orphanaesthesia

Anaesthesia recommendations for

Systemic sclerosis

Disease name: Systemic sclerosis

ICD 10: M34

Synonyms: Progressive systemic sclerosis, Scleroderma, CREST syndrome

Disease summary: Systemic sclerosis (SSc) is an autoimmune connective tissue disorder characterised by excess collagen deposition and fibrosis of the skin and internal organs as well as a small-vessel vasculopathy. This results in a multi-system disorder with a mortality greater than any other rheumatic disease (10-year survival after diagnosis: 66 %) [1]. Clinical features include tightening and thickening of skin (skin sclerosis), Raynaud's phenomenon and involvement of various internal organs (particularly the lungs, kidneys, heart and gastrointestinal system). Two major phenotypes of SSc are recognised based on the degree of skin involvement: limited cutaneous systemic sclerosis, where skin involvement occurs distal to the elbows (+/- face & neck); and diffuse cutaneous systemic sclerosis, where skin involvement occurs more proximally [2].

Approximately 1:10,000 people are affected by systemic sclerosis worldwide, however, there is a marked geographical variation with greater prevalence seen in the USA and Australia than in Europe and Japan. The ratio of women to men affected is around 3:1 and it has a peak incidence in the fifth decade of life [2,3]. Death directly attributable to systemic sclerosis occurs in 55 % of patients, of these the top three causes of death are from: pulmonary fibrosis (19 %), pulmonary arterial hypertension (14 %) and myocardial disease (14 %) [4].

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Typical surgery

Patients affected by systemic sclerosis may require surgery for any type of procedure, but typically present for repeated oesophageal procedures, dental treatment, peripheral orthopaedic/plastics procedures and surgical management of vascular insufficiency including cervical, lumbar and digital sympathectomy in addition to amputation [5,6,7]. In severe forms, lung transplantation may be considered due to severe interstitial disease or pulmonary arterial hypertension [8].

Type of anaesthesia

There is no definite recommendation for either general anaesthesia or regional anaesthesia in patients with systemic sclerosis and the choice of anaesthetic technique will depend on the type of surgery, an understanding of the pathophysiology of the disease and careful pre-operative assessment of the patient.

Complications of general anaesthesia include difficult airway management, a higher risk of aspiration (90 % of SSc patients suffer from gastro-oesophageal reflux (GORD)/oesophageal dysmotility [9]), and the impact of potentially significant cardio-respiratory disease. Interstitial lung disease develops in 80 % of patients with SSc and invasive ventilation in such patients may increase morbidity [2,10].

Regional anaesthesia may offer advantages over general anaesthesia through the avoidance of intubation and ventilation, as an adjunct in the treatment of post-operative pain, and in the prevention of vasospastic crisis. However, technical challenges may occur due to difficulties in patient positioning and altered anatomy [11,12]. Prolonged sensory block has been reported in some cases, however there is no evidence of an increased risk of permanent nerve injury and full sensory function usually returns within 24 hours [13–17]. Underlying autonomic neuropathy and cardiac disease may exacerbate the haemodynamic consequences of neuraxial anaesthesia [10]. Ultrasound guidance is advocated to improve success rates and reduce the volume of local anaesthetic required [10,18].

Necessary additional pre-operative testing (beside standard care)

The multiple systems which may be involved in systemic sclerosis necessitate a thorough pre-operative assessment, in order to produce an optimal anaesthetic plan.

Interstitial lung disease often develops early in the disease course of SSc and is the leading related cause of death [2,4]. To assess the extent of pulmonary disease, patients should have a chest radiograph and pulmonary function tests (PFTs) to demonstrate any reductions in compliance, vital capacity and diffusion capacity. A low diffusion capacity for carbon monoxide (DLCO) is a risk factor for mortality in SSc and in those with a vital capacity of less than 1 litre are at high risk of post-operative respiratory failure [19,20]. Those with symptoms of dyspnoea or abnormal spirometry should be considered for a high resolution CT scan and respiratory review. Inflammatory markers should also be reviewed as a C-reactive protein (CRP) of ≥5 mg/l and erythrocyte sedimentation rate (ESR) of ≥ 20 mm/hr are associated with worsening PFTs and the development of pulmonary arterial hypertension [21]. Functional capacity may be assessed by a 6 minute walk test or cardiopulmonary exercise testing, if available.

Sleep disordered breathing may be present in up to one third of patients with scleroderma [22]. This should be screened for pre-operatively using validated pre-operative screening tools such

as STOP-BANG. In those with moderate-to-high risk, referral for pre-operative sleep studies should be considered. Pre-operative initiation of continuous positive airway pressure (CPAP) therapy may be appropriate and employing an opioid-sparing regional anaesthesia technique is preferable [23].

Pulmonary Arterial Hypertension (PAH) occurs in around 15 % of patients with systemic sclerosis and has a poorer prognosis that PAH associated with other connective tissue diseases [24,25]. Pulmonary hypertension is also an independent risk factor for peri-operative morbidity and mortality [26]. Patients may be asymptomatic or present with exertional dyspnoea, chest pain, fatigue, syncope (in severe cases) and/or signs and symptoms of right heart failure [27]. Pre-operatively, patients should be screened using echocardiography, however, the gold standard test remains right heart catheterisation. A detailed review of the assessment and anaesthetic management of patients with pulmonary arterial hypertension has previously been published [26] and it is vital that patients are made aware of the high-risk nature of surgery with this condition.

Primary cardiac disease in scleroderma (otherwise known as SSc-Cardiomyopathy) may take the form of cardiac failure, arrhythmias, pericarditis or valvular disease. At-risk patients should have a baseline ECG and an echocardiogram. It is worth noting that these tests may have already been recently carried out, with United Kingdom rheumatology best practice recommendations advising at least yearly ECGs, echocardiography, troponin and NT-proBNP testing in patients with systemic sclerosis [28].

The gastro-intestinal (GI) system can be affected at any point throughout its length in SSc. It is the most frequently affected organ system, with more than 90 % of patients affected [29]. Important GI abnormalities include gastro-oesophageal reflux and dysmotility, bleeding from gastric vascular ectasia (resulting in the so-called “watermelon stomach”), small bowel bacterial overgrowth and pseudo-obstruction [5]. These may result in anaemia, malnutrition, impaired absorption of vitamin K and electrolyte disturbance. All patients therefore require a full blood count, urea and electrolytes, liver function tests, bone screen and coagulation screen in addition to a group and save or cross match depending on procedure [18].

Particular preparation for airway management

Airway management may pose a particular challenge in patients with SSc. Microstomia is a common finding and may be compounded by restricted mouth opening due to temporomandibular joint fibrosis [30–38]. Limited neck extension may occur as may atrophied nasal alae and tightening of the skin of the face, neck and mouth [31,33,34,36–39]. Poor dentition is also common [40]. Difficulties with intubation and mask ventilation should therefore be expected and access to difficult intubation equipment should be immediately available. Awake fibreoptic intubation may be appropriate in such patients although may be unsuccessful due to excessive oropharyngeal soft tissue or profuse haemorrhage from mucosal telangiectasia [31]. In such particularly difficult situations, it may be necessary to consider awake tracheotomy with local anaesthesia [20,38].

GORD is common in patients with SSc and an aspiration event whilst in hospital is an independent risk factor for mortality in patients with scleroderma [41]. As such, routine use of pre-operative acid suppression should be considered [20]. Rapid sequence induction should, however, be avoided where possible due to the risk of failed/difficult intubation. Cricoid pressure may also be ineffective due to fibrosis or the oesophagus and may serve only to further impair laryngoscopy [31,42]. Oesophageal strictures are more common in SSc patients (due to prolonged, untreated GORD) and nasogastric tube placement in such patients risks oesophageal perforation [43,44].

Particular preparation for transfusion or administration of blood products

Haematological abnormalities occur less frequently in systemic sclerosis patients than in other rheumatological diseases such as systemic lupus erythematosus or rheumatoid arthritis [45]. Severe anaemia (haemoglobin < 100 g/l) is, however, still present in around 10 % of patients and may be due to GI bleeding, malabsorption/malnutrition or anaemia of chronic disease [45,46]. A haemolytic anaemia and thrombocytopaenia may occur in the context of a scleroderma renal crisis. There are no specific recommendations for transfusion in SSc and administration of blood products should follow routine practice, taking into account the type of surgery, the patient's symptoms and physiology, and advice from senior haematology clinicians.

Particular preparation for anticoagulation

The role of long-term anticoagulation in patients with scleroderma related PAH is debated and the subject of an ongoing randomised control trial [47–49]. As such, these patients may or may not present on established anticoagulation therapy.

Venous thrombosis and pulmonary embolism occur more frequently in patients with scleroderma. Risk factors for venous thromboembolism (VTE) in SSc include: diagnosis within the last year, female sex and comorbidities such as heart failure and atrial fibrillation [50-52]. There is, however, a need to balance this increased risk against the potential bleeding risk from GORD-related ulceration and gastric antral vascular ectasias. Decisions, therefore, on the aggressiveness of VTE prophylaxis (and the management of those on long term anticoagulation) need to be patient-specific and take account of senior clinical advice.

Particular precautions for positioning, transportation and mobilisation

Around a third of patients with SSc with have joint contractures, whilst 27 % will suffer from peripheral neuropathy [53,54]. Given that vascular insufficiency is also common amongst these patients, it is important that great care is taken with positioning, to prevent ischaemic damage, pressure sores and/or worsening of neuropathy. Padding should be used liberally and patients should ideally be positioned on the operating table whilst awake and able to provide feedback [55]. Pressure areas should be checked regularly during the case and saturation probes moved during prolonged surgery to prevent ischaemic damage [20]. A vacuum mattress should be considered for patient transportation.

During the procedure, Trendelenburg positioning may favour pulmonary aspiration and should therefore be avoided, unless the airway is secure. In patients with autonomic neuropathy characterised by orthostatic hypotension, marked hypotension may develop with head-up positioning. Patients should therefore be screened for symptoms of autonomic neuropathy prior to anaesthesia to anticipate such potential issues [10].

Patients are prone to developing dry eyes which may be compounded by scarring of the eyelids preventing complete closure. Eyes should be carefully lubricated and padded to avoid corneal abrasions [6,55].

Interactions of chronic disease and anaesthesia medications

Treatment of SSc is targeted according to the specific organ involvement present. Immunosuppressants (e.g. methotrexate, cyclophosphamide, azathioprine etc.) form the mainstay of treatment. These drugs may increase the risk of post-operative infection; however, no specific guidance exists for scleroderma and decisions should be made in conjunction with the surgeons and parent rheumatology team.

Glucocorticoids are commonly used medications in SSc and steroid supplementation should be provided in the peri-operative period for those taking ≥5 mg prednisolone (or equivalent) as per Association of Anaesthetists of Great Britain and Ireland (AAGBI) guidelines [56]. Care should be taken to ensure that prolonged courses of increased dose steroids are avoided, as glucocorticoid therapy is a risk factor for the development of a scleroderma renal crisis (SRC). One case series showed a 1.5 % increased risk for every mg/day of prednisolone taken in the three months prior to development of scleroderma renal crisis [57]. Post-operative patients should be carefully monitored for the development of scleroderma renal crisis [58].

In those who do develop SRC, early initiation of an angiotensin–converting enzyme inhibitor improves outcome and should be continued long term. These drugs may produce refractory hypotension post induction of anaesthesia [59].

Given the potential for significant cardiac disease in SSc, drugs with pro-arrhythmogenic properties (including anti-emetics such as metoclopramide and droperidol) should be avoided as these may induce dysrhythmias and cardiac arrest [60].

Anaesthetic procedure

Prior to anaesthesia, IV access should be established. This may be challenging due to thickening of the skin and contractures. Ultrasound assistance or establishment of central venous access may, therefore, be required [18,34–36].

In cases where general anaesthesia is indicated, endotracheal intubation is advocated to decrease the risk of aspiration. As discussed, rapid sequence intubation should be avoided in this patient group. Interstitial lung disease may make ventilation challenging due to reduced lung compliance and lung protective ventilatory strategies should be employed to reduce the risk of barotrauma and volutrauma. Invasive ventilation, however, is not without significant risk with evidence from the intensive care unit showing intubation and ventilation to be associated with extremely poor outcomes (in-hospital mortality ~85 %) [61].

Regional anaesthesia may, where possible, provide an attractive alternative to general anaesthesia. For truncal, plexus and peripheral nerve blocks, ultrasound guidance should be utilised to improve the reliability of this technique, as altered fascial planes and suboptimal patient positioning may distort normal anatomical landmarks [18]. Reports of prolonged sensory blockade in some patients with scleroderma are attributed to several potential reasons such as: pre-existing vasoconstriction, altered tissue pH, compression of fibrosed tissue by local anaesthetics, and altered anatomy leading to an increased risk of intraneural injection [18]. Ultrasound guidance may allow for a reduction in the total volume of local anaesthetic used and help protect against intraneural injection, potentially reducing the risk of prolonged blockage [10]. Local anaesthetic mixtures which do not contain adrenaline may be preferable given the already high levels of vasoconstriction and concerns regarding prolonged sensory blockade [7,13].

Systemic sclerosis frequently spares the back and many of the challenges and complications associated with regional anaesthesia are therefore reduced by neuraxial techniques [18]. Positioning may be difficult due to restricted joint movement and, in such cases, the use of ultrasound to identify the point of needle insertion may be helpful [11,62]. Unmodified doses of levobupivacaine have been used for spinal anaesthesia without prolonged sensory blockade [32,63]. Reduction of the pre-existing high vascular tone by neuraxial anaesthesia may, however, cause profound hypotension. This may require high doses of vasopressors, which may worsen Raynaud's phenomenon and lead to a vasospastic crisis. Excessive intravenous fluid, meanwhile, may result in pulmonary oedema [18,32]. Consequently, techniques that enable gradual or incremental adjustment of block height, such as epidural or combined epidural spinal anaesthesia, are preferable [20,32].

Non-steroid anti-inflammatory drugs (NSAIDs) should be avoided, given the strong association of renal and gastrointestinal disease in SSc. Given the higher prevalence of sleep disorders in SSc, opiate use should be minimised and multimodal analgesia is recommended.

Particular or additional monitoring

Routine monitoring, as set out by the AAGBI, should be adhered to in all cases [64]. Dermal thickening, flexion contractures and vasoconstriction may make it difficult to obtain pulse oximetry and non-invasive blood pressure readings, and efforts should be made to address these issues prior to induction of anaesthesia [20,35]. Pulse oximeter probes should also be regularly moved during the case to reduce the risk of ischaemic damage [20].

Patient temperature should be closely monitored throughout the operation. Hypothermia may lead to vasoconstriction with the potential to induce digital ischaemia [18]. Sweating may be impaired in patients leading to the potential to overheat the patient, which may present similarly to malignant hyperthermia [65].

Decisions regarding the need for invasive arterial blood pressure monitoring should be carefully considered. Given the potential for difficult non-invasive readings and potentially significant cardio-respiratory disease in SSc, these may offer significant value in terms of both haemodynamic monitoring and arterial gas sampling. However, radial arterial cannulation may precipitate Raynaud's phenomenon and even subsequent necrosis. Decisions should therefore be made on a case-by-case basis.

Cardiac output monitoring may be an attractive option in patients wither severe cardiac disease and pulmonary hypertension. It should be noted, however, that the accuracy of such devices may be altered by the presence of oesophageal fibrosis, aortic disease and reduced vascular compliance in SSc patients [18].

Possible complications

In patients undergoing non-cardiac surgery, peri-operative myocardial infarction is independently associated with systemic sclerosis [66]. Underling cardiac disease (including heart failure, dysrhythmias and pulmonary hypertension) may worsen peri-operatively and require emergency treatment [10,26]. Stress, pain, dehydration, hypothermia and vasoconstrictor use may also induce a peripheral vasospastic crisis, leading to peripheral ischaemia and ulceration. In severe cases, treatment with intravenous iloprost may be indicated [66]. Pre-existing vasoconstriction also reduces the volume of the intravascular compartment at rest and profound hypotension may occur with anaesthesia [20]. Patients,

therefore, tolerate dehydration and blood loss poorly. Excessive intravenous fluid use, however, may result in pulmonary oedema as vascular tone returns post-procedure [18,32].

As discussed, patients with systemic sclerosis are at increased risk of difficult intubation and aspiration. Interstitial lung disease reduces lung compliance, increasing the risk of both barotrauma and difficulties in extubating patients at the end of the procedure [18]. High rates of sleep disordered breathing may also lead to post-operative respiratory impairment, especially in cases where opiates have been administered [23].

Preoperative malnutrition is common this patient group and increases the susceptibility to infection and poor wound healing. This is exacerbated by immunosuppressant therapy and poor peripheral perfusion, which also predisposes the patient to pressure sores [66].

Post-operative care

Post-operative care will depend on type of surgery and disease severity. Post-operative ventilation may be required given the high risk of postoperative respiratory failure, and admission to High Dependency or the Intensive Care Unit admission may be indicated. Those on pre-operative CPAP for sleep disordered breathing should be advised to bring their machine into hospital and continue to use it post-operatively [23]. Close monitoring for post-operative pulmonary complications (and early treatment) is advised given the poor respiratory reserve found in many patients [10].

A high index of suspicion for peri-operative myocardial infarction should be maintained in this patient group and continuous ECG monitoring and/or invasive monitoring is indicated in the post-operative period in those with known cardiac involvement. In those with pulmonary hypertension, it is particularly important to maintain sinus rhythm, normocapnia, normoxia and avoid acidosis. Pain should also be well controlled, ideally through a multimodal approach [26].

Thromboembolic stockings should be avoided due to peripheral vascular disease and the risk of ischaemia. Pharmacological thromboprophlaxis (where appropriate) should be commenced as soon as possible post-operatively given the propensity for thrombus formation in this patient group [10].

Post-operative analgesia should avoid NSAIDs and opiates should be used with caution. Mobilisation can prove difficult due to contractures, malnutrition and prolonged sensory blockade from regional anaesthesia and additional assistance may be required.

Disease-related acute problems and effect on anaesthesia and recovery

SRC is defined by the development of thrombotic microangiopathy, in the progressive acute kidney injury and (usually) hypertension. A subgroup of patients may be normotensive and this is associated with a worse prognosis [2]. Risk factors for the development of SRC include: the diffuse cutaneous systemic sclerosis phenotype (especially in the early years following diagnosis); rapid, progressive skin disease; glucocorticoid exposure in the previous 3 months; new anaemia; new cardiac events and anti-RNA polymerases III positivity [67]. Clinically, blood pressure is usually significantly elevated (above 150/85) and a greater than 30 % drop in estimated glomerular filtration rate is seen [68]. Patients may be asymptomatic or complain of headaches, visual disturbances and/or shortness of breath. Seizures may also occur, whilst myocardial stress from the increase in afterload may result in congestive heart failure, pericardial effusions and arrhythmias. Urinalysis is usually positive for protein and blood and a

full blood count may reveal a haemolytic anaemia and thrombocytopenia. Treatment is with rapid initiation of angiotensin-converting enzyme (ACE) inhibitor therapy, which has markedly improved survival and reduced the need for dialysis in this patient group [67].

Patients should have their blood pressure and renal function closely monitored in the peri-operative period. Risk factors for the development of SRC should be minimised and a high index of suspicion maintained. If SRC does develop, this should be considered a medical emergency and these patients should be managed in close conjunction with intensive care and renal colleagues [2,66].

Ambulatory anaesthesia

Availability of ambulatory anaesthesia will be guided by the severity of disease, surgical procedure and local guidelines. It is unlikely to be appropriate in any but the mildly affected.

Obstetrical anaesthesia

Pregnant women with systemic sclerosis should have experienced obstetric care and multidisciplinary team involvement. Risk factors for complications during pregnancy include: the diffuse cutaneous systemic sclerosis phenotype (especially within the first 5 years of diagnosis); anti-topoisomerase or anti-RNA polymerase III positivity; and the presence of significant organ involvement at the time of conception (e.g. ILD, PAH, SSc-Cardiomyopathy etc.) [69].

SRC occurs with no greater frequency than outside of pregnancy, however, during pregnancy it may be difficult to differentiate from pre-eclampsia and the HELLP syndrome (Haemolysis, Elevated Liver enzymes, Low Platelets) [70]. Importantly, unlike in pre-eclampsia, SRC does not improve with delivery of the foetus [71]. Due to the high potential mortality of SRC, ACE inhibitors are still recommended for treatment during pregnancy, despite the risk of teratogenicity [66]. Labetalol is relatively contraindicated due to the risk of peripheral vasospasm. Patients should be advised to closely monitor their BP throughout pregnancy.

Patients with pulmonary hypertension represent a particularly high-risk group, with maternal mortality being reported as high as 33 % [72]. These patients should be cared for in a specialist centre, with frequency echocardiography and early elective delivery in severe cases. Nitrous oxide raises pulmonary artery pressures and should be avoided. Wherever possible, anaesthesia for delivery should be provided with an incremental combined spinal-epidural (CSE) technique, to avoid the detrimental haemodynamic effects of general anaesthesia or single-shot spinal anaesthesia [73].

Other complications during pregnancy may include exercise intolerance and need for supplemental oxygen in those with ILD, worsening of upper GI symptoms, and higher rates of pre-term delivery [69,74,75]. Raynaud's phenomenon often improves during pregnancy due to the increased cardiac output seen [71].

Early epidural anaesthesia is recommended for labour as there is a high risk of obstructive labour and need for expedient operative delivery [76]. Where patients are on long term steroids, supplementation during labour should follow AAGBI guidance [56]. General anaesthesia for delivery should only be undertaken with extreme caution given the higher incidence of difficult airways within this population.

Following delivery, a slow infusion of oxytocin is preferable to a bolus dose due to the risk of haemodynamic instability. Ergometrine increases both systemic and pulmonary vascular resistance and should be avoided, whilst carboprost is not recommended in those with cardiac disease [77]. Misoprostol is considered safe [78]. Patients should continue to be closely monitored in a high acuity area for at least 72 hours following delivery for the development of SRC, worsening of cardiac function and progression of skin disease [69].

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