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Intensive Care Management Following Endovascular Clot Retrieval for Acute Stroke: A Systematic Review of the Literature

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Abstract

There has been an increase in the number of patients requiring ICU care following endovascular clot retrieval (ECR) for acute ischemic stroke (AIS). The authors' objective was to systematically assess the evidence surrounding postprocedural care of ECR patients in critical care areas. A systematic literature review was conducted examining the critical care management of adult patients following ECR. The preliminary search results were sorted manually by two authors and conflicts were settled by consensus with a third reviewer. References of key papers were also reviewed for studies meeting the inclusion criteria. In addition, the authors sought to identify all relevant practice guidelines from major neurological and critical care societies. Study quality was assessed using the Newcastle Ottawa Quality Assessment Scale for cohort studies. Medline, Embase, Cochrane Central Register of Controlled Trials databases, Web of Science, and bibliographies of retrieved articles were searched. Studies were limited to human subjects and English language. Studies specific to the post ECR population were limited. In the initial Medline search, 3,882 papers were returned. A total of 16 studies met the inclusion criteria. There were also 10 practice guidelines from relevant scientific bodies. The level of evidence for postprocedural care was found to be variable and mostly based on expert opinion and data extrapolated from general stroke and postthrombolysis patients. There is limited evidence guiding the postprocedural care of ECR patients. Given the increase in both the availability and application of ECR, trials looking specifically at how best to care for this patient population are needed.

Keywords
- mechanical thrombolysis
- balloon embolectomy
- thrombectomy
- endovascular procedures
- intracranial embolism
- stroke
- brain ischaemia
- brain infarction
- critical care
- intensive care units

Introduction

Since 2010, several landmark randomized controlled trials have consistently demonstrated improved functional outcomes associated with endovascular clot retrieval (ECR) over standard stroke care alone in selected acute ischemic strokes.[1,2]

As health services adapt to facilitate emergent endovascular treatment for ischemic strokes, increasing numbers of patients are cared for in the postprocedural period in critical care environments.

The objective of this study is to summarize the recommended critical care management of adult patients who have undergone emergent ECR for acute ischemic stroke and to systematically review the evidence supporting recommended practice.

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Methods

A systematic review of the literature was first conducted to identify all clinical studies relating to the postoperative and critical care management of patients undergoing ECR.

The following electronic databases were searched for relevant studies: Medline (via Ovid interface), Embase, Cochrane Central Register of Controlled Trials databases, and Web of Science. Medical subject heading and keyword searches used are shown in ►**Table 1**.

Two authors (G.M. and L.D.) screened the results of the search and produced a list of potential inclusions. All potentially eligible articles were then obtained and the full text analyzed for inclusion. Discussion between all three authors resolved any disputes over inclusion or exclusion. The bibliographies of all included studies and relevant review articles were also manually reviewed.

Table 1 Medical subject headings and keywords used in search

'brain ischemia' or 'intracranial embolism' or 'thrombosis' or 'intracranial embolism' or 'intracranial thrombosis' or 'stroke' or 'brain infarction' or 'lacunar stroke'
combined with: 'embolectomy' or 'balloon embolectomy' or 'endovascular procedures' or 'angioplasty' or 'thrombectomy' or 'mechanical thrombolysis'.

We included any published clinical study examining the intensive care unit (ICU), critical care, or early postoperative management of adult patients following ECR for acute ischemic stroke. Expert opinion pieces, letters, and review articles were excluded as were articles written in languages other than English. No pediatric trials were included.

All included studies were appraised to ascertain their internal validity and risk of bias by a single author using the Newcastle Ottawa Quality Assessment Scale for Cohort Studies.[3]

In addition to this systematic review, a wide-ranging manual review was undertaken to identify all relevant clinical practice guidelines from all major national and international interventional neuroradiology, neurology, and critical care societies.

Results

The initial search returned a total of 3,885 studies, and after application of the inclusion criteria, 17 clinical studies were identified for inclusion. The full text of one study (a poster presentation) could not be sourced.[4] As such, 16 clinical studies were included in this review.[5-20] The flow of studies and reasons for exclusion are shown in ►**Fig. 1**.

Details of the included studies are shown in ►**Table 2**. Notably, the quality of identified studies was low; no randomized controlled trials were identified and there were few studies testing specific management interventions following

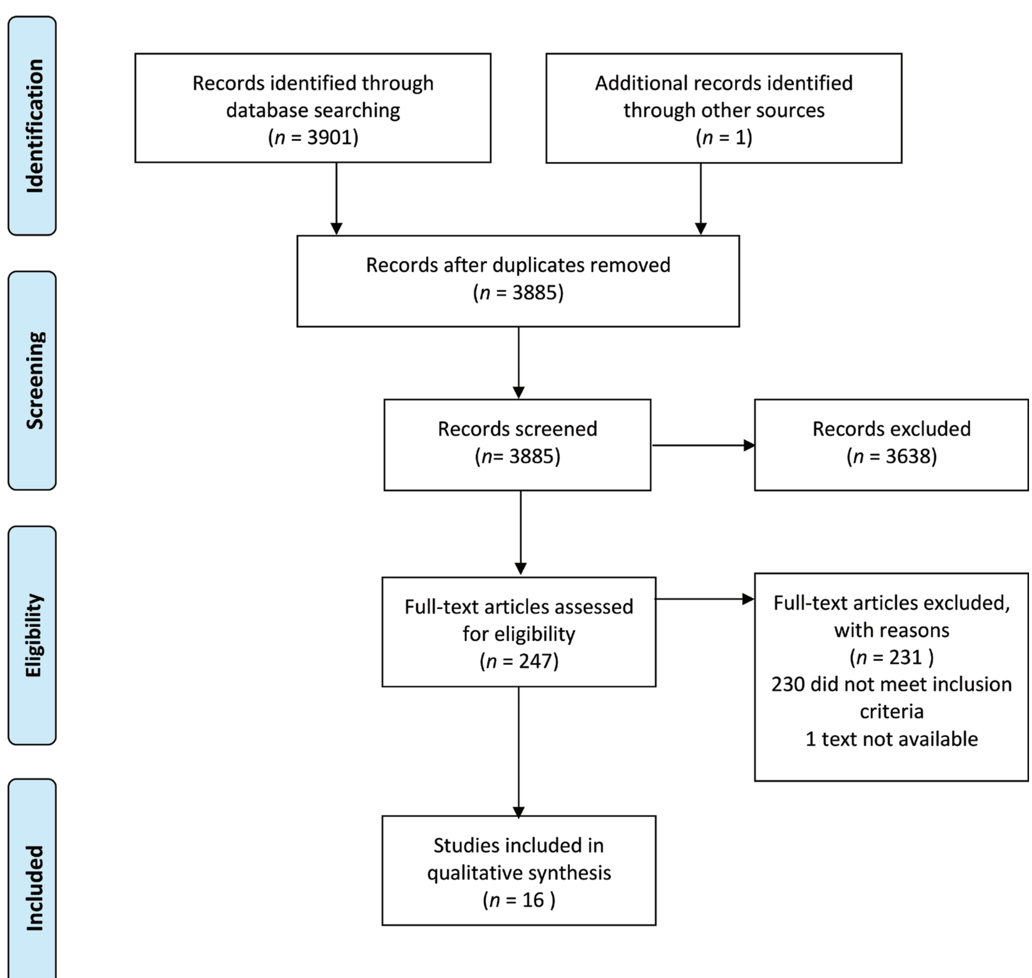

Fig. 1 Flow of inclusions of clinical studies through systematic review.

Table 2 Characteristics of included clinical studies

Study and location	Population	Study type	Exposure	Primary outcome	Stated results	Level of evidence
Khan et al (2018), USA[5]	14 adult patients in an ICU following neuro-endovascular procedure	Retrospective case series	Femoral arterial sheaths left in situ following the completion of interventional procedures	Vascular complications or delayed extubation	7 patients (50%) suffered complications–delayed extubation in 7 (50%), bleeding complications in 4 (28%)	4
Gordon et al (2018), USA[6]	79 AIS patients treated with ECR	Retrospective cohort study	Hyperglycemia (measured in various ways)	mRS at 3 months (0–2 vs. 3–6).	Hyperglycemia measured as "SD of blood glucose in first 24 hours" correlated with poor functional outcome when controlled for other predictors of poor outcome (OR = 1.07, 95% CI =1.02–1.11, p = 0.003)	2b
Chang et al (2018), USA[7]	385 AIS patients receiving IV tPA with or without ECR	Prospective cohort study	tPA with or without ECR	Timing of symptomatic intracranial hemorrhage (sICH)	For those who developed sICH, mean time from tPA dosing to sICH detection was 8.5 hours. Only 4 patients experienced a sICH > 12 hours after dosing. Combination therapy (IV tPA and ECR) substantially increased the risk of sICH (p = 0.002).	2b
Akpinar et al (2018), Turkey[8]	90 AIS patients admitted following ECR	Retrospective cohort study	Anemia (defined as Hb < 12 g/dL for women and < 13 g/dL for men)	NS	No significant difference in outcome for patients with anemia. Hb levels below 10 g/dL were associated with increased risk of mortality (OR = 9.077, 95% CI =1.215–67.823).	2b
Ritzenthaler et al (2017), France[9]	17 AIS patients with LVO of anterior circulation, treated with ECR	Prospective case series	Monitoring with cerebral near infrared spectroscopy (NIRS) during and for 24 hours after mechanical thrombectomy	NS	Frontal tissue oxygen saturations (rSO2) correlated with perfusion parameters seen on MRI (Tmax and MTT).	4
Mistry et al (2017), USA[10]	228 patients following ECR for LVO of anterior circulation	Retrospective cohort study	High blood pressure (measured in various ways)	mRS at 90 days	"Maximum systolic blood pressure" up to 180 mm Hg directly correlated with worse 90-day functional outcomes (OR = 1.02, 95%CI = 1.01–1.03, p = 0.004)	2b
Hwang et al (2017), South Korea[11]	18 patients with AIS from LVO of proximal anterior circulation with substantial ischemic burden (ASPECTS ≤ 5), treated with ECR and/or thrombolysis with successful reperfusion	Prospective case series	"Postreperfusion" targeted temperature management, targeting 34°C for at least 24 hours using an intravascular cooling catheter	NS	10 patients (55.6%) had a favorable functional outcome at 3 months (mRS ≤ 2). Treatment was complicated by pneumonia in 8 (44.4%) patients, and malignant brain edema in 6 (33.3%).	4
Goyal et al (2017), USA[12]	217 AIS patients with LVO treated with ECR	Prospective cohort study	Post ECR hypertension as defined by minimum, mean, and maximum SBP and DBP	Functional independence at 3 months (mRS 0–2)	Mean maximum SBP was significantly lower in those functionally independent at 3 months (179 mm Hg vs. 163 mm Hg, p < 0.001) and those dead at 3 months (166 mm Hg vs. 184 mm Hg, p < 0.001).	2b
Dehkharghani (2017), USA[13]	129 AIS patients with LVO treated with ECR and with confirmed successful endovascular reperfusion	Retrospective cohort study	Fever (> 37.5°C)	CT indicators of infarction growth and favorable functional outcome at 90 days (mRS of 0–2)	Significant correlation between fever and infarction growth (p = 0.002) but not poor functional outcome (p = 0.05)	2b
Nikoubashman et al (2016), Germany[14]	103 patients with AIS due to LVO who underwent ECR within 6 hours of symptom onset	Retrospective cohort study	Early extubation (within 24 h)	Functional outcome (mRS = 0–2) and mortality at 90 days, incidence of VAP	Ventilation for > 24 hours was associated with poor functional outcome, death, and higher incidence of VAP, although correlation not supported in univariate or multivariate analyses	2b

(continued)

Table 2 *(continued)*

Study and location	Population	Study type	Exposure	Primary outcome	Stated results	Level of evidence
Martins et al (2016), Portugal[15]	674 patients with AIS treated with either ECR or IV tPA	Retrospective cohort study	Blood pressure in first 24 hours	NS	Patients with higher mean SBP in the first 24 hours following treatment had worse clinical outcomes, particularly those with early recanalization on imaging who demonstrated a linear relationship between mean systolic BP and poor functional outcome	2b
Jeong et al (2016), South Korea[16]	712 AIS patients treated with IV thrombolysis, ECR, or both	Prospective cohort study	Early initiation of antithrombotic therapy (< 24 h) after recanalization treatment	Hemorrhagic transformation on follow-up imaging	Early initiation of antithrombotics were associated with decreased odds of hemorrhagic transformation (OR = 0.56, 95% CI = 0.35–0.89) but no difference in rates of symptomatic hemorrhage (OR =0.85, 95% CI = 0.35–2.10) or functional outcome (OR = 1.32, 95% CI = 0.90–1.93)	2b
Horn et al (2014), USA[17]	20 patients with AIS from proximal MCA or internal carotid occlusion with ASPECTS score of 5–7, treated with ECR	Prospective case series	Intravascular cooling to 33°C for 12 hours followed by gradual rewarming at 0.2°C/h.	NS (Feasibility study)	6 patients (30%) died due to malignant cerebral edema or due to established limitations in care; 3 patients (15%) developed new hemorrhages on imaging at 24 hours. 6 patients (30%) achieved a good functional outcome at 90 days (mRS = 0–2)	4
Jung et al (2012), Switzerland[18]	805 patients with AIS treated with IA thrombolysis, ECR, or both	Prospective cohort study	Seizures following AIS	NS	Seizures were recorded in 44 patients (5.5%). In multivariable analysis, early seizures (within 24 hours of admission) predicted an unfavorable functional outcome (OR = 4.75, 95% CI = 0.38–3.91, p = 0.014) and mortality (OR = 5.86, 95% CI = 0.77–2.95, p = 0.001)	2b
Natarajan et al (2011), USA[19]	614 patients with AIS treated with ECR	Retrospective cohort study	Hyperglycemia measured as blood glucose at admission and change in blood glucose at 48 hours from the baseline value	90-day good functional outcome (mRS =0–2)	High presenting blood glucose level (≥ 6.4 mmol/L) was significantly associated with poor functional outcome (p < 0.001). Nondiabetic patients whose blood glucose did not drop by > 1.7 mmol/L at 48 hours had a greater chance of a poor outcome (p < 0.001)	2b
Restrepo et al (2009), USA[20]	142 patients with AIS treated with endovascular procedure (tPA, prourokinase or ECR) within 12 hours of symptom onset	Prospective cohort study	Hyperlipidemia and statin use before and after AIS	NS	Elevated cholesterol prior to the stroke was associated with reduced odds of good outcome (mRS = 0–1) at 3 months (OR = 0.36, 95% CI = 0.45–0.88, p = 0.03). Statin use did not alter the odds of improved functional outcome (p = 0.1843).	2b

Abbreviations: AIS, acute ischemic stroke; ASPECTS, Alberta Stroke Program Early CT Score; DBP, diastolic blood pressure; BG, blood glucose; ECR, endovascular clot retrieval; Hb, hemoglobin; ICU, intensive care unit; IA, intra-arterial; IV, intravenous; LVO, large vessel occlusion; MRI, magnetic resonance imaging; MTT, mean transit time; mRS, modified rankin score; rSO2, regional brain oxygen saturation; sICH, symptomatic intracerebral hemorrhage; SD, standard deviation; NA, not applicable; NIRS, near infrared spectroscopy; NS, not stated; OR, odds ratio; tPA, recombinant tissue plasminogen activator; SBP, systolic blood pressure; Tmax, time-to-maximum; VAP, ventilator associated pneumonia; 95% CI, 95% confidence interval.

Note: Level of evidence as described by the Oxford Centre for Evidence-based Medicine.[21]

ECR. Most studies involved retrospective analysis of prognostic variables amongst a cohort of patients undergoing ECR. There were several small prospective case series describing specific interventions following ECR.[9,11,17]

The results of the validity assessment are shown in **Supplementary Table S1** (online only). The overall risk of bias amongst the included studies was high. No randomized studies were identified. Almost all were retrospective cohort studies. While all studies drew the exposed and nonexposed groups from the same cohort, several studies defined the exposure in multiple ways. Most used logistic regression modelling to control for confounding and imbalances between groups, however, few described a blinded method of outcome collection, and few clearly demonstrated that outcome of interest was not present at the start of the study period.

The search for clinical practice guidelines included all major local and international societies for critical care, interventional neuroradiology, and stroke and identified 14 guidelines for inclusion.[22-35] Of these, two were specifically aimed at management following ECR.[26,30] The majority of identified guidelines focused on the management of the broader acute stroke population, with few specifically examining the post ECR patient population. The levels of evidence varied widely within these documents. A summary of the recommendations of the identified clinical practice guidelines is included as **Supplementary Tables S2**, **S3**, and **S4** (online only).

Discussion

Post ECR clinical management strategies, supported by the identified studies and clinical practice guidelines, are summarized below.

Postoperative Monitoring

Ventilation and Oxygenation Management

Extubation is recommended after a successful spontaneous breathing trial and demonstration of adequate sputum clearance and bulbar function. The quality of evidence informing this recommendation is recognized as very low.[22] Tracheostomy should be considered if extubation is not possible within 7 to 14 days[22]

Although the retrospective study by Nikoubashman et al demonstrated worse outcomes in patients who remained intubated beyond 24 hours,[14] it is not clear if this merely reflects a difference in the severity of underlying injury, rather than an effect of prolonged intubation per se.

While intubated, ventilatory support should be adjusted to maintain normal levels of arterial carbon dioxide (CO_2) and oxygen (O_2) saturations > 93%.[36] No studies or guidelines recommend the routine use of low or low-normal CO_2. Intubated patients should be monitored with continuous oximetry and end-tidal capnography.[37]

Following extubation, supplemental oxygen should be provided to achieve O_2 saturations > 93% only; hyperoxia or hyperbaric oxygen are not recommended.[22,37]

Blood Pressure Management

The management of blood pressure (BP) following ECR is made complex by the potential for immediate and complete revascularisation. As such, there is emerging concern that permissive hypertension following ECR may be harmful.

Several identified clinical studies suggested worse 90-day functional outcomes in patients with higher blood pressures in the first 24 hours following ECR.[10,12,15] Martins et al (2016) found that this was particularly true in patients with confirmed recanalization following ECR. In this group, a linear relationship between mean systolic BP and an increasingly poor functional outcome was demonstrated.[15]

Most guidelines provide BP targets reflecting generalized recommendations following acute ischemic stroke (AIS), managed either with or without thrombolysis. Guidelines from The Society of Neurointerventional Surgery recommend hemodynamic augmentation in patients with failed or incomplete recanalization following ECR.[26] They recommend maintaining a mean arterial pressure 10 to 20% above the baseline BP, while keeping the systolic blood pressure to a maximum of 185 mm Hg if intravenous (IV) tissue plasminogen activator (rtPA) has been administered.[26] These guidelines do not provide specific recommended targets in those who have been successfully recanalized.[26]

Temperature Management

Three of the identified clinical studies focused on temperature management following ECR.

Hwang et al and Horn et al both reported small case series of patients with moderate to severe strokes (based on Alberta Stroke Program Early CT Score [ASPECTS] at baseline) from a proximal occlusion who received hypothermia (33–34).[11,17] Despite positive results such studies can only be considered hypothesis testing. As such most guidelines do not recommend induced hypothermia.

Dehkharghani et al[13] reported a significant correlation between fever and infarction growth ($p = 0.002$) but not poor functional outcome ($p = 0.05$). Simple treatment of fevers with antipyretics and investigation of their source is recommended in several guidelines.[24,38]

Management of Blood Sugar

Gordon et al and Natarajan et al both report retrospective cohort studies that suggest a correlation between hyperglycaemia in early acute stroke treated with ECR and poor functional outcome.[6,19] In line with the recommendations of AIS more broadly, most guidelines recommend treatment of hyperglycaemia in excess of 10 mmol/L (180 mg/dL).[24,38,39]

Neuromonitoring Strategies

The identified prospective cohort study by Chang et al may provide some insight into the required length of monitoring in an ICU environment.[7] Few patients suffered a spontaneous intracerebral hemorrhage (ICH) beyond 12 hours after dosing, and all were within 25 hours of admission. As such, it seems reasonable to observe patients within the ICU setting for 12 to 24 hours, assuming no other complications are identified.

Although advanced methods of neuromonitoring, such as those trialed by Ritzenthaler et al offer some promise, no guidelines yet recommend their routine use.[9]

Prevention of Complications

Patient Positioning

Patient positioning can improve cerebral perfusion by increasing cerebral blood flow by as much as 15 to 20%.[26] It is suggested by two society guidelines to maintain a supine position unless there are concerns regarding risk of aspiration[26] or increased intracranial pressure (ICP) in patients with large hemispheric infarcts.[22]

Management of Dysphagia

There were no ECR specific studies identified in our literature review which addressed questions on dysphagia or nutritional management in the post ECR population. Swallowing screening is recommended across all guidelines[22-24,27,33,40] before oral intake in the general stroke population. The recommended timing of this assessment varies from admission, within 4 hours of admission, or soon after extubation. The screening should be performed by a trained health care professional and speech pathology assessment recommended for those who fail screening.[22,23,27,33,40] For those patients suspected of aspiration, an instrumental evaluation is recommended.[23,40]

Nutrition and Hydration

All patients should have hydration status assessed on admission and normal hydration maintained.[33,40] For those with ongoing dysphagia, nasogastric tube insertion is recommended within a range of 24 hours to 7 days.[23,33,40] Those who require nasogastric feeds for greater than 3 to 7 days should be reassessed and percutaneous endoscopic gastrostomy tube insertion considered after 1 to 2 but within 3 weeks of admission.[23,33,40] Routine nutritional supplementation is not recommended except for those who are at risk of malnutrition.[23,33,40]

Deep Venous Thrombosis (DVT) Prophylaxis

In all immobile stroke patients, intermittent compression stockings are recommended.[22,23,25,28] The Neurocritical Care Society Guideline for large hemispheric stroke specifically recommends this also for ECR patients.[22] Elastic compression stockings are more controversial with most major societies not recommending their use.[22]

Only one society has a recommendation specifically for the post ECR patient, the Neurocritical Care Guidelines recommend pharmacological DVT prophylaxis to commence immediately after the procedure for thrombectomy patients.[22] Three of the guidelines recommend low molecular weight heparin over unfractionated heparin for DVT.[23,25,28]

Anticoagulation and Antiplatelet Management

In our literature review, we identified one relevant prospective cohort study which included patients who had received ECR and/or thrombolysis.[16] This study found that early initiation of antithrombotic therapy (i.e., less than 24 hours after treatment) was associated with decreased odds of hemorrhagic transformation (odds ratio [OR] = 0.56, 95% CI = 0.35–0.89), but no difference in rates of symptomatic hemorrhage (OR = 0.85, 95%CI = 0.35–2.10), or functional outcome (OR = 1.32, 95%CI = 0.90–1.93).[16] There are no guidelines that refer to antiplatelet management specifically for the ECR population. For patients who have received thrombolysis, all major society guidelines recommend delaying antiplatelet therapy for 24 hours.[23,27]

Urgent anticoagulation is not recommended post stroke,[23] and a delay between 1 to 4 weeks is recommended depending on infarct size and the underlying thrombotic risk.[22,33,40] Patients should not be routinely anticoagulated unless there is a clear clinical indication.[23,27,33,40]

Management of Postoperative Complications

To decrease the risk of all complications, it is recommended that ECR is only conducted in high volume centers by trained personnel.[41]

Cerebral Edema

Neuronal cell death following stroke causes cerebral edema which peaks from day 2 onwards.[42] Significant mortality and morbidity can follow especially in large volume middle cerebral artery territory infarcts or those in the posterior fossa. No trials address the specific question of how to manage this complication in the post ECR patient.

The societal recommendations do not deviate from standard treatment of raised intracerebral pressure and cerebral edema. Most recommendations are extrapolated from both general stroke populations and other patient groups with cerebral edema.[22-24] Judicious osmotherapy and hyperventilation is advocated only if swelling occurs. The Neurocritical Care Society go further and give guidance on which hyperosmotic agent to use and how (see **Supplementary Table S4,** online only). Prophylactic use of these therapies is not indicated and they should be used solely as a bridge to more definitive care. Barbiturates and steroids are not recommended.[23,24,26]

Neurosurgical opinion should be sought early for a possible neurosurgical intervention.[23,24] Decompressive craniotomy has been extensively debated in the literature[43,44] and may improve mortality at the cost of functional outcome. Extensive conversations with all treating teams and families are needed before undertaking this intervention.

Basic management of cerebral edema should be followed including reduction in mechanical obstruction by using "neuro tapes" and raising the head of the bed[45,46]. Control of variables associated with raised intracerebral pressure, such as $CO2$ and serum sodium are not specifically addressed but seem reasonable. The use of ICP monitors in this patient population has not been explored.[47]

Cerebral Hemorrhage

Postprocedure intracerebral hemorrhage can be a catastrophic complication of ECR. The risk in patients that have undergone both thrombolysis and ECR is not higher than patients who have only had intravenous thrombolysis.[7,23,24] The treatment of intracerebral hemorrhage in the context of thrombolysis is beyond the scope of this review. However, reversal of antifibrinolytic therapy should be strongly considered along with aggressive control of BP to decrease hematoma size.[45] Subarachnoid hemorrhage (SAH) may also occur with subsequent vasospasm.

Seizures

The incidence of seizure in one prospective analysis of ECR patients in a single center was 5.5%.[18] Early seizures which occur within 24 hours of stroke onset have been linked to worse outcomes in the post ECR population.[18] Even considering this, both the American Heart Association (AHA) and the European Stroke Organisation (ESO) guidelines state seizure prophylaxis is not recommended.[23,24,35]

No studies were identified in this review which addressed the acute management of seizures in post ECR patients. If patients have recurrent seizures, consideration for antiepileptic drug (AED) is recommended by the AHA with the agent based on patient characteristics.

Vascular Injury

Femoral sheaths are used during ECR as access points and can be left in situ for reintervention or in the case of overt coagulopathy. Complications related to vascular access include hematomas (retroperitoneal and groin), distal ischemia, and femoral artery pseudoaneurysms.[48] Any unexplained anemia, back pain, or signs of poor perfusion in the associated limb should be investigated. Shah et al found a low complication rate in their retrospective analysis with a rate of 0.4 to 0.8% in patients with large bore sheaths.[48] These sheaths should be removed as soon as possible with data suggesting an increase in complication rates proportional to the duration of time in situ.[5] Sheaths should be removed by staff who are trained to do so.[49]

Pressure on larger arteries during removal may cause vagal episodes.[50] Ongoing bleeding may require surgical intervention.

Intravenous Contrast Agents

Concern over contrast induced nephropathy in ECR patients due to contrast loads from both CT studies and the ECR procedure has been noted. No studies identified in our search looked specifically at how to treat ECR related contrast induced kidney dysfunction.

Conclusion

The evidence base for the care of post procedure ECR patients is limited. The majority of recommendations are extrapolated from the society guidelines aimed at the management of the broader stroke population. The specific ECR population may differ from the broader stroke population in some aspects and this should be considered when applying these recommendations. The small number of studies we identified, which were specifically aimed at post ECR patients, are of limited quality. The areas where further research is essential in the ECR population include postprocedural blood pressure management, and the management of specific complications such as vasospasm.

Conflict of Interest

None declared.

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