IL FOLLOW-UP E L'OUTCOME DELL'ICTUS CRIPTOGENETICO

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ICTUS CRIPTOGENETICO

- 3 entità cliniche con notevoli differenze prognostiche:
  - Valutazione incompleta (morti precoci)
  - Cause multiple (alto rischio)
  - Nessuna causa nonostante work-up diagnostico estensivo (basso rischio)

Diagnostic group	Distribution		Associated medical diseases
	No.	%	
Atherothrombotic	110*	33.1	
With angiographic evidence	50		2
With two or more risk factors	60		7, 15
Cardioembolic	64†	19.2	4, 5, 11, 16, 18, 18, 19
Mixed	15	4.5	15
Other	27	8.1	
Arteritis	2		3, 13
Fibromuscular dysplasia	2		
Arterial dissection	1		
Hematologic and autoimmune diseases	5		1, 9, 12, 14, 18
Migraine with aura	4		
Oral contraceptive use	13‡		
Undetermined	66	19.8	
One risk factor and associated medical disease	62		4, 6, 8, 10, 17, 17
Probably nonembolic cardiac abnormalities	4		
Bundle branch block	2		
Hypertrophic cardiomyopathy	1		
Asymmetrical septal hypertrophy	1		
Unknown	51	15.3	

Stroke 1993; 24: 362-367

ETIOLOGY OF STROKE IN THE YOUNG

	Univariate		Multivariate*	
Outcome Predictor	HR	95% CI	HR	95% CI
Composite outcome event				
Male gender	2.7	(1.3–5.6)	2.1	(1.0–4.4)
Age >35 y	5.9	(2.1–16.7)	4.3	(1.5–12.5)
Stroke at entry	2.9	(1.3–6.4)	2.3	(1.0–5.0)
Carotid territory	0.9	(0.4–1.8)	0.7	(0.3–1.5)
Cardiac diseases	3.0	(1.6–5.7)	2.5	(1.3–4.8)
Carotid abnormalities	2.3	(1.1–4.8)	1.7	(0.8–3.8)
Hypertension	2.0	(1.0–4.0)	1.1	(0.5–2.3)
Diabetes mellitus	1.9	(0.5–8.1)	0.9	(0.2–3.9)

Stroke 1999; 30:2320-2325

PREDICTORS OF STROKE OUTCOME IN THE YOUNG

Outcome	Atherothrombotic (n=109)	Cardioembolic (n=63)	Mixed (n=15)	Miscellaneous (n=143)
New stroke	0.20	0.17	2.36	0.29
	(0.00–0.47)	(0.00–0.52)	(0.00–5.42)	(0.01–0.57)
Myocardial infarction	0.49	0.18	1.68	0.00
	(0.07–0.93)	(0.00–0.55)	(0.00–4.30)	(0.00–0.00)
Death from all causes	0.79	2.31	3.05	0.26
	(0.26–1.34)	(0.85–4.00)	(0.44–6.52)	(0.00–0.57)

Values are percent, with 95% CIs in parentheses.

AVERAGE ANNUAL INCIDENCE RATE OF NEW EVENTS

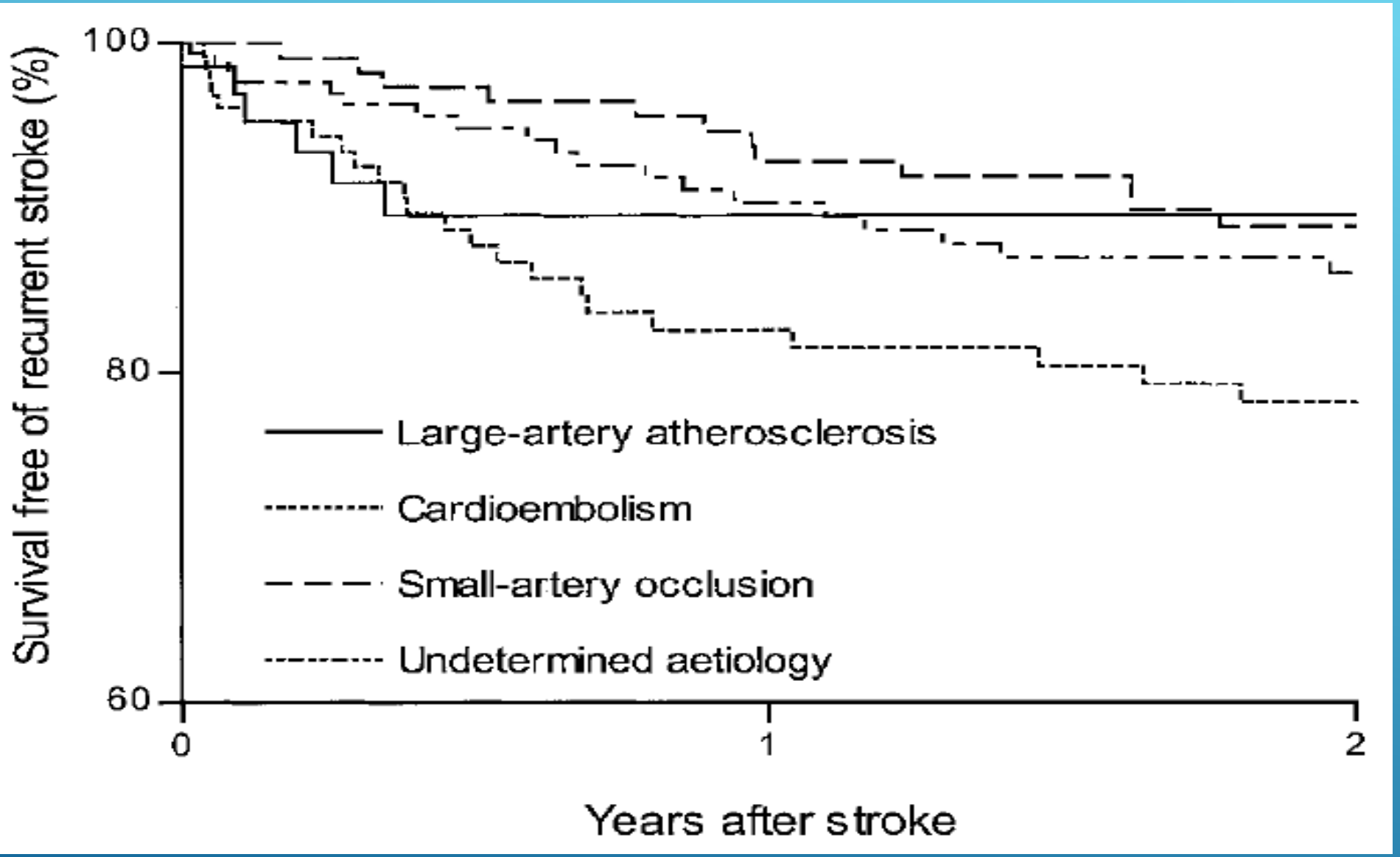
Outcome	Atheroma, n = 24	Cardioembolism, n = 15	Lacune, n = 5	Other, n = 64	Undetermined, n = 179	p^*
Recurrent stroke	1	2	0	0	7	0.61
Myocardial infarction	1	1	0	0	0	NA
Epileptic seizure	2	2	1	4	11	0.49
Death	2	2	0	3	15	0.56

Breakdown of the outcome events in stroke subtypes at the end of the follow-up period. Numbers of patients with the risk factor are given.

* χ^2 test between patients with an undetermined cause and patients with a known cause considered in a single group.

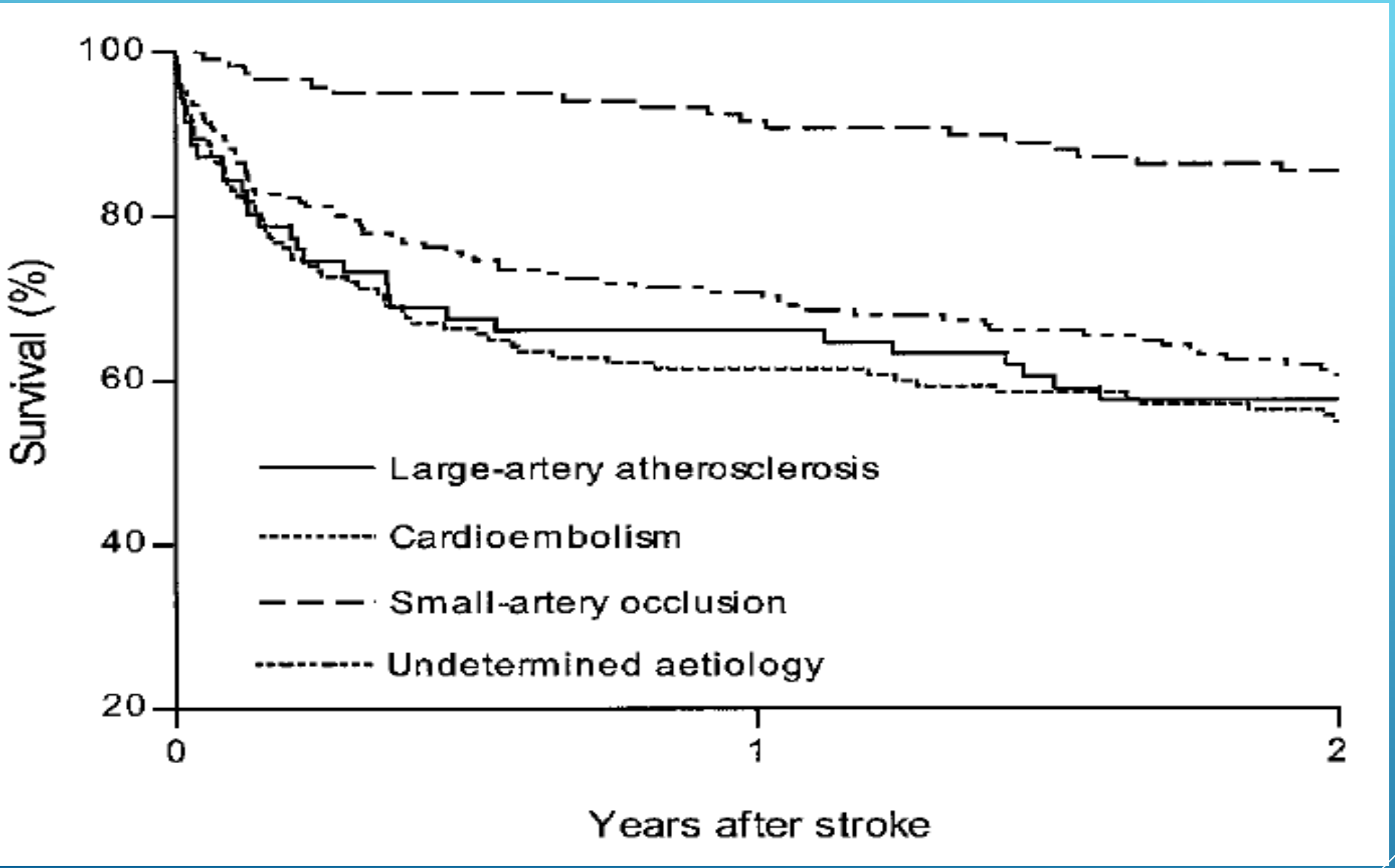
PROGNOSIS OF STROKE IN THE YOUNG

NEUROLOGY 2002;59:26–33



LAA 90%
SAO 89%
UE 86%
CE 78%

ERLANGEN STROKE REGISTRY 1994-1998



SAO 85%

UE 61%
LAA 58%
CE 55%

ERLANGEN STROKE REGISTRY 1994-1998

Evolution of patients	Subgroups of ischemic stroke					Total group
	CS	LAD	CE	SAD	OC	
Recurrence						
No recurrence	70	83	68	46	38	305
Recurrent stroke, n (%)*	4 (5.3)	8 (7.3)	16 (17.2)	7 (12.5)	5 (11.1)	40 (10.5)
Recurrence time						
<3 months	0	0	1	0	0	1
3-6 months	0	1	1	1	1	4
7-12 months†	2	2	5	1	0	10
1-2 years	2	3	8	5	4	22
2-3 years	0	2	1	0	0	3
Long-term outcome						
BI, mean ± SD	77 ± 18	76 ± 9	64 ± 19	88 ± 15	85 ± 13	76 ± 16
mRS score, mean ± SD	2 ± 1	2 ± 1	3 ± 1	1 ± 1	1 ± 1	2 ± 2
Without disability, n‡	20	28	26	21	16	111 (29.2)
Mild disability, n§	20	24	20	13	8	85 (22.3)
Moderate disability, n¶	5	10	10	6	3	39 (8.9)
Severe disability, n‖	3	2	5	0	1	11 (2.9)
Death, n (%)**	6 (8.0)	8 (7.3)	15 (16.1)	0	2 (4.4)	31 (8.1)
Lost to follow-up, n	2	19	9	3	2	35 (9.2)

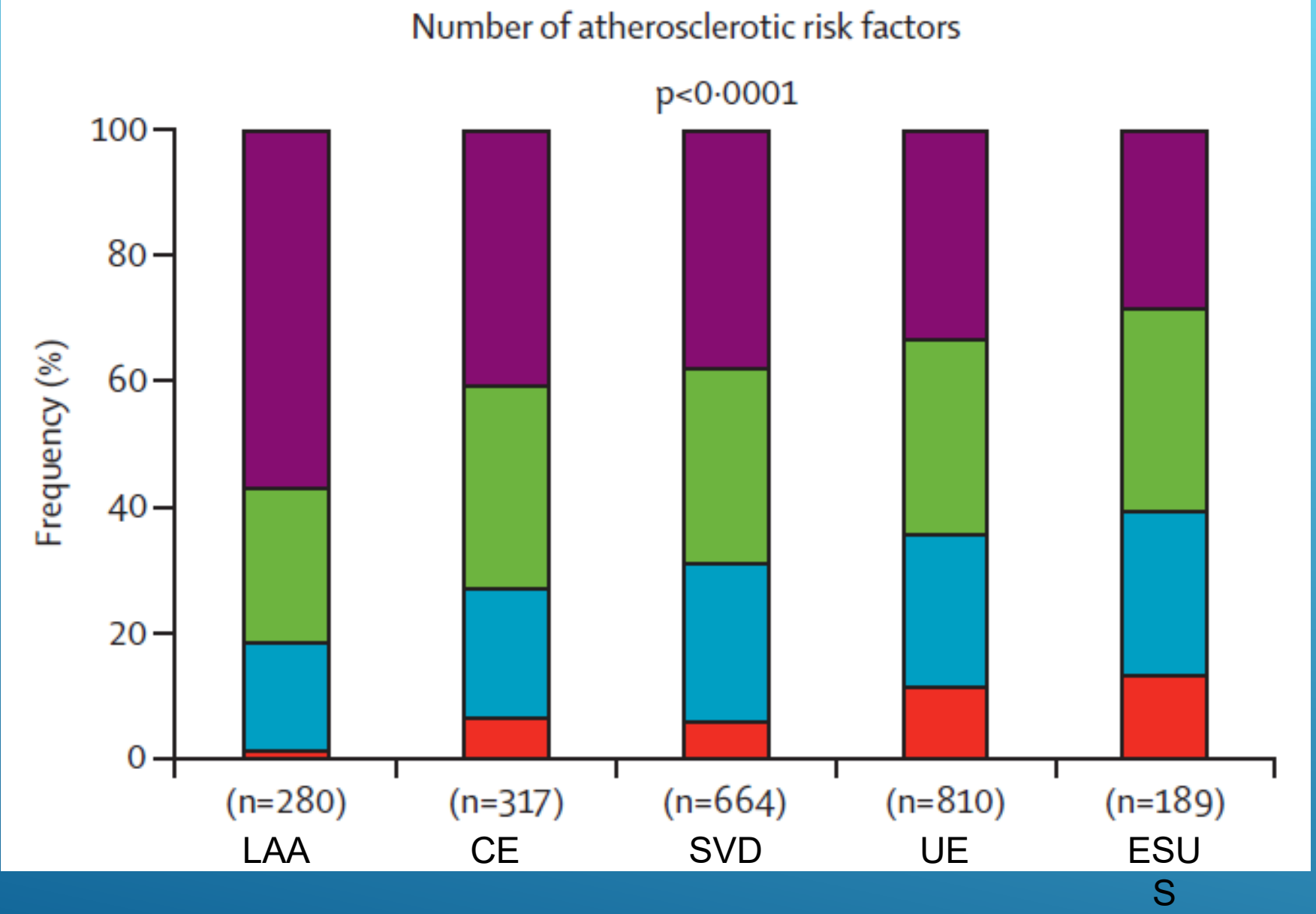
PROGNOSIS OF CRYPTOGENIC STROKE

J Stroke Cerebrovasc Dis 2012;21: 621-628

	Cryptogenic (n=812)	Cardioembolic (n=668)	Large artery disease (n=280)	Small vessel disease (n=317)	Unknown cause (n=331)	More than one cause (n=90)	Other causes (n=57)	Total (n=2555)	p value*
Baseline characteristics									
Age (years)	70·4 (12·8)	77·9 (11·9)	73·3 (10·3)	69·7 (12·6)	81·2 (10·4)	77·2 (10·5)	56·7 (17·7)	73·9 (13·0)	<0·0001
Sex									
Male	402 (50%)	306 (46%)	172 (61%)	182 (57%)	112 (34%)	56 (62%)	32 (56%)	1262 (49%)	<0·0001
Female	410 (50%)	362 (54%)	108 (39%)	135 (43%)	219 (66%)	34 (38%)	25 (44%)	1293 (51%)	..
Hypertension	432 (53%)	477 (71%)	208 (74%)	188 (59%)	203 (61%)	66 (73%)	26 (46%)	1600 (63%)	<0·0001
Diabetes	99 (12%)	81 (12%)	52 (19%)	51 (16%)	55 (17%)	17 (19%)	2 (4%)	357 (14%)	0·004
Myocardial infarction	67 (8%)	117 (18%)	39 (14%)	16 (5%)	34 (10%)	18 (20%)	5 (9%)	296 (12%)	<0·0001
Peripheral vascular disease†	31 (4%)	58 (9%)	40 (14%)	15 (5%)	27 (8%)	16 (18%)	3 (5%)	190 (7%)	<0·0001
Hypercholesterolaemia	265 (33%)	240 (36%)	137 (49%)	105 (33%)	100 (30%)	37 (41%)	18 (32%)	902 (35%)	<0·0001
Smoking status									
Present‡	127 (16%)	45 (7%)	54 (19%)	77 (24%)	30 (9%)	17 (19%)	11 (19%)	361 (14%)	<0·0001
Past§	317 (39%)	302 (45%)	129 (46%)	120 (38%)	120 (37%)	42 (47%)	25 (44%)	1055 (41%)	0·02
Secondary prevention during follow-up									
On antiplatelets									
At 1 month¶	764/809 (94%)	331/555 (60%)	258/273 (95%)	306/317 (97%)	196/244 (80%)	59/86 (69%)	47/55 (86%)	1961/2339 (84%)	<0·0001
At 1 year‖	711/766 (93%)	186/435 (43%)	228/247 (92%)	290/310 (94%)	110/151 (73%)	38/76 (50%)	40/46 (87%)	1603/2031 (79%)	<0·0001
On anticoagulants									
At 1 month¶	9/809 (1%)	221/555 (40%)	12/273 (4%)	2/317 (1%)	19/244 (8%)	27/86 (31%)	8/55 (15%)	298/2339 (13%)	<0·0001
At 1 year‖	11/766 (1%)	239/435 (55%)	11/247 (4%)	2/310 (1%)	2/151 (1%)	36/76 (47%)	4/46 (9%)	305/2031 (15%)	<0·0001
On a statin									
At 1 month¶	650/809 (80%)	379/555 (68%)	232/273 (85%)	266/317 (84%)	132/244 (54%)	65/86 (76%)	31/55 (56%)	1755/2339 (75%)	<0·0001
At 1 year‖	627/766 (82%)	315/435 (72%)	221/247 (89%)	256/310 (83%)	80/151 (53%)	61/76 (80%)	29/46 (63%)	1589/2031 (78%)	<0·0001
On one or more antihypertensives									
At 1 month¶	590/809 (73%)	445/555 (80%)	224/273 (82%)	258/317 (81%)	150/244 (61%)	72/86 (84%)	32/55 (58%)	1771/2339 (76%)	<0·0001
At 1 year‖	574/766 (75%)	358/435 (82%)	213/247 (86%)	246/310 (79%)	89/151 (59%)	65/76 (86%)	27/46 (59%)	1572/2031 (77%)	<0·0001

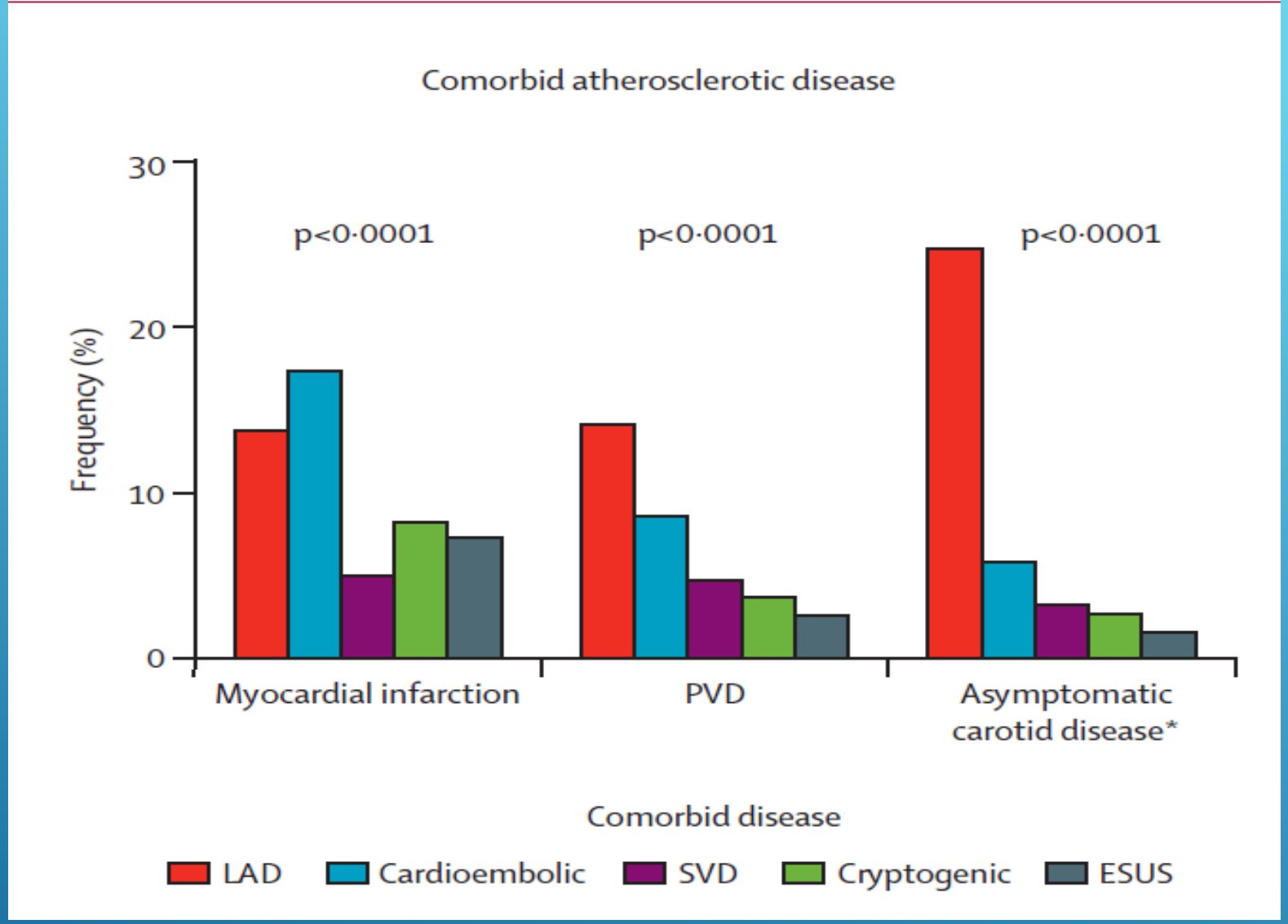
OXVASC: SUBTYPES OF IS

Lancet Neurol 2015; 14: 903–13



OXVASC: N. OF RISK FACTORS

Lancet Neurol 2015; 14: 903–13

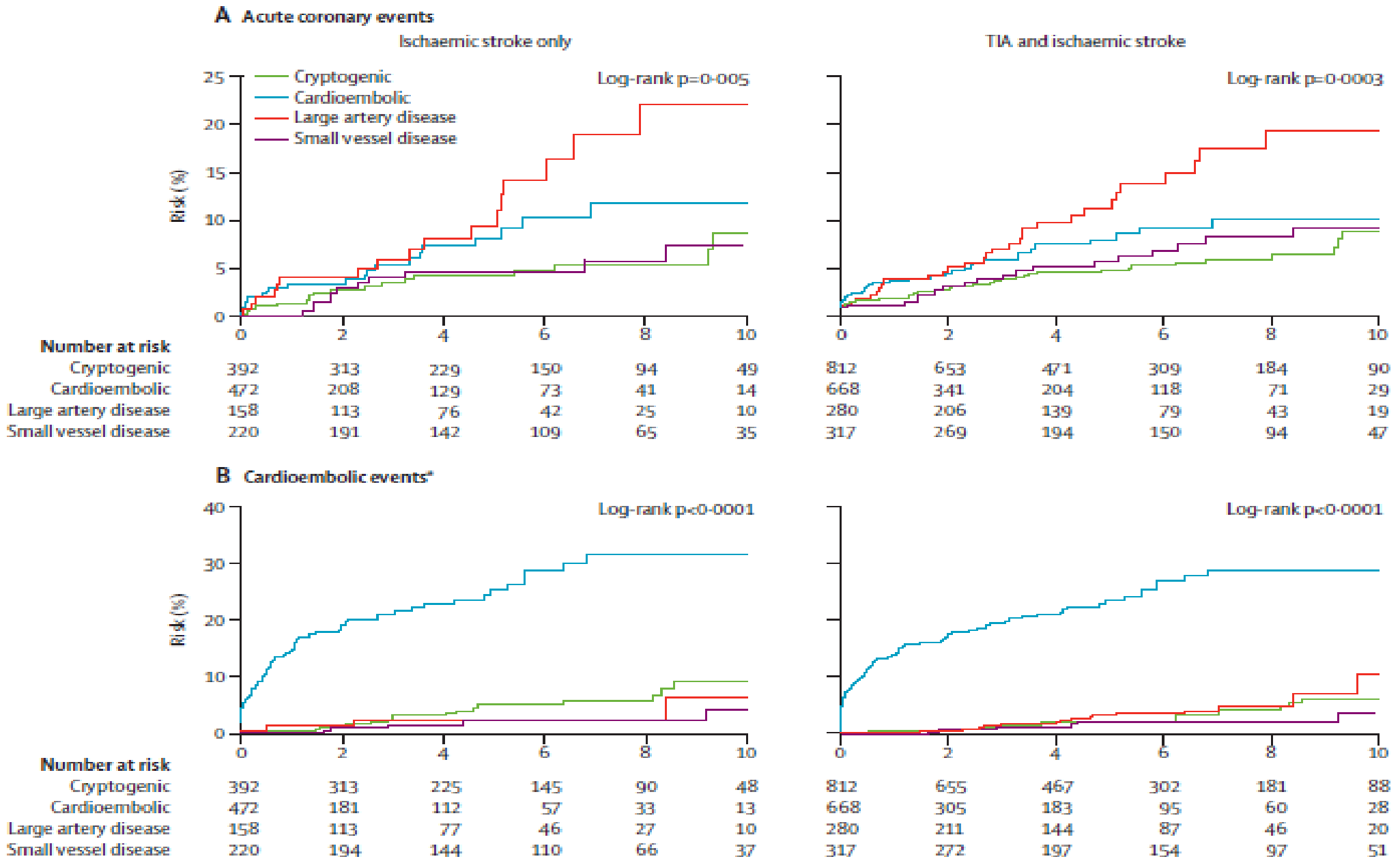


OXVASC: COMORBIDITY

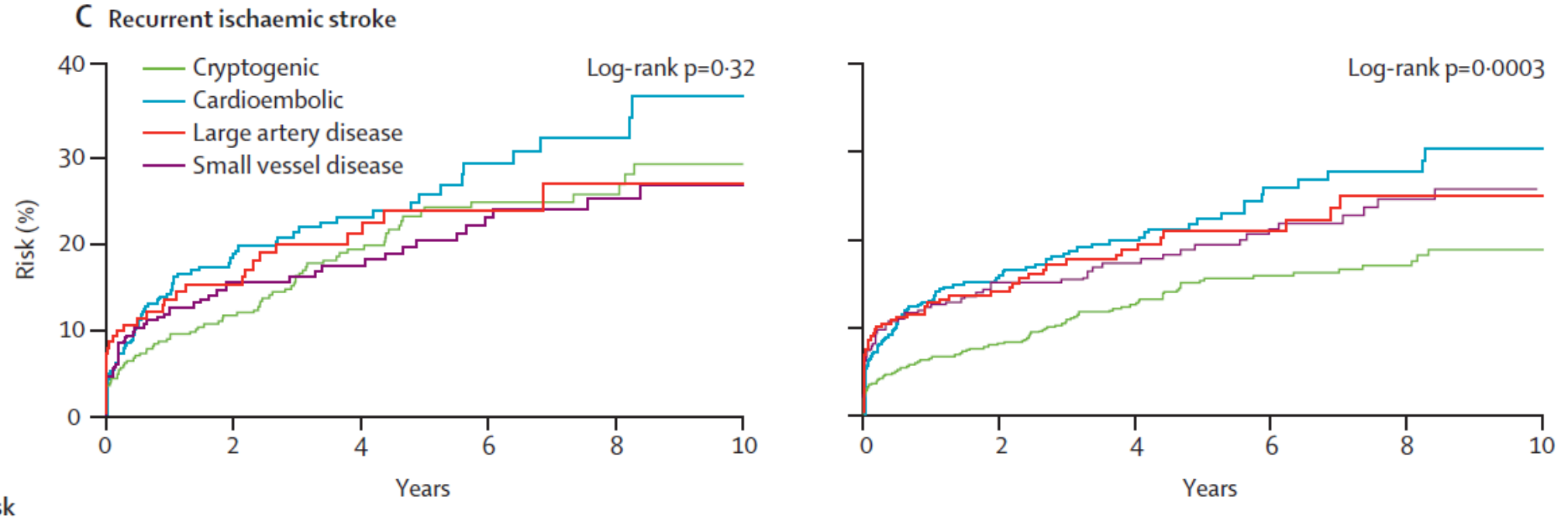
	Cryptogenic (n=392)		Small vessel disease (n=220)		Large artery disease (n=158)		Cardioembolic (n=472)		p value
	Number	% (95% CI)*	Number	% (95% CI)*	Number	% (95% CI)*	Number	% (95% CI)*	
Disability (mRS >2)									
Premorbid†	58	15%‡	18	8%‡	17	11%‡	146	32%‡	p<0·0001§
6 months¶	89	23%‡	50	23%‡	51	32%‡	305	66%‡	p<0·0001§
Mortality									
1 year	23	6·0% (3·6–8·4)	2	0·9% (0·0–2·1)	23	14·7% (9·2–20·2)	196	41·7% (37·2–46·2)	p<0·0001
5 years	80	24·9% (20·0–29·8)	37	19·8% (13·9–25·7)	42	30·9% (22·9–38·9)	280	64·6% (59·9–69·3)	p<0·0001
10 years	114	45·5% (38·4–52·6)	64	44·9% (35·9–53·9)	56	54·9% (42·6–67·2)	317	83·3% (78·2–88·4)	p<0·0001
Vascular death									
1 year	11	2·8% (1·2–4·4)	2	0·9% (0·0–2·1)	12	7·8% (3·5–12·1)	155	34·0% (29·7–38·3)	p<0·0001
5 years	32	10·0% (6·7–13·3)	12	6·4% (2·9–9·9)	14	9·9% (4·8–15·0)	183	43·5% (38·6–48·4)	p<0·0001
10 years	39	15·4% (10·3–20·5)	17	12·2% (6·1–18·3)	18	21·7% (8·6–34·8)	195	53·4% (46·5–60·3)	p<0·0001
Any recurrent stroke									
1 year	35	9·1% (6·2–12·0)	27	12·3% (8·0–16·6)	21	14·0% (8·5–19·5)	54	15·1% (11·4–18·8)	0·11
5 years	76	24·0% (19·1–28·9)	41	20·5% (14·8–26·2)	31	24·1% (16·3–31·9)	79	27·8% (21·9–33·7)	0·25
10 years	85	31·9% (25·2–38·6)	47	26·9% (19·5–34·3)	32	26·9% (17·7–36·1)	87	40·0% (30·6–49·4)	0·13
Any recurrent ischaemic stroke									
1 year	34	8·8% (6·1–11·5)	27	12·3% (8·0–16·6)	20	13·4% (7·9–18·9)	50	14·0% (10·3–17·7)	0·19
5 years	73	23·2% (18·3–28·1)	40	20·0% (14·3–25·7)	30	23·4% (15·8–31·0)	72	25·3% (19·6–31·0)	0·49
10 years	79	28·6% (22·3–34·9)	46	26·4% (19·1–33·7)	31	26·2% (17·0–35·4)	79	36·3% (26·9–45·7)	0·32
Any acute coronary syndrome									
1 year	5	1·3% (0·1–2·5)	0	..	6	4·1% (1·0–7·2)	12	3·3% (1·3–5·3)	0·008
5 years	14	4·2% (2·0–6·4)	9	4·6% (1·7–7·5)	11	9·5% (4·0–15·0)	20	8·2% (4·5–11·9)	0·10
10 years	18	8·7% (3·6–13·8)	11	7·3% (2·6–12·0)	17	22·2% (11·2–33·2)	23	11·8% (6·3–17·3)	0·005
Any recurrent cardioembolic event									
1 year	2	0·5% (0·0–1·3)	0	..	2	1·3% (0·0–3·1)	53	14·5% (10·8–18·2)	p<0·0001
5 years	14	5·1% (2·4–7·8)	4	2·3% (0·0–4·7)	3	2·2% (0·0–4·7)	74	25·0% (19·5–30·5)	p<0·0001
10 years	18	9·2% (4·3–14·1)	5	4·3% (0·0–8·8)	4	6·3% (0·0–14·5)	79	31·3% (23·9–38·7)	p<0·0001

Lancet Neurol 2015; 14: 903–13

OXVASC: OUTCOME AND LT PROGNOSIS



OXVASC: LONG-TERM PROGNOSIS



Number at risk												
Cryptogenic	392	283	193	118	71	35	812	608	423	267	154	71
Cardioembolic	472	181	110	55	33	12	668	307	182	94	60	27
Large artery disease	158	98	64	35	20	7	280	184	123	74	37	15
Small vessel disease	220	168	121	90	51	27	317	232	164	126	72	35

OXVASC: LONG-TERM PROGNOSIS

PROGNOSIS OF ESUS

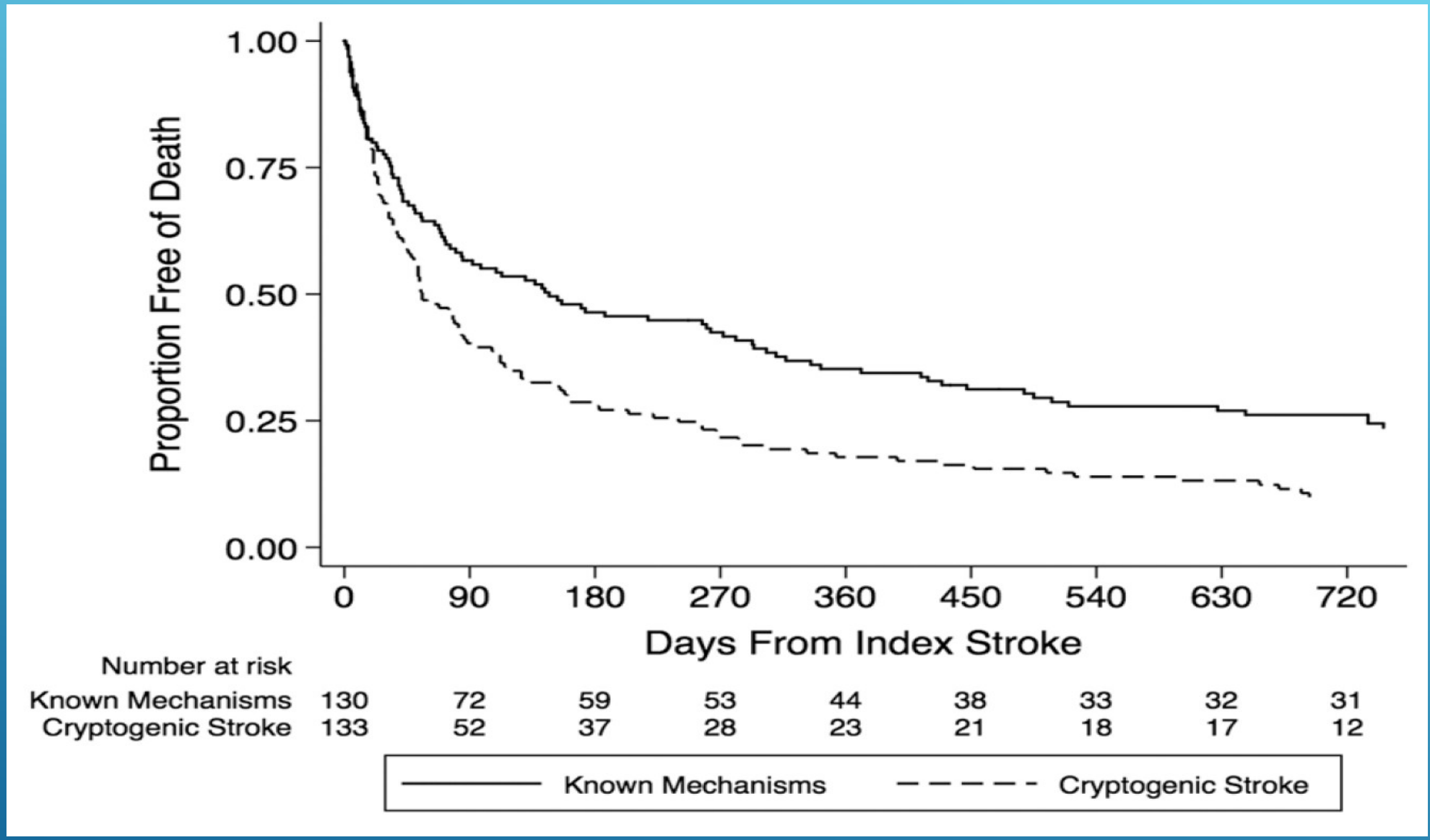
- Athen's retrospective registry: 2731 pts with first IS between 1992 and 2011; 31 months mean fup; 10% were ESUS
- Cumulative probability of stroke recurrence in ESUS was similar to cardioembolic strokes (29% vs. 27%) but higher than in LAA (13%) and lacunar strokes (13%)
- Higher percentage of ESUS pts with a favorable functional outcome (mRS ≤2): 62.5% vs 32.2% in CE

F1000Research 2016, **5**(F1000 Faculty Rev):168

STROKE RECURRENCE AND PFO

- Rate of recurrence in cryptogenic stroke varies widely because of different diagnostic criteria, non-standardised antithrombotic treatment, and prognostic factors (particularly age), but in average is 3–6% per year
- Young patients (mean age mid-40s) with PFO have a recurrence rates of 1–2% per year when given aspirin; but a rate substantially higher in older pts (14% per year)

Lancet Neurol 2014; 13: 429–38



Stroke 2014; 45: 2292–2297

PROGNOSIS OF PTS WITH STROKE AND CANCER

	CE	AAE	LAC	CRYP	PAR	*P* value
Discharge NIHSS (mean)	11.12 (±12.26)	7.49 (±9.63)	4.16 (±3.55)	7.33 (±11.59)	3.67 (±4.90)	.007
Mean difference in discharge NIHSS	0.57	1.96	1.6	2.45	3.22	.516
Discharge Rankin (% poor)	53	48	35	36	17	.011
Disposition (% bad)	37	23	8	28	0	.000
Length of stay (d)	6.69 (±3.77)	7.3 (±4.69)	5.88 (±4.35)	4.76 (±2.76)	5.5 (±1.79)	.011
Mean infarct volume (cm^3)	46.86 (±81.53)	43.62 (±81.68)	1.27 (±.86)	22.42 (±44.40)	16.75 (±19.47)	.007
Respiratory failure (%)	24	16	2	21	11	.012
Pneumonia (%)	8	8	4	5	0	.634
Angioedema (%)	3	7	0	6	0	.259
Use of pressor (%)	3	6	4	3	0	.651
Symptomatic hemorrhagic transformation (%)	9	3	4	10	0	.19
Decompressive hemicraniectomy (%)	3	3	2	3	0	.96

OUTCOME OF THROMBOLYSIS

J Stroke Cerebrovasc Dis 2013;22:e492-e499

Parameter	B	SE	*t*	Significance	95% confidence interval		Partial eta squared
					Lower bound	Upper bound	
Intercept	−.549	.209	−2.626	.009	−.961	−.136	.039
Coronary artery disease	.027	.060	.448	.655	−.092	.146	.001
Congestive heart failure	.150	.071	2.112	.036	.010	.290	.026
Log of admission NIHSS	.651	.100	6.515	.000	.454	.848	.201
Age	.006	.002	2.333	.021	.001	.011	.031
Diabetes history	−.015	.057	−.256	.798	−.127	.098	.000
Smoking history	.093	.064	1.457	.147	−.033	.218	.012
Statin use	−.044	.061	−.713	.477	−.165	.077	.003
Log of infarct volume	.201	.036	5.580	.000	.130	.272	.156
Obesity	−.017	.057	−.303	.762	−.129	.095	.001
CE mechanism	.032	.101	.321	.749	−.166	.231	.001
AAE mechanism	.056	.106	.530	.597	−.153	.265	.002
LAC mechanism	.300	.114	2.619	.010	.074	.526	.039
PAR mechanism	.008	.146	.057	.955	−.281	.297	.000
CRYP mechanism	0*	—	—	—	—	—	—

OUTCOME OF THROMBOLYSIS

J Stroke Cerebrovasc Dis 2013;22:e492-

CONCLUSIONI

- Prognosi in linea con quella dell’ictus in generale, tendenzialmente buona
- Peggiore negli ESUS e migliore nel PFO
- Variabile in funzione della definizione e dell’età dei pazienti
- Dipende dai fattori di rischio coesistenti