Cerebral Venous Sinus Thrombosis (CVST) Assessment and Management of Adult Patients in Greater Manchester, Lancashire and South Cumbria Policy and Guidelines for

Salford Royal NHS
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Summary of Policy

A. Cerebral venous thrombosis (CVT) should be considered in the following groups of patients

- Patients presenting with new, sub-acute headache suggestive of raised intracranial pressure (ICP)
- Pregnant patients in the third trimester or puerperium who present with new headache suggestive of raised ICP
- Patients with new headache suggestive of raised ICP who have a history of venous thromboembolism
- Patients presenting with thunderclap (sudden, maximal at onset) headache
- Patients presenting with progressive neurological decline including any of headache, focal neurological signs, seizures, altered mentation, ENT infection, meningism
- Patients with atypical site of intracerebral haemorrhage (ICH)/multiple sites of haemorrhage
- Patients with ischaemic stroke crossing arterial territories/bilateral stroke

Clinicians should have a higher index of clinical suspicion for all such presentations in patients known to have hereditary thrombophilia or lupus anticoagulant.

B. Patients in whom cerebral venous thrombosis is considered should undergo urgent imaging of the brain and cerebral venous system guided by local radiologists. In most centres this is likely to be CT brain and CT venogram due to ease of access and quality of venous imaging.

C. Patients in whom the diagnosis of cerebral venous thrombosis is made should undergo initial investigation of aetiology, bearing in mind that most cases have more than one risk factor

- FBC/Renal/Liver/Bone/clotting profiles
- D-Dimer (if pre imaging)
- Full thrombophilia screen (Protein C and protein S, and antithrombin, factor V Leiden, and prothrombin gene mutation, lupus anticoagulant should be tested 6 weeks after cessation of anticoagulant therapy as results are unreliable in acute thrombosis and with anticoagulation)
- Full drug history, in particular history of taking the oral contraceptive pill
- Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and antinuclear antibodies

- Urine protein
- Lumbar puncture (LP) should be considered and discussed with the visiting neurologist or the neurology team at the regional neurosciences centre (Salford Royal NHS Foundation Trust (SRFT) or Lancashire Teaching Hospitals NHS Foundation Trust (LTHFT) prior to the initiation of anticoagulation.

D. All patients with a confirmed diagnosis of CVT should be discussed with the on-call regional neurology team at the regional neurosciences centre.
   - The expectation for confirmed cases would be for patients to be transferred to the regional neurosciences centre if safe and appropriate. In most patients transfer could be during normal working hours. If it is felt urgent transfer out of hours is needed then assessment by the local medical and intensive care team should take into account the stability of patient for transfer. It will be important to identify the critical care capacity in the receiving centre for such patients if necessary. If no neuroscience bed is available then transfer to an acute stroke unit should be considered with a view to onward transfer to the neurology unit when a bed becomes available.
   - In exceptional cases it may be considered in the patient's best interests to remain in the local district hospital, where daily contact should be made with the neurology team
   - Cases which are related to surgical complications (such as ENT/neurosurgical) would normally remain under the care of the surgical team if appropriate neurosciences support can be achieved
   - There are no obstetric facilities at SRFT and patients in the Greater Manchester area who are 20 weeks pregnant or more, or immediately post-partum, will not be able to access GMNC. Such patients requiring transfer to a neurosciences centre will need to be discussed with the on-call neurology team at LTHFT.
   - For patients who are pregnant, a case by case discussion should be had as to where the patient's best interests are served but ideally should be where medical and obstetric care is co-located. In Greater Manchester, in general, patients who are 20 weeks pregnant or more would not access GMNC. For many patients, regardless of the stage of pregnancy, it may be more appropriate for them to remain in the district general hospital where their obstetric care is based and ideally this would be on a stroke unit with in-reach from the neuroscience team as appropriate. For patients who require assessment at a regional neurosciences centre this should be discussed with the relevant team, either at SRFT or LTHFT and a decision made as to whether the patient requires transfer. If an inpatient stay is thought

likely then transfer should be to LTHFT. If a discrete assessment/intervention is thought most appropriate then this could be delivered at SRFT.

E. The management of patients with CVT would normally be anticoagulation with heparin even in cases with intracerebral haemorrhage. The standard of care is usually low molecular weight heparin (LMWH) at the same dose ranges as for treatment of pulmonary embolus, though in certain circumstances unfractionated heparin may be used.

- Anticoagulation should be started as soon as possible after diagnosis unless LP is indicated.
- In some cases (large haemorrhage with mass effect, possibility of need for LP, possibility of need for surgical intervention, other active bleeding risk) intravenous (iv) unfractionated heparin may be considered more appropriate, assuming adequate experience in the use of iv heparin for its safe administration.

F. Patients with seizures should be treated early with appropriate antiepileptic medication

G. Early neurological deterioration can be seen in up to 25% of cases. If deterioration occurs despite optimum anticoagulation then surgical/radiological intervention could be considered and discussed with the appropriate team

H. Patients may be considered for transfer back to their local hospital for further care/rehabilitation once the treating consultant considers it safe to do so

- Patients should be referred to their local anticoagulation service for on-going management of anticoagulation.
- Usual practice would be to continue heparin until warfarin therapy achieves an INR within the desired range (2-3)
- Patients should be followed up by their local neurologist at least on one occasion
- It is reasonable for patients to undergo follow up brain and venous imaging 4-6 months after commencement of anticoagulation to look for evidence of recanalization, subject to the discretion of the local neurologist and neuroradiologist.
- Duration of anticoagulation will be dependent on aetiology but the following are broad guidelines:

i. Provoked CVT (associated with a transient risk factor), anticoagulation should be continued for 3 to 6 months, with a target INR of 2.0 to 3.0
ii. Unprovoked CVT, anticoagulation should be continued for at least 6 months or long-term, depending on individual patients, with a target INR of 2.0 to 3.0
iii. Recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia (two thrombophilic factors, or lupus anticoagulant), long-term anticoagulation should be considered, with a target INR of 2.0 to 3.0

Introduction

Aim of the Guideline:

This document aims to provide standards of care for patients with cerebral venous thrombosis throughout Greater Manchester, Lancashire and South Cumbria. The document is primarily aimed at secondary care and whilst it is hoped the information contained within will provide some educational support, it was not conceived nor written as a comprehensive and systematic review of the disease, but can be read in conjunction with the two published and referenced international guidelines (European Federation of Neurological Societies and American Heart Association/American Academy of Neurology). The recommendations within the document for patient transfers and care are mainly on the basis of those patients already diagnosed with cerebral venous thrombosis in a secondary care setting.

Plans for Dissemination of the Guideline:

The agreed final version of the document will be circulated to all NHS Trusts, Health Authorities and Clinical Commissioning Groups throughout Greater Manchester, Lancashire and South Cumbria. It will also be made available on Salford Royal NHS Foundation Trust and Lancashire Teaching Hospitals NHS Foundation Trust intranet sites.

Plans for Updating the Guideline:

After a suitable timeframe the effect of the guideline will be reviewed and amended as necessary.

Key Recommendation:

All patients with proven cerebral venous thrombosis should be referred to and, where safe and appropriate, managed in the regional neurosciences centre at SRFT (Greater Manchester Neurosciences Centre) or LTHFT (Lancashire and South Cumbria) or, if there is no available neurosciences bed, in an acute stroke unit.

List of abbreviations

AED	Anti-epileptic drug
ANU	Acute neurology unit
ASU	Acute stroke unit
CNS	Central nervous system
CRP	C-reactive protein
CT	Computed tomography
CTV	CT Venogram
CVT	Cerebral venous thrombosis
DGH	district general hospital
DVT	Deep vein thrombosis
ENT	Ear, nose and throat
ESR	Erythrocyte sedimentation rate
EVD	External ventricular drain
FBC	Full blood count
GCS	Glasgow Coma Scale
GMNC	Greater Manchester Neurosciences Centre
GRE	Gradient echo
HIV	Human immunodeficiency virus
ICH	Intracranial haemorrhage
ICP	Intracranial pressure
INR	International normalised ratio
LMWH	Low molecular weight heparin
LP	Lumbar puncture
LTHFT	Lancashire Teaching Hospitals NHS Foundation Trust
MCA	Middle cerebral artery
MRI	Magnetic resonance imaging
MRV	Magnetic resonance venogram
NHS	National Health Service
OCP	Oral contraceptive pill
PE	Pulmonary embolus
SRFT	Salford Royal NHS Foundation Trust
SWI	Susceptibility weighted imaging
VPS	Ventriculo-peritoneal shunt
VTE	Venous thromboembolism

Background

Cerebral venous thrombosis (CVT) is a complex disease affecting all age groups. Although there may be many causes, the primary pathology is thrombosis within the draining veins of the brain, and resulting complications. The aetiology is often multifactorial and presentation is varied both in terms of severity and clinical syndrome. The majority (56%) of patients present acutely within 48 hours of symptom onset. A large minority of patients (37%) present in a sub-acute phase (48hrs to 30 days) and a small minority (7%) with a chronic phase (>30 days). The incidence of CVT is variably reported as from 0.5 (Bousser & Ferro, 2007) to 1.2 (Janghirbani, et al., 2008)per 100,000. The majority of cases (78%) occurs in the <50 years age group (Canhao, et al., 2005).

Given the broad range of presentations both in terms of syndromes and timescales, and the complexities of management, international guidelines suggest that care in an organised environment is optimal (Saposnik, et al., 2011). Management of such patients at a regional neurosciences centre may be the most effective way to deliver such care. Organising care in such a centralised way would allow a consistent and high quality care to be provided for each and every patient with this uncommon and difficult to recognise condition.

This document sets out the approach to achieving this aim.

Practice, Evidence and Guideline

1. Recognising patients with cerebral venous thrombosis

1.1. Clinical presentation

1.1.1. Clinical presentation tends to be with one of three types of syndrome
1.1.1.1. Symptoms of raised intracranial pressure (ICP)
1.1.1.2. Focal neurological symptoms
1.1.1.3. Mixed raised pressure and focal symptoms

1.1.2. Symptoms tend to be progressive and diagnostic delay is not uncommon

1.2. Presenting symptoms and signs

1.2.1. Headache is seen in 90% of patients as part of their presentation and is often indicative of raised intracranial pressure (80% of cases). The headache is typically described as diffuse and progresses over days to weeks. 'Thunderclap' headache may also be a presenting feature as can headache with clinical features of migraine. Headache as an isolated symptom has been reported in up to 25% of cases (Patronas, et al., 1981).

1.2.2. Papilloedema is a common finding and represents raised intracranial pressure either from severe venous obstruction, diffuse cerebral oedema, or malignant haemorrhage and infarction and secondary cerebral oedema (associated with lateralising neurological signs).

1.2.3. Diplopia may also be a feature of raised intracranial pressure, a so-called 'false localising sign'

1.2.4. Seizure is frequently seen (approximately 40% of cases) reflecting discrete cortical insult and/or cerebral irritation

1.2.5. Other symptoms or combination of symptoms may often give clues as to the location of thrombus.

1.2.5.1. Superior sagittal sinus: Headache, raised ICP, papilloedema, scalp oedema, dilated scalp veins, motor deficits with or without seizures

1.2.5.2. Lateral sinus: Pain in ear/constitutional symptoms if infected, raised ICP, distension of scalp veins, hemianopia, contralateral weakness, aphasia.

1.2.5.3. Deep sinuses: Rapid neurological/conscious deterioration

1.2.5.4. Cortical veins: Rare, typically stroke or seizure

1.2.6. Always check mental state and Glasgow Coma Scale (GCS)

1.2.7. Always check for signs of meningism

1.2.8. Always perform fundoscopy to look for evidence of raised ICP. If ICP is elevated with visual symptoms, close monitoring of visual fields and severity of papilloedema is important (Saposnik, et al., 2011).

1.2.9. Always perform otoscopy to look for evidence of infection

2. Causes of cerebral venous thrombosis

2.1. The causes of CVT are multiple and varied. They often co-exist in the same patient

2.2. Up to 34% of patients have an inherited or acquired prothrombotic condition (Ferro, et al., 2004).

2.2.1. Compared to the general population patients with CVT are more likely to have Protein S/C deficiency (Martinelli, et al., 1998) (Bombeli, et al., 2002), antiphospholipid/anticardiolipin antibody (Canhao, et al., 2005), hyperhomocysteinaemia or Factor V leiden deficiency or mutation in the prothrombin G20210A gene (Ventura, et al., 2004).

2.2.2. Late stage pregnancy and early post-partum phase, and oral contraceptive use are also amongst the commoner risk factors in younger women (Martinelli, et al., 1998) (Wilterdink & Easton, 2002) (De Bruijn, et al., 1998)

2.2.3. 7.4% of cases are associated with underlying malignancy (Canhao, et al., 2005).

3. Investigation of suspected cerebral venous thrombosis

3.1. Initial blood screening

3.1.1. Immediate routine blood panel including
- 3.1.1.1. FBC
- 3.1.1.2. Renal profile
- 3.1.1.3. Bone profile
- 3.1.1.4. Liver profile
- 3.1.1.5. ESR
- 3.1.1.6. CRP
- 3.1.1.7. Clotting studies
- 3.1.1.8. D-dimer (can be useful if negative unless strong clinical suspicion)

3.1.2. Urine protein

3.1.3. Further blood panel following confirmed diagnosis may include
- 3.1.3.1. Thrombophilia screen
  - 3.1.3.1.1. Antiphospholipid/anticardiolipin antibody, Lupus anticoagulant, (beta 2 glycoprotein 1 antibodies may be considered)
  - 3.1.3.1.2. Factor V Leiden and prothrombin G20210A mutation
  - 3.1.3.1.3. Protein S, Protein C and antithrombin III deficiency testing should be delayed until cessation of anticoagulation therapy
- 3.1.3.2. Anti-nuclear antibodies
- 3.1.3.3. Homocysteine
- 3.1.3.4. HIV

3.2. Imaging studies

3.2.1. Imaging of the cerebral venous sinuses should be considered in the following situations
- 3.2.1.1. Patient with headache preceding stroke
- 3.2.1.2. Patients with bilateral infarction/haemorrhage
- 3.2.1.3. Patients with infarction crossing arterial territory
- 3.2.1.4. Patients with features of raised ICP (headache/papilloedema/VI or III nerve palsy)
- 3.2.1.5. Progressive/Thunderclap/new atypical headache with known thromboembolic risk
- 3.2.1.6. Altered mentation where bilateral thalamic lesions are suspected

3.2.2. Imaging should be carried out urgently after the diagnosis of cerebral venous thrombosis is considered

3.2.3. For practical reasons most centres will have easier access to CT brain and CT venogram (CTV) especially out of hours. CTV is preferable to plain CT or post-contrast CT due to variation in clot density early in the disease (Saposnik, et al., 2011).

3.2.4. Magnetic resonance imaging (MRI) and MR venogram may be preferred in certain instances, such as need to avoid irradiation, need for more sensitive brain parenchymal imaging.

3.2.5. In chronic cases, gradient echo (GRE) or susceptibility weighted imaging (SWI) may be useful to demonstrate low signal in thrombosed sinuses (Saposnik, et al., 2011).

3.2.6. Invasive cerebral angiography/direct venography, by discussion with the vascular Neuroradiologists, is usually only considered where radiological intervention is an option or in the rare instances where CTV/MRV are inconclusive

3.2.7. Follow up imaging in the acute phase is indicated in the following circumstances

3.2.7.1. For patients who are deteriorating despite optimal therapy

3.2.7.2. For patients previously diagnosed who present with symptoms and signs suggestive of recurrence

3.2.8. Most patients (84%) recanalise within 4 months (Baumgartner, et al., 2003)and repeat imaging may be indicated within 3-6 months after initiation of anticoagulation (Saposnik, et al., 2011), though recanalization appears to have no bearing on outcome in adult patients (Strupp, et al., 2002).

4. Cerebrospinal fluid analysis

4.1. Lumbar puncture is not typically helpful in the diagnosis of cases with focal neurology and confirmed CVT (Saposnik, et al., 2011). LP may be considered appropriate in some cases, particularly those in whom intracranial infection is considered a possible aetiology

4.2. Lumbar puncture may also demonstrate abnormalities consistent with CNS inflammatory disease as a possible aetiological factor

4.3. If lumbar puncture is performed, opening pressure should always be measured with the patient in the lateral decubitus position without full flexion of the hips

4.4. Lumbar puncture should be avoided if a large lesion with mass effect is found on imaging or with evidence of severe cerebral oedema with evidence of transtentorial herniation

4.5. British guidelines published in 2013 (Harrop-Griffiths, et al., 2013) recommend the following for spinal anaesthesia. It would seem reasonable to translate this to lumbar puncture:

4.5.1. Anticoagulation with intravenous unfractionated heparin - administer the drug no earlier than 4 hours after spinal anaesthesia completed, and after stopping anticoagulation, spinal anaesthesia should be performed only after 4 hours, or normal APPT.

4.5.2. Anticoagulation with s/c LMWH - administer the drug no earlier than 4 hours after spinal anaesthesia, and do not attempt spinal anaesthesia until 12 hours after the last dose of LMWH.

4.6. If repeat lumbar puncture is thought likely to be needed then patients should be given intravenous unfractionated heparin so this can be stopped at short notice, assuming adequate experience in the use of iv heparin for its safe administration

5. Treatment of cerebral venous thrombosis

5.1. The diagnosis of cerebral venous thrombosis would normally be achieved in the acute secondary care setting.

5.2. Once the diagnosis of cerebral venous thrombosis is secured treatment should be initiated as swiftly as possible.

5.3. Organised care is one of the most effective interventions to reduce morbidity and mortality after stroke (Collaboration, 2007) (Collaboration, 1997) and it therefore seems reasonable to apply this to cerebral venous thrombosis

5.3.1. We recommend early involvement of neurological expertise for all such patients with a view to transfer to the regional neurosciences centre if safe and appropriate.

5.3.1.1. Transfer should be made safely and may be best achieved during normal working hours seven days a week, and avoided if at all possible late at night.

5.3.1.2. If there is delay to transfer, medical and nursing staff should be vigilant to the high chance of deterioration and contact the neurosciences centre again if necessary

5.3.1.3. If urgent transfer out of hours is thought necessary for patients who are deteriorating or who are believed to be at high risk of deteriorating (section 6.5) then the local medical and or critical care team should assess the patient's safety for transfer.

5.3.1.4. Critical care capacity at the receiving hospital should also be identified. In some cases it may not be considered safe for the transfer to go ahead immediately and patients could be admitted to the local critical care unit if necessary.

5.3.1.5. If no bed is available in a neurosciences unit for urgent transfer, patients should be transferred to an ASU in the first instance.

5.3.1.6. In exceptional cases it may be considered in the patient's best interests to remain in their local hospital, provided that neurological support is available or can be sought from the local neurologist or through the on-call neurology services on a daily basis

5.3.1.6.1. Such cases may include patients who are already in a specialised centre for another reason where it is thought the patient's best interests are served in that centre. An example being in patients for acute lymphoid leukaemia treated with asparaginase, where there is a known association to develop cerebral venous thrombosis. On discussion with the neurology team these patients are likely to be better served by remaining in the haematology centre in the absence of any of the observed risk factors for deterioration (see section 6.5, but in particular 6.53 to 6.59)

5.4. Treatment of any acute underlying cause should be a priority (e.g. an intracranial infection)

5.5. Anticoagulation therapy

5.5.1. The decision on when to anticoagulate such patients should only usually be made after a formal diagnosis is achieved.

5.5.2. Cases should be discussed with the regional neurosciences centre and a joint decision on the risks and benefits of anticoagulation made between the treating physician, neurologist and patient

5.5.3. Early anticoagulation is indicated in most cases to prevent clot propagation, promote recanalization and prevent distal thromboembolism

5.5.4. There are only two randomised controlled trials of anticoagulation in CVT and meta-analysis demonstrated a non-statistically significant benefit in terms of death/dependency for anticoagulation (De Bruijm & Stam, 1999) (Einhaupl, et al., 1991)

5.5.5. Anticoagulation appears safe in this patient group, even in the setting of intracranial haemorrhage (Stam, et al., 2001) and this situation is not normally considered a contraindication to therapeutic dose anticoagulation

5.5.6. Low molecular weight heparin (LMWH) is the preferred option in uncomplicated patients (Einhaupl, et al., 2010). A meta-analysis for extracranial venous thromboembolism found a superiority for LMWH with less bleeding risk (Van Dongen, et al., 2004)though there are perceived advantages of UFH for critically ill patients in terms of short bleeding time and reversal. For patients with CVT LMWH might be safer and more efficacious than unfractionated heparin (Coutinho, et al., 2010).

5.5.7. LMWH should be used during pregnancy (Saposnik, et al., 2011) (Bates, et al., 2012)

5.5.8. Once it is considered appropriate, heparin anticoagulation may be converted to oral anticoagulation therapy

5.5.8.1. It would normally be considered the responsibility of the current treating physician to initiate oral anticoagulation

5.5.8.2. If using warfarin, once established with an INR of 2-3 for at least 24 hours, heparin therapy can be stopped. Referral should then be made to the patient's local anticoagulation service for maintenance monitoring

5.6. Thrombolytic therapy

5.6.1. Thrombolytic (mechanical or chemical) therapy may be considered for those patients who are worsening despite adequate anticoagulation. Data are largely anecdotal though suggest more benefit may be achieved in comatose/critically ill patients (Canhao, et al., 2003).

5.6.2. Chemical thrombolysis is not recommended in those who already have ICH or those with impending herniation (Einhaupl, et al., 2010).

5.6.3. Mechanical thrombectomy may be discussed with an interventional neuroradiologist where a patient is worsening despite adequate anticoagulation but there are no randomised controlled trials currently to support its use.

5.7. Management of raised intracranial pressure

Optimum management of raised ICP in the setting of CVT is not known. It may depend on the aetiology of raised ICP (generalised cerebral oedema versus 'malignant' infarction/haemorrhage versus hydrocephalus) but several principles may be followed:

5.7.1. Adequate anticoagulation promotes venous recanalisation and therefore pressure reduction

5.7.2. Lumbar puncture may be considered to reduce ICP

5.7.2.1. There is no randomised controlled evidence to recommend this as standard of practice

5.7.2.2. Performing lumbar puncture may lead to delay in anticoagulation as recommendations are for LMWH starting up to 24 hours after dural puncture (Harrop-Griffiths, et al., 2013)

5.7.2.3. Repeated LP may be considered for pressure management but this would result in interrupted anticoagulation

5.7.3. Acetazolamide is used for ICP reduction in other conditions but it's role in CVT is not proven by trials (Ferro & Canhao, 2008)

5.7.4. Corticosteroids are not efficacious in CVT and in fact may harm the ischaemic brain (Canho, et al., 2008)

5.7.5. Anti-oedema therapies may be considered (head elevation, hyperventilation, iv osmotic diuretics (with caution due to impaired clearance in venous outflow obstruction) (Saposnik, et al., 2011)

5.7.6. Surgical decompressive craniectomy may be considered in certain groups of patients and in a small review of individual cases was associated with a favourable outcome in 86% (Coutinho, et al., 2009)

5.7.6.1. Indication may include large infarction, haemorrhage, or global oedema

5.7.6.2. Decompressive craniectomy is efficacious in select arterial stroke patients with malignant MCA territory infarction and though there is no specific evidence for CVT it may be appropriate to consider in select cases. However, neuronal damage is less pronounced in CVT (Villringer, et al., 1994) and their overall prognosis is better than for acute ischaemic stroke (Vahedi, et al., 2007)

5.7.7. Communicating hydrocephalus may occur in 6.6% of cases of CVT

5.7.7.1. Arachnoid granulations function can become impaired in superior sagittal and lateral dural sinus thrombosis (Wasay, et al., 2008) (Bousser & Russell, 1997)

5.7.7.2. In other cases, particularly internal cerebral venous thrombosis, haemorrhage into the ventricles may result in obstructive hydrocephalus.

5.7.7.3. Due to the potentially already high intracranial pressure, early neurosurgical opinion is advised for consideration of clot evacuation/ventriculostomy/EVD/VPS as lesser degrees of ventricular enlargement may be more significant

5.7.8. In refractory cases, VP shunt may be considered

5.7.9. In cases where vision is threatened ophthalmic opinion should be sought and optic nerve fenestration can be considered.

5.8. Management of other complications

5.8.1. Seizures are common in adult patients and up to 40% of cases present with seizures

5.8.1.1. Early seizures are 4 fold more likely with supratentorial parenchymal lesions but a 70% reduction in likelihood of seizure seen in one study (Ferro, et al., 2008)was not statistically significant, and prophylactic AED therapy is not recommended.

5.8.1.2. AED therapy is recommended in patients with CVT who have suffered a seizure. The duration of AED therapy to recommend is unclear (Einhaupl, et al., 2010)

5.8.1.3. Less than 10% of cases develop late seizures and late seizures are not a predictor of outcome (Ferro, et al., 2003)

5.8.1.4. Late seizures are more common in those with ICH at presentation but almost all occur within the first year (Preter, et al., 1996) (Ferro, et al., 2003)

5.8.2. Headache is a common feature seen in long term follow up in up to 55% of patients

5.8.2.1. Headache tends to be of the migrainous or tension type

5.8.2.2. It may require further vascular imaging or lumbar puncture to exclude recurrent thrombosis or raised ICP, respectively.

5.8.3. Thromboembolism

5.8.3.1. In hypercoagulable states thrombosis may be seen in other sites (limb DVT, vena cava, renal vein, retinal vein) and awareness should prompt appropriate investigation (e.g. worsening renal function)

5.8.3.2. Distal embolism can result in pulmonary embolus

5.8.3.3. Patients should be made aware of risk of thromboembolism so they can report additional symptoms at an early stage

5.8.4. Neurocognitive symptoms

5.8.4.1. Subtle neurocognitive deficits often go unrecognised in this patient group

5.8.4.2. Enquiry should be made at follow up to determine any suggestion of cognitive sequelae and consideration of referral to neuropsychology

6. Clinical course

6.1. Neurological deterioration can occur in up to 23% of patients ranging from worsening headache to death

6.2. Patients with depressed conscious state on admission are more likely to deteriorate and a third of those who deteriorate will have new parenchymal lesion on brain imaging

6.3. The overall death/dependency rates for patients is approximately 15% in prospective cohort registries and studies

6.3.1. Death in the acute phase of the illness is reported to occur in between 3% and 15% of cases (Dentali, et al., 2006)

6.3.2. The main cause of death in the acute phase is trans-tentorial herniation due to a large haemorrhagic lesion. Multiple lesions/diffuse oedema is the next most frequent cause followed by status epilepticus, medical complications and PE

6.3.3. Death at 30 days occurs in between 3.4% (Canhao, et al., 2005)and 13% (Boncoraglio, et al., 2004)of cases

6.3.4. Deaths after the acute phase are predominantly related to underlying conditions such as malignancy

6.4. Risk stratification scores to predict outcome are available though not used widely (Koopman, et al., 2009)

6.5. The following factors have been reported to be poorer prognostic factors:
6.5.1. Age >37
6.5.2. Male sex
6.5.3. Coma/decreased conscious state
6.5.4. Severity of neurological deficit
6.5.5. Encephalopathy
6.5.6. Intracerebral haemorrhage
6.5.7. Venous infarction
6.5.8. Straight sinus thrombosis
6.5.9. Seizures

6.5.10. CNS infection
6.5.11. Underlying malignancy
6.5.12. Hereditary coagulopathy

6.6. Recurrence of cerebral venous thrombosis

6.6.1. The overall risk of recurrence of any thrombotic event (CVT or systemic) after a CVT is approximately 6.5% (Saposnik, et al., 2011)

6.6.2. The risk of recurrent CVT is between 1.3 to 2.2% within 16 months (Canhao, et al., 2005) (Messe, et al., 2009)

6.6.3. Preventing recurrent CVT

6.6.3.1. Long term anticoagulation for secondary prevention of VTE/CVT should be considered as for other venous thrombo-embolic diseases (Saposnik, et al., 2011)

6.6.3.2. Testing for prothrombotic conditions may be considered in patients with CVT though clinical assessment is a superior predictor of recurrent events (Baglin, et al., 2010)

6.6.3.2.1. Testing for protein C, protein S, and antithrombin deficiency is should be delayed to 4 weeks after cessation of anticoagulation therapy. There is a very limited value of testing in the acute setting or in patients taking warfarin

6.6.3.3. Testing for D-dimer once off anticoagulation for 4 weeks may be helpful in identifying those patients at higher risk of recurrence (Verhovsek, et al., 2008).

6.6.3.4. For patients with provoked CVT (associated with a transient risk factor), anticoagulation may be continued for 3 to 6 months, with a target INR of 2.0 to 3.0 (Saposnik, et al., 2011)

6.6.3.5. For patients with unprovoked CVT, anticoagulation may be continued for at least 6 months, or long-term depending on individual patients, with a target INR of 2.0 to 3.0 (Saposnik, et al., 2011)

6.6.3.6. For patients with recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia, indefinite anticoagulation may be considered, with a target INR of 2.0 to 3.0 (Saposnik, et al., 2011)

6.6.3.7. Patients on long-term anticoagulation therapy should undergo regular review of bleeding risk to ensure risk-benefit profile remains in favour of continuing anticoagulation (kearon, et al., 2012)

6.7. Cerebral venous thrombosis and future pregnancy

6.7.1. For CVT associated with pregnancy the risk of recurrence is low

6.7.2. In the absence of other predisposing factors, future pregnancy is not contraindicated

6.7.3. Prophylaxis with LMWH would be reasonable for future pregnancies (Saposnik, et al., 2011)

6.8. Oral contraceptive use and hormone replacement therapy after cerebral venous thrombosis

6.8.1. For women who have suffered current or previous VTE, the Royal College of Gynaecologists recommends against the use of combined hormonal contraception as this poses an unacceptable health risk. It seems reasonable to apply this to CVT (Royal College of Obstetricians and Gynaecologists, 2010)

6.8.2. For women with current venous thromboembolism on anticoagulants or previous venous thromboembolism the benefits of use of progestogen-only contraception outweigh the risks (Royal College of Obstetricians and Gynaecologists, 2010)

6.8.3. Given age as a risk factor and oestrogen content, HRT should also be avoided in patients with current or previous CVT

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Appendix A

CVT Referral Proforma for Greater Manchester

Demographics

Name_____ M/F____ DOB___/___/___

Hospital number_____ NHS number_____

Referring clinician_____ Referring hospital_____ Referring ward_____

Clinical features

GCS (E__V__M__)

Headache □

Seizure □

Encephalopathy □

Hemiparesis □

Hemisensory disturbance □

Cranial nerve signs □

Visual disturbance □

Other_____

Risk factors

Hereditary coagulopathy □

Pregnancy □

OCP □

Dehydration □

Infection □

Inflammatory disorder □

Malignancy □

CNS Infection □

Other_____

Imaging findings

Cerebral infarction ☐ Cerebral haemorrhage ☐

Venous thrombosis

saggital sinus ☐ torcula ☐ R transverse sinus ☐

L transverse sinus ☐ R sigmoid sinus ☐ L sigmoid sinus ☐

R jugular vein ☐ L jugular vein ☐ straight sinus ☐

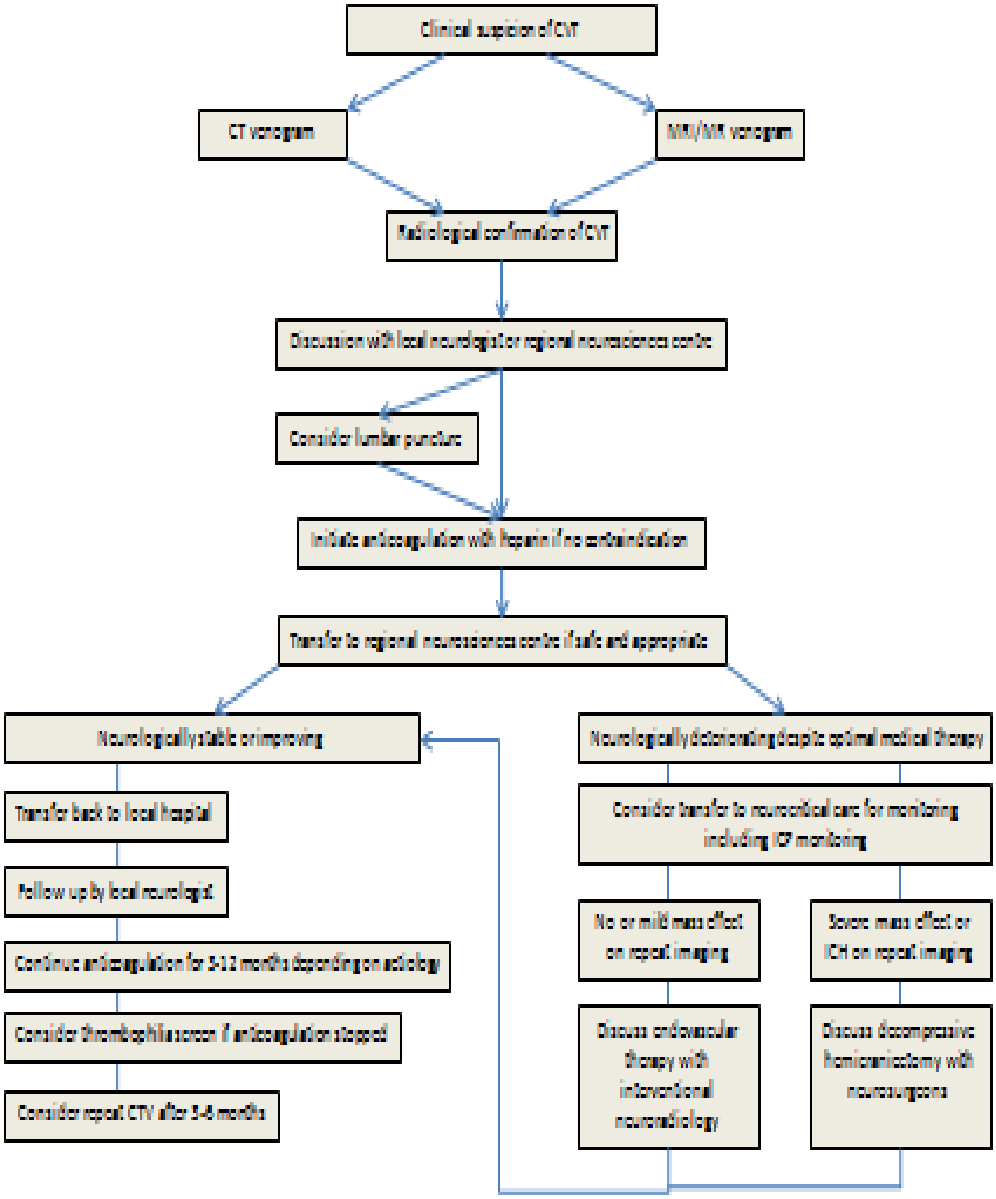
cortical vein thrombosis ☐

Lumbar Puncture

Opening pressure_____ mm CSF Constituents_____

Appendix B

Algorithm for CVT management in Greater Manchester, Lancashire and South Cumbria



Document Control Information

Cerebral Venous Sinus Thrombosis (CVST) Assessment and Management of Adult Patients in Greater Manchester, Lancashire and South Cumbria Policy and Guidelines for	Salford Royal NHS NHS Foundation Trust University Teaching Trust safe • clean • personal
Lead Author: Martin Punter, Consultant Neurologist & Mark Kellet, Consultant Neurologist. **Additional authors:** See page 2 of document **Document owner:** Martin Punter **Contact details:** martin.punter@srft.nhs.uk	
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Associated Documents: • None	
Unique Identifier: TWCG22(14) **Issue number:** 2 **Replaces:** 1 **Authorised by:** Clinical Effectiveness Committee, May 2014 **Authorisation date:** November 2016 **Next review:** November 2018	

Policy Implementation Plan

This policy has already been sent to all acute trusts around the region. It has been debated and discussed within the medical neurosciences directorate meeting and accepted. It is fully implemented as of 1st June 2014.

Monitoring and Review

The impact of the policy on service provision will be the subject of monitoring and will be initially reviewed after approximately 6 months.

Although the main aim of the policy is to transfer cases to SRFT as there are many reasons for patients to remain in their local/referring hospital, deviation from transfer should not necessarily be considered a deviation from the protocol.

There is scope to audit many aspects of the policy and this will be done as appropriate through the medical neurosciences audit programme.

Endorsement

Endorsed by:		
Name of Lead Clinician/Manager or Committee Chair	Position of Endorser or Name of Endorsing Committee	Date
Pete Turkington	Chair, Clinical Effectiveness Committee	May 2014
Mark Kellett	Clinical Director Medical Neurosciences	May 2014
Jane Molloy	Clinical Lead, Stroke Service	May 2014
Pete Turkington	Chair, Clinical Effectiveness Committee	November 2016

Screening Equality Analysis Outcomes

The Trust is required to ensure that all our policies/procedures meet the requirements of its service users, that it is accessible to all relevant groups and **furthers the aims of the Equality Duty for all protected groups by age, religion/ belief, race, disability, sex, sexual orientation, marital status/ civil partnership, pregnancy/ maternity, gender re-assignment. Due consideration may also be given to carers & socioeconomic factors.**

Have you been trained to carryout this assessment? **If 'no' contact Equality Team 62598 for details.**	
Name of policy or document : Policy and Guidelines for Assessment and Management of Adult Patients with Cerebral Venous Thrombosis in Greater Manchester, Lancashire & South Cumbria, Version 1.10 **Key aims/objectives of policy/document:** To improve access to acute neurological care for patients with cerebral venous sinus thrombosis across Greater Manchester, Lancashire and Cumbria. (impact on both staff & service users)	
1) a) Who is this document or policy aimed at?	All acute trusts in the region.
2) a) Is there any evidence to suggest that your 'end users' have different <u>needs</u> in relation to this policy or document; (e.g. health/ employment inequality outcomes) (**NB If you do not have any evidence you should put in section 8 how you will start to review this data)**	No
3) a) Does the document require any decision to be made which could result in some individuals receiving different treatment, care, outcomes to other groups/individuals?	No
b) If yes, on what basis would this decision be made? **(It must be justified objectively)**	n/a
4) a) Have you included where you may need to make reasonable adjustments for disabled users or staff to ensure they receive the same outcomes to other groups ?	n/a

5) a) Have you undertaken any consultation/ involvement with service users or other groups in relation to this document?	No
b) If yes, what format did this take? Face/face or questionnaire? (please provide details of this)	n/a
c) Have any amendments been made as a result?	n/a
6) a) Are you aware of any complaints from service users in relation to this policy?	No
b) If yes, how was the issue resolved? Has this policy been amended as a result?	n/a

7) a) To summarise; is there any evidence to indicate that any groups listed below receive different outcomes in relation to this document?

	Yes		No	unsure
	Positive	Negative*		
Age			X	
Disability			X	
Sex			X	
Race			X	
Religion & Belief			X	
Sexual orientation			X	
Pregnancy & Maternity			X	
Marital status/civil partnership			X	
Gender Reassignment			X	
Carers *1			X	
Socio/economic**2			X	

1: That these two categories are not classed as protected groups under the Equality Act.
2: Care must be taken when giving due consideration to socio/economic group that we do not inadvertently discriminate against groups with protected characteristics

Negative Impacts

*If any negative impacts have been identified you must either a) state below how you have eliminated these within the policy or b) conduct a full impact assessment:

8) How will the future outcomes of this policy be monitored? The impact of the policy

on service provision will be the subject of monitoring and will be initially reviewed after approximately 6 months
9) **If any negative impact has been highlighted by this assessment, you will need to undertake a full equality impact assessment:** Will this policy require a full impact assessment? No (if yes please contact Equality Team, 62598/67204, for further guidance) Low Type/sign Martin Punter date: November 2016