenting.[5,7,11] Our experience of carotid stenting echoes their observation. In our study, the majority (71%) of significant ISR were identified during the 6-month or 12-month ultrasound follow-up. The average time interval of reintervention for significant ISR from the initial CAS procedure in our series was 11 months ranging from 1 month to 24 months. We have also observed decreased ultrasound velocities over time in selected patients who presented with moderately elevated velocity during the initial follow-up ultrasound. However, we were not able to identify factors predictive of ultrasound progression or regression. Particularly, one patient presented with multiple bilateral severe ISR that required interventions. His bilateral ISR occurred consecutively, thus, the ultrasound velocity of the suspected side was not affected by the contralateral side as the contralateral side had relatively normal velocity. We, therefore, decided not necessary to exclude this patient from our study. Ultimately, the progress of the ultrasound velocity on this patient had reduced 36 months following the initial stenting procedure. The incidence of hemodynamically significant ISR in our study is 7.6% over a 32-month follow-up period, which remained consistent with other clinical series. However, two patients refused diagnostic angiogram or any further intervention despite significantly elevated ultrasound velocities. Among whom, one patient had an isolated increase in ICA PSV 18 months following cutting balloon angioplasty for severe ISR. We, therefore, estimate that the true incidence of ISR may be slighter higher. Although we did not find difference in ISR rates, perioperative mortality or morbidities among different carotid stents used, the small cohort of patients who received ACCULINK or Xact stents precluded us from draw a valid conclusion.

Several investigators have attempted to establish ultrasound criteria for ISR following CAS. Lal and associates compared post-carotid stenting ultrasound velocities with angiographically measured residual in-stent stenosis following CAS and proposed a new criteria of PSV > 150 cm/s

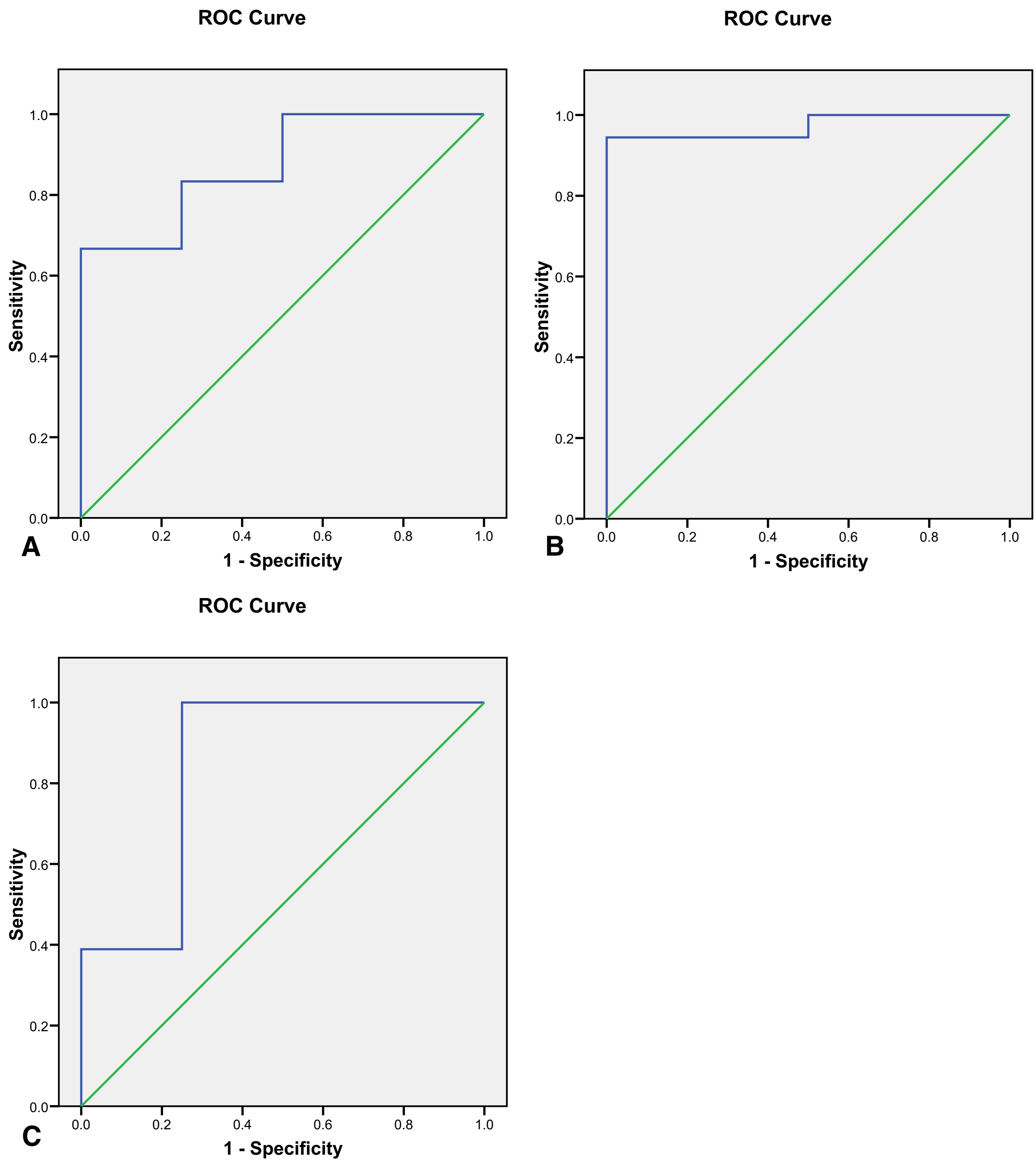

Fig 1. **A**, Receiver operator characteristic curve for ICA peak systolic velocity to differentiate between ≥70% and <70% stenosis in the stented arteries. **B**, Receiver operator characteristic curve for ICA end diastolic velocity to differentiate between ≥70% and <70% stenosis in the stented arteries. **C**, Receiver operator characteristic curve for peak systolic velocity ratio of internal carotid artery and common carotid artery to differentiate between ≥70% and <70% stenosis in the stented arteries

with ICA/CCA > 2.16 defining over 20% ISR.[14] Ultrasound criteria for severe ISR were, however, not examined in their study. Stanziale and colleagues retrospectively reviewed 118 stented carotid arteries and identified 19 patients with >50% ISR.[16] However, only six patients had >70% ISR. Their analyses showed that PSV ≥ 350 cm/s and ICA/CCA ratio ≥4.75 correlate best with ≥ 70% ISR following CAS. Similarly, Peterson and associates reviewed ultrasound velocities following CAS to identify ultrasound criteria indicative of severe ISR and found four patients

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PSV	.875	.087	.022	.705	1.045
EDV	.972	.033	.004	.907	1.037
Ratio	.847	.138	.033	.577	1.117

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig 2. The area under the ROC curve (area ± SE) and significance (P) were calculated for various ultrasound velocity values including PSV, EDV, and ICA/CCA ratio. Our analysis showed that EDV provided the best discriminative power.

with severe ISR.[19] They concluded that ISR can reliably be detected by carotid duplex using cut-off values of 170 cm/s PSV, 120 cm/s EDV, and >50% increase over immediate postoperative values. Like others, we have previously examined moderate ISR (>60%).[9] However, a moderate ISR typically does not warrant urgent treatment. In this study, we examined follow-up ultrasound evaluations of 237 patients to determine clinically significant ISR that require prompt intervention. Although the consensus is still lacking on treatment threshold for ISR, it is generally accepted that 70% ISR is considered significant and should be intervened. We, therefore, determined to evaluate ultrasound velocity criteria correlating to 70% ISR. In addition, diameter reduction on gray-scale and significant color flow disturbance were also considered. Although we did not analyze the progress of ultrasound velocity following CAS procedures, we have observed reduction of velocities over time in selected patients as mentioned previously. We, therefore, postulate that the initial ultrasound does not predict the risk of ISR and serial follow-up ultrasound evaluations are necessary to detect significant ISR.

Unlike other studies, our analysis showed that ultrasound velocity criteria for greater than 70% ISR is surprisingly similar to the criteria for non-stented arteries in our vascular laboratory in spite of much higher observed values of PSV, EDV, and ICA/CCA ratios in the arteries with severe ISR. This observation likely reflects the operator and laboratory-dependent nature of ultrasound measurement. To determine the optimal value, ROC curves were analyzed for PSV, EDV, and ICA/CCA. Our ROC analysis showed no optimal value for ISR, and that EDV greater than 90 cm/s or ICA/CCA greater than 4.0 corresponded to the most accurate ultrasound velocity profiles. Although PSV of 300 cm/s is less sensitive than PSV of 250 cm/s, the small but definitive risks of carotid angiograms prompted us to choose PVS of 300 cm/s as the threshold for significant ISR. Our chosen criteria, particularly PSV, may sacrifice sensitivity in change for specificity. Additionally, statistical selection bias can not be excluded as we only included those patients with elevated velocities and high likelihoods for significant ISR. Despite our effort of intentionally lowering velocity criteria for selective angiogram, the total patient cohort for ROC analysis was relatively small due to low incidence of severe ISR. In order to minimize the statistical bias, we will need to subject an additional number of patients to invasive angiograms and contrast exposure. We believe that it is unnecessary to expose patients to these potential risks. Moreover, we analyzed the ultrasound velocity of the patients who did not meet velocity criteria for carotid angiograms, and compared the ultrasound velocities of the patients who underwent carotid angiograms with those who did not receive angiograms. Using a student *t* test analysis with unequal variances, we demonstrated that the velocities of these two groups had minimal overlap ($P <$ .05). The significantly different distribution patterns of the two groups further confirmed that the number of patients with significant ISR but did not receive carotid angiogram was extremely small. Therefore, we advocate utilizing the aforementioned velocity thresholds along with color flow disturbance and gray-scale imaging to detect significant ISR. Nonetheless, other noninvasive diagnostic modalities, such as computed tomography (CT) angiogram and magnetic resonance imaging (MR) angiogram, perhaps should be utilized to validate ultrasound velocity criteria in future studies.

In addition to identifying severe ISR using ultrasound velocity criteria, our study also showed significant changes in velocity parameters following a successful intervention for ISR, particularly PSV and EDV. ICA/CCA ratio did not reach statistical significant despite marked decrease in value. Although we did not find a correlation between the postintervention velocity and the likelihood of recurrent ISR ($P >$ .05), we demonstrated that postintervention ultrasound velocities can be used to indicate success of interventions and as a baseline for long-term follow-up after CAS procedures.

Admittedly, there are certain limitations to our study. Although it is the largest series of significant ISR following CAS to date, our series only comprised of 18 carotid arteries with >70% ISR during a mean follow-up of 32-months. This relatively limited patient cohort is largely due to a low incidence of severe ISR following CAS and inadequate detection criteria to identify the patients for repeat carotid angiogram. The ultrasound evaluations of carotid stents were retrospectively reviewed, and only patients with markedly increased ultrasound velocities underwent angiographic confirmation. We, therefore, may have underestimated a small number of stented arteries with false negative ultrasound values. However, the incidence of presumed false negative studies is extremely low, and we did not believe that it is justified to perform angiograms on a wide sample of our patient population as mentioned previously. It is also important to recognize that our velocity criteria is established in our own laboratory where all duplex ultrasounds were performed by experienced registered vascular technologists using Phillips/ATL HDL 5000 SonoCT or Phillips IU 22 ultrasound imaging system. We did not compare our results with other laboratories or other scanner models. Therefore, it is crucial for individual vascular laboratory to validate its own duplex criteria to establish reliable ultrasound criteria for clinically significant ISR.

In conclusion, our study demonstrated that PSV > 300 cm/s, EDV > 90 cm/s, and ICA/CCA > 4 correlated well

Table IV. Ultrasound velocity changes in patients undergoing interventions for >70% ISR

Total n = 18	*Preintervention ISR*	*One month postintervention*	P *value*
ICA PSV (cm/s)	421.1 ± 22 (266-601)	153.2 ± 19 (82-352)	.03
ICA EDV (cm/s)	181 ± 23 (75-306)	44.2 ± 5 (28-75)	.02
ICA/CCA	8.2 ± 2 (3.9-28.6)	2.16 ± 0.37 (0.95-4.03)	.17

ICA, Internal carotid artery; *PSV,* peak systolic velocity; *EDV,* end diastolic velocity; *ICA/CCA ratio*, internal carotid artery to common carotid artery peak systolic velocity ratio.

with >70% ISR in our laboratory. These velocity criteria combined with color flow pattern and gray-scale image can reliably predict severe ISR. Our study also demonstrated that postintervention ultrasound criteria were useful in confirming the success of the procedures and can be used as a baseline for long-term follow-up after carotid artery stenting. The proposed velocity thresholds in this study form the basis for additional multicentered prospective validation studies to further establish standard post-CAS ultrasound surveillance criteria. Moreover, each vascular laboratory may need to establish local ultrasound criteria for detecting significant ISR.

AUTHOR CONTRIBUTIONS

Conception and design: WZ
Analysis and interpretation: WZ
Data collection: DF, ME, SM, PK, HE, AL
Writing the article: WZ
Critical revision of the article: WZ, PL
Final approval of the article: WZ, DF, ME, SM, PL, PK, HE, AL
Statistical analysis: WZ
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Overall responsibility: WZ

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