

***ACE* Statistical Analysis**

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¹Taking study ASA 2 or more days prior to CE and taking less than 650mg ASA prior to randomization.

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1 Patient Accrual and Follow-up

1.1 Patient Accrual and Follow-up

	81 mg	325 mg	650 mg	1300 mg	Total
Patients Randomized	709	708	715	717	2849
Patients Excluded ¹					
- surgery cancelled by patient	1	3	0	0	4
- surgery cancelled by surgeon	8	6	8	10	32
- surgery cancelled due to medical event	2	2	4	0	8
- scheduled for external CE	0	0	0	1	1
Days Between Randomization and Surgery					
< 1 day	11	12	18	10	51
1 day	286	272	274	282	1114
2 days	79	85	77	74	315
3 days	64	53	56	61	234
4 days	47	58	43	58	206
5 days	40	36	40	43	159
> 5 days	171	181	195	178	725
Follow-ups Completed					
- none, patient lost to follow-up	0	0	0	0	0
- baseline only	0	0	1	0	1
- to hospital discharge only	8	7	8	8	31
- to 1 month follow-up only	6	2	5	4	17
- to final 3 month follow-up	684	688	689	694	2755

Notes

1. Patients Excluded are not included in subsequent tables or analyses except for Table 7.12 which summarizes the follow-up of these patients.

2 Baseline Characteristics

2.1 Baseline Demographics

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Gender:						
male	477	495	499	491	1962	(70%)
female	221	202	204	215	842	(30%)
Age:						
median	69	69	69	69	69	
range	38–88	40–92	43–93	35–93	35–93	
Race:						
caucasian	662	663	666	671	2662	(95%)
black	21	22	27	17	87	(3%)
asian	1	1	1	6	9	(0%)
other	14	11	9	12	46	(2%)
Prior ASA:						
none	162	133	141	141	577	(21%)
< 325	287	305	305	301	1198	(43%)
325–649	169	175	163	165	672	(24%)
650–1299	65	66	73	77	281	(10%)
≥ 1300	15	18	21	22	76	(3%)
Days on Study Drug Before Surgery:						
post-op	0	3	1	2	6	(0%)
0 days	40	35	34	41	150	(5%)
1 day	330	301	317	319	1267	(45%)
2 days	128	142	126	116	512	(18%)
3 days	59	53	66	67	245	(9%)
4 days	40	39	36	48	163	(6%)
≥ 5 days	101	124	123	113	461	(16%)

Notes

For “Prior ASA” the average dose in the past five days is used.

2.2 Stenosis Measured by Angiography

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Ipsilateral						
No Angiography	114	111	122	119	466	(17%)
< 50%	12	19	14	18	63	(2%)
50–69%	74	76	78	66	294	(10%)
70–79%	148	134	122	144	548	(20%)
80–89%	159	121	138	145	563	(20%)
90–99%	191	236	229	214	870	(31%)
100%	0	0	0	0	0	(0%)
<i>Other</i>	0	0	0	0	0	(0%)
Contralateral						
No Angiography	127	128	134	126	515	(18%)
< 50%	324	318	353	350	1345	(48%)
50–69%	92	86	84	95	357	(13%)
70–79%	42	42	27	30	141	(5%)
80–89%	24	26	16	28	94	(3%)
90–99%	27	29	35	25	116	(4%)
100%	62	68	54	52	236	(8%)
<i>Other</i>	0	0	0	0	0	(0%)

2.3 Baseline CT/MRI Scan Results

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Not Done	306	313	317	314	1250	(45%)
Ipsilateral Infarction						
none	232	249	259	249	989	(35%)
old	72	63	60	70	265	(9%)
recent	39	35	25	34	133	(5%)
unknown	49	37	42	39	167	(6%)
Contralateral Infarction						
none	296	304	298	303	1201	(43%)
old	69	46	56	57	228	(8%)
recent	11	10	10	7	38	(1%)
unknown	16	24	22	25	87	(3%)

Notes

none = none on both CT and MRI

old = old on CT or MRI and not recent on CT or MRI

recent = recent on CT or MRI (\pm old on other exam)

unknown = infarction observed but age unknown (on both CT and MRI)

2.4 Ipsilateral Stenosis and Corresponding Symptoms at Baseline

Stenosis	Symptomatic ¹	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
≥ 70%	Yes	249	255	243	256	1003	(36%)
≥ 70%	No	233	226	228	235	922	(33%)
< 70%	Yes	34	39	47	31	151	(5%)
< 70%	No	48	56	37	42	183	(7%)
N/A	Yes	36	27	42	33	138	(5%)
N/A	No	98	94	106	109	407	(15%)

Notes

1. Patients are considered symptomatic if they have had symptoms (TIA or stroke) in the past six months on the same side as the *ACE* carotid endarterectomy was performed. Patients with only vertebrobasilar symptoms are considered asymptomatic.
2. Stenosis is determined from the angiogram reading performed by the center. Central review of angiograms was not done in the *ACE* trial.
3. The “Stenosis: N/A” categories include patients with no angiography in the past year.

2.5 History of Stroke and TIA

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Ipsilateral Events¹						
stroke - hemispheric	175	153	156	158	642	(23%)
- retinal	20	25	21	18	84	(3%)
TIA - hemispheric	197	195	208	187	787	(28%)
- retinal	104	119	108	117	448	(16%)
none	297	310	300	320	1227	(44%)
Most Recent Ipsi. Stroke or TIA						
< 30 days	135	164	188	158	645	(23%)
31-90 days	118	99	94	97	408	(15%)
91-180 days	66	58	50	65	239	(9%)
> 180 days	82	66	71	66	285	(10%)
never	297	310	300	320	1227	(44%)
unknown	0	0	0	0	0	(0%)
Number of Ipsi. Strokes						
none	520	536	551	546	2153	(77%)
one	166	151	135	144	596	(21%)
two or more	12	10	17	16	55	(2%)
Number of Ipsi. TIAs						
none	413	405	413	421	1652	(59%)
one	112	100	91	116	419	(15%)
two or more	173	192	199	169	733	(26%)
Contralesional/VB Events²						
stroke	249	231	215	216	911	(32%)
TIA	89	90	66	84	329	(12%)
none	391	396	436	432	1655	(59%)
Summary						
Ipsilateral only	186	185	216	200	787	(28%)
Contralesional/VB only	92	99	80	88	359	(13%)
Both	218	216	197	195	826	(29%)
None	202	197	210	223	832	(30%)

Notes

1. Patients are counted once for each type of ipsilateral stroke or TIA they have had prior to randomization.
2. Patients are counted once for each type of contralesional event suffered prior to randomization.

2.6 Medical History

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Hypertension:	468	457	459	473	1857	(66%)
On Treatment	442	431	429	448	1750	(62%)
Controlled/Resolved	445	443	443	448	1779	(63%)
Duration (yrs)						
median	10	8.5	9	8	9	
range	0.08–52	0.08–60	0.08–57	0.08–53	0.08–60	
Atrial Fibrillation:	19	26	24	21	90	(3%)
On Treatment	15	16	14	9	54	(2%)
Controlled/Resolved	16	23	22	20	81	(3%)
Duration (yrs)						
median	1.71	4.25	5	3	3	
range	0.08–30	0.08–16	0.08–30	0.08–22	0.08–30	
Other Cardiac Arrhythmia:	41	31	33	40	145	(5%)
On Treatment	18	9	12	16	55	(2%)
Controlled/Resolved	36	27	31	36	130	(5%)
Duration (yrs)						
median	5	6	4	3	4.04	
range	0.08–40	0.08–27	0.08–25	0.08–50	0.08–50	
Valvular Heart Disease:	17	21	16	16	70	(2%)
On Treatment	5	7	7	2	21	(1%)
Controlled/Resolved	17	20	16	14	67	(2%)
Duration (yrs)						
median	9.165	5.25	7	4	6	
range	0.25–62	0.08–27	0.08–70	0.5–55	0.08–70	
Other Organ Failure:	52	63	65	59	239	(9%)
On Treatment	31	39	27	30	127	(5%)
Controlled/Resolved	49	54	62	55	220	(8%)
Duration (yrs)						
median	3.5	6	4.25	5.5	5	
range	0.08–46	0.08–49	0.08–88	0.25–76	0.08–88	
Diabetes:	176	170	169	167	682	(24%)
On Insulin	60	46	47	55	208	(7%)
Duration (yrs)						
median	9	6	6.085	9.96	8	
range	0.08–50	0.08–39	0.08–34	0.08–50	0.08–50	
Current Cigarette Smoker:	206	194	202	193	795	(28%)
Cigarettes/day						
median	20	20	20	20	20	
range	2–80	1–70	1–60	1–60	1–80	
Duration (yrs)						
median	40	40	40	44	40	
range	1–69	1–68	1–70	1–73	1–73	

2.7 Surgical History

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)
None	240	233	208	218	899 (32%)
Carotid Endart. Right	32	40	40	40	152 (5%)
Carotid Endart. Left	36	48	43	36	163 (6%)
CABG Surgery	116	117	110	134	477 (17%)
Other Surgery	388	382	411	403	1584 (56%)
<i>Unknown</i>	0	0	0	0	0 (0%)

Notes

1. Patients who have had more than one type of surgery are counted in each surgery type.
2. *Unknown* is indicated when all four surgical procedures listed on Plate 2 (Form 1.1) are "NA" or Plate 2 was not received.

2.8 Carotid Investigations

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)
None	0	0	1	1	2 (0%)
Angiography Only	83	76	71	83	313 (11%)
Ultrasound Only	107	106	116	113	442 (16%)
Both	508	515	515	509	2047 (73%)
<i>Unknown</i>	0	0	0	0	0 (0%)

Notes

1. *Unknown* is indicated when both Angiography and Ultrasound on Plate 4 (Form 1.3) are "NA" or Plate 4 was not received.

2.9 Cardiac History

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
None	448	442	464	416	1770	(63%)
MI	149	142	119	154	564	(20%)
CHF	32	27	22	29	110	(4%)
Angina	138	152	148	182	620	(22%)
<i>Unknown</i>	0	0	0	0	0	(0%)

Notes

1. Patients who have had more than one type of event are counted in each event type.
2. *Unknown* is indicated when “NA” is entered on Plate 3 (Form 1.2) for “Cardiac Events History” or Plate 3 was not received.

2.10 Cardiac Examination at Baseline

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
No Abnormalities	562	590	586	592	2330	(83%)
Arrhythmia	17	14	9	15	55	(2%)
Heart Murmur	88	71	74	74	307	(11%)
Other	42	27	40	32	141	(5%)
<i>Unknown</i>	0	1	0	0	1	(0%)

Notes

1. Patients who have more than one type of abnormality are counted in each relevant abnormality.
2. *Unknown* is indicated when “NA” is entered on Plate 4 (Form 1.3) for “Cardiac Examination” or Plate 4 was not received.

2.11 Neurological Examination at Baseline

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Language Function:						
Normal	642	652	645	663	2602	(93%)
Abnormal	55	45	57	43	200	(7%)
Unknown	1	0	1	0	2	(0%)
Cranial Nerves and Eye Examination:						
Normal	542	552	581	576	2251	(80%)
Abnormal	155	144	121	130	550	(20%)
Unknown	1	1	1	0	3	(0%)
Sensory System:						
Normal	577	588	614	620	2399	(86%)
Abnormal	120	109	88	86	403	(14%)
Unknown	1	0	1	0	2	(0%)
Motor System:						
Normal	425	435	462	485	1807	(64%)
Abnormal	272	262	240	221	995	(35%)
Unknown	1	0	1	0	2	(0%)

2.12 Baseline Physical Examination

		81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)
Height (cm)	Range	124–203	125–198	107–201	137–203	107–203
	Mean	169	169	170	169	169
	SD	10.1	9.4	10	9.9	9.9
Weight (kg)	Range	42–159	38–128	42–141	29–132	29–159
	Mean	76	77	77	77	77
	SD	14.8	14.3	15.3	15	14.9
BMI (kg/m ²)	Range	16–50	16–50	17–52	12–48	12–52
	Mean	27	27	27	27	27
	SD	4.7	4.5	4.6	4.6	4.6
Diastolic BP	Range	49–188	46–117	50–170	52–178	46–188
	Mean	79	79	80	79	79
	SD	11.8	10.9	11.7	10.8	11.3
Systolic BP	Range	92–220	84–210	92–231	90–212	84–231
	Mean	147	146	148	147	147
	SD	20.1	21.2	20.7	20.3	20.6
Heart Rate	Range	39–126	40–115	47–122	45–110	39–126
	Mean	73	73	74	72	73
	SD	10.5	10.9	10.7	10.7	10.7

3 ASA: Compliance and Contamination

3.1 Dose of ASA in the 5 Days Before Randomization

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Average Dose per Day						
none	162	133	141	141	577	(21%)
≤ 81 mg	63	76	78	75	292	(10%)
82–325 mg	321	336	339	341	1337	(48%)
326–650 mg	102	102	83	83	370	(13%)
≥ 651 mg	50	50	62	66	228	(8%)
1st quartile	65	80	65	65	65	
median	226	259	250	260	250	
3rd quartile	325	325	325	325	325	

Notes

1. ASA dose is determined from the ASA question at randomization.

3.2 Compliance With Study ASA

	81 mg (<i>N</i> = 693)	325 mg (<i>N</i> = 696)	650 mg (<i>N</i> = 696)	1300 mg (<i>N</i> = 703)	Total (<i>N</i> = 2788)
Weeks 1–2					
<i>N</i> complete ¹	658	671	658	668	2655
<i>N</i> partial	21	18	28	28	95
90–100%	89.5%	88.7%	88.3%	90.5%	89.3%
80–89%	1.8%	1.2%	2.2%	1.3%	1.6%
< 80%	8.7%	10.2%	9.5%	8.2%	9.1%
Weeks 3–4					
<i>N</i> complete	656	669	655	663	2643
<i>N</i> partial	2	2	3	5	12
90–100%	87.4%	87.0%	85.4%	88.2%	87.0%
80–89%	0.3%	0.6%	1.5%	1.8%	1.1%
< 80%	12.3%	12.4%	13.1%	10.0%	11.9%
Weeks 5–12					
<i>N</i> complete	648	666	649	655	2618
<i>N</i> partial	7	3	6	8	24
90–100%	81.1%	78.5%	80.0%	82.7%	80.5%
80–89%	2.9%	3.0%	2.0%	3.5%	2.8%
< 80%	16.0%	18.5%	18.0%	13.9%	16.6%

Notes

1. Each patient is categorized according to the percentage of active study medication taken during each of the three periods shown above. Patients who did not provide data for the whole period, due to death or other reason, have their compliance rate determined from the days on which compliance data is available. For each period, the number of patients with “complete” and “partial” compliance data are shown.
2. If a patient has a stroke or dies, compliance is not considered on or beyond the day of the event.
3. There are 16 patients excluded from this table due to difficulties in determining compliance (11 had CE postponed which upset study scheduling).

3.3 Compliance With Study ASA By Week

	81 mg (N = 693)	325 mg (N = 696)	650 mg (N = 696)	1300 mg (N = 703)	Total (N = 2788)
Week 1	95.3%	94.7%	95.3%	96.1%	95.3%
Week 2	92.6%	92.1%	91.2%	93.0%	92.2%
Week 3	90.9%	89.6%	89.4%	91.2%	90.3%
Week 4	89.5%	87.8%	87.9%	90.5%	88.9%
Week 5	89.0%	86.4%	85.7%	89.0%	87.6%
Week 6	88.3%	84.6%	86.1%	88.8%	86.9%
Week 7	87.2%	83.7%	84.6%	88.4%	86.0%
Week 8	85.9%	83.5%	84.1%	87.5%	85.3%
Week 9	85.1%	82.7%	83.8%	87.0%	84.6%
Week 10	84.9%	82.2%	83.3%	86.5%	84.2%
Week 11	84.0%	81.5%	82.0%	86.1%	83.4%
Week 12	82.0%	78.8%	80.7%	83.5%	81.2%
Total	88.0%	85.7%	86.2%	89.0%	87.2%

Notes

1. For each patient, the percentage of active meds actually taken each week is determined. These percentages are then averaged to give the figures in this table. Patients who did not provide data for the whole period, due to death or other reason, have their compliance rate determined from the days on which compliance data is available
2. If a patient has a stroke or dies, compliance is not considered from the day of the event on.
3. There are 16 patients excluded from this table due to difficulties in determining compliance (11 had CE postponed which upset the study scheduling).

3.4 Actual ASA Dose From Rand. to the 15th Day Following CE Considering: Study Medication, Contamination and Compliance

	81 mg (N = 693)	325 mg (N = 696)	650 mg (N = 696)	1300 mg (N = 703)	Total (N = 2788)	
Actual Dose of ASA ¹						
none	13	7	10	7	37	(1%)
≤ 81 mg	640	15	7	2	664	(24%)
82–325 mg	36	661	65	20	782	(28%)
326–650 mg	4	9	612	61	686	(25%)
≥ 651 mg	0	4	2	613	619	(22%)
1st quartile	62	250	459	957	76	
median	69	279	552	1105	289	
3rd quartile	71	287	574	1147	578	

Notes

1. Average daily dose over the time period from randomization to the 15th day following carotid endarterectomy is used.
2. If a patient has a stroke or dies, ASA dose is not considered on or beyond the day of the event.
3. There are 16 patients excluded from this table due to difficulties in determining compliance (11 had CE postponed which upset study scheduling).
4. There were 21 patients known to have taken non-study ASA between randomization and the 30 day follow-up. However, the exact timing of the use of the ASA is unknown. These patients are included above based on study medication and compliance only.

4 Surgical Report

4.1 Surgical Technique

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Side:						
Right	329	333	347	334	1343	(48%)
Left	369	364	356	372	1461	(52%)
Anesthesia:						
General	598	606	611	616	2431	(87%)
Local	100	91	92	90	373	(13%)
Time (min)	172	174	177	177	175	
Shunt Used:						
No	372	382	384	365	1503	(54%)
Total cross clamp time (min)	35	36	36	36	36	
Yes	326	315	319	340	1300	(46%)
Pre-shunt insertion (min)	10	9	11	10	10	
Post-shunt removal (min)	10	10	10	11	10	
Time shunt in place (min)	35	37	35	36	35	
Heparin Used:	679	679	685	689	2732	(97%)
Heparin Reversed:	293	301	307	300	1201	(43%)
Arteriotomy Closure:						
Simple Closure	450	458	446	453	1807	(64%)
Vein Patch	68	57	69	52	246	(9%)
Fabric Patch	163	165	167	184	679	(24%)
Other	15	16	19	15	65	(2%)
Missing	2	1	2	2	7	(0%)

	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Cerebral Monitoring:						
None	408	400	405	429	1642	(59%)
EEG	169	171	175	163	678	(24%)
Transcranial Doppler	27	32	23	25	107	(4%)
Evoked Potentials	19	20	21	22	82	(3%)
Carotid stump pressure after clamping	67	58	57	56	238	(8%)
Action if change in monitoring:						
None	38	36	34	32	140	(55%)
Shunt Inserted	21	23	26	30	100	(39%)
Procedure Stopped	1	1	0	2	4	(2%)
Other	5	2	2	2	11	(4%)
CE Not Completed:	4	4	3	3	14	(0%)
Surgeon:						
Vascular	398	400	402	395	1595	(57%)
Neurosurgeon	300	297	301	311	1209	(43%)
NASCET	599	616	612	617	2444	(87%)

Notes

1. The mean time is given for "Anesthesia Time," "Total cross clamp time," "Pre-shunt insertion time," "Post-shunt removal time" and "Time shunt in place."

4.2 Severity of Non-Endpoint Surgical Complications

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
None	509	514	510	545	2078	(74%)
Mild	105	94	121	106	426	(15%)
Moderate	73	78	64	46	261	(9%)
Severe	11	11	8	9	39	(1%)

Notes

1. Data taken from Hospital Discharge Form.
2. *Mild* indicates the complication did not result in prolonged hospital stay and did not result in a permanent disability.
3. *Moderate* indicates the complication did result in prolonged hospital stay but did not result in a permanent disability.
4. *Severe* indicates the complication resulted in a permanent disability at the time of hospital discharge.
5. Patients with more than one complication are classified according to their most severe complication.

4.3 Number of Non-Endpoint Surgical Complications

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
0	509	514	510	545	2078	(74%)
1	137	139	146	127	549	(20%)
2	33	30	32	25	120	(4%)
≥ 3	19	14	15	9	57	(2%)

4.4 Type and Severity of Non-Endpoint Surgical Complications

	Mild (N = 583)	Moderate (N = 364)	Severe (N = 51)	Total (N = 998)	
Wound Hematoma	123	51	3	177	(18%)
Wound Infection	2	2		4	(0%)
Wound Dehiscence				0	(0%)
Other wound complication	18	3	1	22	(2%)
Cranial Nerve Injury - facial	26	1	2	29	(3%)
Cranial Nerve Injury - vagus	16	1	6	23	(2%)
Cranial Nerve Injury - spinal accessory	2		1	3	(0%)
Cranial Nerve Injury - hypoglossal	38	6	8	52	(5%)
Cranial Nerve Injury - other	6	2		8	(1%)
Seizure: stroke related	2	4	5	11	(1%)
Seizure: non-stroke related	3	4	1	8	(1%)
Arrhythmia (requiring medication)	31	22	3	56	(6%)
Congestive heart failure	8	18	1	27	(3%)
Uncontrolled hypertension	5	15	1	21	(2%)
Hypotension	82	20	3	105	(11%)
Other cardiovascular	41	42		83	(8%)
Other vascular	4	2	3	9	(1%)
Respiratory	8	36	5	49	(5%)
Renal failure	1	6	1	8	(1%)
Trauma	3	2		5	(1%)
Depression requiring medication	1			1	(0%)
Confusion requiring restraint	8	16		24	(2%)
TIA	24	14		38	(4%)
Other	130	97	7	234	(23%)

Notes

1. Mild, Moderate and Severe complications are defined as above.
2. All complications are counted in this table. Thus, patients with multiple complications contribute more than once to this table

4.5 Mild Non-Endpoint Surgical Complications

	81 mg (N = 152)	325 mg (N = 133)	650 mg (N = 163)	1300 mg (N = 135)	Total (N = 583)	
Wound Hematoma	30	33	34	26	123	(21%)
Wound Infection			1	1	2	(0%)
Wound Dehiscence					0	(0%)
Other wound complication	2	3	4	9	18	(3%)
Cranial Nerve Injury - facial	8	7	6	5	26	(4%)
Cranial Nerve Injury - vagus	4	3	7	2	16	(3%)
Cranial Nerve Injury - spinal accessory			1	1	2	(0%)
Cranial Nerve Injury - hypoglossal	14	7	11	6	38	(7%)
Cranial Nerve Injury - other	2	2		2	6	(1%)
Seizure: stroke related	1		1		2	(0%)
Seizure: non-stroke related		1	1	1	3	(1%)
Arrhythmia (requiring medication)	11	10	6	4	31	(5%)
Congestive heart failure	3	1	3	1	8	(1%)
Uncontrolled hypertension	1	1	1	2	5	(1%)
Hypotension	18	19	19	26	82	(14%)
Other cardiovascular	7	9	16	9	41	(7%)
Other vascular		1	1	2	4	(1%)
Respiratory	2	1	4	1	8	(1%)
Renal failure				1	1	(0%)
Trauma	2		1		3	(1%)
Depression requiring medication	1				1	(0%)
Confusion requiring restraint	1	2	4	1	8	(1%)
TIA	6	5	7	6	24	(4%)
Other	39	28	35	28	130	(22%)

Notes

1. As above, *mild* complications did not result in a prolonged hospital stay, and did not result in a permanent disability.
2. All mild complications are counted in this table. Thus, patients with multiple mild complications contribute more than once to this table

4.6 Moderate Non-Endpoint Surgical Complications

	81 mg (N = 107)	325 mg (N = 102)	650 mg (N = 92)	1300 mg (N = 63)	Total (N = 364)	
Wound Hematoma	13	19	10	9	51	(14%)
Wound Infection		1	1		2	(1%)
Wound Dehiscence					0	(0%)
Other wound complication	2	1			3	(1%)
Cranial Nerve Injury - facial			1		1	(0%)
Cranial Nerve Injury - vagus	1				1	(0%)
Cranial Nerve Injury - spinal accessory					0	(0%)
Cranial Nerve Injury - hypoglossal	2		3	1	6	(2%)
Cranial Nerve Injury - other	1		1		2	(1%)
Seizure: stroke related	1		1	2	4	(1%)
Seizure: non-stroke related	2	1		1	4	(1%)
Arrhythmia (requiring medication)	7	7	5	3	22	(6%)
Congestive heart failure	3	4	8	3	18	(5%)
Uncontrolled hypertension	2	4	7	2	15	(4%)
Hypotension	3	4	5	8	20	(5%)
Other cardiovascular	15	12	6	9	42	(12%)
Other vascular		1		1	2	(1%)
Respiratory	9	9	12	6	36	(10%)
Renal failure	3	2	1		6	(2%)
Trauma	1		1		2	(1%)
Depression requiring medication					0	(0%)
Confusion requiring restraint	6	2	6	2	16	(4%)
TIA	6	3	3	2	14	(4%)
Other	30	32	21	14	97	(27%)

Notes

1. As above, *moderate* complications result in a prolonged hospital stay, but no permanent disability
2. All moderate complications are counted in this table. Thus, patients with multiple moderate complications contribute more than once to this table

4.7 Severe Non-Endpoint Surgical Complications

	81 mg (N = 17)	325 mg (N = 13)	650 mg (N = 8)	1300 mg (N = 13)	Total (N = 51)
Wound Hematoma	1		1	1	3 (6%)
Wound Infection					0 (0%)
Wound Dehiscence					0 (0%)
Other wound complication	1				1 (2%)
Cranial Nerve Injury - facial	1			1	2 (4%)
Cranial Nerve Injury - vagus	2	2	1	1	6 (12%)
Cranial Nerve Injury - spinal accessory				1	1 (2%)
Cranial Nerve Injury - hypoglossal	2	2	1	3	8 (16%)
Cranial Nerve Injury - other					0 (0%)
Seizure: stroke related	1	1	1	2	5 (10%)
Seizure: non-stroke related	1				1 (2%)
Arrhythmia (requiring medication)	2		1		3 (6%)
Congestive heart failure	1				1 (2%)
Uncontrolled hypertension		1			1 (2%)
Hypotension	1	1		1	3 (6%)
Other cardiovascular					0 (0%)
Other vascular		2		1	3 (6%)
Respiratory	2	1	1	1	5 (10%)
Renal failure	1				1 (2%)
Trauma					0 (0%)
Depression requiring medication					0 (0%)
Confusion requiring restraint					0 (0%)
TIA					0 (0%)
Other	1	3	2	1	7 (14%)

Notes

1. As above, *severe* complications result in a permanent disability at the time of hospital discharge.
2. All severe complications are counted in this table. Thus, patients with multiple severe complications contribute more than once to this table

4.8 Severity of Surgical Bleeding Complications

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Wound Hematoma						
mild	30	33	34	26	123	(4%)
moderate	13	19	10	9	51	(2%)
severe	1	0	1	1	3	(0%)
Total	44	52	45	36	177	(6%)

Notes

1. Mild, moderate and severe are defined as above.
2. If more than one wound hematoma was reported, the most severe is counted.

5 Medical Report

5.1 Possible ASA Adverse Side Effects

5.1.1 Overall Summary

	81 mg	325 mg	650 mg	1300 mg	Total	
At Hospital Discharge	51/698	66/697	58/702	55/706	230/2803	(8%)
At 30 Day Follow-up	84/690	104/690	100/693	104/698	392/2771	(14%)
At 3 Month Follow-up	77/684	66/688	69/689	84/694	296/2755	(11%)
At Any Time During Trial	160/698	177/697	175/702	177/706	689/2803	(25%)

Notes

1. The denominators change over time due to deaths and missed visits.

5.1.2 At Hospital Discharge

	81 mg (N = 698)		325 mg (N = 697)		650 mg (N = 702)		1300 mg (N = 706)		Total (N = 2803)	
Indigestion, heartburn, epigastric discomfort	32	(5%)	38	(5%)	32	(5%)	33	(5%)	135	(5%)
- Study ASA Suspended	8	(1%)	7	(1%)	9	(1%)	9	(1%)	33	(1%)
Spontaneous bruising, skin hemorrhage	17	(2%)	21	(3%)	24	(3%)	22	(3%)	84	(3%)
- Study ASA Suspended	0	(0%)	0	(0%)	1	(0%)	1	(0%)	2	(0%)
Melena	3	(0%)	1	(0%)	1	(0%)	4	(1%)	9	(0%)
- Study ASA Suspended	1	(0%)	0	(0%)	0	(0%)	1	(0%)	2	(0%)
Hematemesis	1	(0%)	1	(0%)	0	(0%)	3	(0%)	5	(0%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Other	1	(0%)	6	(1%)	4	(1%)	1	(0%)	12	(0%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Patients with none of the above	647	(93%)	631	(91%)	644	(92%)	651	(92%)	2573	(92%)

Notes

1. Patients with more than one adverse effect are counted once for each adverse effect in this table.
2. "Study ASA Suspended" includes both permanent and temporary stoppages of study ASA

5.1.3 At 30 Day Follow-up

	81 mg (N = 690)		325 mg (N = 690)		650 mg (N = 693)		1300 mg (N = 698)		Total (N = 2771)	
Indigestion, heartburn, epigastric discomfort	62	(9%)	75	(11%)	77	(11%)	73	(10%)	287	(10%)
- Study ASA Suspended	16	(2%)	34	(5%)	29	(4%)	27	(4%)	106	(4%)
Spontaneous bruising, skin hemorrhage	18	(3%)	23	(3%)	12	(2%)	24	(3%)	77	(3%)
- Study ASA Suspended	0	(0%)	0	(0%)	1	(0%)	3	(0%)	4	(0%)
Melena	5	(1%)	5	(1%)	6	(1%)	5	(1%)	21	(1%)
- Study ASA Suspended	2	(0%)	1	(0%)	2	(0%)	2	(0%)	7	(0%)
Hematemesis	2	(0%)	4	(1%)	3	(0%)	5	(1%)	14	(1%)
- Study ASA Suspended	0	(0%)	2	(0%)	0	(0%)	0	(0%)	2	(0%)
Other	5	(1%)	5	(1%)	7	(1%)	9	(1%)	26	(1%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Patients with none of the above	606	(88%)	586	(85%)	593	(86%)	594	(85%)	2379	(86%)

Notes

1. Patients with more than one adverse effect are counted once for each adverse effect in this table.
2. "Study ASA Suspended" includes both permanent and temporary stoppages of study ASA

5.1.4 At 90 Day Follow-up

	81 mg (N = 684)		325 mg (N = 688)		650 mg (N = 689)		1300 mg (N = 694)		Total (N = 2755)	
Indigestion, heartburn, epigastric discomfort	54	(8%)	44	(6%)	48	(7%)	65	(9%)	211	(8%)
- Study ASA Suspended	13	(2%)	10	(1%)	17	(2%)	15	(2%)	55	(2%)
Spontaneous bruising, skin hemorrhage	19	(3%)	24	(3%)	16	(2%)	22	(3%)	81	(3%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	4	(1%)	4	(0%)
Melena	2	(0%)	2	(0%)	1	(0%)	4	(1%)	9	(0%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	3	(0%)	3	(0%)
Hematemesis	0	(0%)	1	(0%)	3	(0%)	1	(0%)	5	(0%)
- Study ASA Suspended	0	(0%)	0	(0%)	2	(0%)	0	(0%)	2	(0%)
Other	5	(1%)	5	(1%)	5	(1%)	6	(1%)	21	(1%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Patients with none of the above	607	(89%)	622	(90%)	620	(90%)	610	(88%)	2459	(89%)

Notes

1. Patients with more than one adverse effect are counted once for each adverse effect in this table.
2. "Study ASA Suspended" includes both permanent and temporary stoppages of study ASA

5.1.5 At Any Time During Trial

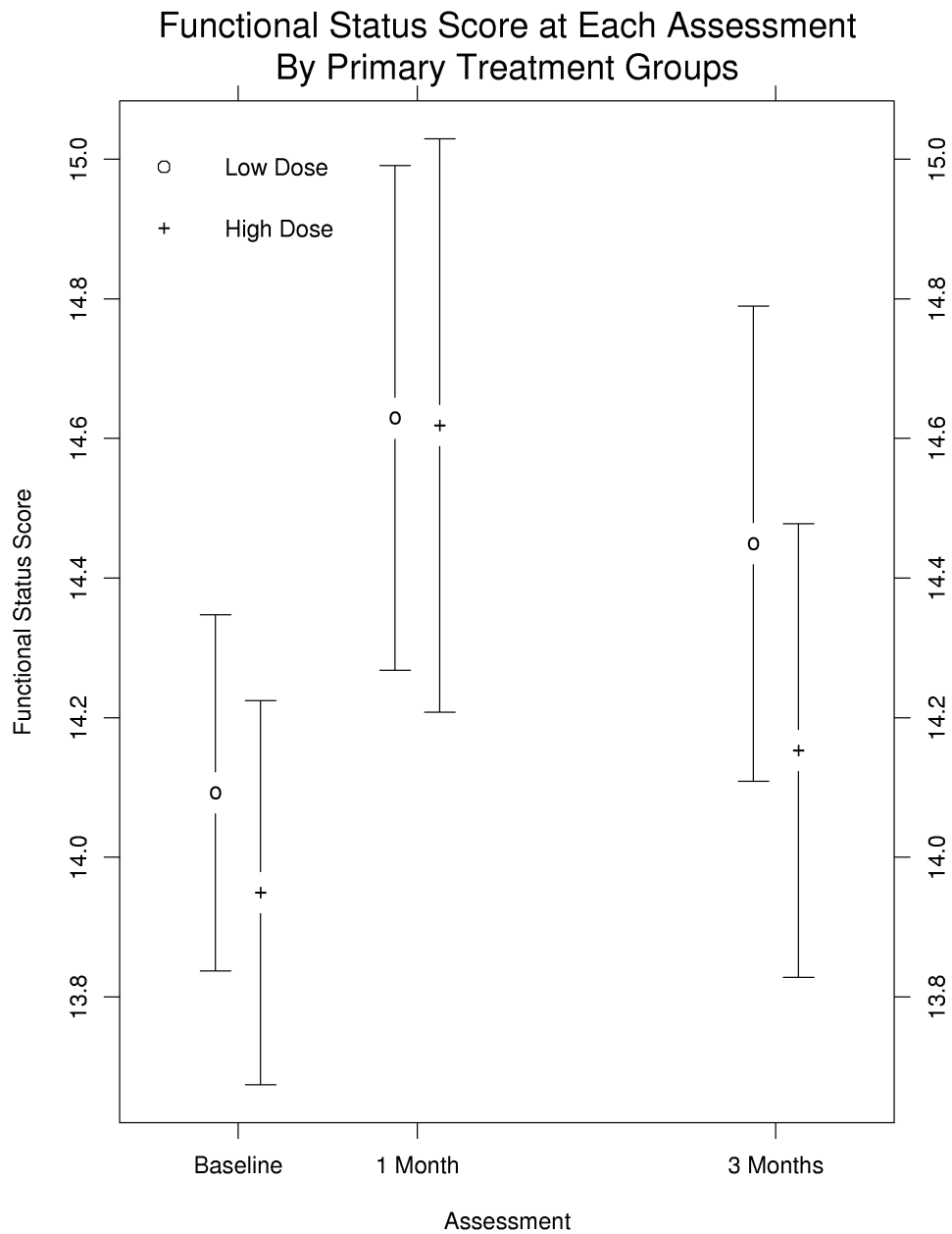
	81 mg (N = 698)		325 mg (N = 697)		650 mg (N = 702)		1300 mg (N = 706)		Total (N = 2803)	
Indigestion, heartburn, epigastric discomfort	111	(16%)	119	(17%)	119	(17%)	126	(18%)	475	(17%)
- Study ASA Suspended	31	(4%)	42	(6%)	43	(6%)	41	(6%)	157	(6%)
Spontaneous bruising, skin hemorrhage	47	(7%)	58	(8%)	48	(7%)	55	(8%)	208	(7%)
- Study ASA Suspended	4	(1%)	1	(0%)	3	(0%)	5	(1%)	13	(0%)
Melena	8	(1%)	6	(1%)	8	(1%)	8	(1%)	30	(1%)
- Study ASA Suspended	2	(0%)	1	(0%)	2	(0%)	3	(0%)	8	(0%)
Hematemesis	3	(0%)	5	(1%)	6	(1%)	7	(1%)	21	(1%)
- Study ASA Suspended	0	(0%)	2	(0%)	2	(0%)	1	(0%)	5	(0%)
Other	11	(2%)	15	(2%)	14	(2%)	15	(2%)	55	(2%)
- Study ASA Suspended	0	(0%)	0	(0%)	0	(0%)	0	(0%)	0	(0%)
Patients with none of the above	538	(77%)	520	(75%)	527	(75%)	529	(75%)	2114	(75%)

Notes

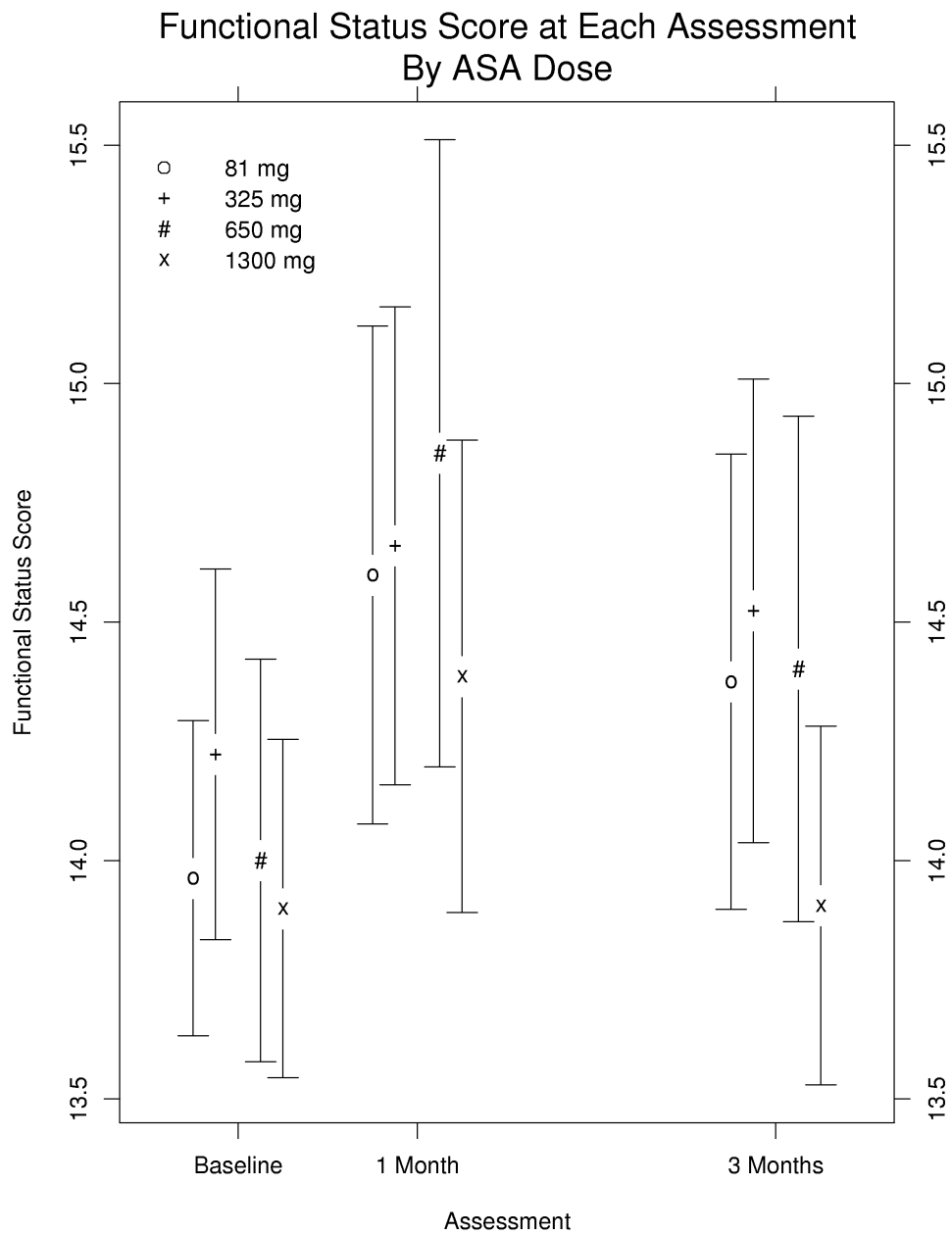
1. Patients with more than one adverse effect are counted once for each adverse effect in this table.
2. "Study ASA Suspended" includes both permanent and temporary stoppages of study ASA

6 Functional Status

6.1 High Dose vs. Low Dose



6.2 Comparison Among All Four Doses



7 Outcome Events

7.1 All Stroke and All Causes of Death Within 30 Days of Surgery

7.1.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose		
Event	66	(4.7%)	86	(6.1%)	
Event Free	1329	(95.3%)	1323	(93.9%)	
					2804

$$\chi^2_{(1)} = 2.58, p = 0.109$$

Absolute Risk Reduction = -1.4% (95% CI -3% to 0.3%)

7.1.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	39	(5.6%)	27	(3.9%)	45	(6.4%)	41	(5.8%)
Event Free	659	(94.4%)	670	(96.1%)	658	(93.6%)	665	(94.2%)
$\chi^2_{(1)} = 2.27, p = 0.132$				$\chi^2_{(1)} = 0.22, p = 0.642$				

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	28	4.0	14	2.0	42	3.0	31	4.4	28	4.0	59	4.2
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	5	0.7	4	0.6	9	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	2	0.3	2	0.3	4	0.3
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	3	0.4	6	0.4
Cardiovascular Death	1	0.1	4	0.6	5	0.4	4	0.6	1	0.1	5	0.4
Other Death	0	0.0	2	0.3	2	0.1	0	0.0	3	0.4	3	0.2
Event Free	659	94.4	670	96.1	1329	95.3	658	93.6	665	94.2	1323	93.9

7.1.3 Perioperative Stroke and Death Stratified by Prior ASA and Study ASA Duration Prior to Surgery

Time on Study Treatment	Pre-Randomization ASA Dose	Randomized Study Treatment (ASA Dose)			
		Low Dose		High Dose	
≥ 2 Days	< 650 mg/day	19/566	3.4%	38/550	6.9%
≥ 2 Days	≥ 650 mg/day	9/120	7.5%	14/145	9.7%
< 2 Days	< 650 mg/day	32/665	4.8%	32/666	4.8%
< 2 Days	≥ 650 mg/day	6/ 44	13.6%	2/ 48	4.2%

Hypothesis: If high dose ASA is beneficial, this effect will be:

1. *Strongest* among those patients with the least contamination by prior ASA (ie. group 1: on study treatment for ≥ 2 days with pre-randomization ASA dose < 650 mg).
2. *Weakest* among those patients with the most contamination by prior ASA (ie. group 4: on study treatment for < 2 days with pre-randomization ASA dose ≥ 650 mg).

Note

Logistic regression modelling will be used to examine the effects and interactions among the three factors summarized in this table.

7.1.4 Logistic Regression

Outcome: Any stroke or death within 30 days following surgery.

Variables: Treatment (high dose vs. low dose), *ACE* contamination variables (prior ASA, days on study ASA prior to CE), risk factors found important in NASCET, whether or not patients were symptomatic at baseline, all first order interactions between treatment and risk factors.

	Observed Univariate Results					Interaction
	Present	Absent	RR	95% CI	p-value	p-value
Treatment (< 650 mg)	66/1395	86/1409	0.78	0.57–1.06	0.109	—
Prior ASA (< 650 mg)	121/2447	31/357	0.57	0.39–0.83	0.00356	0.282
Days on Rx pre CE (< 2 days)	80/1381	72/1423	1.14	0.84–1.56	0.391	0.0238
History of Diabetes	58/682	94/2122	1.92	1.4–2.63	< 0.001	0.256
History of MI or Angina	48/984	104/1820	0.85	0.61–1.19	0.351	0.513
Contralateral Occlusion	27/236	101/1996	2.26	1.51–3.38	< 0.001	0.0824
Appropriate Lesion on CT/MRI	36/565	54/989	1.17	0.78–1.76	0.459	0.585
DBP > 90 mmHg	20/283	130/2507	1.36	0.87–2.15	0.183	0.721
CE on Left Side	96/1461	56/1343	1.58	1.14–2.17	0.00503	0.74
Female Gender	53/842	99/1962	1.25	0.9–1.72	0.181	0.543
Symptomatic	83/1292	69/1512	1.41	1.03–1.92	0.0301	0.72

7.2 All Stroke and All Causes of Death Within 3 Months of Surgery

7.2.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose		
Event	79	(5.7%)	100	(7.1%)	
Event Free	1316	(94.3%)	1309	(92.9%)	
					2804

$$\chi^2_{(1)} = 2.41, p = 0.120$$

Absolute Risk Reduction = -1.4% (95% CI -3.2% to 0.4%)

7.2.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	46	(6.6%)	33	(4.7%)	51	(7.3%)	49	(6.9%)
Event Free	652	(93.4%)	664	(95.3%)	652	(92.7%)	657	(93.1%)
	$\chi^2_{(1)} = 2.25, p = 0.134$				$\chi^2_{(1)} = 0.05, p = 0.818$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	31	4.4	17	2.4	48	3.4	34	4.8	31	4.4	65	4.6
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	5	0.7	4	0.6	9	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	3	0.4	2	0.3	5	0.4
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	3	0.4	6	0.4
Cardiovascular Death	4	0.6	5	0.7	9	0.6	6	0.9	3	0.4	9	0.6
Other Death	1	0.1	4	0.6	5	0.4	0	0.0	6	0.8	6	0.4
Event Free	652	93.4	664	95.3	1316	94.3	652	92.7	657	93.1	1309	92.9

7.3 Ipsilateral Stroke and All Causes of Death Within 30 Days of Surgery

7.3.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	58	(4.2%)	81	(5.7%)
Event Free	1337	(95.8%)	1328	(94.3%)
	2804			

$$\chi^2_{(1)} = 3.77, p = 0.052$$

Absolute Risk Reduction = -1.6% (95% CI -3.2% to 0%)

7.3.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	33	(4.7%)	25	(3.6%)	43	(6.1%)	38	(5.4%)
Event Free	665	(95.3%)	672	(96.4%)	660	(93.9%)	668	(94.6%)
	$\chi^2_{(1)} = 1.14, p = 0.286$				$\chi^2_{(1)} = 0.35, p = 0.554$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	22	3.2	12	1.7	34	2.4	30	4.3	25	3.5	55	3.9
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	4	0.6	4	0.6	8	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	2	0.3	2	0.3	4	0.3
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	2	0.3	5	0.4
Cardiovascular Death	1	0.1	4	0.6	5	0.4	4	0.6	1	0.1	5	0.4
Other Death	0	0.0	2	0.3	2	0.1	0	0.0	3	0.4	3	0.2
Fatal Stroke (Non-Ipsilateral)	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1
Event Free	665	95.3	672	96.4	1337	95.8	660	93.9	668	94.6	1328	94.3

7.4 Ipsilateral Stroke and All Causes of Death Within 3 Months of Surgery

7.4.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	68	(4.9%)	91	(6.5%)
Event Free	1327	(95.1%)	1318	(93.5%)
	2804			

$$\chi^2_{(1)} = 3.29, p = 0.070$$

Absolute Risk Reduction = -1.6% (95% CI -3.3% to 0.1%)

7.4.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	39	(5.6%)	29	(4.2%)	47	(6.7%)	44	(6.2%)
Event Free	659	(94.4%)	668	(95.8%)	656	(93.3%)	662	(93.8%)
	$\chi^2_{(1)} = 1.53, p = 0.216$				$\chi^2_{(1)} = 0.12, p = 0.729$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	23	3.3	13	1.9	36	2.6	31	4.4	26	3.7	57	4.0
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	4	0.6	4	0.6	8	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	2	0.3	2	0.3	4	0.3
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	2	0.3	5	0.4
Cardiovascular Death	5	0.7	5	0.7	10	0.7	6	0.9	3	0.4	9	0.6
Other Death	1	0.1	4	0.6	5	0.4	0	0.0	6	0.8	6	0.4
Fatal Stroke (Non-Ipsilateral)	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	2	0.1
Event Free	659	94.4	668	95.8	1327	95.1	656	93.3	662	93.8	1318	93.5

7.5 All Stroke, All MI and All Causes of Death Within 30 Days of Surgery

7.5.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	75	(5.4%)	99	(7.0%)
Event Free	1320	(94.6%)	1310	(93.0%)
	2804			

$$\chi^2_{(1)} = 3.28, p = 0.070$$

Absolute Risk Reduction = -1.6% (95% CI -3.4% to 0.1%)

7.5.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	42	(6.0%)	33	(4.7%)	53	(7.5%)	46	(6.5%)
Event Free	656	(94.0%)	664	(95.3%)	650	(92.5%)	660	(93.5%)
	$\chi^2_{(1)} = 1.13, p = 0.288$				$\chi^2_{(1)} = 0.56, p = 0.452$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	28	4.0	14	2.0	42	3.0	30	4.3	27	3.8	57	4.0
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	4	0.6	4	0.6	8	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	2	0.3	2	0.3	4	0.3
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	3	0.4	6	0.4
Non-Fatal MI	2	0.3	7	1.0	9	0.6	11	1.6	6	0.8	17	1.2
Fatal MI	2	0.3	1	0.1	3	0.2	3	0.4	1	0.1	4	0.3
Other Cardiovascular Death	0	0.0	3	0.4	3	0.2	0	0.0	0	0.0	0	0.0
Other Death	0	0.0	1	0.1	1	0.1	0	0.0	3	0.4	3	0.2
Event Free	656	94.0	664	95.3	1320	94.6	650	92.5	660	93.5	1310	93.0

7.6 All Stroke, All MI and All Causes of Death Within 3 Months of Surgery

7.6.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	87	(6.2%)	118	(8.4%)
Event Free	1308	(93.8%)	1291	(91.6%)
	2804			

$$\chi^2_{(1)} = 4.73, p = 0.030$$

Absolute Risk Reduction = -2.1% (95% CI -4.1% to -0.2%)

7.6.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	49	(7.0%)	38	(5.5%)	61	(8.7%)	57	(8.1%)
Event Free	649	(93.0%)	659	(94.5%)	642	(91.3%)	649	(91.9%)
	$\chi^2_{(1)} = 1.47, p = 0.226$				$\chi^2_{(1)} = 0.17, p = 0.683$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	31	4.4	17	2.4	48	3.4	33	4.7	30	4.2	63	4.5
Non-Fatal Stroke (hemorrhagic)	2	0.3	4	0.6	6	0.4	5	0.7	4	0.6	9	0.6
Fatal Stroke (non-hemorrhagic)	6	0.9	1	0.1	7	0.5	3	0.4	2	0.3	5	0.4
Fatal Stroke (hemorrhagic)	2	0.3	2	0.3	4	0.3	3	0.4	3	0.4	6	0.4
Non-Fatal MI	3	0.4	7	1.0	10	0.7	12	1.7	11	1.6	23	1.6
Fatal MI	2	0.3	1	0.1	3	0.2	4	0.6	1	0.1	5	0.4
Other Cardiovascular Death	2	0.3	3	0.4	5	0.4	1	0.1	1	0.1	2	0.1
Other Death	1	0.1	3	0.4	4	0.3	0	0.0	5	0.7	5	0.4
Event Free	649	93.0	659	94.5	1308	93.8	642	91.3	649	91.9	1291	91.6

7.7 Primary Outcome Events Within 3 Months of Surgery

Outcome Event	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)	
Stroke:						
Mild	16	14	26	24	80	(2.9%)
Moderate	9	1	5	5	20	(0.7%)
Severe	6	6	7	6	25	(0.9%)
Fatal	9	3	7	5	24	(0.9%)
Total Strokes	40	24	45	40	149	(5.3%)
Myocardial Infarction:						
Non-fatal	3	9	15	15	42	(1.5%)
Fatal	3	1	4	1	9	(0.3%)
Total Myocardial Infarctions	6	10	19	16	51	(1.8%)
Death:						
Stroke	9	3	7	5	24	(0.9%)
Myocardial Infarction	3	1	4	1	9	(0.3%)
Other Ischemic Heart Disease	2	2	2	2	8	(0.3%)
Sudden Death		2			2	(0.1%)
Other Cardiovascular			1	1	2	(0.1%)
Other Vascular				1	1	(0.0%)
Other Cause	1	4	1	5	11	(0.4%)
Total Deaths	15	12	15	15	57	(2.0%)

Notes

1. Patients are only counted once under each of the three types of outcome event: stroke (most severe counted), myocardial infarction (most severe counted) and death.
2. Mild moderate and severe strokes had Rankin scores (assessed at 3 months) of 1, 2 and ≥ 3 respectively.

7.8 Total Mortality Within 30 Days of Surgery

Cause of Death	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)
Stroke	8	2	5	5	20 (0.7%)
Myocardial Infarction	1	1	4	1	7 (0.2%)
Other Cardiovascular	0	3	0	1	4 (0.1%)
Other	0	2	0	3	5 (0.2%)
Total	9	8	9	10	36 (1.3%)

7.9 Total Mortality Within 3 Months of Surgery

Cause of Death	81 mg (N = 698)	325 mg (N = 697)	650 mg (N = 703)	1300 mg (N = 706)	Total (N = 2804)
Stroke	9	3	7	5	24 (0.9%)
Myocardial Infarction	3	1	4	1	9 (0.3%)
Other Cardiovascular	2	4	3	3	12 (0.4%)
Other	1	4	1	5	11 (0.4%)
Total	15	12	15	15	57 (2.0%)

Notes

1. "Other Cardiovascular" includes other ischemic heart disease, sudden death and other cardiovascular (with no further breakdown provided).
2. "Other" includes pulmonary embolism, other vascular, CNS malignancy, systemic malignancy, respiratory disease, other known cause (not further divided) and uncertain/unknown.

7.10 Most Serious Outcome Event in the 30 Day Perioperative Period

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Non-Fatal MI	3	6	8	5	22	(0.8%)
Mild Non-Fatal Stroke	16	13	25	22	76	(2.7%)
Moderate Non-Fatal Stroke	9	1	5	5	20	(0.7%)
Severe Non-Fatal Stroke	5	5	6	4	20	(0.7%)
Death	9	8	9	10	36	(1.3%)
Total	42	33	53	46	174	(6.2%)

7.11 Most Serious Outcome Event Within 3 Months of Surgery

	81 mg (<i>N</i> = 698)	325 mg (<i>N</i> = 697)	650 mg (<i>N</i> = 703)	1300 mg (<i>N</i> = 706)	Total (<i>N</i> = 2804)	
Non-Fatal MI	3	5	10	8	26	(0.9%)
Mild Non-Fatal Stroke	17	14	24	24	79	(2.8%)
Moderate Non-Fatal Stroke	8	1	5	5	19	(0.7%)
Severe Non-Fatal Stroke	6	6	7	5	24	(0.9%)
Death	15	12	15	15	57	(2.0%)
Total	49	38	61	57	205	(7.3%)

7.12 Follow-up of Patients Excluded Due to Cancelled Surgery

	81 mg	325 mg	650 mg	1300 mg	Total
Patients Excluded	11	11	12	11	45
Follow-ups Completed					
- none, lost to follow-up	0	0	0	0	0
- baseline only	0	0	0	0	0
- to 1 month follow-up only	0	0	0	0	0
- to 3 month follow-up	11	11	12	11	45

Strokes and Deaths

Patient ID	Rx	Type	Days Since Randomization
A	650 mg	Stroke	7
A	650 mg	Death	90
B	650 mg	Death	49

8 Efficacy Analysis¹

8.1 All Stroke and All Causes of Death Within 30 Days of Surgery

8.1.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	19	(3.4%)	38	(6.9%)
Event Free	547	(96.6%)	512	(93.1%)
	1116			

$$\chi^2_{(1)} = 7.26, p = 0.007$$

Absolute Risk Reduction = -3.6% (95% CI -6.1% to -1%)

8.1.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	9	(3.3%)	10	(3.4%)	21	(7.5%)	17	(6.3%)
Event Free	263	(96.7%)	284	(96.6%)	260	(92.5%)	252	(93.7%)
	$\chi^2_{(1)} = 0.00, p = 0.951$				$\chi^2_{(1)} = 0.28, p = 0.594$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	7	2.6	6	2.0	13	2.3	16	5.7	12	4.5	28	5.1
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	2	0.7	1	0.4	3	0.5
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	2	0.7	2	0.4
Cardiovascular Death	0	0.0	2	0.7	2	0.4	3	1.1	0	0.0	3	0.5
Other Death	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4	1	0.2
Event Free	263	96.7	284	96.6	547	96.6	260	92.5	252	93.7	512	93.1

¹Taking study ASA 2 or more days prior to CE and taking less than 650mg ASA prior to randomization.

8.2 All Stroke and All Causes of Death Within 3 Months of Surgery

8.2.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose		
Event	22	(3.9%)	45	(8.2%)	
Event Free	544	(96.1%)	505	(91.8%)	
					1116

$$\chi^2_{(1)} = 9.12, p = 0.003$$

Absolute Risk Reduction = -4.3% (95% CI -7.1% to -1.5%)

8.2.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	11	(4.0%)	11	(3.7%)	24	(8.5%)	21	(7.8%)
Event Free	261	(96.0%)	283	(96.3%)	257	(91.5%)	248	(92.2%)
	$\chi^2_{(1)} = 0.03, p = 0.852$				$\chi^2_{(1)} = 0.10, p = 0.753$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	8	2.9	6	2.0	14	2.5	17	6.0	15	5.6	32	5.8
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	2	0.7	1	0.4	3	0.5
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	2	0.7	2	0.4
Cardiovascular Death	1	0.4	2	0.7	3	0.5	5	1.8	0	0.0	5	0.9
Other Death	0	0.0	1	0.3	1	0.2	0	0.0	2	0.7	2	0.4
Event Free	261	96.0	283	96.3	544	96.1	257	91.5	248	92.2	505	91.8

8.3 Ipsilateral Stroke and All Causes of Death Within 30 Days of Surgery

8.3.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	17	(3.0%)	36	(6.5%)
Event Free	549	(97.0%)	514	(93.5%)
	1116			

$$\chi^2_{(1)} = 7.74, p = 0.005$$

Absolute Risk Reduction = -3.5% (95% CI -6% to -1%)

8.3.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	7	(2.6%)	10	(3.4%)	20	(7.1%)	16	(5.9%)
Event Free	265	(97.4%)	284	(96.6%)	261	(92.9%)	253	(94.1%)
	$\chi^2_{(1)} = 0.33, p = 0.564$				$\chi^2_{(1)} = 0.31, p = 0.579$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	5	1.8	6	2.0	11	1.9	16	5.7	11	4.1	27	4.9
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	1	0.4	1	0.4	2	0.4
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	1	0.4	1	0.2
Cardiovascular Death	0	0.0	2	0.7	2	0.4	3	1.1	0	0.0	3	0.5
Other Death	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4	1	0.2
Fatal Stroke (Non-Ipsilateral)	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4	1	0.2
Event Free	265	97.4	284	96.6	549	97.0	261	92.9	253	94.1	514	93.5

8.4 Ipsilateral Stroke and All Causes of Death Within 3 Months of Surgery

8.4.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	20	(3.5%)	41	(7.5%)
Event Free	546	(96.5%)	509	(92.5%)
	1116			

$$\chi^2_{(1)} = 8.30, p = 0.004$$

Absolute Risk Reduction = -3.9% (95% CI -6.6% to -1.3%)

8.4.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	9	(3.3%)	11	(3.7%)	23	(8.2%)	18	(6.7%)
Event Free	263	(96.7%)	283	(96.3%)	258	(91.8%)	251	(93.3%)
	$\chi^2_{(1)} = 0.08, p = 0.781$				$\chi^2_{(1)} = 0.44, p = 0.505$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	6	2.2	6	2.0	12	2.1	17	6.0	12	4.5	29	5.3
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	1	0.4	1	0.4	2	0.4
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	1	0.4	1	0.2
Cardiovascular Death	1	0.4	2	0.7	3	0.5	5	1.8	0	0.0	5	0.9
Other Death	0	0.0	1	0.3	1	0.2	0	0.0	2	0.7	2	0.4
Fatal Stroke (Non-Ipsilateral)	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4	1	0.2
Event Free	263	96.7	283	96.3	546	96.5	258	91.8	251	93.3	509	92.5

8.5 All Stroke, All MI and All Causes of Death Within 30 Days of Surgery

8.5.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	21	(3.7%)	45	(8.2%)
Event Free	545	(96.3%)	505	(91.8%)
	1116			

$$\chi^2_{(1)} = 10.02, p = 0.002$$

Absolute Risk Reduction = -4.5% (95% CI -7.2% to -1.7%)

8.5.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	9	(3.3%)	12	(4.1%)	25	(8.9%)	20	(7.4%)
Event Free	263	(96.7%)	282	(95.9%)	256	(91.1%)	249	(92.6%)
	$\chi^2_{(1)} = 0.24, p = 0.627$				$\chi^2_{(1)} = 0.39, p = 0.532$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	7	2.6	6	2.0	13	2.3	16	5.7	12	4.5	28	5.1
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	2	0.7	1	0.4	3	0.5
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	2	0.7	2	0.4
Non-Fatal MI	0	0.0	2	0.7	2	0.4	5	1.8	3	1.1	8	1.5
Fatal MI	0	0.0	1	0.3	1	0.2	2	0.7	0	0.0	2	0.4
Other Cardiovascular Death	0	0.0	1	0.3	1	0.2	0	0.0	0	0.0	0	0.0
Other Death	0	0.0	0	0.0	0	0.0	0	0.0	1	0.4	1	0.2
Event Free	263	96.7	282	95.9	545	96.3	256	91.1	249	92.6	505	91.8

8.6 All Stroke, All MI and All Causes of Death Within 3 Months of Surgery

8.6.1 Low Dose vs. High Dose ASA (primary analysis)

	Low Dose		High Dose	
Event	24	(4.2%)	55	(10.0%)
Event Free	542	(95.8%)	495	(90.0%)
	1116			

$$\chi^2_{(1)} = 14.07, p = 0.0002$$

Absolute Risk Reduction = -5.8% (95% CI -8.8% to -2.8%)

8.6.2 81 mg vs. 325 mg and 650 mg vs. 1300 mg (secondary analysis)

	81 mg		325 mg		650 mg		1300 mg	
Event	11	(4.0%)	13	(4.4%)	28	(10.0%)	27	(10.0%)
Event Free	261	(96.0%)	281	(95.6%)	253	(90.0%)	242	(90.0%)
	$\chi^2_{(1)} = 0.05, p = 0.824$				$\chi^2_{(1)} = 0.00, p = 0.977$			

	81 mg		325 mg		Total Low Dose		650 mg		1300 mg		Total High Dose	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-Fatal Stroke (non-hemorrhagic)	8	2.9	6	2.0	14	2.5	17	6.0	15	5.6	32	5.8
Non-Fatal Stroke (hemorrhagic)	0	0.0	0	0.0	0	0.0	2	0.7	1	0.4	3	0.5
Fatal Stroke (non-hemorrhagic)	1	0.4	0	0.0	1	0.2	0	0.0	1	0.4	1	0.2
Fatal Stroke (hemorrhagic)	1	0.4	2	0.7	3	0.5	0	0.0	2	0.7	2	0.4
Non-Fatal MI	0	0.0	2	0.7	2	0.4	5	1.8	6	2.2	11	2.0
Fatal MI	0	0.0	1	0.3	1	0.2	3	1.1	0	0.0	3	0.5
Other Cardiovascular Death	1	0.4	1	0.3	2	0.4	1	0.4	0	0.0	1	0.2
Other Death	0	0.0	1	0.3	1	0.2	0	0.0	2	0.7	2	0.4
Event Free	261	96.0	281	95.6	542	95.8	253	90.0	242	90.0	495	90.0

8.7 Primary Outcome Events Within 3 Months of Surgery

Outcome Event	81 mg (<i>N</i> = 272)	325 mg (<i>N</i> = 294)	650 mg (<i>N</i> = 281)	1300 mg (<i>N</i> = 269)	Total (<i>N</i> = 1116)	
Stroke:						
Mild	5	5	14	12	36	(3.2%)
Moderate	2		2	1	5	(0.4%)
Severe		1	2	3	6	(0.5%)
Fatal	3	2	1	3	9	(0.8%)
Total Strokes	10	8	19	19	56	(5.0%)
Myocardial Infarction:						
Non-fatal		4	7	8	19	(1.7%)
Fatal		1	3		4	(0.4%)
Total Myocardial Infarctions	0	5	10	8	23	(2.1%)
Death:						
Stroke	3	2	1	3	9	(0.8%)
Myocardial Infarction		1	3		4	(0.4%)
Other Ischemic Heart Disease	1		2		3	(0.3%)
Sudden Death		1			1	(0.1%)
Other Cardiovascular			1		1	(0.1%)
Other Vascular					0	(0.0%)
Other Cause		1		2	3	(0.3%)
Total Deaths	4	5	7	5	21	(1.9%)

Notes

1. Patients are only counted once under each of the three types of outcome event: stroke (most severe counted), myocardial infarction (most severe counted) and death.
2. Mild moderate and severe strokes had Rankin scores (assessed at 3 months) of 1, 2 and ≥ 3 respectively.