Supplementary Information I – Search Strategy

The search strategy will be piloted initially, and if insufficient articles are returned will be revised and re-piloted. The search will be limited to studies in humans, but not by language. We will search the following databases: Medline, EMBASE, Web of Science, Cochrane database, PsycINFO. Reference lists of included articles will also be searched and we will use the Pubmed “related articles” feature to identify additional literature. Citation searching will be completed with tools such as Web of Science and Scopus. We will search grey literature databases and contact authors working in the field to identify any additional, unpublished data.

Population
Acute ischaemic stroke
Acute stroke
Stroke
AIS

Intervention
Cerebral blood flow*
dCA
Cerebral autoregulate*
Dynamic cerebral autoregulate*
Cerebral haemodynamic*
Autoregulatory index
ARI
Transfer function analysis
TFA
Phase
Gain
Coherence
Sit to stand
Squat stand
Thigh cuff
Outcome
Modified Rankin Scale
mRS
Mortality
Death
Dependent
National Institute of Stroke Severity Scale
NIHSS
Glasgow Coma Scale
GCS
Barthel
Infarct size
Infarct volume
Infarct extension
Infarct growth
Haemorrhagic transformation
Parenchymal haematoma
Cerebral oedema
Supplementary Information II – list of all pre-defined variables for which data will be collected

Demographic variables:

Age
Sex
Ethnicity
Time to randomisation
Time to thrombolysis/thrombectomy
Glasgow Coma Scale (GCS)
National Institute of Health Stroke Severity Scale (NIHSS)
Modified Rankin Scale (mRS) (baseline and pre-morbid)
Barthel index

Medical co-morbidities: diabetes mellitus, hypertension, previous stroke, atrial fibrillation, carotid artery disease (present/absent at >70% (NASCET criteria (1)), ischaemic heart disease, heart failure (with and without reduced ejection fraction), smoker, antihypertensive and statin therapy, frailty (as determined by a clinical frailty score, e.g. Clinical Frailty Scale (2)).

Stroke characteristics:

Affected hemisphere
Sub-type (large vessel occlusion (LVO)/non-LVO),
CT angiography (ICA, T, M1, M2 or M3)
Haemorrhagic transformation (European Cooperative Acute Stroke Study (ECASS II) classification (3))
Oedema

Physiological parameters:

Heart rate, blood pressure
End-tidal CO₂ (EtCO₂)

Outcome variables:

mRS
Phase
Gain
ARI
Mortality
mRS (Dead or dependent/independent)

NIHSS

GCS

Barthel

Infarct size/volume

Infarct extension (infarct growth measured as the difference in in infarct volume between baseline and follow-up (4))

Predicted or actual infarct size/volume (Alberta Stroke Program early CT score (ASPECTS) at baseline (5))

Haemorrhagic transformation (ECASS II criteria subtypes: HT1, HT2, and parenchymal haematoma (PH) type 1 and 2 (3))

Cerebral oedema
**Supplementary Information III – Pre-specified heterogeneity and sensitivity analyses**

*Heterogeneity analyses*

Heterogeneity will be investigated using the $I^2$ index (6), where $I^2 < 25\%$ corresponds to low, $50\%$ moderate, and $> 75\%$ high heterogeneity, and is summarised in the following equation:

$$I^2 = \frac{Q - df}{Q} \times 100$$

Where: $Q$ is Chi-square statistic, df is degrees of freedom.

Heterogeneity will be considered significant where $p < 0.05$. The traditional method of $I^2$ was originally developed for a two-stage analysis, but has recently been adapted for one-stage IPD analyses (7).

In addition to quantitative evaluation of heterogeneity, the following areas will be investigated as part of a pre-specified analysis:

*Case mix*

It is anticipated there will be significant differences between studies in terms of: the age of participants, their ethnicity, study location, severity and type of stroke, and co-morbidities. The relationship between dCA parameters and clinical outcome are likely to vary significantly between these factors, and will be investigated through pre-specified sub-group analyses outlined below.

*Stroke diagnosis and assessment*

There is likely to be significant heterogeneity between centres in the methods and classifications used to diagnose and sub-type AIS. The quality of stroke assessment and diagnosis will be assessed using the quality assessment tools (QUADAS-2, STROBE, and CONSORT).

*dCA assessment*
There is likely to be significant differences between centres in the protocols used to collect and analyse the dCA parameters. Data will be collected on the protocols and procedures used by individual centres for the collection and analysis of dCA parameters.

**Pre-specified sub-group analyses**

Where sufficient data are present, pre-specified analyses will include the following:

1. The relationship between key risk factors, dCA parameters and outcome in AIS including
2. The relationship between outcome from intervention (thrombolysis and thrombectomy) and dCA parameters in AIS
3. The relationship between neuroimaging outcomes and dCA parameters in AIS
4. The relationship between outcome and dCA parameters at varying time points
5. DTA test properties will be investigated within high risk sub-groups

**Sensitivity analysis**

Sensitivity analyses will be performed to identify the effect of any studies classified at high risk of bias on summary estimates. Initially, all studies will be included in analyses, and those identified to be at high risk of analysis will be removed, and the summary statistics re-calculated.
References