Carotid Stent Fractures Are Not Associated With Adverse Events

Results From the ACT-1 Multicenter Randomized Trial (Carotid Angioplasty and Stenting Versus Endarterectomy in Asymptomatic Subjects Who Are at Standard Risk for Carotid Endarterectomy With Significant Extracranial Carotid Stenotic Disease)

BACKGROUND: The impact of carotid artery stent fractures on the incidence of adverse clinical events remains unclear. The objective of this study is to report the stent fracture rate and its association with in-stent restenosis and adverse outcomes in the ACT-1 trial (Carotid Angioplasty and Stenting Versus Endarterectomy in Asymptomatic Subjects Who Are at Standard Risk for Carotid Endarterectomy With Significant Extracranial Carotid Stenotic Disease).

METHODS: ACT-1 is a prospective multicenter trial of patients who have standard surgical risk with severe asymptomatic carotid artery stenosis randomly assigned to carotid artery stenting or carotid endarterectomy (Abbott Vascular). The primary end point was a composite of death, stroke, or myocardial infarction during the 30 days after the procedure or ipsilateral stroke during the 365 days after the procedure. After 771 patients were enrolled, successively randomly assigned patients were required to undergo annual radiographic (x-ray) analysis for stent fracture. Images were independently adjudicated by a core laboratory.

RESULTS: Of 1021 patients treated with carotid artery stenting during a mean follow-up of 3.1±1.6 years, 939 had at least 1 x-ray during the follow-up period. Stent fracture was reported in 51 (5.4%) patients. With a maximum follow-up period of 5 years, adverse clinical outcomes occurred in 39 patients with at least 1 x-ray during the follow-up. Of 826 (80.9%) subjects who underwent both duplex ultrasound and x-ray, 822 (99.5%) were interpretable. There was no association between stent fracture and the primary end point (P=0.86) or with restenosis (P=0.53).

CONCLUSIONS: In this large, independently adjudicated, multicenter study, the stent fracture rate was low and not associated with major adverse clinical events or in-stent restenosis.

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Clinical Perspective

What Is New?

- Carotid stent fracture is uncommon, and not associated with in-stent restenosis or with serious adverse clinical outcomes.
- Adverse events associated with carotid artery stenting including death, stroke, myocardial infarction, and clinically driven target lesion revascularization are uncommon.

What Are the Implications?

- Routine surveillance for carotid stent fracture is unnecessary.
- If a fracture is identified in an asymptomatic patient, intervention will rarely be required.

Treatment with carotid artery stenting (CAS) and carotid endarterectomy (CEA) has been compared in several prospective randomized trials of carotid artery stenosis.[1–5] Because the neck is mobile, and carotid stents undergo repeated flexion, extension, and rotation, carotid stent fractures have been reported.[6–18] Stent fracture, a complication found only with CAS in carotid revascularization, may affect the late outcomes of CAS. Reported rates of carotid stent fracture have been variable, ranging from 0% to 29%,[18,19] but the true incidence of carotid stent fractures has not been systematically studied and remains unknown. The current association of carotid stent fracture with in-stent restenosis, neurological and cardiac events, or death is derived from small, uncontrolled series lacking uniform event and stent fracture adjudication.[15]

ACT-1 (Carotid Angioplasty and Stenting Versus Endarterectomy in Asymptomatic Subjects Who Are at Standard Risk for Carotid Endarterectomy With Significant Extracranial Carotid Stenotic Disease) is a prospective multicenter trial for asymptomatic patients with carotid artery stenosis. This study compared the outcomes of CAS with embolic protection and CEA in standard-risk, asymptomatic patients with severe carotid artery

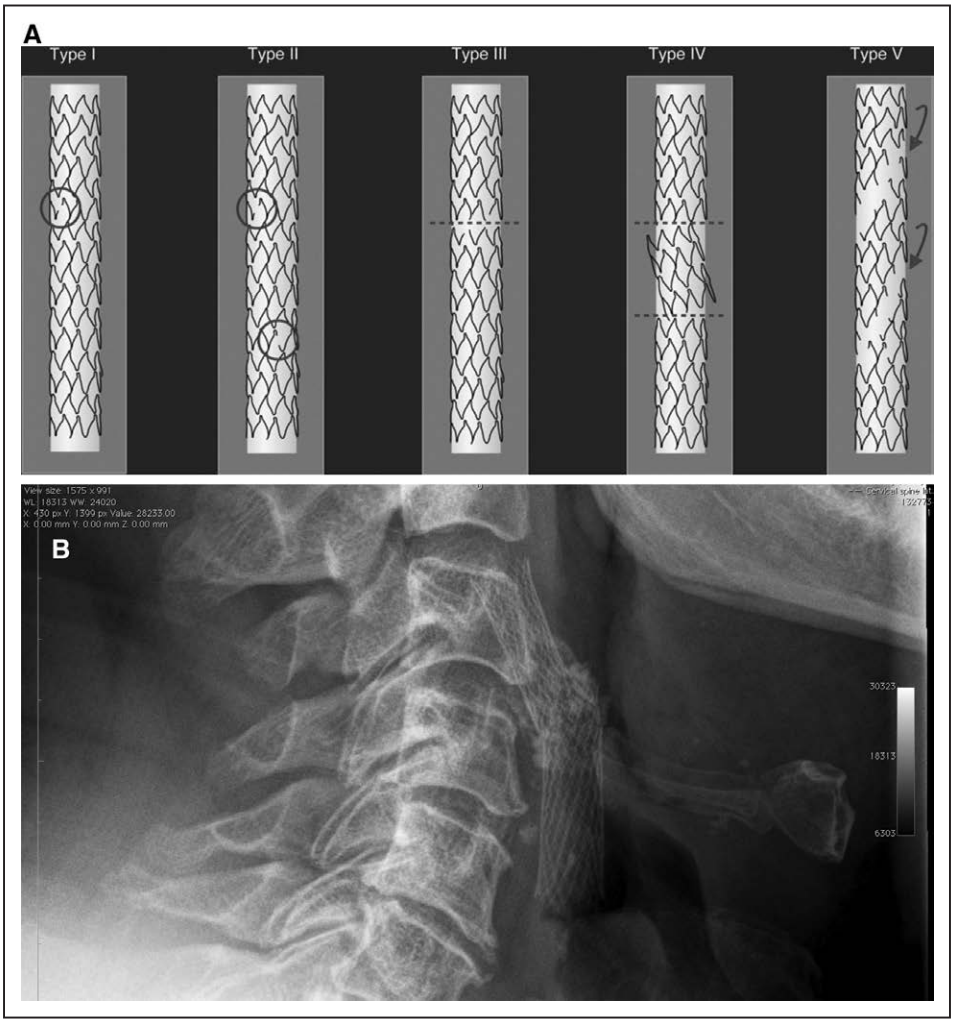

Figure 1. A, Stent integrity grading scale. B, Lateral x-ray of the neck depicting a grade IV stent fracture.
A, Reproduced from Rocha-Singh et al[21] with permission. Copyright © 2007, Wiley-Liss Inc.

stenosis. In addition, it included prospective imaging analysis to determine the incidence of stent fracture by independent, core-laboratory adjudication.[20]

The objectives of the current study were to determine the stent fracture rate of the Xact stent (Abbott Vascular) used in ACT-1, and its association with clinically meaningful adverse outcomes and carotid in-stent restenosis.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. ACT-1 is a prospective multicenter trial of asymptomatic patients with severe atherosclerotic carotid artery stenosis at standard risk for surgical complications from CEA.[20] Patients were randomly assigned to undergo stenting with embolic protection or CEA at a 3:1 CAS:CEA randomization rate. The study was sponsored by Abbott Vascular, reviewed by the US Food and Drug Administration, and approved by the institutional review board at each study site; all patients provided written informed consent.

The primary outcome of this study was defined as the composite of death, stroke (ipsilateral or contralateral, major or minor), or myocardial infarction within 30 days of the procedure or ipsilateral stroke within 365 days of the procedure. An independent clinical events committee adjudicated all primary end point events.

All patients were required to undergo annual duplex ultrasound (DUS) surveillance. After 771 patients had been enrolled, because of external reports of clinical events associated with stent fracture, all subsequent randomly assigned patients were also required to undergo annual radiographic (x-ray) analysis for stent fracture. All DUS and x-ray images were independently adjudicated by a vascular core laboratory (VasCore, Massachusetts General Hospital).

Stent fractures were identified exclusively by x-ray and were graded as previously described (Figure 1): single tine (grade I), multiple tines (grade II), stent fracture with transection and preserved alignment (grade III), stent fracture with transection and malalignment of the components (grade IV), and stent fracture in a transaxial spiral configuration (grade V).[21,22] It is noteworthy that this stent fracture grade system was first described in relation to superficial femoral artery stent fractures, and was adapted to describe carotid stent fractures. Stent fracture location was further pinpointed to the proximal, middle, or distal segment of the stent. Stent fractures were graded by examiners blinded to clinical data.

In-stent restenosis was defined as >70% in stent restenosis and identified with DUS. DUS criteria for in-stent restenosis were defined as spectral broadening and peak systolic velocity ratio of the internal carotid artery in comparison with the ipsilateral common carotid artery ≥4.0. When no ratio was available, a peak systolic velocity of >150 cm/s and end-diastolic velocity of >100 cm/s were used; both criteria had to be present. Carotid calcifications were determined by the angiographic core laboratory.

Clinical outcomes were adjudicated by an independent clinical events committee from the Harvard Clinical Research Institute (Boston, MA). Before randomization, asymptomatic

Table 1. Baseline Characteristics of Patients With and Without Stent Fracture

Patient Characteristic	CAS Subjects With Stent Fracture (n=51)	CAS Subjects Without Stent Fracture but With X-ray Follow-Up (n=888)	*P* Value*
Age, mean±SD (n)	68.1±7.7 (51)	67.5±6.9 (888)	0.58
Range (min, max)	(44.4, 79.9)	(47.0, 79.8)	
[95% CI]†	[65.9–70.2]	[67.0–67.9]	
Male sex	66.7% (34/51)	61.4% (545/888)	0.55
[95% CI]‡	[52.1–79.2%]	[58.1–64.6%]	
Coronary artery disease	47.1% (24/51)	52.8% (469/888)	0.47
[95% CI]‡	[32.9–61.5%]	[49.5–56.1%]	
Clinical congestive heart failure	3.9% (2/51)	4.3% (38/888)	1.0
[95% CI]‡	[0.5–13.5%]	[3.0–5.8%]	
Hypertension	92.2% (47/51)	90.7% (805/888)	1.0
[95% CI]‡	[81.1–97.8%]	[88.5–92.5%]	
Hyperlipidemia requiring medication	90.2% (46/51)	90.9% (807/888)	0.80
[95% CI]‡	[78.6–96.7%]	[88.8–92.7%]	
History of cigarette smoking	68.6% (35/51)	73.5% (653/888)	0.42
[95% CI]†	[54.1–80.9%]	[70.5–76.4%]	
Current cigarette smoker	29.4% (15/51)	24.0% (213/888)	0.40
[95% CI]‡	[17.5–43.8%]	[21.2–26.9%]	
Diabetes mellitus	37.3% (19/51)	34.5% (306/888)	0.76
[95% CI]‡	[24.1–51.9%]	[31.3–37.7%]	
Previous carotid endarterectomy	13.7% (7/51)	5.0% (44/888)	0.02
[95% CI]†	[5.7–26.3%]	[3.6–6.6%]	
History of stroke	3.9% (2/51)	6.5% (58/888)	0.77
[95% CI]‡	[0.5–13.5%]	[5.0–8.4%]	
History of ipsilateral stroke	2.0% (1/51)	1.5% (13/888)	0.55
[95% CI]‡	[0.0–10.4%]	[0.8–2.5%]	
History of TIA	11.8% (6/51)	5.9% (52/888)	0.12
[95% CI]‡	[4.4–23.9%]	[4.4–7.6%]	
History of amaurosis fugax	3.9% (2/51)	1.7% (15/888)	0.24
[95% CI]‡	[0.5–13.5%]	[0.9–2.8%]	
History of renal insufficiency	9.8% (5/51)	8.0% (71/888)	0.60
[95% CI]‡	[3.3–21.4%]	[6.3–10.0%]	
History of cancer	15.7% (8/51)	13.7% (122/888)	0.68
[95% CI]‡	[7.0–28.6%]	[11.5–16.2%]	

CAS indicates carotid artery stenting; CI, confidence interval; max, maximum; min, minimum; and TIA, transient ischemic attack.

**P* values were derived from the Student *t* test for age and from the Fisher exact test for the other variables.

†By normal approximation.

‡Clopper-Pearson exact CI.

status was confirmed by a neurologist or neurosurgeon. Independent neurological assessment was performed before, on the day after the procedure, and at 1, 6, and 12 months, and annually thereafter, until 5 years after the procedure.[20]

In the current analysis, stent fractures were examined in association with the ACT-1 study primary end point and its components, as well. Stent fractures were also examined in association with in-stent restenosis.

Statistical Analysis

Because stent fracture could only occur in patients who received a stent and can only be identified by x-ray, the analysis was performed on a per-protocol population of patients with CAS who had at least 1 x-ray image during the follow-up period. It is noteworthy that only 1 patient crossed over from CEA to CAS and no stent fracture was observed for this patient. Patients who were randomly assigned to CAS and then crossed over from CAS to CEA were excluded from the per-protocol analysis. Baseline variables are summarized with the use of descriptive statistics. Continuous variables are summarized as mean, median, SD, minimum and maximum values, and 95% confidence intervals (CIs). Categorical variables are summarized as counts, percentages, and exact 95% Clopper-Pearson CIs. For time-to-event variables, Kaplan-Meier estimates were used. The starting day was the day of the procedure.

RESULTS

In total, 1021 patients were randomly assigned and treated with CAS without crossover to CEA. Mean follow-up was 3.1±1.6 years. Of these, 939 (92.0%) had at least 1 x-ray image, and 822 (80.5%) had both interpretable DUS and x-ray images. During the follow-up period, 51 (5.4%) stent fractures were noted.

Baseline patient characteristics are shown in Table 1; 61.7% of the patients were men. More patients underwent previous contralateral CEA in the stent fracture group than in the nonfracture group (13.7% versus 5.0%, *P*=0.02). There were no significant differences in baseline characteristics between patients who did and those who did not have an x-ray available for interpretation (Table I in the online-only Data Supplement).

X-ray data are available in Table II in the online-only Data Supplement and Figure 2. Most stent fractures were grade I. During subsequent follow-up, the percentage of available x-rays increased, whereas the proportion of stent fractures remained stable and low (Figure I in the online-only Data Supplement). During this time, worsening of the fracture grade was detected in 6 patients, and in 2 patients another fracture of the same grade as the original fracture was seen. No correlation was found between fracture grade and location (*P*=0.89, Table III in the online-only Data Supplement).

Angiographic data are shown in Table 2. In patients with stent fracture in comparison with those without, respectively, lesions were more likely to be contiguous with the carotid bulb (98.0% versus 89.1%, *P*=0.05) and closer to the bulb (4.9±5.9 mm versus 6.7±5.7 mm, *P*=0.05). More severe calcification was noted in the stent fracture group than in the nonfracture group (35.4% versus 20.1%, *P*=0.02). No association was found between postdilatation and stent fracture. Postdilatation was performed in 100% and 95.3% of the fracture and nonfracture groups, respectively (*P*=0.16).

At 5 years, the primary outcome occurred in 2 and in 37 subjects (4.1% and 4.7%) in the fracture and nonfracture groups, respectively (*P*=0.86). Similarly, stroke and death rates did not differ between the fracture and nonfracture groups (Figure 3). No correlation was found between stent fracture grade and clinical outcomes (*P*=0.53 for clinically driven target lesion revascularization, *P*=0.08 for all stroke, and *P*=0.58 for death, Table IV in the online-only Data Supplement); however, event numbers were small (Tables V through VIII in the online-only Data Supplement). In-stent restenosis, defined as >70%, did not differ between the fracture versus the nonfracture groups (4.4% versus 5.3%, *P*=1.0). Furthermore, there was no difference in clinically driven

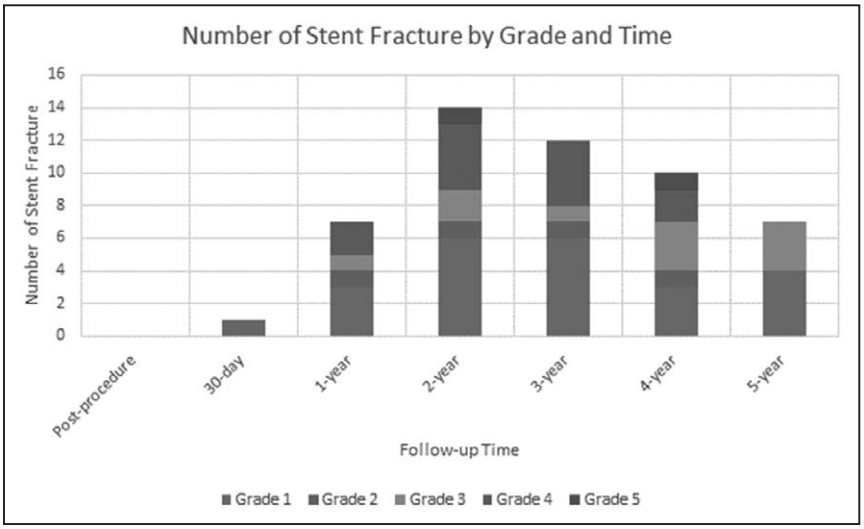

Figure 2. Number of stent fractures by grade and time.

Table 2. Angiographic Characteristics of Patients With and Without Stent Fracture

Lesion Characteristic	CAS Subjects With Stent Fracture (n=51)	CAS Subjects Without Stent Fracture but With X-Ray Follow-Up (n=888)	Total (N=939)	*P* Value
Lesion location				
Left internal carotid	2.0% (1/50)	5.2% (45/871)	5.0% (46/921)	0.51†
[95% CI]*	[0.1–10.6%]	[3.8–6.9%]	[3.7–6.6%]	
Left internal and common carotid	40.0% (20/50)	45.7% (398/871)	45.4% (418/921)	0.47†
[95% CI]	[26.4–54.8%]	[42.3–49.1%]	[42.1–48.7%]	
Right internal carotid	0.0% (0/50)	4.9% (43/871)	4.7% (43/921)	0.16†
[95% CI]*	[0.0–7.1%]	[3.6–6.6%]	[3.4–6.2%]	
Right internal and common carotid	58.0% (29/50)	44.2% (385/871)	45.0% (414/921)	0.06†
[95% CI]*	[43.2–71.8%]	[40.9–47.6%]	[41.7–48.2%]	
Lesion location relative to the bulb				
Contiguous	98.0% (49/50)	89.1% (776/871)	89.6% (825/921)	0.05†
[95% CI]*	[89.4–99.9%]	[86.8–91.1%]	[87.4–91.5%]	
Remote	2.0% (1/50)	10.1% (88/871)	9.7% (89/921)	0.08†
[95% CI]*	[0.1–10.6%]	[8.2–12.3%]	[7.8–11.8%]	
Both	0.0% (0/50)	0.8% (7/871)	0.8% (7/921)	1.0†
[95% CI]*	[0.0–7.1%]	[0.3–1.6%]	[0.3–1.6%]	
Lesion distance from the ostium, mm				
Mean±SD (n)	4.9±5.9 (50)	6.7±5.7 (870)	6.6±5.7 (920)	0.05‡
Range (min, max)	(0.0, 23.0)	(0.0, 39.6)	(0.0, 39.6)	
[95% CI]§	[3.2–6.6]	[6.3–7.0]	[6.2–6.9]	§
Lesion length, mm				
Mean±SD (n)	19.4±6.8 (50)	19.2±5.7 (871)	19.2±5.8 (921)	0.83‡
Range (min, max)	(5.9, 38.8)	(2.5, 39.6)	(2.5, 39.6)	
[95% CI]§	[17.5–21.3]	[18.8–19.6]	[18.8–19.6]	
Calcification	54.2% (26/48)	45.9% (386/841)	46.3% (412/889)	0.30†
[95% CI]*	[39.2–68.6%]	[42.5–49.3%]	[43.0–49.7%]	
None/mild	45.8% (22/48)	54.1% (455/841)	53.7% (477/889)	0.30†
[95% CI]*	[31.4–60.8%]	[50.7–57.5%]	[50.3–57.0%]	
Moderate	18.8% (9/48)	25.8% (217/841)	25.4% (226/889)	0.31†
[95% CI]*	[8.9–32.6%]	[22.9–28.9%]	[22.6–28.4%]	
Severe	35.4% (17/48)	20.1% (169/841)	20.9% (186/889)	0.02†
[95% CI]*	[22.2–50.5%]	[17.4–23.0%]	[18.3–23.7%]	

CAS indicates carotid artery stenting; CI, confidence interval; max, maximum; and min, minimum.
*Clopper-Pearson exact CI.
†From Fisher exact test.
‡From Student *t* test.
§By normal approximation.

target lesion revascularization in the fracture versus the nonfracture groups, respectively (2.0% versus 1.8%, *P*=0.86).

DISCUSSION

In this prospective study independently assessing the presence and impact of carotid stent fracture, we have demonstrated that stent fracture was uncommon, and it was not associated with in-stent restenosis or with serious adverse clinical outcomes.

Carotid stent fracture has been reported infrequently.[6–18] Furthermore, previous publications included case reports and single-center studies that lacked rigorous adjudication methodology. In these reports, stent fracture infrequently associated with symptoms, but did

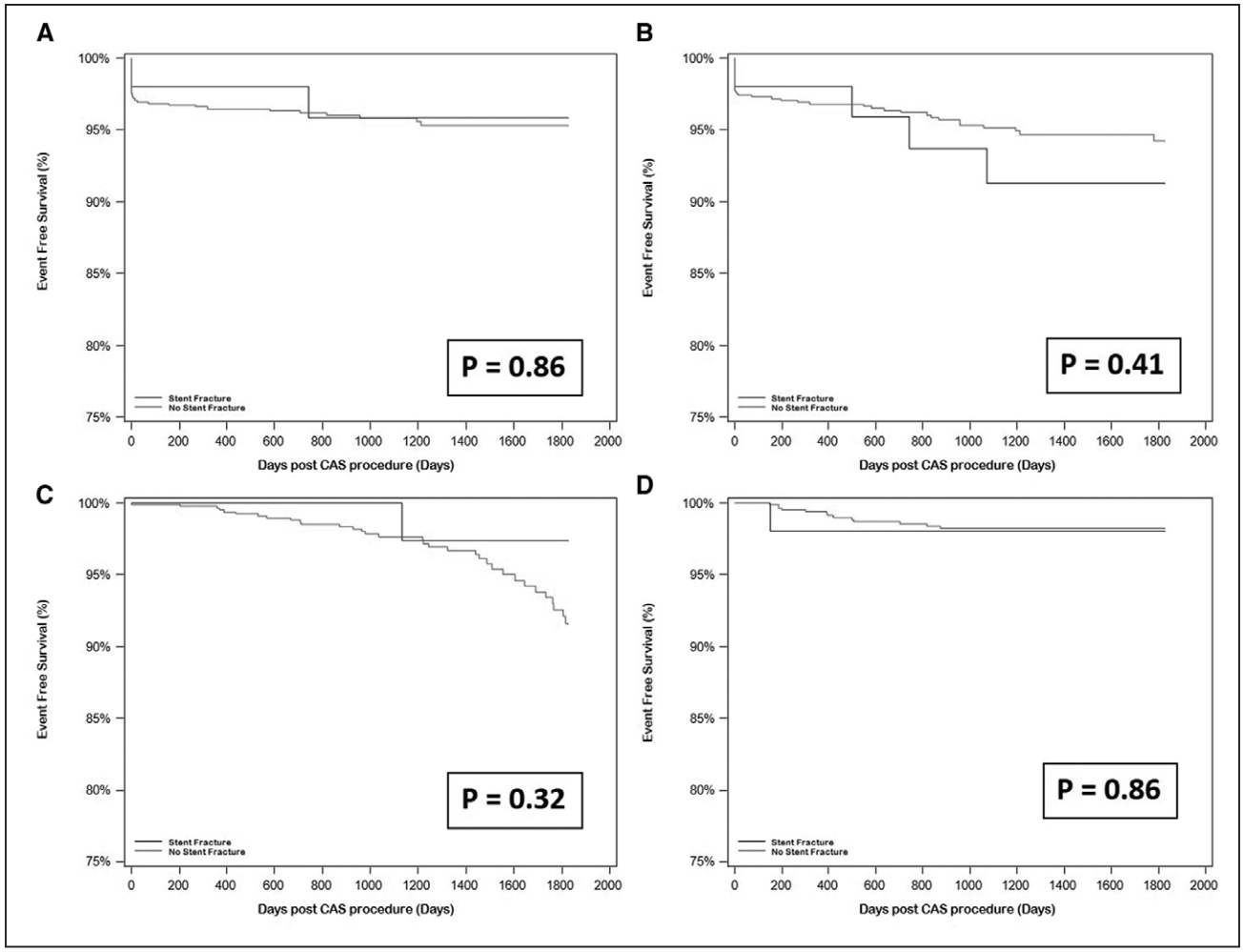

Figure 3. Stent fracture and patient outcomes.
Kaplan-Meier curves comparing patients with (black line) and without (green line) stent fractures for the primary outcome (**A**), stroke (**B**), death (**C**), and clinically driven target lesion revascularization (**D**). CAS indicates carotid artery stenting.

associate with in-stent restenosis in as many as 55% of cases.[15] Neurological symptoms have rarely been described in patients also found to have a carotid stent fracture.[10] Once a fracture is diagnosed, clinical management varies and ranges from observation to surgical extraction.[6,7,13,17]

Several single-center retrospective series have reported outcomes with carotid stent fracture (Table 3). These reports lacked a standardized protocol for x-ray and DUS acquisition and analysis, and for detection and reporting of clinical outcomes, as well. Given the nature of these reports, the true rate of stent fracture, its association with restenosis and clinical events, and the rationale for clinical management were unknown. Nonetheless, these previously published reports support the low incidence of stent fractures noted in the current study. Most fractures were grade I and most fractures were stable; the fracture severity increased over time in 6 patients and a second fracture of the same grade was noted in 2 patients. No clinical events occurred in any of these patients. These results do not suggest prevalent material fatigue. Furthermore, the relationship between stent fractures and clinical outcomes is further diminished by an inverse timing of events. Clinical outcomes in the stent-fracture group were noted most frequently before a fracture had occurred.

Stent fractures were more prevalent in patients with prior contralateral CEA and with closer lesion proximity to the carotid bulb. As reported previously, stent fracture was more prevalent when dense lesion calcification was present. In contrast, fractures did not occur more frequently with longer lesions. The current study was not designed to evaluate the mechanism of stent fracture, and these observations merit further study. Similarly, the optimal management of carotid artery stent fracture cannot be inferred from the current study.

Limitations of this study include the use of 1 stent design. Previous reports have postulated that closed-cell stents such as the Xact stent may be more prone to fracture.[7,14] Thus, results may not be generalizable to other stents. Most patients did not have an x-ray available at all time points. However, 92% of patients

Table 3. Summary of Stent Fracture–Related Data in Retrospective Series

Reference	Number of Stents	X-Ray Timing	Fracture Rate, %	Comments
Coppi et al[23]	323	12 mo	3.4	Stent fractures were not associated with adverse outcomes
Eskandari et al[9]	73	N/A	5.5	X-ray protocol was not defined
Garcia-Toca et al[16]	106	32 mo	7.6	Six of 8 stent fractures were in arteries exhibiting dense calcifications; stent fractures were not associated with adverse outcomes.
Chang et al[18]	116	4 y	4.0	Stent fractures were associated with dense calcifications; stent fractures were not associated with adverse outcomes.
Ling et al[24]	48	15 mo	29.0	Three of 14 fractured stents also developed in-stent restenosis; x-ray protocol was not defined.

Case reports are not displayed in this table. N/A indicates not available.

did undergo an x-ray and most patients had >1 x-ray. Furthermore, incident fractures did not progress as time elapsed. Specifically, at 5 years, 77.9% of available subjects underwent x-ray, and fracture incidence was not higher than in other time points (Figure I in the online-only Data Supplement). Finally, although not all patients had at least 1 pair of interpretable x-ray and DUS, clinical follow-up was invariably available. Despite these limitations, this study remains the largest objectively adjudicated study of stent fractures, clinical events, and DUS correlates.

In conclusion, the carotid stent fracture rate independently assessed during the ACT-1 study was low and was not associated with severe adverse events or in-stent restenosis. More research is required to delineate the correlation between lesion location, the presence of calcification or prior CEA, and stent fracture. With the ever declining adverse events with CAS, our findings support the safety of this strategy for patients with severe extracranial carotid artery stenosis in those with standard surgical risk who have asymptomatic severe carotid stenosis.

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DISCLOSURES

Dr Beckman has consulted for Astra Zeneca, Sanofi, Aralez, and Abbott. Dr Beckman serves on the data safety and monitoring board for Bayer; received a research grant from Merck; has ownership in EMX and Janacare; and serves on a nonprofit board for VIVA. Dr Matsumura has received research grants from Abbott, Gore, Cook, Endologix, and Medtronic. Dr Rosenfield serves on advisory boards for Abbott Vascular, Cardinal Health, Surmodics, Inari Medical, Volcano/Philips, and Proteon; receives fees and stock options for serving on advisory boards for Cruzar Systems, Valcare, and Eximo; receives stock options for serving on advisory boards for Capture Vascular, Shockwave, Micell, Endospan, and Silk Road Vascular; receives stock options for serving on the advisory boards of and holding equity positions in Contego, Access Vascular, and MD Insider; holds stock/stock options in Embolitech, Janacare, Primacea, and PQ Bypass; will receive a future payout from a previous equity position in Vortex; and receives grant support paid to his institution from Abbott Vascular, Atrium/Maquet, and Lutonix/Bard. Dr Ansel consults for Abbott Vascular, Medtronic, and Boston Scientific. Dr Chaturvedi is an executive committee member of ACT-1 and CREST-2. Dr Metzger receives proctor fees and symposia honoraria from Abbott. Dr Shu is an employee of Abbott Vascular. Dr Wechsler is on the steering committee of ACT I; holds stock in Silk Road Medical; and is an investigator for CREST-2. Dr Jaff is a noncompensated advisor for Abbott Vascular, Boston Scientific, Cordis, and Medtronic; is a consultant for Philips/Volcano; has equity investment in PQ Bypass, Primacea, Vascular Therapies, and Venarum; and is a board member for VIVA Physicians, a 501(c)(3) not-for-profit education and research organization. The other authors report no conflicts.

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FOOTNOTES

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Supplemental Material

Supplemental Tables

Table 1S: Baseline Characteristics of Patients with and without Available Stent X-Ray			
	CAS Subjects with X-ray N = 939	**CAS Subjects without X-ray N = 82**	**P Value[‡]**
Age Mean ± SD (N) **Range (min, max)** **[95% Conf. Interval][*]**	67.5 ± 6.9 (939) (44.4, 79.9) [67.1, 67.9]	69.3 ± 8.3 (82) (46.9, 79.8) [67.5, 71.1]	0.06
Male **[95% Conf. Interval] [†]**	61.7% (579/939) [58.5%, 64.8%]	63.4% (52/82) [52.0%, 73.8%]	0.81
Coronary Artery Disease **[95% Conf. Interval] [†]**	52.5% (493/939) [49.3%, 55.7%]	53.7% (44/82) [42.3%, 64.7%]	0.91
Clinical Congestive Heart Failure **[95% Conf. Interval] [†]**	4.3% (40/939) [3.1%, 5.8%]	7.3% (6/82) [2.7%, 15.2%]	0.26
Hypertension **[95% Conf. Interval] [†]**	90.7% (852/939) [88.7%, 92.5%]	91.5% (75/82) [83.2%, 96.5%]	1.0
Hyperlipidemia requiring medication **[95% Conf. Interval] [†]**	90.8% (853/939) [88.8%, 92.6%]	86.6% (71/82) [77.3%, 93.1%]	0.24
History of cigarette smoking **[95% Conf. Interval] [†]**	73.3% (688/939) [70.3%, 76.1%]	74.4% (61/82) [63.6%, 83.4%]	0.90
Current cigarette smoker **[95% Conf. Interval] [†]**	24.3% (228/939) [21.6%, 27.2%]	26.8% (22/82) [17.6%, 37.8%]	0.59
Diabetes mellitus **[95% Conf. Interval] [†]**	34.6% (325/939) [31.6%, 37.8%]	45.1% (37/82) [34.1%, 56.5%]	0.07

Previous carotid endarterectomy [95% Conf. Interval] †	5.4% (51/939) [4.1%, 7.1%]	8.5% (7/82) [3.5%, 16.8%]	0.22
History of stroke [95% Conf. Interval] †	6.4% (60/939) [4.9%, 8.1%]	11.0% (9/82) [5.1%, 19.8%]	0.11
History of ipsilateral stroke [95% Conf. Interval] †	1.5% (14/939) [0.8%, 2.5%]	3.7% (3/82) [0.8%, 10.3%]	0.15
History of TIA [95% Conf. Interval] †	6.2% (58/939) [4.7%, 7.9%]	4.9% (4/82) [1.3%, 12.0%]	0.81
History of amaurosis fugax [95% Conf. Interval] †	1.8% (17/939) [1.1%, 2.9%]	0.0% (0/82) [0.0%, 4.4%]	0.39
History of renal insufficiency [95% Conf. Interval] †	8.1% (76/939) [6.4%, 10.0%]	9.8% (8/82) [4.3%, 18.3%]	0.53
History of cancer [95% Conf. Interval] †	13.8% (130/939) [11.7%, 16.2%]	13.4% (11/82) [6.9%, 22.7%]	1.0

CAS – Carotid artery stenting

* – By normal approximation

† – Clopper-Pearson exact confidence interval

‡ – P values were derived from the Student's t-test for Age and from the Fisher's Exact test for the other variables.

Table 2S: Stent Fracture Rate and Grade								
	X-ray			Severity Grade				
Visit	**Number of Eligible Subjects**	**% of X-ray Completed**	**% of Stent Fracture**	**1**	**2**	**3**	**4**	**5**
Post-procedure	1021	21.2% (216/1021)	0.0% (0/216)	0	0	0	0	0
30-day	1020	17.7%(181/1020)	0.6% (1/181)	1	0	0	0	0
1-year	927	47.4% (439/927)	1.6% (7/439)	3	1	1	2	0
2-year	804	57.7% (464/804)	3.0% (14/464)	6	1	2	4	1
3-year	643	68.7% (442/643)	2.7% (12/442)	6	1	1	4	0
4-year	465	76.8% (357/465)	2.8% (10/357)	3	1	3	2	1
5-year	271	77.9% (211/271)	3.3% (7/211)	4	0	3	0	0
Overall	1021	92.0% (939/1021)	5.4% (51/939)	23	4	10	12	2

Table 3S: Fracture grade and location				
Highest Grade	**Proximal**	**Mid**	**Distal**	**Total**
V	2	0	0	2
IV	4	3	4	11
III	5	3	2	10
II	3	3	1	4[*]
I	10	8	7	24[†]

[*] One (1) subject had a Grade 2 stent fractures on proximal, mid and distal; 1 subject had a Grade 2 stent fractures on proximal and mid stent.

[†] One (1) subject had a Grade 1 stent fracture on mid and distal stent.

Table 4S: Stent Fracture Grade and Clinical Events					
Highest Grade	**Primary Outcome**	**CDTLR**	**All Stroke**	**Death**	**Total**
5	1	0	1	0	2
4	0	1	0	0	11
3	0	0	1	1 *	10
2	1	0	1	0	4
1	0	0	1	1	24

CD-TLR – Clinically driven target lesion revascularization

* Death even occurred 1829 days post-procedure, hence it does not show in the Kaplan-Meier curve of all-cause death.

Table 5S: Kaplan-Meier Analysis of Freedom from Primary Outcome Event through 5 Years

Time After Index Procedure (days)							
	0	**30**	**365**	**730**	**1095**	**1460**	**1825**
Stent Fracture # At Risk	51	49	48	46	39	26	14
# Events	0	1	1	1	2	2	2
Survival Rate (%)	100%	98.0%	98.0%	98.0%	95.9%	95.9%	95.9%
No Stent Fracture # At Risk	888	847	738	632	474	318	134
# Events	11	27	31	33	35	37	37
Survival Rate (%)	98.8%	97.0%	96.5%	96.2%	95.8%	95.3%	95.3%
Test Between Stent Fracture and No Stent Fracture	**Log-Rank Test**	**Chi-Square**	**DF**	**p-value**			
		0.032	1	0.8580			

Note: Number of events displayed in the table is a cumulative count from Day 0.

Table 6S: Kaplan-Meier Analysis of Freedom from All Stroke Event through 5 Years

Time After Index Procedure (days)							
	0	**30**	**365**	**730**	**1095**	**1460**	**1825**
Stent Fracture # At Risk	51	49	48	45	37	25	13
# Events	0	1	1	2	4	4	4
Survival Rate (%)	100%	98.0%	98.0%	95.9%	91.3%	91.3%	91.3%
No Stent Fracture # At Risk	888	850	740	633	472	317	133
# Events	11	23	28	32	38	40	41
Survival Rate (%)	98.8%	97.4%	96.8%	96.2%	95.2%	94.7%	94.3%
Test Between Stent Fracture and No Stent Fracture	**Log-Rank Test**	**Chi-Square**	**DF**	**p-value**			
		0.678	1	0.4104			

Note: Number of events displayed in the table is a cumulative count from Day 0.

Table 7S: Kaplan-Meier Analysis of Freedom from All Cause Death to 5 Years

Time After Index Procedure (days)							
	0	**30**	**365**	**730**	**1095**	**1460**	**1825**
Stent Fracture # At Risk	51	50	49	47	41	28	15
# Events	0	0	0	0	0	1	1
Survival Rate (%)	100%	100%	100%	100%	100%	97.4%	97.4%
No Stent Fracture # At Risk	888	872	762	653	491	331	139
# Events	0	1	3	11	16	22	33
Survival Rate (%)	100%	99.9%	99.6%	98.5%	97.7%	96.1%	91.6%
Test Between Stent Fracture and No Stent Fracture	**Log-Rank Test**	**Chi-Square**	**DF**	**p-value**			
		0.986	1	0.3207			

Note: Number of events displayed in the table is a cumulative count from Day 0.

Table 8S: Kaplan-Meier Analysis of Freedom from Clinically Driven Target Lesion Revascularization Events through 5 Years

Time After Index Procedure (days)							
	0	**30**	**365**	**730**	**1095**	**1460**	**1825**
Stent Fracture # At Risk	51	50	48	46	40	27	15
# Events	0	0	1	1	1	1	1
Survival Rate (%)	100%	100%	98.0%	98.0%	98.0%	98.0%	98.0%
No Stent Fracture # At Risk	888	872	757	642	480	326	137
# Events	0	0	5	11	13	13	13
Survival Rate (%)	100%	100%	99.4%	98.5%	98.2%	98.2%	98.2%
Test Between Stent Fracture and No Stent Fracture	**Log-Rank Test**	**Chi-Square**	**DF**	**p-value**			
		0.030	1	0.8631			

Note: Number of events displayed in the table is a cumulative count from Day 0.

Supplemental Figures

Figure 1S:

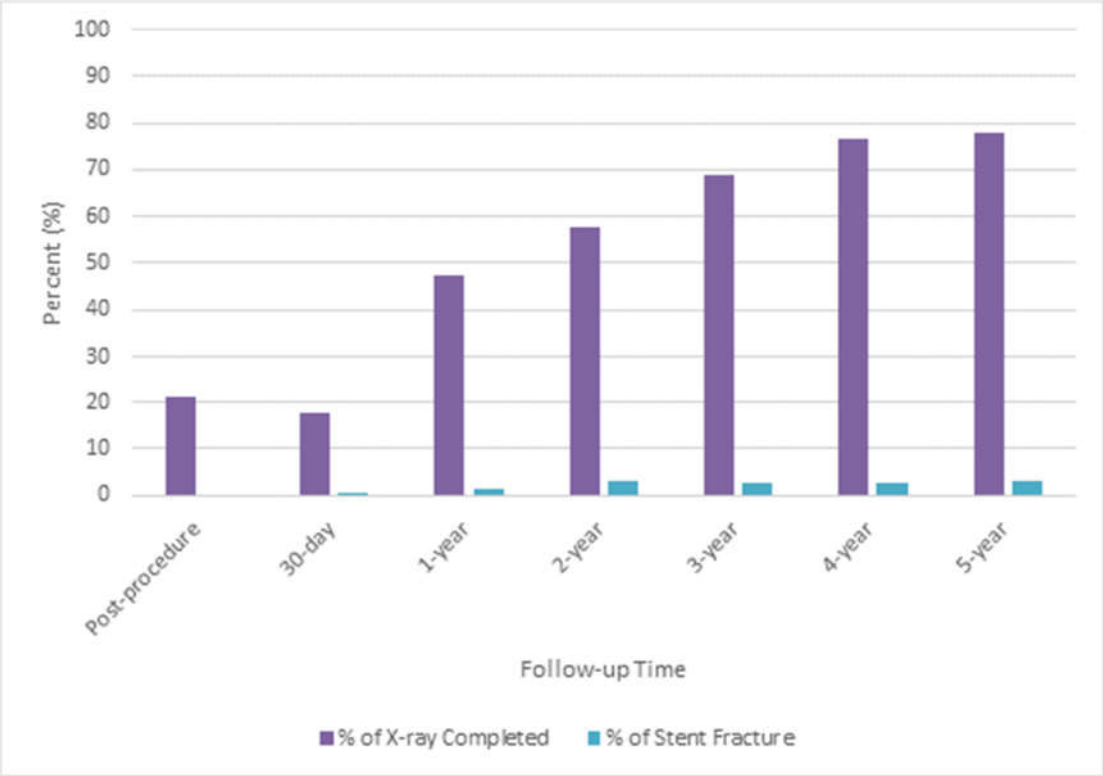

Figure Legend:

Figure 1S – Proportion of X-rays and proportion of stent fractures over time