carotid hyperperfusion syndrome

A. Ross Naylor MD, FRCS

Professor of Vascular Surgery

Leicester Vascular Institute

Leicester UK

arnaylor@hotmail.com

I have no disclosures relating to this talk

hyperperfusion syndrome (HS)

constellation of symptoms including; headache, seizures, impaired consciousness, neurological deficit secondary to either ischaemia or intracranial haemorrhage

uncontrolled surges in blood flow after CEA/CAS, but complex relationship with post-CEA hypertension

meta-analysis: 3.4% after CEA *vs* 2.2% after CAS (OR 1.43 (95%CI 1.01-1901), p=0.015), *Galyfos J Neurol Sci 2017*

risk factors: bilateral severe ICA disease, impaired autoregulation, poorly controlled BP, impaired cerebral vascular reserve, poor collateralization via circle of Willis

clinical symptoms

REVIEW

EJVES 2011;41:229

Hypertension and the Post-carotid Endarterectomy Cerebral Hyperperfusion Syndrome CME

S. Bouri, A. Thapar, J. Shalhoub, G. Jayasooriya, A. Fernando, I.J. Franklin, A.H. Davies *

	Hyperperfusion Syndrome (n=42)	Intracranial Haemorrhage (n=36)
seizures	36%	31%
hemiparesis	31%	31%
both	33%	31%

onset of symptoms

REVIEW

EJVES 2011;41:229

Hypertension and the Post-carotid Endarterectomy Cerebral Hyperperfusion Syndrome CME

S. Bouri, A. Thapar, J. Shalhoub, G. Jayasooriya, A. Fernando, I.J. Franklin, A.H. Davies *

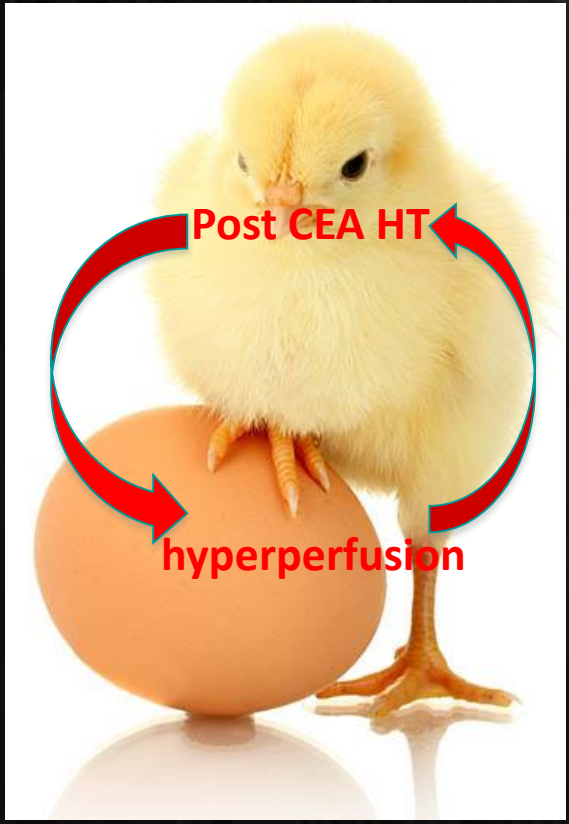
median delay = 5 days (IQR 3-6)
92% had onset of HS symptoms within 1 week
earliest presentation = 17 hours
latest presentation = 28 days

REVIEW

EJVES 2011;41:229

Hypertension and the Post-carotid Endarterectomy Cerebral Hyperperfusion Syndrome CME

S. Bouri, A. Thapar, J. Shalhoub, G. Jayasooriya, A. Fernando, I.J. Franklin, A.H. Davies *



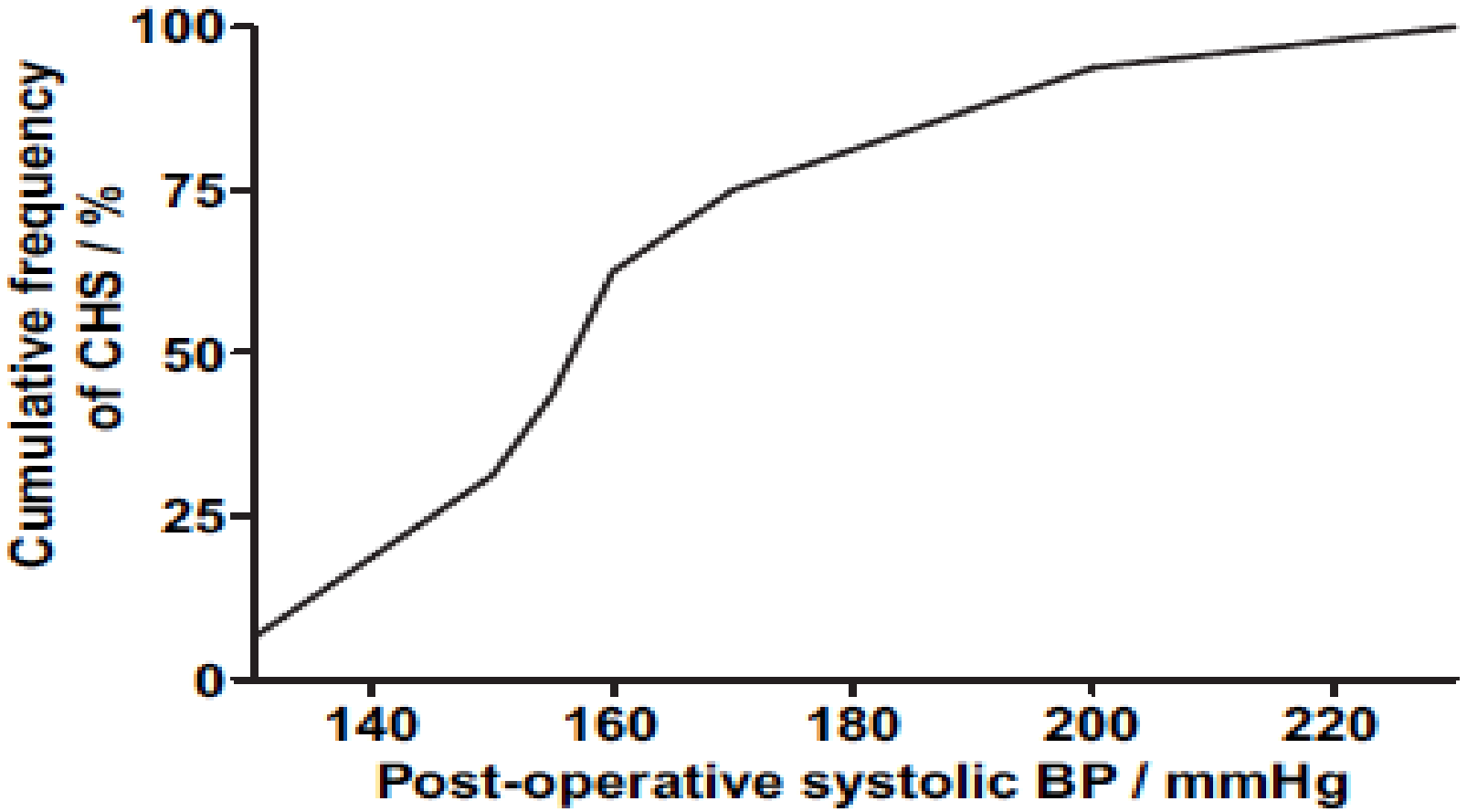
81% of HS/ICH patients had severe HT 'at onset' of symptoms *Bouri EJVES 2011*

BUT some are normotensive *Naylor EJVES 2003*

rapid treatment of post-CEA HT can reverse headache/seizures and prevent progression on to HS stroke or ICH *Naylor EJVES 2013*

HS and post-CEA hypertension

meta-analysis



Bouri EJVES 2011;41:229

factors associated with PEH?

significant association

Pre-op

undiagnosed / poorly controlled hypertension

baroreceptor dysfunction

Intra-op

severe hypertension on induction of anaesthesia

NOT Associated with PEH

Pre-op

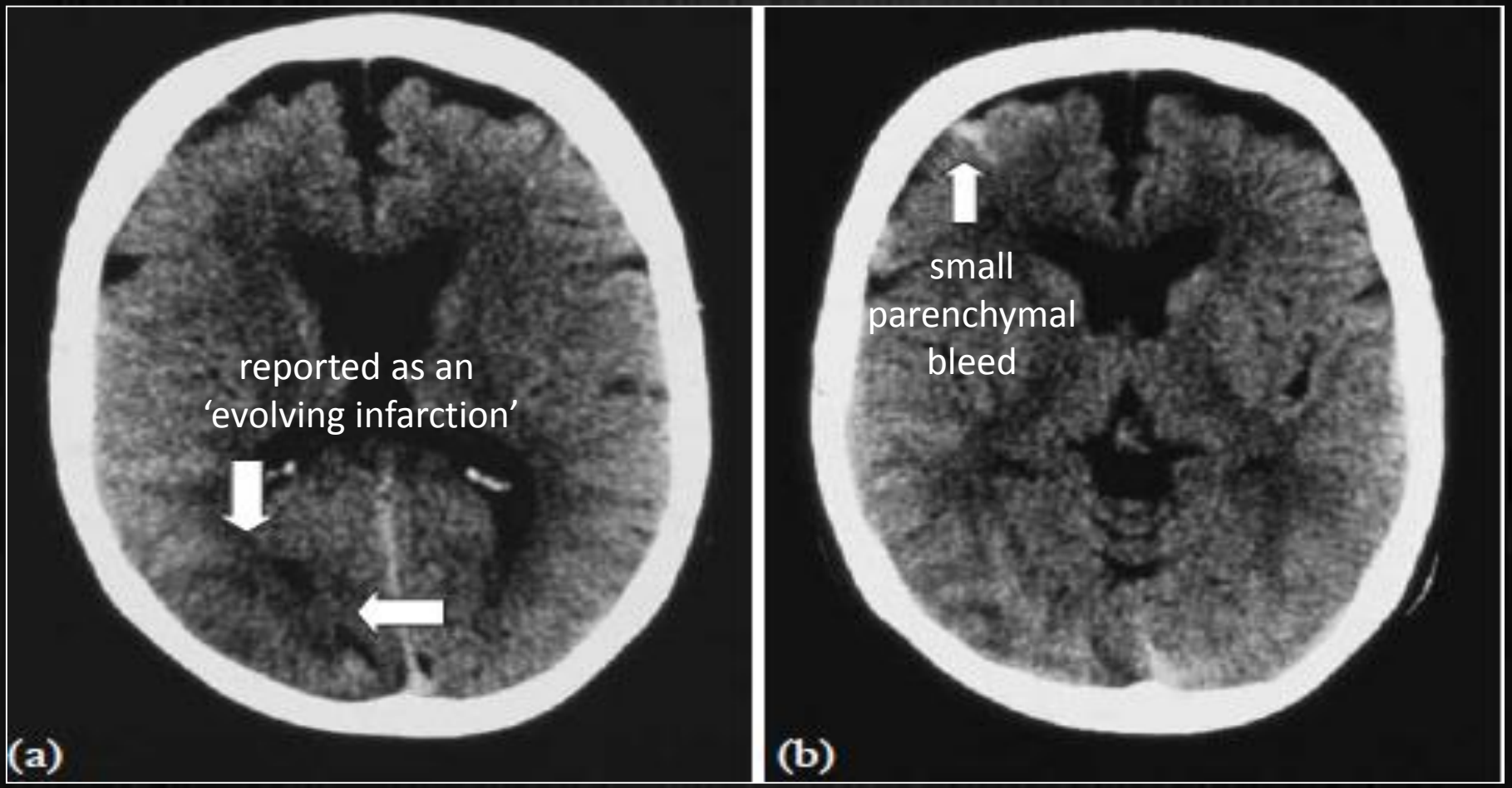
Impaired autoregulation
Presenting symptoms
Time since index event
Timing of surgery
Central aortic pressure
Degree of carotid stenosis
Diabetes Mellitus
antihypertensive
PVD
heart disease
smoking
NIHSS score
raised lipids
MCAV
class of

Intra-op

Induction agents
Vasoactive agents
post-clamp MCAV
intra-op BP

Newman EJVES 2017

beware of ‘evolving infarction’ diagnosis



Naylor EJVES 2003;26:39

anomalies

if this is mainly a high-flow phenomenon, how does an increase in CBF cause severe hypertension?

if autoregulation is defective pre-operatively, why do most CEA patients have a surge in MCAV after clamp release, which then declines over the next 10 minutes, suggesting that autoregulation is intact?

if this is purely a high flow phenomenon with abnormal auto-regulation, why are there not consistently large increases in MCAV at restoration of flow or at 3 hours post clamp release in patients destined to develop HS?

anomalies

if this is a high-flow pathology, why have studies found no CBF increase when some patients became symptomatic?

how does HS/HE account for patchy white matter oedema where CBF is either normal or increased?

if cerebral oedema is such an important factor in triggering onset of seizures, why do some patients exhibit this abnormality predominantly in the posterior (rather than in the carotid) circulation?

possible pathopysiology

extravasation of protein and vasogenic oedema consistent with breakthrough of the autoregulation mechanism, rather than being secondary to true ischaemia

absent autoregulation, fuelled by worsening hypertension, increases CBF; aggravating microcirculatory changes with increasing breakdown of blood brain barrier

impairment of endothelial permeability, activation of coagulation cascade and inhibition of endogenous fibrinolysis, leading to either intravascular thrombosis (ischaemic stroke) or intracerebral haemorrhage

can ‘high-risk’ patients for HS be predicted?

YES

Prediction of Cerebral Hyperperfusion after Carotid Endarterectomy with Transcranial Doppler

C.W.A. Pennekamp [a], S.C. Tromp [b], R.G.A. Ackerstaff [b], M.L. Bots [c], R.V. Immink [d], W. Spiering [e], J.P.P.M. de Vries [f], L.J. Kappelle [g], F.L. Moll [a], W.F. Buhre [d], G.J. de Borst [a,*]

NO

Changes in Middle Cerebral Artery Velocity after Carotid Endarterectomy do not Identify Patients at High-risk of Suffering Intracranial Haemorrhage or Stroke due to Hyperperfusion Syndrome

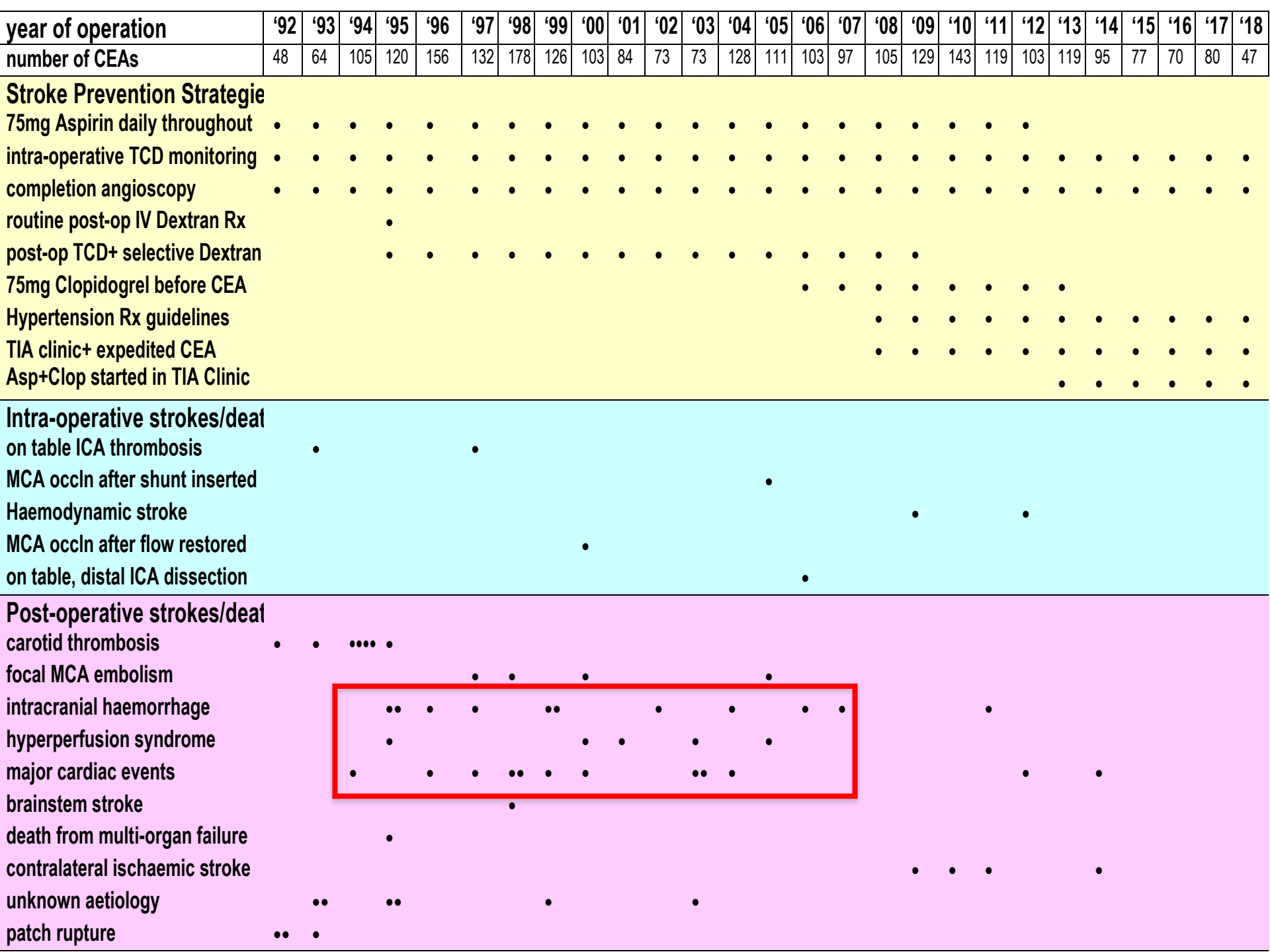
J.E. Newman [a,*], M. Ali [a], R. Sharpe [b], M.J. Bown [a], R.D. Sayers [a], A.R. Naylor [a]

can HS stroke/ICH be prevented?

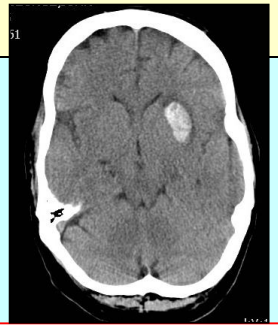
measuring MCAV changes with flow restoration ineffective

vast majority of HS/ICH patients have post-CEA hypertension

“needs of the many outweigh the needs of the few”!

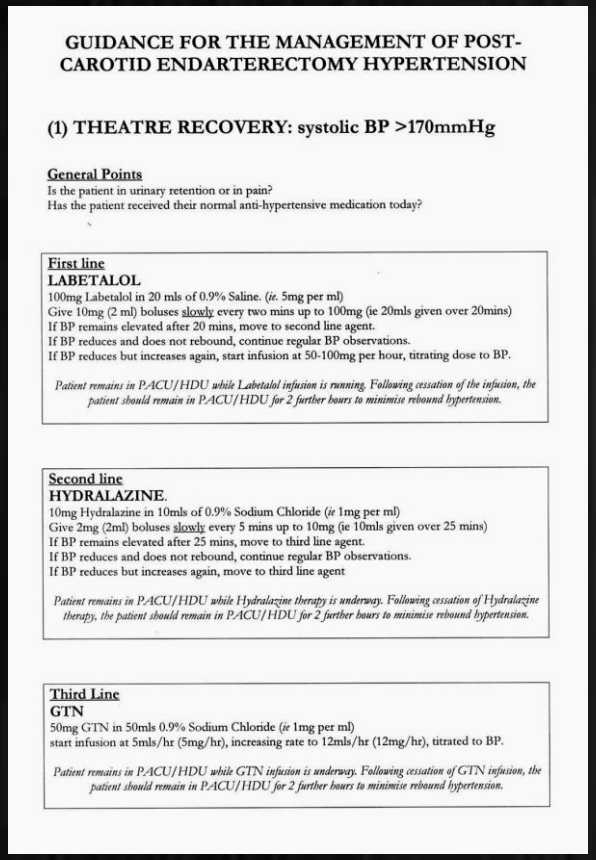

year of operation
'92 '93 '94 '95 '96 '97 '98 '99 '00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13 '14 '15 '16 '17 '18
number of CEAs
48 64 105 120 156 132 178 126 103 84 73 73 128 111 103 97 105 129 143 119 103 119 95 77 70 80 47
Stroke Prevention Strategie
75mg Aspirin daily throughout
intra-operative TCD monitoring
completion angioscopy
routine post-op IV Dextran Rx
post-op TCD+ selective Dextran
75mg Clopidogrel before CEA
Hypertension Rx guidelines
TIA clinic+ expedited CEA
Asp+Clop started in TIA Clinic
Intra-operative strokes/deat
on table ICA thrombosis
MCA occln after shunt inserted
Haemodynamic stroke
MCA occln after flow restored
on table, distal ICA dissection
Post-operative strokes/deat
carotid thrombosis
focal MCA embolism
intracranial haemorrhage
hyperperfusion syndrome
major cardiac events
brainstem stroke
death from multi-organ failure
contralateral ischaemic stroke
unknown aetiology
patch rupture

year of operation	'92	'93	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17	'18
number of CEAs	48	64	105	120	156	132	178	126	103	84	73	73	128	111	103	97	105	129	143	119	103	119	95	77	70	80	47
Stroke Prevention Strategie																											
75mg Aspirin daily throughout	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•						
intra-operative TCD monitoring	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
completion angioscopy	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
routine post-op IV Dextran Rx				•																							
post-op TCD+ selective Dextran				•	•	•	•	•	•	•	•	•	•	•	•	•	•	•									
75mg Clopidogrel before CEA															•	•	•	•	•	•	•	•					
Hypertension Rx guidelines																	•	•	•	•	•	•	•	•	•	•	•
TIA clinic+ expedited CEA																	•	•	•	•	•	•	•	•	•	•	•
Asp+Clop started in TIA Clinic																						•	•	•	•	•	•
Intra-operative strokes/deat																											
on table ICA thrombosis		•				•																					
MCA occln after shunt inserted																											
Haemodynamic stroke																		•			•						
MCA occln after flow restored									•																		
on table, distal ICA dissection																											
Post-operative strokes/deat																											
carotid thrombosis	•	•	••••	•																							
focal MCA embolism						•	•		•					•													
intracranial haemorrhage				••	•	•		••				•			•	•				•							
hyperperfusion syndrome				•					•	•		•		•													
major cardiac events			•		•	•	••	•	•			••	•								•		•				
brainstem stroke							•																				
death from multi-organ failure				•																							
contralateral ischaemic stroke																		•	•	•			•				
unknown aetiology		••		••				•				•															
patch rupture	••	•																									



severe hypertension
at 4am: 18hrs after CEA

Guidelines for treating post-CEA hypertension



GUIDANCE FOR THE MANAGEMENT OF POST-CAROTID ENDARTERECTOMY HYPERTENSION

(1) THEATRE RECOVERY: systolic BP >170mmHg

General Points
Is the patient in urinary retention or in pain?
Has the patient received their normal anti-hypertensive medication today?

First line
LABETALOL
100mg Labetalol in 20 mls of 0.9% Saline. (*ie.* 5mg per ml)
Give 10mg (2 ml) boluses slowly every two mins up to 100mg (ie 20mls given over 20mins)
If BP remains elevated after 20 mins, move to second line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, start infusion at 50-100mg per hour, titrating dose to BP.

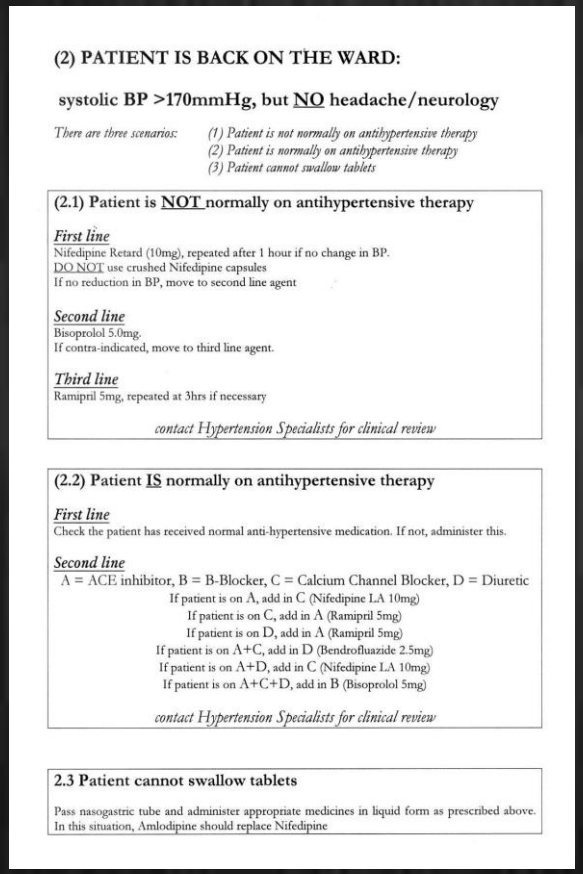
Patient remains in PACU/HDU while Labetalol infusion is running. Following cessation of the infusion, the patient should remain in PACU/HDU for 2 further hours to minimise rebound hypertension.

Second line
HYDRALAZINE.
10mg Hydralazine in 10mls of 0.9% Sodium Chloride (*ie* 1mg per ml)
Give 2mg (2ml) boluses slowly every 5 mins up to 10mg (ie 10mls given over 25 mins)
If BP remains elevated after 25 mins, move to third line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, move to third line agent

Patient remains in PACU/HDU while Hydralazine therapy is underway. Following cessation of Hydralazine therapy, the patient should remain in PACU/HDU for 2 further hours to minimise rebound hypertension.

Third Line
GTN
50mg GTN in 50mls 0.9% Sodium Chloride (*ie* 1mg per ml)
start infusion at 5mls/hr (5mg/hr), increasing rate to 12mls/hr (12mg/hr), titrated to BP.

Patient remains in PACU/HDU while GTN infusion is underway. Following cessation of GTN infusion, the patient should remain in PACU/HDU for 2 further hours to minimise rebound hypertension.



(2) PATIENT IS BACK ON THE WARD:

systolic BP >170mmHg, but NO headache/neurology

There are three scenarios:
(1) Patient is not normally on antihypertensive therapy
(2) Patient is normally on antihypertensive therapy
(3) Patient cannot swallow tablets

(2.1) Patient is NOT normally on antihypertensive therapy

First line
Nifedipine Retard (10mg), repeated after 1 hour if no change in BP.
DO NOT use crushed Nifedipine capsules
If no reduction in BP, move to second line agent

Second line
Bisoprolol 5.0mg.
If contra-indicated, move to third line agent.

Third line
Ramipril 5mg, repeated at 3hrs if necessary

contact Hypertension Specialists for clinical review

(2.2) Patient IS normally on antihypertensive therapy

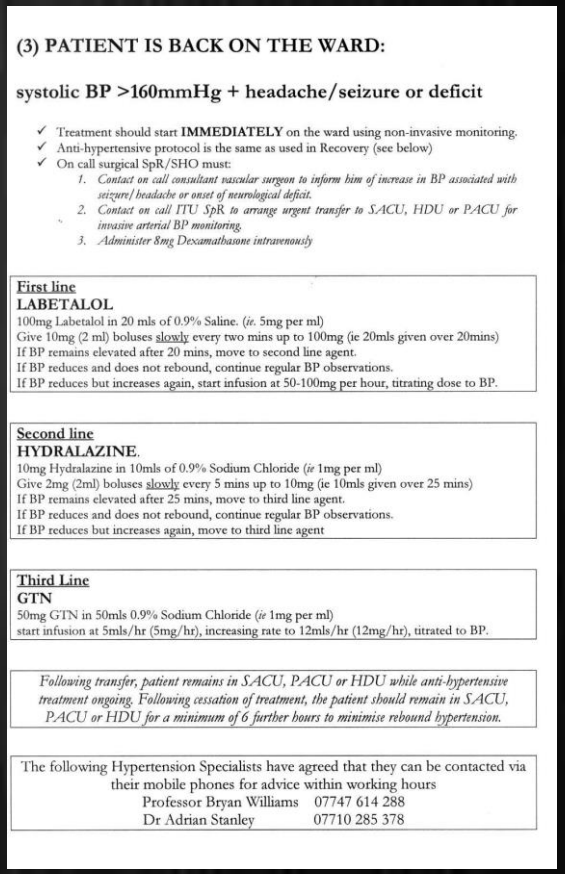
First line
Check the patient has received normal anti-hypertensive medication. If not, administer this.

Second line
A = ACE inhibitor, B = B-Blocker, C = Calcium Channel Blocker, D = Diuretic
If patient is on A, add in C (Nifedipine LA 10mg)
If patient is on C, add in A (Ramipril 5mg)
If patient is on D, add in A (Ramipril 5mg)
If patient is on A+C, add in D (Bendrofluazide 2.5mg)
If patient is on A+D, add in C (Nifedipine LA 10mg)
If patient is on A+C+D, add in B (Bisoprolol 5mg)

contact Hypertension Specialists for clinical review

2.3 Patient cannot swallow tablets

Pass nasogastric tube and administer appropriate medicines in liquid form as prescribed above.
In this situation, Amlodipine should replace Nifedipine



(3) PATIENT IS BACK ON THE WARD:

systolic BP >160mmHg + headache/seizure or deficit

- ✓ Treatment should start **IMMEDIATELY** on the ward using non-invasive monitoring.
- ✓ Anti-hypertensive protocol is the same as used in Recovery (see below)
- ✓ On call surgical SpR/SHO must:
  1. *Contact on call consultant vascular surgeon to inform him of increase in BP associated with seizure/ headache or onset of neurological deficit.*
  2. *Contact on call ITU SpR to arrange urgent transfer to SACU, HDU or PACU for invasive arterial BP monitoring.*
  3. *Administer 8mg Dexamathasone intravenously*

First line
LABETALOL
100mg Labetalol in 20 mls of 0.9% Saline. (*ie.* 5mg per ml)
Give 10mg (2 ml) boluses slowly every two mins up to 100mg (ie 20mls given over 20mins)
If BP remains elevated after 20 mins, move to second line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, start infusion at 50-100mg per hour, titrating dose to BP.

Second line
HYDRALAZINE.
10mg Hydralazine in 10mls of 0.9% Sodium Chloride (*ie* 1mg per ml)
Give 2mg (2ml) boluses slowly every 5 mins up to 10mg (ie 10mls given over 25 mins)
If BP remains elevated after 25 mins, move to third line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, move to third line agent

Third Line
GTN
50mg GTN in 50mls 0.9% Sodium Chloride (*ie* 1mg per ml)
start infusion at 5mls/hr (5mg/hr), increasing rate to 12mls/hr (12mg/hr), titrated to BP.

Following transfer, patient remains in SACU, PACU or HDU while anti-hypertensive treatment ongoing. Following cessation of treatment, the patient should remain in SACU, PACU or HDU for a minimum of 6 further hours to minimise rebound hypertension.

The following Hypertension Specialists have agreed that they can be contacted via their mobile phones for advice within working hours
Professor Bryan Williams 07747 614 288
Dr Adrian Stanley 07710 285 378

arnaylor@hotmail.com

GUIDANCE FOR THE MANAGEMENT OF POST-CAROTID ENDARTERECTOMY HYPERTENSION

(I) THEATRE RECOVERY: systolic BP >170mmHg

General Points
Is the patient in urinary retention or in pain?
Has the patient received their normal anti-hypertensive medication today?

First line
LABETALOL
100mg Labetalol in 20 mls of 0.9% Saline. (ie. 5mg per ml)
Give 10mg (2 ml) boluses slowly every two mins up to 100mg (ie 20mls given over 20mins)
If BP remains elevated after 20 mins, move to second line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, start infusion at 50-100mg per hour, titrating dose to BP.

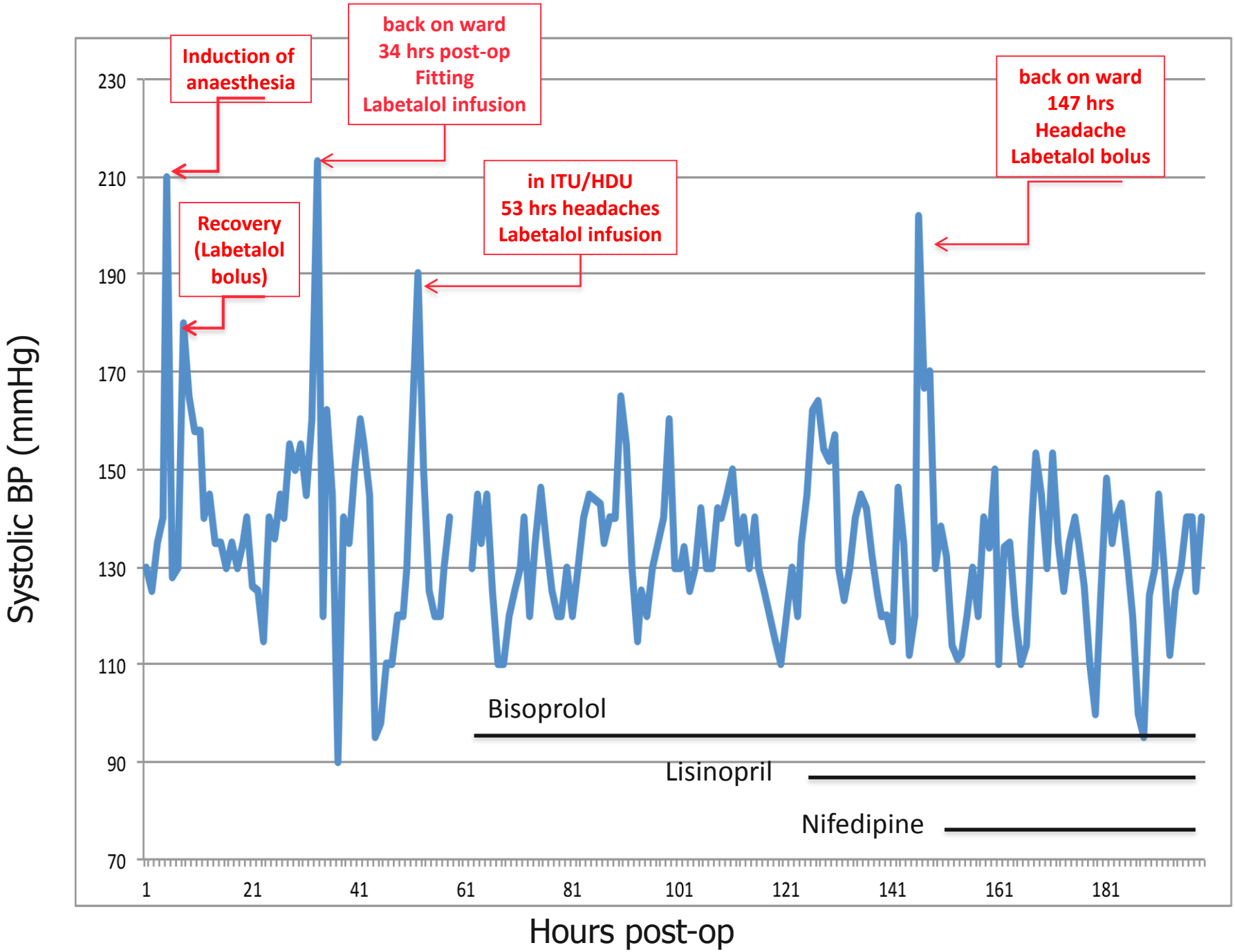
Patient remains in PACU/HDU while Labetalol infusion is running. Following cessation of the infusion, the patient should remain in PACU/HDU for 2 further hours to minimize rebound hypertension.

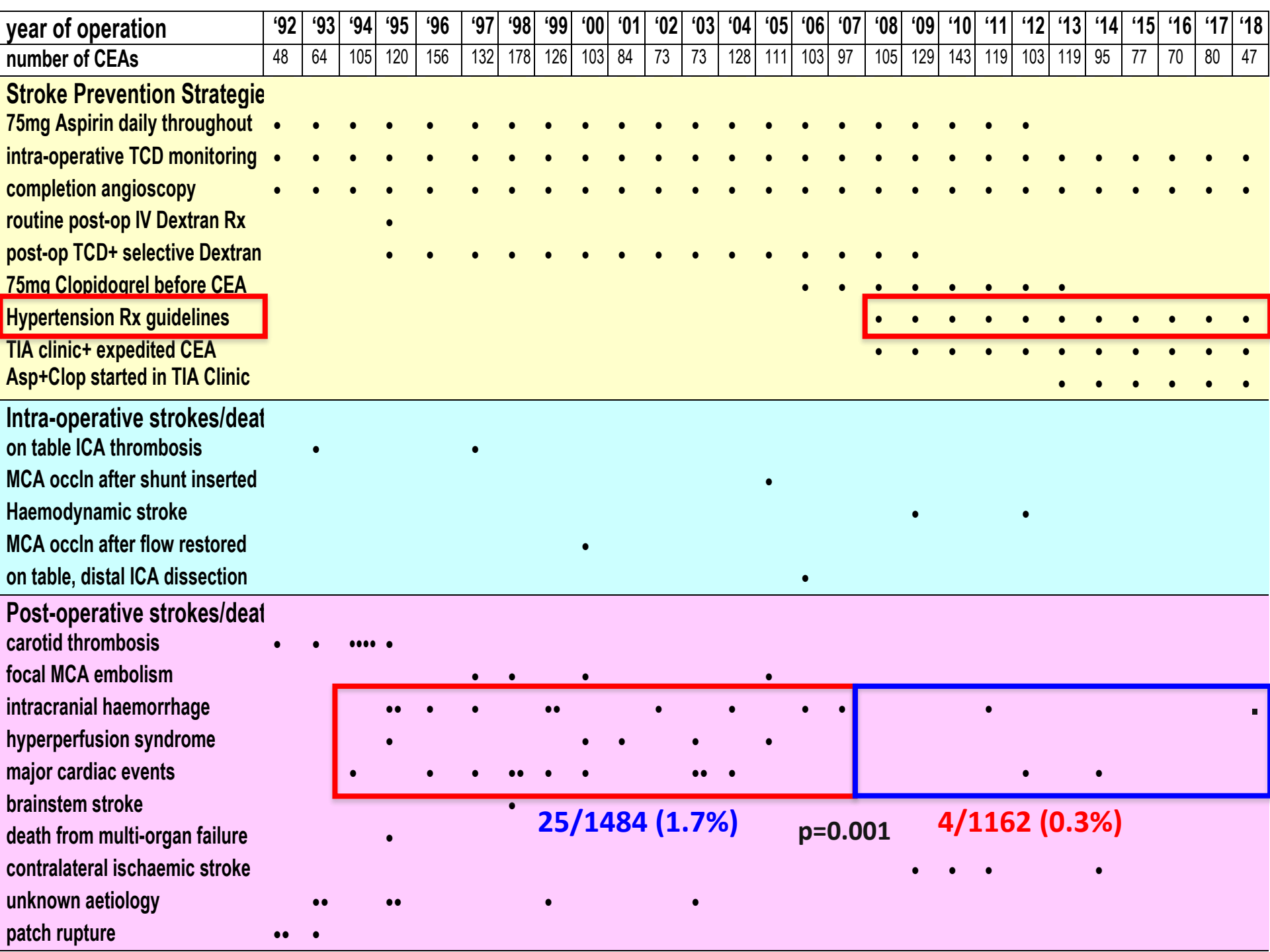
Second line
HYDRALAZINE
10mg Hydralazine in 10mls of 0.9% Sodium Chloride (ie 1mg per ml)
Give 2mg (2ml) boluses slowly every 5 mins up to 10mg (ie 10mls given over 25 mins)
If BP remains elevated after 25 mins, move to third line agent.
If BP reduces and does not rebound, continue regular BP observations.
If BP reduces but increases again, move to third line agent.

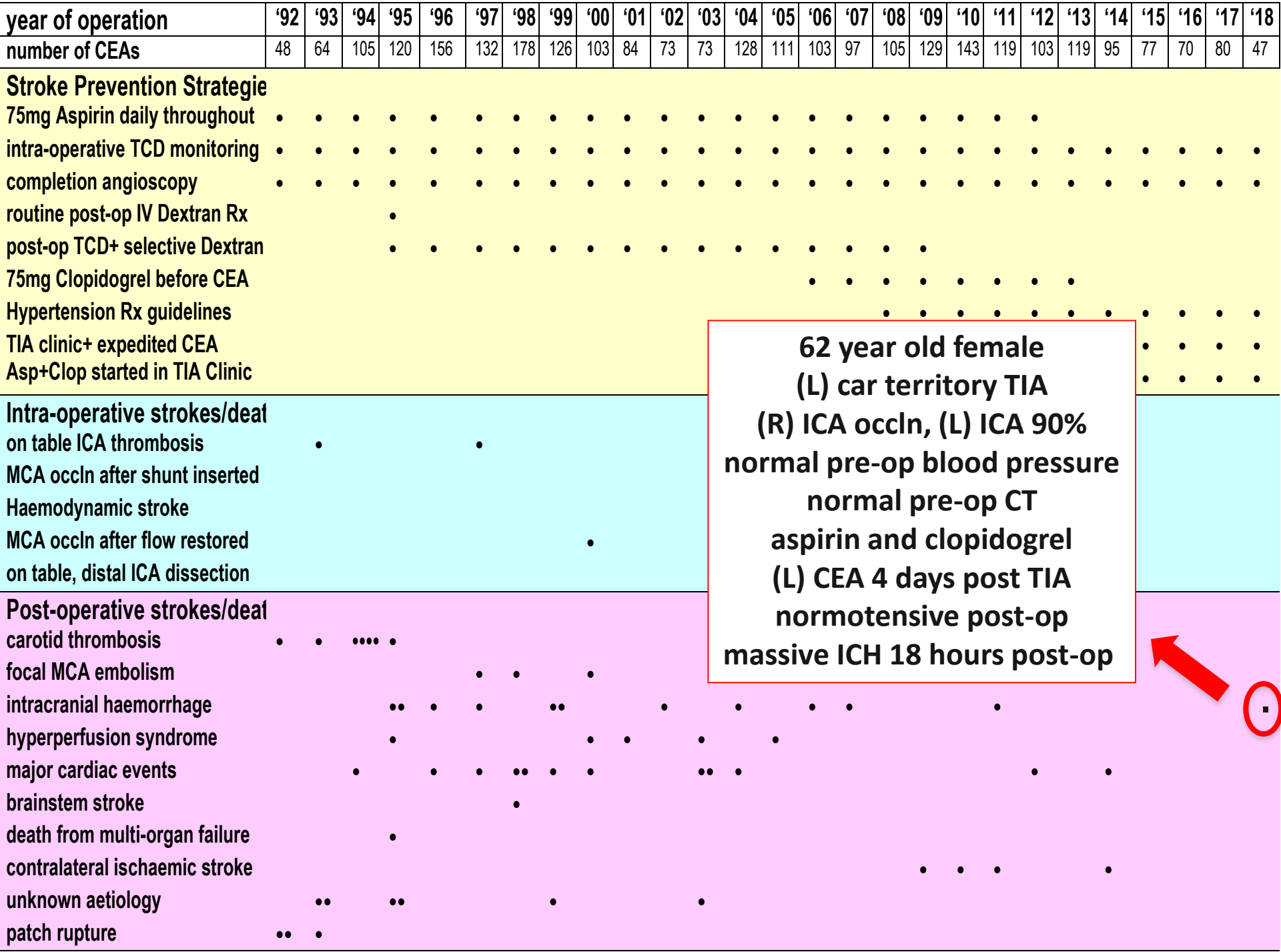
Patient remains in PACU/HDU while Hydralazine therapy is underway. Following cessation of Hydralazine therapy, the patient should remain in PACU/HDU for 2 further hours to minimize rebound hypertension.

Third Line
GTN
50mg GTN in 50mls 0.9% Sodium Chloride (ie 1mg per ml)
start infusion at 5mls/hr (5mg/hr), increasing rate to 12mls/hr (12mg/hr), titrated to BP.

Patient remains in PACU/HDU while GTN infusion is underway. Following cessation of GTN infusion, the patient should remain in PACU/HDU for 2 further hours to minimize rebound hypertension.


Induction of anaesthesia
back on ward 34 hrs post-op Fitting Labetalol infusion
back on ward 147 hrs Headache Labetalol bolus
in ITU/HDU 53 hrs headaches Labetalol infusion
Recovery (Labetalol bolus)
Systolic BP (mmHg)
230
210
190
170
150
130
110
90
70
Bisoprolol
Lisinopril
Nifedipine
1
21
41
61
81
101
121
141
161
181
Hours post-op


year of operation
'92 '93 '94 '95 '96 '97 '98 '99 '00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13 '14 '15 '16 '17 '18
number of CEAs
48 64 105 120 156 132 178 126 103 84 73 73 128 111 103 97 105 129 143 119 103 119 95 77 70 80 47
Stroke Prevention Strategie
75mg Aspirin daily throughout
intra-operative TCD monitoring
completion angioscopy
routine post-op IV Dextran Rx
post-op TCD+ selective Dextran
75mg Clopidogrel before CEA
Hypertension Rx guidelines
TIA clinic+ expedited CEA
Asp+Clop started in TIA Clinic
Intra-operative strokes/deat
on table ICA thrombosis
MCA occln after shunt inserted
Haemodynamic stroke
MCA occln after flow restored
on table, distal ICA dissection
Post-operative strokes/deat
carotid thrombosis
focal MCA embolism
intracranial haemorrhage
hyperperfusion syndrome
major cardiac events
brainstem stroke
death from multi-organ failure
contralateral ischaemic stroke
unknown aetiology
patch rupture
25/1484 (1.7%)
p=0.001
4/1162 (0.3%)


year of operation
'92 '93 '94 '95 '96 '97 '98 '99 '00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13 '14 '15 '16 '17 '18
number of CEAs
48 64 105 120 156 132 178 126 103 84 73 73 128 111 103 97 105 129 143 119 103 119 95 77 70 80 47
Stroke Prevention Strategie
75mg Aspirin daily throughout
intra-operative TCD monitoring
completion angioscopy
routine post-op IV Dextran Rx
post-op TCD+ selective Dextran
75mg Clopidogrel before CEA
Hypertension Rx guidelines
TIA clinic+ expedited CEA
Asp+Clop started in TIA Clinic
Intra-operative strokes/deat
on table ICA thrombosis
MCA occln after shunt inserted
Haemodynamic stroke
MCA occln after flow restored
on table, distal ICA dissection
Post-operative strokes/deat
carotid thrombosis
focal MCA embolism
intracranial haemorrhage
hyperperfusion syndrome
major cardiac events
brainstem stroke
death from multi-organ failure
contralateral ischaemic stroke
unknown aetiology
patch rupture
62 year old female
(L) car territory TIA
(R) ICA occln, (L) ICA 90%
normal pre-op blood pressure
normal pre-op CT
aspirin and clopidogrel
(L) CEA 4 days post TIA
normotensive post-op
massive ICH 18 hours post-op

Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS)

Writing Group [a], A.R. Naylor, J.-B. Ricco, G.J. de Borst, S. Debus, J. de Haro, A. Halliday, G. Hamilton, J. Kakisis, S. Kakkos, S. Lepidi, H.S. Markus, D.J. McCabe, J. Roy, H. Sillesen, J.C. van den Berg, F. Vermassen,
ESVS Guidelines Committee [b], P. Kolh, N. Chakfe, R.J. Hinchliffe, I. Koncar, J.S. Lindholt, M. Vega de Ceniga, F. Verzini,
ESVS Guideline Reviewers [c], J. Archie, S. Bellmunt, A. Chaudhuri, M. Koelemay, A.-K. Lindahl, F. Padberg, M. Venermo

Keywords: Carotid, Vertebral, Stroke, Transient ischaemic attack, Endarterectomy, Stenting, Medical therapy, Screening, Dementia, Asymptomatic, Symptomatic, Thrombolysis, Imaging, Bypass, Surgical techniques, Complications, Patch infection, Restenosis