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Sedation versus general anaesthesia in endovascular therapy for anterior circulation acute ischaemic stroke: the multicentre randomised controlled AMETIS trial study protocol

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ABSTRACT

Introduction Endovascular thrombectomy is the standard of care for anterior circulation acute ischaemic stroke (AIS) secondary to emergent large vessel occlusion in patients who qualify. General anaesthesia (GA) or conscious sedation (CS) is usually required to ensure patient comfort and avoid agitation and movement during thrombectomy. However, the question of whether the use of GA or CS might influence functional outcome remains debated. Indeed, conflicting results exist between observational studies with better outcomes associated with CS and small monocentric randomised controlled trials favouring GA. Therefore, we aim to evaluate the effect of CS versus GA on functional outcome and periprocedural complications in endovascular mechanical thrombectomy for anterior circulation AIS.

Methods and analysis Anesthesia Management in Endovascular Therapy for Ischemic Stroke (AMETIS) trial is an investigator initiated, multicentre, prospective, randomised controlled, two-arm trial. AMETIS trial will randomise 270 patients with anterior circulation AIS in a 1:1 ratio, stratified by centre, National Institutes of Health Stroke Scale (≤15 or >15) and association of intravenous thrombolysis or not to receive either CS or GA. The primary outcome is a composite of functional independence at 3 months and absence of perioperative complication occurring by day 7 after endovascular therapy for anterior circulation AIS. Functional independence is defined as a modified Rankin Scale score of 0–2 by day 90. Perioperative complications are defined as intervention-associated arterial perforation or dissection, pneumonia or myocardial infarction or cardiogenic acute pulmonary oedema or malignant stroke evolution occurring by day 7.

Ethics and dissemination The AMETIS trial was approved by an independent ethics committee. Study began in august 2017. Results will be published in an international peer-reviewed medical journal.

Trial registration number NCT03229148.

Strengths and limitations of this study

- Anesthesia Management in Endovascular Therapy for Ischemic Stroke trial is the first multicentre randomised controlled trial comparing conscious sedation (CS) and general anaesthesia (GA) in thrombectomy for anterior circulation (internal carotid artery and/or proximal middle cerebral artery) acute ischaemic stroke.
- The multicentre setting and large pragmatic inclusions criteria compatible with current practice and recommendations will allow external validity.
- Stratification based on centre, stroke severity and concomitant administration of intravenous thrombolysis will allow groups homogeneity and comparability.
- Composite primary outcome measure will allow evaluation of functional independence at 3 months and neurological and non-neurological periprocedural complications. Secondary outcomes will measure different important aspects of care.
- Despite the absence of specific anaesthetic protocol concerning CS and GA management in order to reinforce external validity, perfusion pressure determinants (arterial blood pressure and carbon dioxide tension) will have to be maintained in strict limits.

INTRODUCTION

Background and rationale

Endovascular mechanical thrombectomy dramatically changed management of acute ischaemic stroke (AIS). Randomised controlled trials demonstrated improved outcome associated with the procedure using stent retrievers in anterior circulation AIS.[1–6] The American Heart Association/American

Stroke Association, as others national medical societies, rapidly endorsed this strategy as a level 1 recommendation in association if possible with intravenous thrombolysis.[7] Nevertheless, periprocedural management in the field added complexity since immobility and cardiorespiratory stability could be incompatible with acute neurological failure in these frail patients. Notably, the optimal management strategy during thrombectomy, using either general anaesthesia (GA) or conscious sedation (CS), remains controversial. It was traditionally assumed that CS was superior since GA could negatively affect brain physiology especially cerebral blood flow (CBF) in the penumbra area related to induced systemic hypotension and carbon dioxide modulation.[8] Also, it was stressed the possible excessive delay associated with GA initiation that counteract a 'time is brain' strategy. Nevertheless, evidence-based medicine supporting this concept is scarce with methodological issues associated with observational data.[9] Notably, sickest patients were prone to receive GA and the anaesthetic strategy was not protocolised nor randomised.[10] We could conceptually argue possible benefits of GA providing systemic hypotension is treated and avoided: (1) immobility that could facilitate an easier, rapid and effective technical procedure; (2) airway protection since AIS patients are prone to aspiration pneumonia related to neurological injury and (3) patient comfort in a highly stressful environment with sometimes prolonged procedures.[9] Recently, three small monocentric randomised controlled trials specifically addressed effect of anaesthesia care on stroke outcome. First, the SIESTA (Sedation vs. Intubation for Endovascular Stroke TreAtment) trial randomised 150 patients between CS and GA.[11] No difference occurred in the National Institutes of Health Stroke Scale (NIHSS) at 24 hours, which was the primary outcome. More patients were functionally independent after 3 months, defined as a modified Rankin Scale (mRS, which ranges from 0 (no symptom) to 6 (death)) of 0–2, in the GA group. Second, the AnStroke (Anesthesia during Stroke) trial randomised 90 patients between CS and GA.[12] No difference was achieved concerning the primary outcome mRS at 3 months and others secondary outcomes. Finally, the GOLIATH (General Or Local Anaesthesia in Intra Arterial THerapy) trial randomised 128 patients between CS and GA.[13] There was no difference in the volume of infarct growth as a primary outcome despite significantly higher successful reperfusion and better mRS score at 3 months in the GA group. On the assumption of these discrepancies, a multicentre randomised controlled trial comparing CS and GA is urgently needed.[14 15]

Objectives

Primary objective

The primary objective of the study is to determine whether CS or GA is associated with improved outcome defined as a dichotomous composite of functional independence at 3 months and absence of perioperative complication occurring by day 7 after endovascular therapy for anterior circulation AIS. Functional independence is defined as an mRS score 0–2 by day 90. Perioperative complications are defined as intervention-associated arterial perforation or dissection, pneumonia or myocardial infarction or cardiogenic acute pulmonary oedema or malignant stroke evolution occurring by day 7.

Secondary objectives

The study will also explore if CS or GA in endovascular therapy for anterior circulation AIS is associated with difference in several outcomes: functional independence by day 90, intraprocedural haemodynamic and ventilatory conditions, intervention-associated vessel and others complications, procedural time delays, successful recanalisation, stroke unit and hospital length of stay, perioperative complications by day 7, unexpected intensive care unit admission by day 7, mortality by day 7 and day 90.

Trial design

The Anesthesia Management in Endovascular Therapy for Ischemic Stroke (AMETIS) trial is an investigator initiated, national, multicentre, prospective, open-labelled, stratified, randomised controlled two-arm trial.

CONSORT diagram

Figure 1 shows the Consolidated Standards of Reporting Trials (CONSORT) diagram of the AMETIS trial.[16]

METHODS AND ANALYSIS

Participants, interventions and outcomes

This manuscript was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials guidelines.[17]

Study setting

The AMETIS trial takes place in 11 university hospitals in France (Clermont-Ferrand, Paris Pitié-Salpêtrière, Paris Saint-Antoine, Lyon, Toulouse, Marseille, Montpellier, Rouen, Lille, Poitiers and Saint-Etienne).

Eligibility criteria

Inclusion criteria

Adult patients admitted for anterior circulation (internal carotid artery and/or proximal middle cerebral artery) AIS, eligible for thrombectomy as decided by the neurology/neuroradiology teams based on current guidelines using brain imaging selection.[15]

Exclusion criteria

Patients with one or more criteria are not included

- Age <18 years.
- Coma or altered vigilance defined as a score ≥2 on the level of consciousness 1A subscale of the NIHSS.[18]
- Premorbid loss of autonomy defined as an mRS >1.[19]
- Posterior circulation stroke.
- Associated cerebral haemorrhage.
- Stroke complicating another acute illness or postoperative stroke.

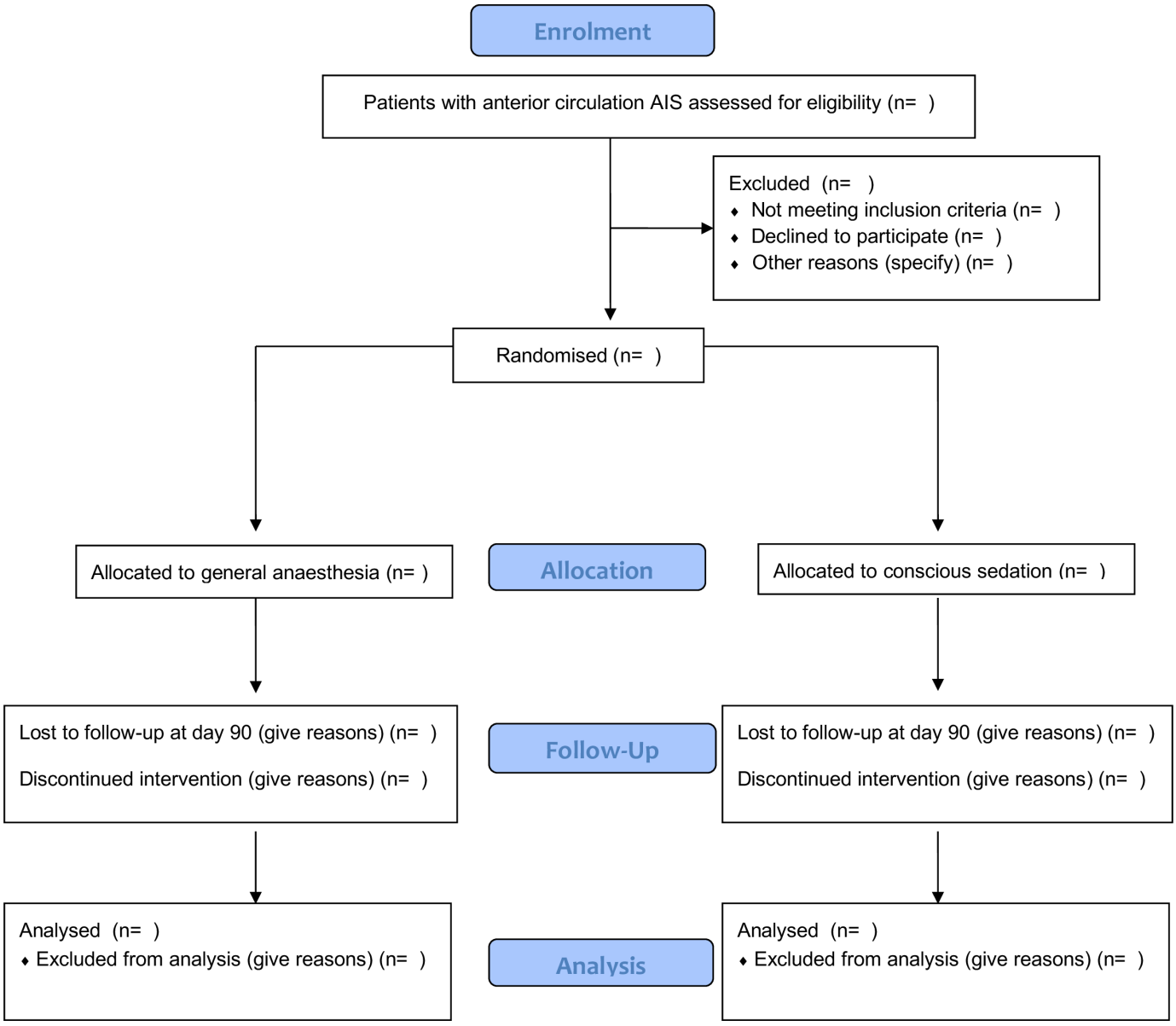

Figure 1 CONSORT diagram of the Anesthesia Management in Endovascular Therapy for Ischemic Stroke trial illustrating the randomisation and flow of patients in the study. AIS, acute ischaemic stroke; CONSORT, Consolidated Standards of Reporting Trials.

- Pregnant or breastfeeding women.
- Adult under the protection of the law.

Interventions

Patients eligible for inclusion will be randomly assigned to CS or GA after a routine medical anaesthetic emergency evaluation has been made by a certified senior anaesthesiologist. As required by French law, all contraindications and/or known allergy to anaesthetics will be registered.

Modality of the CS and GA protocols are left to the attending anaesthesiologist in accordance with current and local guidelines providing systolic blood pressure is maintained between 140 and 180 mm Hg (with vasopressor infusion if necessary) and arterial pulse oximetry (SpO2) >94%.[15]

Under GA, tracheal intubation is mandated and mechanical ventilation should be managed to maintain an end-tidal CO_2 level between 30 and 35 mm Hg.

Under CS, a minimal to moderate sedation level has to be targeted as defined by the American Society of Anesthesiologists recommendations.[20] Clinical sedation level will be evaluated using the Richmond Agitation Sedation Scale (RASS) with an objective between 0 and −3 (defined as a patient alert and calm or drowsy with sustained awakening (eye opening/eye contact) to voice ≥10 s or briefly awake to voice with eye contact <10 s or movement/eye opening to voice).[21 22] Effective spontaneous ventilation has to be maintained.

In the CS group, a crossover to GA with tracheal intubation is recommended in case of severe agitation, coma

defined as a −4 or −5 RASS value (no response to voice but movement or eye opening to physical stimulation or no response to physical stimulation) despite stopping sedative drugs, loss of airway protective reflexes, respiratory failure and incoercible vomiting.

Stent retrievers are the preferred devices to perform thrombectomy. Nevertheless, alternative devices could be used.

At the end of intervention, GA and CS have to be immediately stopped and in the GA group extubation should occur as soon as possible

After the intervention, depending on each hospital organisation and anaesthesia modality (GA or CS), patients are transferred to the postanaesthesia care unit or neurological or general intensive care unit.

Outcomes

Primary outcome measure

The primary outcome measure is a binary composite of functional independence at 3 months and absence of perioperative complication occurring by day 7 after endovascular therapy for anterior circulation AIS. Functional independence is defined as an mRS score 0–2 by day 90. Perioperative complications are defined as intervention-associated arterial perforation or dissection, pneumonia or myocardial infarction or acute cardiogenic pulmonary oedema or malignant stroke evolution occurring by day 7.

Secondary outcome measures

- mRS by day 90.[19 23 24]
  - Ordinal score on the mRS by day 90.
  - Functional independence by day 90 defined as an mRS score 0–2.
  - Excellent recovery by day 90 defined as an mRS score 0–1.
  - Moderate recovery by day 90 defined as an mRS score 0–3.
  - Shift analysis of day 90 mRS adjusted for initial prognostic factors (baseline mRS, age, initial NIHSS and carotid top occlusion).
  - Good recovery defined with sliding dichotomy responder analysis relating day 90 mRS with baseline NIHSS score: mRS 0 for NIHSS ≤7, mRS 0–1 for NIHSS 8–14 and mRS 0–2 for NIHSS >14.
- Intraprocedural haemodynamic and ventilatory conditions and complications defined as hypotension, blood pressure variability, hypoxaemia and aspiration.
- Intervention-associated vessel and others complications defined as arterial dissection or perforation, groin haematoma, embolisation in another arterial territory.
- Stroke onset to door delay, door to groin puncture delay, door to reperfusion delay, stroke onset to groin puncture delay, GA/CS induction to groin puncture delay, duration of the procedure, stroke onset to reperfusion delay (see online supplementary file 1 for definitions).
- Successful reperfusion defined by the modified Treatment In Cerebral Ischaemia (mTICI) reperfusion scale of 2b or 3 (with a grade of 2b or 3 indicating reperfusion of >50% of the affected territory).[25]
- NIHSS by day 1 and day 7.[18]
- Stroke unit and hospital length of stay.
- Perioperative complications by day 7 defined as pneumonia, acute cardiogenic pulmonary oedema, myocardial infarction, extra pulmonary infection, venous thromboembolism, new event of AIS, epilepsy, gastrointestinal bleeding or other symptomatic bleeding.[26]
- Malignant stroke evolution by day 7.[27]
- Symptomatic intracranial haemorrhage by day 7 defined as brain haemorrhage on imaging associated with an increase of at least four points in the NIHSS score.[28]
- Unexpected intensive care unit admission by day 7.
- Mortality by day 7 and day 90.
- Procedural feasibility score estimated by the radiologist and the anaesthesiologist and patient acceptability score.[29]

Recruitment

Patients are expected to be included during a 2-year period starting in august 2017.

2016–2017: Protocol, approvals from ethics committee (CPP Sud-Est I) and the French Medicine Agency (Agence Nationale de Sécurité du Médicament et des produits de santé, ANSM); trial tool development (online case report form (CRF) and randomisation system).

2017-2019: Inclusion of patients.

2019: cleaning and closure of the database, data analyses, writing of the manuscript and submission for publication.

Trial status

The current protocol is .4.0. Study started enrolment in august 2017. To date (28^{h} October 2018), 186 patients have been randomised in the study.

Patient and public involvement

Patients will not be invited to comment on study design or conduction of the trial.

METHODS: ASSIGNMENT OF INTERVENTIONS

Allocation and sequence generation

Randomisation will be conducted over a dedicated password-protected, SSL-encrypted website (CSOnline, Clinsight) to allow concealed allocation. Each patient will be given a unique patient number and randomisation number. The allocation sequence will be generated with the use of a minimisation algorithm stratified according to centre, NIHSS score (≤15 or >15) and association of intravenous thrombolysis or not. The participant allocation will be carried out by local investigators who will log

into the randomisation system using a personal ID and will enter any relevant information.

Blinding

This is an open-label, unblinded trial for the patient and the physician in charge, related to the nature of the intervention (GA with endotracheal intubation or CS). Assessor blinded evaluation of the primary outcome will be performed since the assessor and statistician will be masked to the subjects' assignment group.

METHODS: DATA COLLECTION, MANAGEMENT AND ANALYSIS

Data collection and management

At each participating centre, data will be collected and entered into the web-based electronic CRF (eCRF) (CSOnline, Clinsight) by trial or clinical trained personal (clinical research associate), blinded to the allocation group, under the supervision of the trial site investigators. From the eCRF, the trial database will be created. Paper CRF will be used in case of technical problems with the eCRF. Trained research coordinators will monitor data collection. Data collected are presented in online supplementary file 1.

Patient withdrawal

Evaluated procedure is tested during endovascular thrombectomy. Nevertheless, participant can withdraw consent at any time without need for further explanation. Data will be destroyed and a new patient will be randomised for the complete sample size.

Statistical methods

Sample size estimation

According to literature analysis based on five international randomised controlled trials about endovascular thrombectomy in anterior circulation AIS, frequency of events constitutive of the composite primary outcome was expected at 50%.[1–5] Then, we postulated that 124 patients per group would provide 90% statistical power to detect an absolute between-group difference equals 20% (50% vs 30%) for a two-sided type I error at 5%. Assuming lost to follow-up and modified intention-to-treat (mITT) population requirements (as defined in online supplementary file 2) between 5% and 10%, 270 patients have to be recruited for the study.

Interim analysis

A safety interim analysis is planned after 50% of inclusions. The independent data and safety monitoring board (DSMB) could recommend stopping the study if prolongation of the trial clearly compromises patient safety (in case of serious adverse reactions (SARs) or suspected unexpected serious adverse reactions (SUSARs)). The steering committee will be responsible to continue, hold or stop the study based on the DSMB recommendations.

Statistical analysis

A predefined statistical analysis plan will be followed (online supplementary file 2). All analyses will be conducted with Stata software (V.13, StataCorp) and R (http://cran.r-project.org/) before the breaking of randomisation code, in line with the International Conference on Harmonization Good Clinical Practice guidelines. A two-sided p value of less than 0.05 will be considered for statistical significance. Primary analysis will be done in mITT. Then, a per-protocol analysis will also be done to take into account protocol deviations notably crossover from CS to GA. Patients who withdraw consent will not be included in these analyses.

Continuous variables will be presented as mean and SD or as median and quartiles otherwise. Normality will be assessed using the Shapiro-Wilk test and homoscedasticity will be assessed using the Fisher-Snedecor test.

Concerning the comparison of the primary binary composite outcome between CS and GA, a X^2 test or a Fisher's exact test will be performed as appropriate. Binary outcomes are commonly analysed by applying a logistic regression model to obtain ORs. Although this is often appropriate, there may be situations in which it is more desirable to estimate a relative risk (RR) instead of OR.[30 31] Knol *et al*. 'illustrate the difference between risk ratios and OR using clinical examples, and describe the magnitude of the problem in the literature.[32]' Interestingly, the authors reviewed available methods to obtain adjusted risk ratios and evaluated these methods by means of simulations, and concluded that 'The Mantel-Haenszel risk ratio method, log-binomial regression, Poisson regression with robust SEs and the doubling-of-cases method with robust SEs gave correct risk ratios and CIs.' Also, adjusted analysis will be conducted with the use of robust (SEs) random-effects Poisson generalised linear regression (package gllamm) will be used (1) to take into account adjustment on possible confounding covariates selected according to clinical relevance and stratification variables (including stratification parameters) and (2) to consider within and between centre variability (as random effect). A particular attention will be paid to the covariates used in multivariable regressions, especially quantitative covariates for which convergence issues can be raised due to log-link in the binomial distribution. As presented in statistical analysis plan, only 'time delays' will be concerned. Sensitivity analysis considering these covariates, dichotomising according to the statistical distribution and to the clinical relevance, should be proposed. The results will be presented as RRs and 95% CIs. The Hochberg procedure will be used to adjust for multiple testing of components of the composite primary outcome.

Due to the lack of consensus concerning the categorisation of mRS as a stroke outcome measure, this parameter will be treated by different ways according to literature notably as an ordinal variable.[15 33] A shift analysis will also be performed: Cochran-Mantel-Haenszel for the univariate analysis and random-effects ordinal logistic regression adjusted on initial prognostic factors (baseline mRS, age, initial NIHSS and carotid top occlusion) for multiple regression.

Concerning the comparisons of secondary outcomes between groups, Student's t-test or non-parametric Mann-Whitney test as appropriate will be used for quantitative parameters such as intraoperative blood pressure, oxygen saturation, timing delays or length of stays. X^2 test or Fisher's exact test will be used for categorical parameters such as NIHSS and ordinal and nominal (dichotomised) mRS, intervention-associated and perioperative complications, mTICI score, functional independence at day 90 and mortality. Results will be reported as effect sizes and absolute differences with 95% CIs. Then, multiple regression will be conducted using random-effects models taking into account between and within centre variability: linear mixed models for quantitative endpoints and generalised linear mixed regression for categorical endpoints. The results will be expressed, respectively, as regression coefficients and RRs, with 95% CIs.

Time-to-event curves will be calculated with the use of the Kaplan-Meier method in univariable analysis. For multiple regression, marginal Cox proportional hazards model (with centre as random effect) will be performed. Proportional hazard assumption will be verified using the Schoenfeld test and plotting residuals. Results will be reported as HRs with 95% CIs.

Concerning the study of parameters collected longitudinally (in particular NIHSS score at day 1 and day 7, arterial pressure and arterial oxygen saturation), mixed models will be used to take into account between and within patient variability, in addition to centre random effect. The following fixed effect will be analysed: randomisation group, time and their interaction (time x group).

According to clinical relevance and to European Medicines Agency and CONSORT recommendations, post hoc analyses will be proposed after the study of subgroup ×randomisation group interaction in regression models (for repeated data or not). Missing values will be notified and analysed. A sensitivity analysis will be performed and the nature of missing data will be studied (missing at random or not). If the frequency is >5%, additional analyses will be performed using the multiple imputation method.[34]

METHODS: MONITORING

Data monitoring

Before the start of the study, anaesthetic, neurological and radiological medical and paramedical teams are trained at each site for the study protocol by study coordinators. Physicians are in charge of patient screening and inclusion. Patients admitted for stroke treated by endovascular mechanical thrombectomy and not included in the study will be recorded anonymously at each centre into a screening log. Data will be collected in a web-based eCRF by trial personnel. Each centre will only have access to site-specific data. Each patient will receive a unique trial identification number. Only the investigators and research team will have access to any protected health information of study participants and any study data.

Data monitoring and quality control will be conducted in each centre after the first 10 inclusions then after the next 20 inclusions and at the end of the study by official representatives of the study promoter (Department of Clinical Research and Innovation, Clermont-Ferrand University Hospital).

Data will be handled according to the French law. All originals records (including consent forms, reports of SUSARs and relevant correspondences) will be archived at trial sites for 15 years. The clean trial database file will be anonymised and maintained for 15 years. Only the principal investigators and the statistician will have access to the final dataset.

Harms

Every adverse events that could be related to the trial will be reported to the trial coordinating centre. According to the French law, all suspected serious adverse events will be reported to the ANSM. The DSMB will also be informed. DSMB is independent from the trial investigators and will perform an ongoing review of safety parameters and study conduct. DSMB members are two independent physicians in anaesthesia/critical care medicine and neurology, and a biostatistician that have skills and expertise in anaesthesia, clinical neuroscience and clinical research. The DSMB will be responsible for safeguarding the interests of trial participants, assessing the safety of the interventions during the trial and for monitoring the overall conduct of the trial. DSMB could also formulate recommendations related to the recruitment/retention of participants, their management, improving adherence to protocol-specified regimens, and the procedures for data management and quality control. No formal criteria are set to stop the study. However, recommendations for pausing or stopping the study could be made by DSMB in case of SARs and SUSAR. The scientific committee will be responsible for promptly reviewing the DSMB recommendations and to decide whether to continue, hold or stop the study, and to determine whether amendments to the protocol are needed.

ETHICS AND DISSEMINATION

Any change to eligibility criteria, outcomes and analyses will be communicated to investigators, the ethics committee and the ANSM to obtain their approval.

Consent or assent

Whenever possible to include the patient, written inform consent will be searched. Nevertheless, related to neurological injury and emergency, the patient may be unable to provide written informed consent. In this case, written informed consent could be obtained from the patient next of kin if immediately available. Otherwise, an emergency consent procedure is used with investigator signature countersigned by an independent physician. As soon as possible after recovery, written informed consent from the patient will be searched to continue the study.

DISCUSSION

We recently observed the 'thrombectomy revolution' in anterior circulation AIS.[35] Emergency interventional procedures in frail stroke patients often require skills from anaesthesia providers since immobility is needed and severe intraprocedural complications may occur (eg, coma, agitation or aspiration pneumonia).

Taking into account the increasing volume of procedures and the potential effect of the anaesthetic strategy on outcome with discrepancy in literature, it appears essential to provide a multicentre randomised controlled trial to enhance external validity as suggested by recent recommandations.[15]

Concurrent ongoing trials with day 90 mRS as a primary outcome are planning to recruit 635 patients to demonstrate non-inferiority between CS and GA,[36] 350 patients to demonstrate superiority of CS versus GA (NCT02822144) or 260 patients to demonstrate superiority of GA versus CS (NCT03263117).

Some limitations could be opposed to the AMETIS trial protocol. First, no specific anaesthetic protocol will be used. We choose this strategy in a pragmatic way since no data demonstrate that a drug is better than another even if modulation of CBF could be variable. However, the protocol requires strict objectives for systolic blood pressure and 'normal' blood carbon dioxide tension in GA group.[37 38] Drugs and dose will be monitored. Second, no maximal time delay from stroke onset or maximal/minimal NIHSS values are recommended in order to adhere to a pragmatic investigator-based approach. This strategy complies with recent trials and recommendations: patient selection for thrombectomy is made on angioCT or MRI scans with eventual mismatch evaluation especially when delay is >6 hours and for wake-up strokes.[15 39 40] Delays and imaging modality used for selection will be monitored. Notably, despite published trials mentioned NIHSS limits as inclusion/exclusion criteria, providing thrombectomy is indicated based on actual recommendations, the optimal anaesthetic strategy deserves evaluation whatever the NIHSS is. Stratification on NIHSS score with a cut-off of 15 will provide homogeneous groups in term of initial severity. As recommended, outcome measures will include adjustments for baseline severity.[15] Third, despite thrombectomy might benefit to patients with premorbid mRS>1, we excluded these patients since evaluation is difficult in emergency condition and inclusion of dependent patients could strongly affect the primary outcome. This strategy was adopted by others.[3–5 40] Fourth, we choose a composite principal outcome measure since anaesthesia strategy could affect functional independence at 3 months but also peri-interventional morbidity. The effect size that we could expect on functional independence at 3 months is probably far less than thrombectomy on its own. Based on actual literature, SIESTA trial found dramatically decreased functional independence associated with CS with only 18% of mRS 0–2 compared with 37% in GA.[11] Eighteen per cent of patients being independent is far less than in thrombectomy trials where it barely represents controlled groups (intravenous thrombolysis alone).[1–6] With these proportions, 240 patients would have been necessary to demonstrate a statistical difference with a beta power of 90%, but we could expect important centre effect in SIESTA trial. On the contrary, ANSTROKE trial did not find any difference between groups, with functional independence in respectively 42% and 40% of patients between GA and CS.[12] Based on these two trials, functional independence could be obtained in roughly 40% of patients under GA. Providing a 20% variation in positive or negative effect on functional independence, more than 1000 patients would be required with a 80% beta power. An anaesthesia size effect of more than 20% appeared unrealistic.

Fifth, even if possible in selected patients, we will not study local anaesthesia alone. Management solely under local anaesthesia is difficult regarding comfort and immobility particularly in sickest patients, in left hemisphere strokes with aphasia and in tandem lesions (associated cervical carotid artery occlusion). In the CS group, we provide only clinical sedation objectives based on RASS score between 0 and −3. There is no recommended drug to achieve this goal and local anaesthesia is systematically used under CS.

In conclusion, AMETIS trial is the first multicentre randomised controlled study exploring the effect of CS versus GA on functional outcome and periprocedural complications in endovascular mechanical thrombectomy for anterior circulation AIS. The results of this study could have significant clinical and public health implications.

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