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Guidelines

# Anaesthetic and peri-operative management for thrombectomy procedures in stroke patients☆

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ABSTRACT

*Purpose:* To provide recommendations for the anaesthetic and peri-operative management for thrombectomy procedure in stroke patients
*Design:* A consensus committee of 15 experts issued from the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation, SFAR), the Association of French-language Neuro-Anaesthetists (Association des Neuro-Anesthésistes Réanimateurs de Langue Francaise, ANARLF), the French Neuro-Vascular Society (Société Francaise de Neuro-Vasculaire, SFNV), the French Neuro-Radiology Society (Société Francaise de Neuro-Radiologie, SFNR) and the French Study Group on Haemostasis and Thrombosis (Groupe Français d'Études sur l'Hémostase et la Thrombose, GFHT) was convened, under the supervision of two expert coordinators from the SFAR and the ANARLF. A formal conflict-of-interest policy was developed at the outset of the process and enforced throughout. The entire guideline elaboration process was conducted independently of any industry funding. The authors

☆ Text validated by the par le *Comité des Référentiels Cliniques* (clinical reference committee) of the SFAR on 16/05/2022, by the *Conseil d'Administration* (board of directors) of the SFAR le 29/06/2022, by the bureau of the ANARLF on 29/06/2022, by the *Conseil d'Administration* (board of directors) of the SFNV on 07/10/2022 and by the *Conseil Scientifique* (scientific council) of the SFNR on 16/08/2022.

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were required to follow the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to guide their assessment of quality of evidence.
*Methods:* Four fields were defined prior to the literature search: (1) Peri-procedural management, (2) Prevention and management of secondary brain injuries, (3) Management of antiplatelet and anticoagulant treatments, (4) Post-procedural management and orientation of the patient. Questions were formulated using the PICO format (Population, Intervention, Comparison, and Outcomes) and updated as needed. Analysis of the literature was then conducted and the recommendations were formulated according to the GRADE methodology.
*Results:* The SFAR/ANARLF/SFNV/SFNR/GFHT guideline panel drew up 18 recommendations regarding anaesthetic management of mechanical thrombectomy procedures. Due to a lack of data in the literature allowing to conclude with high certainty on relevant clinical outcomes, the experts decided to formulate these guidelines as "Professional Practice Recommendations" (PPR) rather than "Formalized Expert Recommendations". After two rounds of rating and several amendments, a strong agreement was reached on 100% of the recommendations. No recommendation could be formulated for two questions.
*Conclusions:* Strong agreement among experts was reached to provide a sizable number of recommendations aimed at optimising anaesthetic management for thrombectomy in patients suffering from stroke.


## Introduction

Management of ischemic cerebrovascular accident (ICVA) must be undertaken with maximum urgency, and represents a major issue in public health. Up until 2015, ICVA treatment was based on rapid recanalization of the occluded artery by means of intravenous thrombolysis. The advent of mechanical thrombectomy (MT) enlarged the therapeutic arsenal and modified management policies. MT is indicated either in association with intravenous thrombolysis or as a second or third option (following failure of IV thrombolysis or alone, in case of contraindication to IV thrombolysis), within six hours after symptom onset in acute ICVA patients with occlusion of a large arterial trunk in the anterior circulation, and possibly in the posterior circulation, which is visible on imagery. Considering the results of recent randomized controlled studies, some indications can be prolonged for as many as 24 h. Vascular occlusion must be diagnosed by means of a non-invasive first-line method (angio-tomodensitometry or magnetic resonance angiography) before considering a therapeutic phase involving MT. Any decision to carry out MT must be made by a multidisciplinary team including at least one neurologist and/or a physician with competence in neurovascular pathologies from the establishment's neurovascular care unit, and a doctor qualified to perform mechanical thrombectomy. The latest French health authority (HAS) guidelines (https://www.has-sante.fr/jcms/c_2757616/fr/organisation-de-la-prise-en-charge-precoce-de-l-accident-vasculaire-cerebral-ischemique-aigu-par-thrombectomie-mecanique) also insist on the need for an anaesthesia team and, more specifically, an anaesthetist with experience in the management of patients treated by interventional neuroradiology, as well as a registered nurse anaesthetist (the French IADE). Patient eligibility for MT must be discussed collegially in a consultation involving the vascular neurologist, the interventional neuroradiologist, and the anaesthetist in charge.

The clinicians responsible for MT routinely use several scores corresponding to the different steps of management and treatment:

**- The NIHSS score** [1]: The clinical NIHSS (NIH Stroke Scale) is a diagnostic scale used following ischemic or haemorrhagic cerebrovascular accidents to measure the intensity of neurological signs in view of appraising their severity and monitoring their evolution. The NIHSS [1] is based on the collection of 15 neurological items; it permits precise and rapid assessment of the deficits observed and is closely associated with patient outcomes. Correlated with the volume of the cerebral infarction, it has a quantitative as well as a prognostic function. It is associated with high inter-observer reliability. An NIHSS score between 1 and 4 signifies a minor CVA; between 5 and 15, a moderate CVA; between 15 and 20, a moderate/severe CVA; and over 20 points, a severe CVA.

**- The ASPECTS score** [2]: This 10-point radiological scale (Alberta Stroke Program Early CT Score) assesses ischemic strokes in the area of the middle cerebral artery (MCA) by means of CT without injection. In clinical practice, the score divides the MCA into 10 sectors: 3 deep or subcortical regions, and 7 superficial or cortical regions. For each sector, the absence of hypodensity yields 1 point. A score $\leq$7 is predictive of a pejorative prognosis in terms of both residual handicap and risk of haemorrhagic transformation. An ASPECTS score of 0 corresponds to hypodensity of the entire MCA area.

**- The TICI score** [3]: The angiographic TICI score (Treatment In Cerebral Ischemia Scale revisited) quantifies the degree of revascularization. TICI 3 corresponds to complete radiological success; TICI 2c to almost complete filling of the vascular territory, but which in some parts is slower than normal; TICI 2b to filling covering half of the revascularized territory; TICI 2a to less than half of the territory; TICI 1 to penetration of the contrast product with minimal perfusion (absence of recanalization); and, lastly, TICI 0 corresponds to no perfusion/absence of revascularization. TICI 2c/3 is considered as a good thrombectomy outcome.

**- The modified Rankin score** [4]: As a global and clinical assessment of handicap, the modified Rankin score is determined in five minutes. As a six-level scale, it ranges from 0 for no symptom at all; (1) for no significant disability despite symptoms (able to carry out all usual duties and activities); (2) for slight disability (unable to carry out all previous activities, but able to look after own affairs without assistance); (3) for moderate disability (requiring some help, but able to walk without assistance); (4) for moderately severe disability (unable to walk without assistance, and unable to attend to own bodily needs without assistance); (5) for severe disability (bedridden, incontinent and requiring constant nursing care and attention); to (6) for death.

## Objectives of the recommendations

The objective of these recommendations is to produce a framework to facilitate decision-making in a situation of extreme urgency, face to a patient requiring management for a thrombectomy procedure. The group strove to put together a minimum

number of recommendations to highlight the main points, which have been grouped into four predefined fields: (1) peri-procedural management, (2) prevention and management of secondary brain injuries, (3) management of antiplatelet and anticoagulant treatments, (4) post-procedural management, and orientation of the patient. The golden rules for good medical practice are considered well-known, and consequently excluded from the recommendations; pre-hospital management is likewise not considered. The targeted public is large-scale, corresponding to all of the health professionals (neurologists, radiologists, anaesthetists-intensivists, etc.) involved in management.

## General organization

These recommendations result from work by a group of experts brought together by the SFAR and the ANARLF, in collaboration with the SFNV and the SFNR. Prior to the analysis, each expert filled out a declaration concerning possible competing interests. As a first step, the organizing committee defined the objectives, the methodology, the field(s) of application, and the questions to be addressed in the recommendations. These different elements were subsequently modified and validated by the experts.

To the greatest possible extent, the questions were formulated in accordance with the PICO (Population – Intervention – Comparison – Outcome) format. The population for whom these recommendations are addressed is composed of ''patients presenting with a cerebral artery occlusion and eligible for endovascular treatment'' (this is not repeated in each of the recommendations).

## The recommendation fields

For the present recommendations, the experts unanimously decided to focus on the following fields:

FIELD 1 – Peri-procedural management

FIELD 2 – Prevention and management of secondary brain injuries FIELD 3 – Management of antiplatelet and anticoagulant treatments

FIELD 4 – Post-procedural management and orientation of the patient.

## Methodology of the bibliographic research and formulation of the recommendations

Up until March 2022, extensive bibliographic research was carried out on the MEDLINE PubMed™ and clinicaltrials.gov databases by at least two experts in each field of application in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology for systematic reviews.

Were included in the analysis: meta-analyses, randomized controlled trials, non-randomized prospective trials, retrospective cohorts, case series, and case reports conducted in patients presenting with cerebral artery occlusion and eligible for endovascular treatment, published in English or French.

Analysis of the literature was then carried out in accordance with the GRADE® (Grade of Recommendation Assessment, Development, and Evaluation) methodology. The endpoints were preliminarily defined as follows:

- Primary endpoint: neurological prognosis at 3 months (assessed by the Rankin score) (importance 8).
- Secondary endpoints: short-term neurological morbidity (importance 7), success of the thrombectomy (assessed by the TICI score) (importance 6).

Given the very low number of available studies presenting sufficient power with regard to the most substantive primary endpoint, it was decided before the recommendations were drafted to adopt a Professional Practice Recommendations (PPR) rather than a Formalized Expert Recommendations (FER) format. The GRADE® methodology was applied in the analysis of the literature and in the drafting of summary tables recapitulating the data in the literature. A level of evidence was determined for each of the cited bibliographic references according to the type of study. It could subsequently be re-evaluated according to the methodological quality of the study, consistency of the results between the different studies, the direct or indirect nature of the evidence, and analysis of the cost and extent of benefit. The recommendations were then written out, using the SFAR terminology for PPRs: ''the experts suggest to do'' or ''the experts suggest not to do''. The proposed recommendations were then presented to the experts and discussed, one by one. The goal was not necessarily to arrive at a single and convergent opinion on all the proposals, but rather to distinguish points of convergence from points of divergence or indecision.

## Results

### *The recommendation fields*

During the first PPR organizing meeting, the experts consensually decided to address 15 questions distributed in four fields. The following questions were chosen for the collection and analysis of the literature:

### FIELD 1 – Peri-procedural management

**Questions:**

- In a patient presenting with cerebral artery occlusion and who is eligible for endovascular treatment, does local anaesthesia alone, compared to general anaesthesia or sedation, lead to an improved neurological prognosis at 3 months?
- In a patient presenting with cerebral artery occlusion and who is eligible for endovascular treatment, does sedation, compared to general anaesthesia, lead to an improved neurological prognosis at 3 months?

### FIELD 2 – Prevention and management of secondary brain injuries

**Questions:**

- In a patient having presented with cerebral artery occlusion and received endovascular treatment, is the use of target blood pressure (BP) levels during post-recanalization associated with improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment, does the setting of target saturation as an objective lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment under general anaesthesia, does per-procedure monitoring of $CO_2$ lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment under sedation, does per-

procedure monitoring of $CO_2$ lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment, does per-procedure monitoring of glycemia lead to improved neurological prognosis at 3 months?

**FIELD 3 – Management of antiplatelet and anticoagulant treatments**

**Questions:**

- In a patient having presented with cerebral artery occlusion and received endovascular treatment after having been preliminarily treated by intravenous thrombolysis, does systemic per-procedure heparinization lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment without having been preliminarily treated by intravenous thrombolysis, does systemic per-procedure heparinization lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and received endovascular treatment, does per-procedure anti-aggregation lead to improved neurological prognosis at 3 months?
- In a patient having presented with cerebral artery occlusion and receiving endovascular treatment necessitating emergency stenting, does anti-aggregation of blood platelets lead to improved neurological prognosis at 3 months?

**FIELD 4 – Post-procedural management and orientation of the patient**

**Questions:**

- In a patient having undergone cerebral thrombectomy under general anaesthesia, does implementation of an early neurological assessment strategy (end of sedation, early extubation) lead to improved morbi-mortality?
- In a patient having undergone cerebral thrombectomy under general anaesthesia, does implementation of an early scale-guided extubation strategy (VISAGE score, etc.), lead to improved morbi-mortality?
- In a patient having undergone cerebral thrombectomy, does orientation toward an adapted care structure (critical care *vs.* stroke unit) according to severity criteria lead to improved morbi-mortality?
- In a patient having undergone cerebral thrombectomy, does extended stay in an expert center, usually according to orientation criteria, lead to improved morbi-mortality?

*Synthesis of the results*

Following a synthesis of the experts' work and application of the GRADE® method, 18 recommendations were formalized, whereas, for 2 questions, the experts refrained from issuance of the latter. All of the recommendations were submitted to the expert group for assessment, using the GRADE® Grid method. After 2 rounds of rating, a strong agreement was reached on 100%.

The present PPRs replace the preceding SFAR guidelines for the same fields of application. The SFAR and the ANARLF strongly urge all the professionals involved in the management of patients treated by endovascular thrombectomy to comply with the recommendations put forward. However, when they are being effectively applied, each practitioner is called upon to exercise his own judgment, taking into full account his area of expertise and the specificities of his establishment, so as to decide on the means of intervention best suited to the state of the patient of whom he is in charge.

**FIELD 1. Peri-procedural management**

*Experts: Y. Launey (ANARLF) – S. Saleme (SFNR) – O. Naggara (SFNR) - L. Meuret (SFAR)*

**Question: In a patient presenting with cerebral artery occlusion and who is eligible for endovascular treatment, does local anaesthesia alone, compared to general anaesthesia or sedation, lead to improved neurological prognosis at 3 months?**

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**R1.1.1 - The experts suggest that general anaesthesia with orotracheal intubation, carried out by an anaesthesia team, be preferred to local anaesthesia alone, the objective being to improve the neurological prognosis at 3 months, when at least one of the following situations is present:**
**- in the event of impaired posterior circulation**
**- in the event of difficult planned radiological neuro-navigation**
**- in the event of NIHSS score $\geq$ 15**
**- in the event of diminished mental alertness**
**- in the event of respiratory failure**
**- in the event of patient agitation**
**- in the event of vomiting**

**Expert opinion (Strong agreement)**

**R1.1.2 – With the exception of situations necessitating intubation (see above), the experts suggest not to prefer general anaesthesia to local anaesthesia monitored by an anaesthesia team, the objective being to achieve an improved neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

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**Argumentation:** The distinction between local anaesthesia (LA) and procedural sedation (PS) was relatively recently drawn in studies aiming to assess the impact of anaesthesia strategy on the prognosis of patients undergoing treatment for acute cerebral artery occlusion. As an example, post-hoc analysis of the IMS-III trial reported higher morbi-mortality following endovascular treatment under general anaesthesia (GA), as compared to treatment under "local anaesthesia", which in this study was an entity bringing together all forms of anaesthesia without intubation (with or without sedation) [5].

*For occlusions of the anterior circulation*

Most of the studies dealing with the differences between LA alone and PS are observational or retrospective, and consequently not methodologically robust [6,7]. Even though a meta-analysis of randomized trials [8] in which GA and LA with and without sedation are compared, as well as two analyses of the Dutch prospective and observational thrombectomy registry [9,10] have been published, the results are at times contradictory and riddled with several potential biases (methodologies, definition of LA, missing data). For example, the study by Benvegnù *et al.* seems unfavourable to LA compared to PS insofar as the former is associated with less satisfactory functional neurological evolution, a lower rate of reperfusion, and higher 3-months mortality [11]; whereas the analyses of the MR CLEAN registry [9,10] found that LA

was associated with a better functional prognosis than PS. In an Italian prospective cohort study involving 4429 patients treated by endovascular thrombectomy [12], GA was associated with a worse 3-months functional prognosis than LA or conscious sedation (CS). It bears mentioning that in this study, the initial median NHISS score was lower in the LA group than in the PS or GA group, and that the reasons for conversion to GA were not reported (a major source of bias). In fact, it is not possible to prioritize one technique for endovascular thrombectomy following an ischemic anterior circulation stroke. While awaiting the results of more robust randomized controlled studies in which LA would be more clearly defined with regard to the other anaesthesia techniques (NCT02677415), it seems reasonable to privilege optimized anaesthesia management through an approach adopted to patient characteristics and reliant on local expertise.

*For occlusions of the posterior circulation*

Acute occlusion of posterior arterial circulation, which involves the vertebral artery or the basilar artery, is responsible for more severe strokes with less favourable prognosis than those affecting anterior circulation. In the event of basilar occlusion, it occasions brainstem dysfunction (ascending reticular activating system, long motor and sensory pathways, mixed cranial nerves, autonomic nervous system). Endovascular revascularization by thrombectomy is realizable in this indication, notwithstanding the absence of formal scientific validation. The pathophysiology differs from that of anterior circulation, with a mechanism more atherosclerotic than embolic. The concepts of collaterality, ischemic penumbra, time lapse and subsequent patient selection on radiological criteria are likewise different from those having to do with anterior circulation. Indications are frequently ''compassionate'', particularly in case of severe forms, with individual benefits often found only after an extended lapse of time. Procedures are technically more challenging than in anterior circulation, and correspondingly lengthier. The literature assessing anaesthetic management of posterior circulation occlusions is limited and uniquely observational, with databases including very few patients (at most 298 patients in a Spanish series) [13]. Definition of a ''general anaesthesia'' group is generally restricted to ''intubated patient'', and that of a ''sedation/local anaesthesia'' group to ''non-intubated patient''. Some trials only include basilar occlusion, while others involve all occlusion of the posterior circulation. Out of the 7 analysed trials, 4 pertain to an Asian population presenting much more atherosclerotic aetiology than others and possibly markedly different healthcare organization, which may be a source of selection bias and external validity bias. An ongoing single-center randomized controlled Chinese study [14] is attempting to demonstrate the equivalence of the different forms of anaesthesia, and even the greater benefits of PS and LA as compared to GA in the selected patients, who are among the least severely impaired. While awaiting the results of this study and of other randomized studies yet to come, and given the possibility of severe forms with coma and/or respiratory distress, the experts have positioned themselves in favour of GA with intubation during endovascular thrombectomy procedures for occlusion of the posterior circulation.

When GA is contemplated according to the above-mentioned criteria, the presence to monitor the operation of a specifically experienced and available anaesthesia team is of paramount importance.

**Question: In a patient presenting with cerebral artery occlusion, and who is eligible for endovascular treatment, does sedation, compared to general anaesthesia, lead to improved neurological prognosis at 3 months?**

**R1.2 – With the exception of situations necessitating orotracheal intubation (cf. R1.1.1), the experts suggest not to prefer general anaesthesia to procedural sedation by an anaesthesia team, the objective being to improve the neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

**Argumentation:**

*For occlusions of the anterior circulation:*

The literature concerning anaesthesia management [general anaesthesia (GA) or procedural sedation (PS)] for cerebral artery occlusions of the anterior circulation is sizable but of poor quality. Numerous sets of observational data with meta-analyses characterized by selection bias (non-controlled anaesthetic intervention, severe patients managed under GA…) exist. In these series, definition of the GA and sedation groups is imprecise (patients treated with local anaesthesia alone in the sedation group, or patients secondarily intubated due to complications, and analysed in the GA group). Since 2015, observational meta-analyses have found sedation to be beneficial in terms of functional autonomy at 3 months (modified Rankin score ''mRS'' $\leq$ 2). However, only 3 randomized controlled studies dealing specifically with anaesthesia management exist [15–17]. These studies were single-center, European, and included few patients. In addition, all except one [16] had an intermediate primary endpoint (NIHSS at D1 or infarct volume in MRI). What is more, the patients, who were treated during the 8 h following symptom onset, were peculiarly selected, as some were excluded due to NIHSS $<$ 10, agitation, vomiting and/or loss of airway protective reflexes, or when the anaesthesia team was unavailable. About 40% of the patients eligible for a thrombectomy were not randomized. The teams managing the patients were specialized in neuro-anaesthesia and/or neuro-intensive care, and they fully respected the therapeutic objectives defined in the study protocol, particularly in terms of blood pressure. In these studies, time to reperfusion did not increase under GA, notwithstanding a slight lengthening of time to vascular access. While no significant difference was found regarding the primary endpoint, 2 of the studies found signs favouring GA for the functional prognosis at D90. A meta-analysis of these trials based on individual data [18] found GA to be beneficial in terms of autonomy at D90. Unfortunately, its power remained limited; only 368 patients were included, and the confidence interval was wide (mRS $\leq$ 2: 65/185 PS (35.1%) *vs.* 90/183 GA (49.2%), OR = 0.46, 95%CI (0.28−0.76), $p$ = 0.003).The inhomogeneity of sedation was also due to the types of anaesthetic molecules used and to the fact that the rates of conversion to GA observed during the studies ranged from 6 to 16%, and were associated with a less favourable functional prognosis [18]. Lastly and more recently, 2 multicentred randomized controlled French trials, GASS [19] and AMETIS [20], which compared GA to PS, found no significant difference concerning their respective primary endpoints (GASS: mRS $\leq$ 2 at D90: 40% PS *vs.* 36% GA, OR = 0.91 (0.64–1.31), and AMETIS: composite criteria associating functional autonomy (mRS $\leq$ 2) at D90 and absence of major complications at D7: 39.1% PS *vs.* 33.3% GA, OR = 1.18 (0.86–1.61), $p$ = 0.80).

*For occlusions of the posterior circulation*

In the absence of well-conducted studies on procedural sedation in thrombectomy for arterial occlusion of posterior cerebral circulation, and for the same reasons as those put forward in the R1.1.1 argumentation, general anaesthesia with orotracheal intubation should probably be prioritized during thrombectomy, particularly in the event of basilary artery occlusion.

## FIELD 2. Prevention and management of secondary brain injuries

*Experts: T. Geeraerts (ANARLF) – M. Mazighi (SFNV) - S. Figueiredo (SFAR) – JM Olivot (SFNV)*

**Question: In a patient having presented with cerebral artery occlusions and received endovascular treatment, is use of target blood pressure (BP) levels in post-recanalization associated with improved neurological prognosis at 3 months?**

**R2.1.1 - The experts suggest that in the event of TICI <2b recanalization, post-procedure systolic blood pressure should be maintained between 130 and 180 mmHg, the objective being to achieve an improved neurological prognosis at 3 months.**

**Expert opinion (Strong agreement)**

**R2.1.2 - The experts suggest that in the event of TICI ≥2b recanalization, post-procedure systolic blood pressure should be maintained between 130 et 160 mmHg, the objective being to achieve improved neurological prognosis at 3 months.**

**Expert opinion (Strong agreement)**

**Argumentation:** Blood pressure management has multiple therapeutic objectives: to ensure adequate cerebral perfusion; and to avoid haemorrhagic phenomena or the development of cerebral oedema or other malignant complications. If targets for adequate blood pressure during the first 24 post-thrombectomy hours are met, the patient's prognosis could be improved, and postoperative complications reduced.

The guidelines put forward by the AHA/ASA (American Heart Association/American Stroke Association) are mainly based on the literature concerning intravenous thrombolysis. They recommend maintaining systolic blood pressure (SBP) at < 180 mmHg and diastolic blood pressure (DBP) at < 105 mmHg after revascularization TICI 2b or 3 [21]. The SNACC (Society for Neuroscience in Anaesthesiology and Critical Care) recommends per-procedural SBP between 140 and 180 mmHg, and DBP < 105 mmHg [22].

The degree of recanalization of the artery is an important point, especially insofar as spontaneously lowered blood pressure has been observed following successful recanalization and normalized intracranial haemodynamics [23].

The one presently available work on the subject is the BP-TARGET study (Blood Pressure Target in Acute Stroke to Reduce Haemorrhage After Endovascular Therapy) [24]. It is a multicenter randomized controlled prospective study including successfully recanalized patients (TICI 2b and 3) in which an intensive strategy (target SBP 100-129 mmHg) *vs.* a standard strategy (target SBP 130–185 mmHg) was proposed. The primary endpoint consisted in appearance of haemorrhage on CT at 24–36 hours. All in all, the 158 randomized patients in the intensive arm had the same incidence of cerebral haemorrhage as the 160 patients in the standard arm, and a comparable functional prognosis at 3 months. That is why, according to the currently available evidence on haemorrhagic risk and functional prognosis at 3 months, it would be of no interest to maintain SBP targets at <130 mmHg.

Numerous retrospective studies have reported congruent results regarding the upper limit of SBP. The retrospective study by Matusevicius *et al.,* in which 2920 patients were included, concluded that SBP > 160 mmHg was associated with a poor prognosis for satisfactorily reperfused patients (TICI > 2b) [25]. In the retrospective study by An *et al.,* maximum SBP of 155 mmHg was determined to be the threshold value associated with increased risk of intracranial haemorrhage [26]. Ding *et al.* reported a similar result, as threshold values of 151 mmHg (AUROC 0.74 95%CI (0.66 – 0.82), $p <$ 0.001) were associated with a poor neurological prognosis and threshold values of 155 mmHg (AUROC 0.64 (0.55 – 0.73), $p =$ 0.006) associated with intracranial haemorrhage [27]. Lastly, in the retrospective observational study by Gigliotti *et al.,* SBP > 180 mmHg occurring at least once over the course of the 25 h following thrombectomy was associated with a poor mRS score at discharge [28].

Blood pressure targets must be individualized according to the characteristics of a given patient. Underlying chronic high blood pressure, for example, may necessitate specific post-thrombectomy targets. In 2 studies, only in patients with a history of chronic high blood pressure did excessive blood pressure variations during the 24 h after thrombectomy represent a risk factor for intracerebral haemorrhage [25,29].

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment, does the setting of target saturation as an objective lead to an improved neurological prognosis at 3 months?**

**R2.2 – The experts suggest maintaining patient $SpO_2$ at ≥ 95% during and after surgery so as to avoid aggravating the neurological prognosis at 3 months.**

**Expert opinion (Strong agreement)**

**Argumentation:** As of today, no study has dealt with the influence on patients' neurological prognoses of different $SpO_2$ levels during mechanical thrombectomy procedures.

While several randomized controlled studies have assessed the interest of systematic oxygen administration in patients presenting with ischemic CVA, none of them have shown this to be effective with regard to neurological evolution at 3 months [30–32]. That much said, none of the studies have dealt specifically with patients having undergone thrombectomy, and the rate of recanalization among these patients has not been reported.

Only 1 study has tested the effect of normobaric oxygen therapy in the framework of a thrombectomy procedure [33]. It was a single-center study carried out on a population consisting in patients having been admitted for ischemic CVA of the anterior circulation and having received thrombectomy with recanalization without general anaesthesia. The intervention consisted in the administration subsequent to recanalization of 15 $L.min^{-1}$ of $O_2$ supplied by a Venturi mask for 6 h. The control group received low-flow oxygen therapy by nasal cannula (3 $L.min^{-1}$) during the same 6 h period. In the intervention group 98 patients were included, and 87 in the control group. A beneficial effect of oxygen therapy at 15 $L.min^{-1}$ regarding the neurological prognosis at 3 months was reported [adjusted OR = 2.20 (1.26–3.87)], as well as benefit concerning mortality [RR = 0.35 (0.13–0.93)]. Taken alone, however, these outcomes do not suffice to justify a recommendation for systematic high-flow supplemental oxygen following recanalization by thrombectomy as other studies are needed for confirmation.

**Question: In a patient having presented with cerebral artery occlusion and receiving endovascular treatment under general anaesthesia, does per-procedure monitoring of $CO_2$ lead to improved neurological prognosis at 3 months?**

**R2.3 - The experts suggest that during thrombectomy procedures carried out under general anaesthesia, end-tidal $CO_2$ should be monitored and maintained at 35–40 mmHg, so as to avoid worsening the neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

**Argumentation:** Cerebral autoregulation (modification of cerebral blood flow in response to a modification of mean blood pressure) is profoundly impacted by $PaCO_2$ level [34]. In a patient treated by thrombectomy for ischemic CVA, the vasoconstriction

induced by excessive hypocapnia may transform the ischemic penumbra zone into an irreversibly infarcted zone. With this in mind, an incremental diminution (1 mmHg) of $PaCO_2$ induces a 3.5% reduction of blood flow in the middle cerebral artery [35]. Conversely, alveolar hypoventilation not only exposes the patient to a risk of hypoxemia, but also provokes cerebral arteriolar vasodilatation, which can lead to intracranial hypertension and to a phenomenon of "vascular steal" to the detriment of insufficiently perfused regions. Observational studies have highlighted spontaneous hypocapnia during acute ischemic stroke [36,37], which may be provoked by somatic and psychological stress along with the perturbed respiratory patterns associated with the cerebral insult [38]. It has also been demonstrated that cerebral autoregulation, neurovascular coupling and vascular reactivity to $CO_2$ are modified in the ischemic CVA patient [36]. The influence of capnia on the prognosis of patients having undergone thrombectomy has been analysed in only two prospective cohort studies [39,40], and a before-after study [41]. In the 2014 study by Takahashi *et al.* [39] on patient data collected prospectively from 2007 to 2010 and analysed retrospectively, patients with a good neurological prognosis at 3 months (mRS 0–3) presented higher $etCO_2$ measurements at 60 and 90 min than those with a poor neurological prognosis (mRS 4–6) (respectively 35.2 *vs.* 32.2 mmHg at 60 min; OR = 0.76 95%CI (0.65−0.92), $p$ = 0.03; and 34.9 *vs.* 31.9 mmHg at 90 min; OR = 0.76 95%CI (0.61—0.93), $p$ = 0.01). Published in 2018, the work by Athiraman *et al.* [40] is a single-center, retrospective study based on data concerning 88 patients having undergone thrombectomy under general anaesthesia between 2010 and 2014. After adjustment for age and NIHSS score, the authors observed that the patients with a good neurological prognosis (mRS 0–2) presented a higher maximum $etCO_2$ level than those with a poor neurological prognosis (mRS 3–6) (49 ± 8 *vs.* 45 ± 7 mmHg; OR = 1.14 95%CI (1.02–1.28); $p$ = 0.02). However, no difference was found in median $etCO_2$ level between the "good" and the "poor" neurological prognosis groups (36 [34–40] *vs.* 35 [33–37] mmHg; $p$ = 0.09). Published in 2016, the work by Mundiyanapurath *et al.* [41] is a before-after study including patients having undergone thrombectomy under general anaesthesia. It was initially carried out with retrospective collection of data from 2008 to 2010 on 60 patients, and then, after implementation of a protocol imposing strict $etCO_2$ control (between 40 and 45 mmHg) by retrospective collection of data from 2012 on 64 patients. In univariate analysis only, the authors found a statistically significant association between a prolonged time lapse (>105 min) of $etCO_2$ between 40 and 45 mmHg and a poor prognosis (mRS 3–6). As a result, when $etCO_2$ is measured in patients under general anaesthesia with an invasive airway approach, values outside of the physiological norms (<35 and >40 mmHg) seem to be associated with an unfavourable neurological prognosis, leading the experts to suggest $etCO_2$ target values between 35 and 40 mmHg.

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment under sedation, does per-procedure monitoring lead to improved neurological prognosis at 3 months?**

### R2.4 – The experts suggest, during thrombectomy procedures carried out under sedation, that end-tidal $CO_2$ be monitored, so as to verify the persistence of the patient's spontaneous ventilation.

**Expert opinion (Strong agreement)**

**Argumentation:** As regards the recommendation of systematic monitoring of $etCO_2$ during thrombectomy under sedation, it is essentially based on the contribution of this technique to the reduction of per-procedure episodes of desaturation and hypoxemia; this was illustrated in 2 meta-analyses [42,43]. Over recent years, $etCO_2$ monitoring has been substantially improved [44–46], and it now ensures reliable surveillance of respiratory frequency and early detection of hypoventilation episodes in spontaneously breathing patients. In these situations, however, non-invasive evaluation of $PaCO_2$ by $etCO_2$ is neither reliable nor precise; moreover, it is influenced by supplemental oxygen flow rates, contamination by atmospheric air, and preferential ventilation of dead space in patients suffering from chronic respiratory disease [44,45,47]. In a prospective clinical pilot study, every 30 min for 2 h, Lemurzeaux *et al.* compared $etCO_2$, transcutaneous pressure in $CO_2$ ($PtcCO_2$), and $PaCO_2$ in 25 non-intubated patients in respiratory distress [47]. In this population, the correlation (R = 0.62), mean bias (13.9 mmHg) and limits of agreement (-5.6–33.6 mmHg) between the measurements provided by the 2 techniques did not suffice to render them interchangeable. Conversely, the values provided by measurement of $PtcCO_2$ were better correlated with $PaCO_2$ (R = 0.97), mean bias (1.7 ± 3.9 mmHg) and limits of agreement (-5.8–9 mmHg), which were more compact and closer to those recommended by the American Association for Respiratory Care (1.96 ± 7.5 mmHg) [46]. Present-day limitations to widespread utilization of $PtcCO_2$ technology stem from its high cost, its uneven availability, a need for regular calibration and an incompressible time lapse (a few minutes) between its installation on a patient's skin, and complete calculation of a value [46].

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment, does per-procedure monitoring of glycemia lead to improved neurological prognosis at 3 months?**

### R2.5 - The experts suggest that hyperglycaemia episodes be monitored and treated, while nevertheless avoiding hypoglycaemia, which may be induced by the treatment, so as to avoid worsening the neurological prognosis at 3 months.

**Expert opinions (Strong agreement)**

**Argumentation:** Hyperglycaemia on hospital admission is observed in 40–50% of the patients admitted due to ischemic cerebrovascular accident (iCVA), whether or not they are diabetic [48]. Numerous studies have demonstrated that hyperglycaemia is associated with unfavourable neurological evolution, whatever the means of revascularization (thrombolysis or mechanical thrombectomy (TM): more extended infarct, more numerous haemorrhagic complications, less satisfactory functional recovery at 6 months, higher death rate at D30 [49–54]. From a pathophysiological standpoint, hyperglycaemia increases lactic acidosis and cytotoxic oedema, decreases cerebral vaso-reactivity and collateral circulation, and alters the haemato-encephalic (blood-brain) barrier, thereby increasing the risk of haemorrhagic transformation after revascularization. In light of these data, it has been hypothesized that strict glycaemic control could be favourable to patient outcomes. To this day, however, analysis of the published meta-analyses and randomized studies shows that strict glycaemic control by means of continuous intravenous infusion improves neither functional recovery nor mortality in patients presenting with iCVA, particularly those eligible for MT. Quite on the contrary, it increases the risk of hypoglycaemia, which in this context is probably just as deleterious as hyperglycemia [48,55–57].

## FIELD 3. Management of antiplatelet and anticoagulant treatments

*Experts: V. Seguret (GFHT) – J. Pottecher (SFAR) – JM.Olivot (SFNV) – M. Mazighi (SFNV) –S. Richard (SFNV)*

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment after having**

**been preliminarily treated by intravenous thrombolysis, does systemic per-procedure heparinization lead to improved neurological prognosis at 3 months?**

**R3.1 – The experts suggest not to carry out systemic per-procedure heparinization of cerebral endovascular revascularization in patients having preliminarily received intravenous thrombolysis, the objective being to avoid aggravating the neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

**Argumentation:** In the context of cerebral revascularization, systemic per-procedure heparinization is aimed at preventing: (a) non-perfusion in distal microcirculation; (b) thrombosis around catheters and at the level of the generated endothelial lesions; and (c) the formation de neutrophil extracellular traps (NETs). These different effects, which can contribute to improved distal revascularization (evaluated by a TICI score equal or superior to 2b) are counterbalanced by a theoretical risk of increasingly frequent intraparenchymal cerebral haemorrhage (ICH). More specifically, the effect of systemic heparinization on the neurological prognosis at 3 months (mRS at 90 days) is to be evaluated in terms of: (a) the quality of cerebral revascularization and (b) the consequences of symptomatic intra-parenchymal haemorrhage (sIPH).

The oldest studies [58,59] and/or those with the smallest population are those that report a beneficial effect, with odds ratios higher than 5, of systemic heparinization in terms of mRS at 3 months. Conversely, the retrospective studies bringing together a larger population have reported a lack of effect [60–63], or even an unfavourable effect [64] on the mRS at 3 months. The one randomized multicenter prospective study with a factorial or crossed-treatment design [65] utilizing aspirin as well as heparin (at low or moderate dose) was prematurely halted due to indication of excess mortality [adjusted odds ratio (aOR) 5.85 95% CI (1.7–20.2)] in the group of patients receiving moderate doses of heparin (5000 units as a bolus followed by 1250 UI/hour for 6 h).

Concerning the quality of cerebral revascularization at the end of the procedure (TICI 2b and 3), the results of systemic heparinization were either non-significant [58–61,63,64] or unfavourable [62].

Lastly, as concerns an association of systemic per-procedure heparinization with the risk of sIPH, the results of the retrospective analyses of the large-scale prospective registries are either non-significant [58–62], or unfavourable to heparin [63,64,66]. In the 2 most recent studies, there existed either a threshold effect [66] or a concentration-dependent effect [63], marked by increased sIPH incidence in association with the heparin concentration used in the rinsing liquid. The aforementioned randomized prospective study by van der Steen *et al.* [65] found a highly significant increase of sIPH in the group of heparin-treated patients (13%, across all doses) compared to non-heparin-treated patients [7%; aOR = 1.98 (1.14–3.46)].

To conclude, in patients having received primary intravenous thrombolysis followed by endovascular cerebral revascularization, systemic heparinization seemed neither to increase the proportions of favourable neurological prognosis nor to improve the quality of revascularization, especially in the most recent trials. Quite on the contrary, systemic intravenous heparin administration exposed patients to increased risk of apparently dose-dependent symptomatic intra-parenchymal hematoma. As a result, systemic heparinization is not recommended, and when it is necessitated for procedural reasons, small doses should probably be used.

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment without having been preliminarily treated by intravenous thrombolysis, does systemic per-procedure heparinization lead to improved neurological prognosis at 3 months?**

**ABSENCE OF RECOMMENDATION – At this time, the available literature does not allow to make a recommendation on the possible interest of systemic heparinization in patients presenting with cerebral artery occlusion treated by endovascular thrombectomy without having been preliminarily treated by intravenous thrombolysis.**

**Argumentation:** The data pertaining to systemic heparinization in patients treated by thrombectomy alone (without prior thrombolysis) are few and far between. They concern either patients contraindicated for intravenous thrombolysis [67], or patients admitted subsequent to the time frames provided for thrombolysis and included in an interventional study comparing medical treatment alone to medical treatment associated with interventional revascularization [68].

In a retrospective analysis of the French prospective registry ETIS (6 centers), 751 patients, of whom 27% were receiving heparin, were contraindicated for thrombolysis [67]. In this study, heparin administration was significantly associated with a poor neurological prognosis (aOR 1.58 (1.05–2.40); p = 0.03). The quality of cerebral revascularization was either increased in the heparin group (when TICI grades 2b and 3 are taken into consideration; aOR = 1.62 (1.06–2.48); $p = 0.03$) or decreased (taking into consideration only complete revascularization: TICI grade 3; aOR = 0.68 (0.49−0.95); $p = 0.02$), whereas counter-intuitively, the frequency of haemorrhagic complications was reduced (OR = 0.48 (0.34−0.68); $p < 0.001$).

In a retrospective analysis of the 107 patients included in the DAWN study having received cerebral revascularization, 30% were treated by systemic heparinization [68]. Favourable neurological status at 3 months (mRS 0–2) was observed in 37.5% of the patients treated by par heparin and in 52.1% of the untreated patients, a non-significant difference ($p = 0.17$). Cerebral revascularization (TICI 2b-3) was achieved in 65.3% of the patients treated with heparin and in 75.3% of the non-treated patients ($p = 0.35$), and haemorrhagic complications were not reported.

Among the 162 patients in the MR CLEAN MED study not having preliminarily received intravenous thrombolysis and included in the "systemic heparinization" arm, there was no significant difference with regard to favourable neurological status at 3 months or in intra-cerebral haemorrhage incidence [65].This result shows a lack of statistical power and cannot be extrapolated to the general population.

**Question: In a patient having presented with cerebral arterial occlusions and received endovascular treatment, does per-procedure anti-aggregation lead to improved neurological prognosis at 3 months?**

**R3.2 – In the absence of preliminary intravenous thrombolysis, the experts suggest not to systematically administer to all patients an anti-GPIIb/IIIa platelet aggregation inhibitor or a direct thrombin inhibitor; this treatment can nonetheless be proposed in case of distal embolisms during mechanical thrombectomy or in the event of persistent occlusion at the end of the procedure, the objective being to improve the neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

**Argumentation:** Utilization of platelet aggregation inhibitors during mechanical thrombectomy (MT) may have as a goal to

prevent the migration of distal emboli and to favour optimal reperfusion. Platelet aggregation inhibitors are also used as second-line treatment for occlusions or stenoses that persist following MT [69,70].

The overwhelming majority of studies in this context are designed to assess the use of tirofiban (an inhibitor of the binding of fibrinogen to the GPIIb/IIIa receptor, with a half-life approximating 2 h) [69–80], or of argatroban (a direct inhibitor of thrombin, which also inhibits platelet aggregation, and possesses a half-life inferior to one hour) [81]. There exists only 1 study in which none of patients included had undergone preliminary intravenous thrombolysis (IVT) [73]. In the other studies, a proportion ranging from 24 to 88% of the patients had undergone IVT prior to MT [72,80]. On this subject, there exists only 1 randomized trial, which included 60 patients by group (treated or not treated by tirofiban), with univariate analyses alone as judgment criteria [78]. The other studies were prospective observational or retrospective. A meta-analysis grouped together 844 patients treated with tirofiban during the MT procedure *vs.* 1645 who were not [79].

As regards functional prognosis, a gain in terms of independence at 3 months (modified Rankin score 0–2) was observed in 5 studies for the patients treated with tirofiban, with the highest odds ratio at 2.99 (1.01–8.85) [70]. The beneficial effect was confirmed in the randomized study by Zhang *et al.* [78], with a higher proportion of patients treated with tirofiban having achieved independence at 3 months compared to those who were not (61.7 % *vs.* 45%, $p = 0.024$); and likewise observed in the meta-analysis by Zhang *et al.,* who reported a significant association between tirofiban treatment and functional independence at 3 months [OR = 1.29 (1.05–1.58)] [79].

As regards quality of reperfusion, optimal reperfusion (TICI 2b-3) was more frequently achieved in the tirofiban group in the retrospective study by Kim *et al.* (86.4% *vs*. 42.4%, $p = 0.016$) [70] and in the randomized study by Zhang *et al.* (88.3% *vs*. 66.7%, $p = 0.036$) [78], that said, in multivariate analysis in the literature, particularly in the meta-analysis by Zhang *et al.* [OR = 1.32 (0.97–1.79)] [79], no significant association was highlighted.

As regards antiplatelet safety during the MT procedure, from 3.3–17.6% of the patients presented with symptomatic intraparenchymal haemorrhage (sIPH) after utilization of tirofiban [78,80] and 1% after utilization of argatroban [81]. Only 1 out of the 12 studies found more frequent sIPH occurrence in patients treated with tirofiban (14.6% *vs.* 5.7%, $p = 0.027$ and OR = 2.8 (1.0–7.9), $p = 0.049$) [72]. This did not translate in any of the studies into significantly increased mortality.

As regards local complications related to the MT procedure, only Kim *et al.* reported 2 cases of arterial dissection (1 in the argatroban group *vs.* 1 in the non-treatment group), and 3 cases of arterial perforation in the argatroban group [81].

All in all, utilization of tirofiban and argatroban during MT seems favourable to a return to functional independence in patients treated for cerebral artery occlusion. As regards safety, very few significant increases have been reported in IPH occurrence, local complications inherent to the MT procedure, or mortality. That much said, these conclusions have been drawn from studies in some of which, the level of evidence is low; what is more, the populations have been heterogeneous, particularly as regards preliminary IVT treatment.

Since the publication of these relatively small-scale studies, a multicenter Chinese randomized placebo-controlled study has dealt with the effects of Tirofiban in 948 ischemic stroke patients less than 24 h before treatment, with occlusion of the internal carotid artery or the proximal part of the middle cerebral artery and with an NIHSS score $\leq 30$, and no benefit was observed in terms of functional prognosis at D90 (mRS = 3 (1–4) in the 2 groups, aOR = 1.08 (0.86–1.36), $p = 0.50$) [82]. While there was no difference between the 2 groups regarding incidence of major intracranial haemorrhage [9.7% *vs* 6.4%, aOR 1.56 (0.97–2.56)], overall incidence of radiological intracranial haemorrhage was higher in the tirofiban group (34.9% *vs.* 28.0%, aOR = 1.40 (1.06–1.86), $p = 0.02$) [82].

**R3.3 – The experts suggest not to administer aspirin during a cerebral endovascular revascularization procedure, regardless of whether the patient has undergone preliminary intravenous thrombolysis, the objective being to avoid the risk of symptomatic intraparenchymal haemorrhage.**

**Expert opinion (Strong agreement)**

**Argumentation:** Published in 2022, the randomized multicenter prospective MR CLEAN MED study by Van der Steen *et al.* reported a doubled risk of symptomatic intracerebral haemorrhage in patients treated with aspirin during MT (300 mg administered intravenously following arterial puncture), as compared to those who had not received aspirin [14% *vs*. 7%; aOR = 1.95 (1.13–3.35)] [65]. This result was confirmed in the overall population (628 patients having received or not received preliminary thrombolysis). As regards the population limited to patients preliminarily treated by IVT (n = 466), even though the odds ratio remained unfavourable to aspirin (aOR = 1.72 (0.93–3.18) for risk of ICH), it did not reach statistical significance. By the same token, in the sub-group of patients not having preliminarily undergone IVT, aspirin administration did not lead to an improved neurological prognosis at 3 months and was associated with a substantial increase of ICH [OR = 3.01 (0.88–10.26)] that was nonetheless non-significant, possibly because the sub-group analyses were lacking in power.

**Question: In a patient having presented with cerebral artery occlusion and received endovascular treatment necessitating emergency stenting, does anti-aggregation of blood platelets lead to improved neurological prognosis at 3 months?**

**R3.4.1 – The experts suggest (single or double) anti-aggregation of blood platelets during stenting, the objectives being to avoid thrombosis and to improve the neurological prognosis at 3 months.**

**Expert opinions (Strong agreement)**

**R3.4.2 – The experts suggest to initiate anti-aggregation of blood platelets postoperatively, only after having ruled out cerebral haemorrhage by CT-scan during the 24 h following the procedure, the objective being to avoid aggravating the neurological prognosis.**

**Expert opinions (Strong agreement)**

**Argumentation:** There exists no randomized prospective study evaluating the potential gain of anti-aggregation medication when an MT procedure includes stenting. All of the published studies are retrospective, and their anti-aggregation indications and strategies were heterogeneous (tandem procedures through a stenosis of the carotid artery, etc. . .) [66,83–86]. The aforementioned studies have never compared stenting alone to stenting with anti-aggregation.

Given the specificities of the study methodologies, it is not possible to draw conclusions on potential gain in terms of functional independence due to the use of anti-platelet medication during stenting for tandem occlusions. At 3 months, functional independence (mRS 0–2) has been achieved for 37.4%–50% of the patients with stenting and antiplatelet drugs [85,86], notably with unassisted walking for 53.1–62% (mRS 0–3) [83,85]. Da Ros *et al.* found a significant association between use of dual anti-aggrega-

tion after stenting, and functional independence (OR = 6.03 (1.87–19.4), $p$ = 0.003) [66].

The observed percentages for optimal reperfusion (TICI 2b-3) are excellent: 90% and 61.1% of patients with stenting and anti-aggregation in the studies by Lee *et al.* and Da Ros *et al.* [66] respectively, and 100% of the patients reported by Elhorany *et al.* [86].

Concerning safety, between 3.2 and 27.7% of the patients treated with anti-aggregation medication presented with ICH during stenting over the course of the MT procedure [66,84]. The study by Neuberger *et al.* found no association between use of tirofiban, or of dual anti-aggregation, and ICH occurrence [85]. Da Ros *et al.* observed a negative association between post-MT dual anti-aggregation and ICH occurrence (OR = 0.21 (0.06–0.78), $p$ = 0.02) [66]. Bücke *et al.* reported higher ICH frequency in a patient population under dual anti-aggregation when aspirin is associated with ticagrelor (7.1%), in comparison with an association with clopidogrel (no ICH observed) [84]. As was the case with the different anti-aggregation strategies outlined above, of which the power was limited in some cases by small populations, the observed differences did not entail excess mortality.

To summarize, the observational studies in the literature do not permit assessment of functional prognosis gains that would be due to platelet anti-aggregation during a stenting procedure carried out in the overall framework of mechanical thrombectomy (MT). That much said, while platelet anti-aggregation stenting does not seem to be associated with ICH occurrence, there exists no comparator on stenting without anticoagulation. As a result, given the state of current practice and while awaiting studies with higher levels of evidence, the experts agree to recommend the use of platelet aggregation inhibitors in stenting during the MT procedure; however, they are currently unable to indicate an optimal therapeutic scheme.

And to conclude, recent data reporting an increased risk of intracranial haemorrhage following preliminary IVT [65] have persuaded the experts to recommend the introduction of the antiplatelet treatment only after post-MT CT-scan. This approach appears safe, while awaiting the publication of more robust studies on the subject.

## FIELD 4 – Post-procedural management and orientation of the patient

*Experts: R. Chabane (ANARLF) – S. Richard (SFNV) – F. Rapido (SFAR) – T. Geeraerts (ANARLF)*

**Question: In a patient having undergone cerebral thrombectomy under general anaesthesia, does implementation of an early neurological assessment strategy (end of sedation, early extubation) lead to improved morbi-mortality?**

**R4.1.1 – The experts suggest to stop administering anaesthesia drugs as soon as the thrombectomy procedure is over, except in the event of ventilatory failure or complications suggesting intracranial hypertension or status epilepticus, the objective being to avoid worsening morbi-mortality.**

**Expert opinion (Strong agreement)**

**R4.1.2 – The experts suggest extubation of the patient immediately after the thrombectomy procedure, provided that the usual prerequisites are present and that state of alertness is satisfactory (visual component of the Glasgow score $\geq$ 3) to avoid worsening morbi-mortality. However, responding to verbal commands is not necessary. Swallowing and coughing must also be assessed for occlusions of the posterior circulation.**

**Expert opinion (Strong agreement)**

**Argumentation:** In the literature there does not exist any study having compared, following thrombectomy with general anaesthesia, early evaluation to delayed evaluation, during which sedation and mechanical ventilation would be pursued postoperatively. It is widely recognized that one of the theoretical drawbacks of management under general anaesthesia is that it does not allow clinical monitoring of a patient as regards not only possible neurological improvement, but also – and especially – early detection of neurological complications [87]. As it does not appear logical to unduly prolong general anaesthesia and thereby forgo reliable clinical examination, it is recommended, when the usual prerequisites to extubation are fulfilled, to extubate the patient as rapidly as possible after surgery (*cf.* SFAR guidelines "Difficult intubation and extubation in adult anaesthesia" [88]). Moreover, prolonged mechanical ventilation is associated with complications such as nosocomial pneumonia, and time to extubation is associated with increased mortality in CVA patients admitted to intensive care [89]. And yet, delayed extubation remains quite frequent. In the SIESTA study, delayed extubation (defined as absence of extubation 2 hours after the end of MT) occurred in 49% of the patients in the general aneasthesia group, and due to malignant CVA, cerebral haemorrhage or pneumonia, 9.2% of patients were still intubated at H24 [15].

In a single-center Austrian observational trial including 441 patients treated by MT of the anterior circulation under general anaesthesia (not including malignant CVA), median mechanical ventilation was 3 [1–530] hours [90]. Fifty-eight percent of patients could be extubated within 6 h, 34% between 6 and 24 h, and 8% after 24 h. Early extubation ($<$ 6 h) was associated with a more favourable neurological prognosis (mRS $\leq$ 2) at 3 months than extubation carried out between 6 and 24 h and, *a fortiori*, more than 24 h. Time before extubation of 6–24 hours *vs.* $<$ 6 h was associated with admission during the "permanence of care" period, a factor conducive to undue delays in extubation. In addition to being associated with the prognosis at 3 months, mechanical ventilation duration was significantly associated with occurrence of pneumonia and increased length of hospital stay [90].

We must nonetheless remember that due to frequent comorbidities, the population of patients undergoing endovascular thrombectomy is particularly at risk of failed ventilator weaning and/or failed extubation. More specifically, in a large-scale American cohort composed of patients having undergone MT, heart failure, diabetes and chronic respiratory disease were associated with prolonged mechanical ventilation ($>$ 96 h) [91]. There also exists a risk of Ear-Nose-Throat bleeding in patients having undergone thrombolysis, as well as possible occurrence of an oedema related to rt-PA (incidence from 0.9 to 7.9%) [92]. Lastly, more failures occur in iCVA of the posterior circulation, representing a major independent marker of extubation failure [93]. In fact, these CVAs often have respiratory repercussions due to altered states of consciousness and dysfunction of the mixed nerves of the cerebral trunk, impaired upper airway protective reflexes and, at times, disruption of respiratory control mechanisms on account of bulbo-pontine lesion [94]. In addition, revascularization by MT is quite difficult to achieve in procedures concerning the posterior circulation rather than anterior circulation, frequently leading to irreversible ischemic lesions and heightened clinical severity. Some patients can nonetheless be easily extubated, provided that the basilar artery (vertebral artery, posterior cerebral artery) is not damaged, or if revascularization has been carried out in the absence of fully constituted cerebral infarction.

**Question: In a patient having undergone cerebral thrombectomy under general anaesthesia, does implementation of an early scale-guided extubation strategy (VISAGE score,** etc.**), lead to improved morbi-mortality?**

**ABSENCE OF RECOMMENDATION – At this time, the available literature does not allow us to make a recommendation on the possible interest of scales or scores to guide early extubation and improve the morbi-mortality of patients having undergone thrombectomy with general anaesthesia.**

**Argumentation:** As of now, no study has specifically defined criteria for extubation after MT. A single-center observational study including 133 CVA patients was designed to determine a score predictive of extubation failure [93]. While 77% of the patients had received MT of the anterior (69%) or the posterior (8%) circulation, haemorrhagic CVAs were also included in the study. The independent criteria entering into the score were: duration of mechanical ventilation > 24 h (1 point), oral motor function score ≥ 4 (2 points), infratentorial CVA (2 points), and NIHSS before extubation (5−15 = 1 point; > 15 = 2 points). The area under the curve (AUC) of the score averaged 0.89 (0.83−0.95); for an overall score ≥ 4, sensitivity of 81.3% and specificity of 78.2% in predicting extubation success was attained; however, the score was not externally validated [1].

Lioutas *et al.* proposed as neurological criteria to assess extubation success: NIHSS ≤ 15 and absence of dysarthria prior to intubation [95].

There also exist extubation scores defined with regard to diverse neurologic intensive care populations. However, in the studies by Godet *et al.* [96] and Asehnoune *et al.* [97], only 8.6% et 5% of patients respectively were hospitalized in intensive care following an iCVA. Thus, the results obtained in these heterogeneous populations of brain-damaged patients (cranial trauma, subarachnoid haemorrhage, spontaneous intracerebral hematoma) are not necessarily transposable to patients having recently undergone MT.

In a systematic review with meta-analysis, Wang *et al.* identified lung disease, atelectasis, prolonged mechanical ventilation, low GCS score and inability to execute certain orders (closing the eyes, in particular), "thick" secretions and altered gag reflex as factors predictive of extubation failure in neurologic intensive care [98]. However, inability to execute other types of orders was not found to be predictive of extubation failure [98].

**Question: In a patient having undergone cerebral thrombectomy, does orientation toward an adapted care structure (intermediate care unit, stroke unit, intensive care unit) according to severity criteria lead to improved morbi-mortality?**

**R4.2 – The experts suggest that a patient having just undergone a MT procedure be admitted to a critical care unit, in priority in a stroke unit ("USI Neuro-Vasculaire", in France), with clinical surveillance (glycaemia, temperature…) and monitoring (measurement of blood pressure and oxygen saturation, ECG recording…), at least until the realisation of the control brain CT-scan at 24 h; the objective being to ensure neuroprotection, and to early detect and treat complications.**

**Expert opinion (Strong agreement)**

**Argumentation:** As of now, the validation of criteria for post-MT orientation of patients to a stroke unit or a critical care unit (intermediate care unit or intensive care unit) is difficult, for the following reasons:

- Very few studies have dealt with the question, 1 following MT [99] and 2 others following IVT [100,101].
- The methodology of these studies, of which the objective was to identify the predictive criteria for referral to critical care unit, was retrospective and observational, and could not demonstrate possible gain in terms of morbi-mortality.
- Indications and criteria for admission to intensive care unit differs between France and the United States, where the studies were conducted; as does the level of care carried out in the French "USINV" and the American "stroke units". In France, admission to intensive care unit is strongly conditioned by impairment of consciousness and airway protection, whereas in the USA, blood pressure monitoring may be sufficient grounds for admission.

Based on a cohort of post-MT patients, Duan *et al.* established some predictive factors for admission to critical care units [99]: suboptimal recanalization (TICI < 2b) (OR = 3.63), ASPECT score < 8 (OR = 3.64), and persistence of spontaneous hypodensity of the occluded artery on post-procedure CT (OR = 2.49). In a small-scale study (16 patients referred to critical care *vs.* 30 patients not requiring intensive care), Faigle *et al.* found an association between increased ischemia volume in MRI diffusion sequence and need for critical care after IVT [100]. Lastly, in 2016 the same team established a clinical predictive score for referral to intensive care unit after IVT including the following variables: black skin (OR = 3.81 (1.46–9.93), $p$ = 0.006), male gender (OR = 3.79 (1.42–10.1), $p$ = 0.008), level of systolic blood pressure on admission to hospital (OR = 1.45 (1.19–1.77) by increment of 10 mmHg, $p$ < 0.001), and NIHSS score (OR = 1.09 (0.99–1.19), $p$ = 0.07) [101].

**Question: In a patient having undergone cerebral thrombectomy, does extended stay in an expert center, possibly according to orientation criteria, lead to improved morbi-mortality?**

**R4.3 - The experts suggest not to refer the patient back, immediately after thrombectomy, to the initial admission center, the objective being to rapidly deal with a severe secondary neurological complication, if the patient presents:**
**- a haemodynamic instability;**
**- and/or a severe neurological deficit (NIHSS ≥ 15);**
**- and/or an incomplete result after control of the procedure (TICI < 2b).**

**Expert opinion (Strong agreement)**

**Argumentation:** The current literature does not justify a definitive answer to questions regarding criteria for orienting the patient immediately following MT to either maintaining her/him in the center where MT has been carried out or returning to the territorial neuro-vascular unit of initial admission. More specifically, there exists no study directly comparing the 2 strategies. Only 1 study has reported on 10 cases of post-MT patients, 8 of whom were sent back to the center to which they were initially admitted, while the other 2 were maintained in the center where the MT was performed, due to hemodynamic instability or malignant sylvian infarction, without any outcome having been indicated [102]. As a result, a strong recommendation cannot be issued. While awaiting the results of future studies, the authors propose as a precautionary measure, during the immediate post-procedural period, to maintain near the technical theatre any patients who are hemodynamically unstable, are suffering from highly severe neurological deficits, or whose thrombectomy has yielded non-optimal results (TICI < 2b), the objective being to avoid short-term neurological aggravation and an emergency return to the radiology platform and to specialized critical care.

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**Competing interests of the SFAR and ANARLF experts during the five years preceding the date of validation by the SFAR board of directors**

*Pierre Boussemart* has no direct or indirect competing interest with regard to the contents of the present PPR.

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