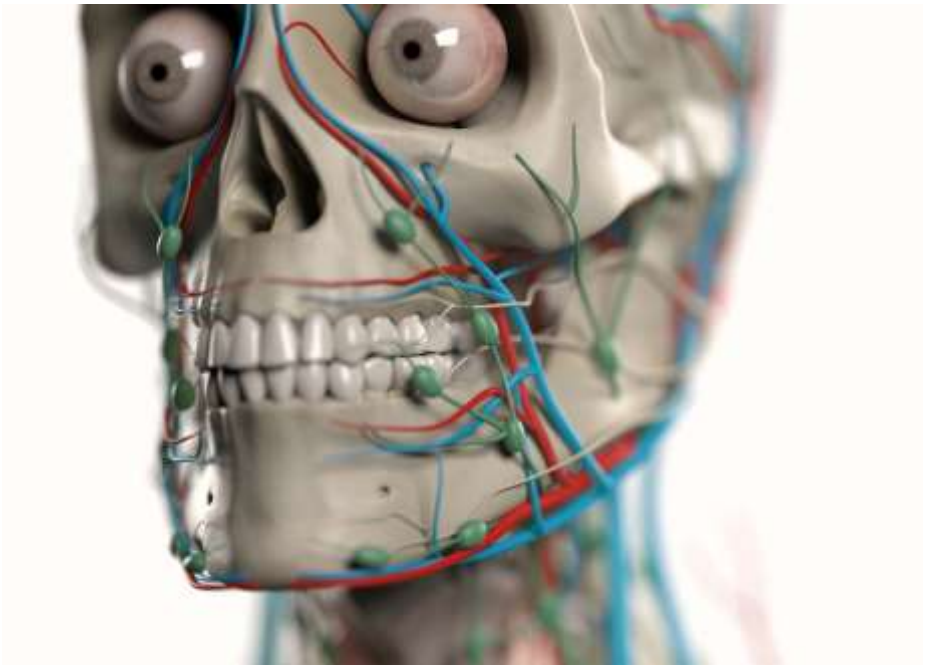
Management of a vascular occlusion associated with cosmetic injections



Seriousness of complication		Frequency of complication	
Major complication	x	Infrequent	x

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Abstract:

Vascular occlusion has been cited as the most severe and feared early complication in aesthetic treatment[1] and the incidence appears to be on the increase. There are several steps practitioners can take to minimise this risk and early identification and treatment of this complication is paramount. This guideline undertakes to educate and inform practitioners on steps to minimise risk, diagnose and manage a vascular occlusion in order to prevent skin necrosis.

Keywords:

Dermal filler, complication, injectable, skin necrosis, vascular compromise, vascular occlusion, cosmetic medicine.

Definition:

A vascular occlusion occurs when blood is no longer able to pass through a blood vessel. It may be a complete occlusion or may be partial resulting in a diminished blood supply. A vascular occlusion may be the result of an internal obstruction, such as a blood clot or a foreign body such as filler material, or a blood vessel may be occluded due to external compression. If left untreated, a vascular occlusion of a blood vessel supplying the skin may result in skin necrosis and tissue death.

Necrosis can be defined as ”The death of most or all of the cells in an organ or tissue due to disease, injury, or failure of the blood supply.”[2]

Unlike normal cell death (apoptosis), which is a programmed and ordered phenomenon, necrosis is the accidental death of the cell caused by various mechanisms such as an insufficient supply of oxygen, thermal or mechanical trauma or irradiation. Cells that are undergoing necrosis swell and then burst (cytolysis), releasing their contents into the surrounding area. This results in a locally triggered inflammatory reaction characterised by swelling, pain, heat and redness. The necrotic cells are subsequently phagocytosed and removed by the immune system.

Introduction:

The three proposed mechanisms of vascular occlusion associated with cosmetic injection[3] are:

1) Intravascular embolism
2) Extravascular compression
3) Vascular Spasm

A study by Chang, 2016[4] failed to show that vascular compression was reproducible in an animal model, although a case report by Lima, 2019[5] showed that tissue hypoperfusion occurred following vascular compression identified using high frequency ultrasound. Vascular occlusion is possible via several mechanisms following cosmetic injections, however intravascular embolism is the pathophysiology best supported by the evidence[3].

When a blood vessel is inadvertently injected with filler material, the normal circulation may be impaired leading to reduced tissue perfusion and compromise of the tissue relating to its angiosome[6]. Most soft tissue fillers used in cosmetic practice consist of hyaluronic acid and

although hyaluronic acid is well tolerated outside the vessel wall, it is highly inflammatory within blood vessels. One experimental study has shown that biphasic hyaluronic acid globules within an arterial vessel lumen produces intense vessel wall inflammation and spasm using histopathologic analysis of tissue obtained from rabbit ears[6]. It is speculated that this inflammation and spasm aims to restrict blood flow and further dispersal of foreign material into the adjacent vascular territory. It is apparent that complications associated with hyaluronic acid injection into an artery involve not just embolus with inflammation of the vessel wall, but spasm of the surrounding anastomoses to limit further spread and protection against wider areas of necrosis[6].

Many cases of vascular compromise occur immediately with injection[1] and the practitioner needs to be aware of the signs of this. However, there are several published papers describing delayed onset of symptoms of vascular occlusion[1,7,8,9].

Although the exact mechanism for a delayed onset of presentation is not properly understood, there are several proposed mechanisms:

1) Due to the hydrophilic nature of hyaluronic acid fillers in attracting water molecules, this can lead to delayed swelling post-treatment and a subsequent external compression of a vessel.

2) An embolus may obstruct a vessel to an area of skin which has a poor collateral circulation and although immediate signs of occlusion fail to manifest, the poor collateral supply fails to deliver enough nutrition to the skin over the following hours when signs of vascular compromise then occur[1].

3) Delayed vascular occlusion may be due an intra-arterial injection which does not initially occlude the vessel but creates a nidus for platelet aggregation which subsequently leads to a blockage.

4) An intra-arterial injection may initially occur in a larger vessel or at a bifurcation point where it initially remains but may later become dislodged leading to an occlusion in a terminal branch.

Incidence:

Although necrosis may occur as a result of many aesthetic treatments, it is most commonly associated with the injection of soft tissue fillers. The incidence of necrosis related to the injection of collagen has been reported at 9 in 100,000 cases of which 50% of cases were in the glabellar region[10] and for all dermal fillers an incidence of 1 in 100,000 cases[11]. However, it is widely recognised that although the prevalence of vascular occlusions following injection of soft tissue filler is increasing due to the rising popularity for these treatments and procedures being performed by less experienced practitioners, incidence data is very poor due to under-reporting. An internet-based survey conducted on 52 experienced injectors worldwide concluded that 62% reported one or more intravascular event[12,13].

Skin necrosis has occurred as a result of injection of all types of dermal filler including collagen, hyaluronic acid, PMMA (Polymethylmethacrylate beads), calcium hydroxylapatite and autologous fat[7].

Signs and symptoms of vascular occlusion (Table 1):

1) Pain[1,7,8,10,13,14,15]

Severe pain is usually experienced by the patient at the time of injection. However, if local anaesthetic has been used (either topically, a nerve block or administered with the product) this symptom may be less reliable.

Remember: Extraordinary pain is not a feature of soft tissue filler treatments and if a patient complains of sudden or escalating pain during treatment or in the subsequent hours after treatment, this should alert the practitioner to the possibility that a vascular occlusion has occurred and warrants an urgent review. Injectors should also be aware that pain distant from the area that has been injected may also be a warning sign of vascular occlusion.

2) Blanching[1,7,10,13,14,15]

When the vasculature is affected, the area will often initially look pale, white or dusky due to the reduction in blood supply to the affected tissue. This colour will remain after removal of the needle or cannula. The blanching may initially be transient and local, but if unresolved, the pattern of the blanching becomes reticulated or irregular, following the same path as the blood supply that has been restricted. This blanching may be masked initially, if adrenaline or certain topical anaesthetics have been used[8,15].

3) Dusky, purple discolouration[1,7,15]

This is more typical several hours later following treatment and is due to the accumulation of deoxygenated blood in the affected tissues. The appearance can mimic that of bruising, but bruises do not blanch as they are caused by blood leaking into the skin.

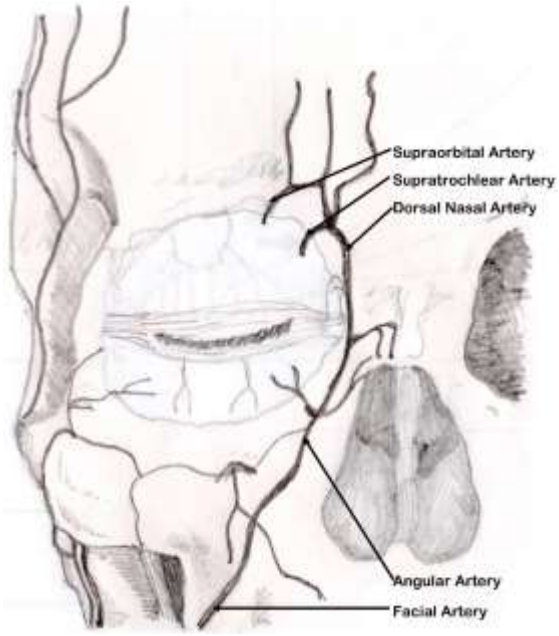
4) **Coolness**[15]

When the blood supply has been affected, the tissues are not being perfused so the temperature will be reduced, this will not be apparent immediately following injection.

Areas of caution:

It is essential to consider that there are no safe areas of the face and all areas should be treated with the same respect and anatomical knowledge. Special attention should be given when injecting into the midline as this area appears to be a more dangerous area to inject for vascular occlusion and cases of visual loss as documented in a world literature review[16,17].

Evidence dictates that there are two main areas on the face that have a higher incidence of vascular occlusion following soft tissue augmentation with filler.



1) Glabellar region[1,15]

Supratrochlear artery, supraorbital artery and cutaneous branches of the ophthalmic artery.

50% of cases of vascular occlusion occur as a result of intravascular injection of dermal fillers into the glabellar region due to the poor collateral circulation in this watershed area[10,11,13,17].

2) Nasolabial Fold[1,15], nasal tip and alar triangle

Facial artery[15], angular artery[15] and lateral nasal artery.

The nasal tip and alar are also commonly affected due to these being supplied by an end artery with limited collateral blood flow[1]. The angular artery turns sharply within the alar triangle and is prone to external compression or inadvertent injection leading to vascular occlusion[10,11,15].

Minimising the risk of a vascular occlusion:

1) Having a detailed knowledge of the 3-dimensional anatomy of the area being treated[15,18]. Practitioners need to understand the distribution and depth of vessels of the target area and possible variations of these.

2) Aspiration prior to injection to try and ascertain that the injection is not intravascular. Although it is well known that aspiration may not always be possible, even if the needle tip is within a vessel[1,7,15,17,19].

   Practitioners should not depend solely on aspiration as a stand-alone test for safety. Published evidence from Casabona, 2015[20] showed reliability of aspiration at 53%, Van Loghem, 2017[21] recorded reliability between 33%-63%, depending on various factors including needle size, pull back time and needle length. Torbeck, 2019[22] suggested that the rheology of the filler used is a major factor in gaining a true positive aspirate. Rheology determines amount of pull back and time of pull back, these parameters ranged from 0.5 to 30 seconds using either 0.2ml or 0.5ml[22]. Therefore, injectors should adjust amount of time to aspirate and adjust the volume pulled back on the syringe if this test is to have any reliance.

3) Slow injection technique under low pressure with the filler delivered at the appropriate depth and tissue plane[7,13].

4) The smallest possible volume to achieve the desired effect should be used, avoid overfilling an area[1] and if more product is required, a repeat treatment in 7-14 days may be more appropriate and safe[13,15,17].

5) Avoid areas of previous scarring as deep tissue scars may fix arteries in place and make them easier to penetrate[1,15].

6) Avoid bolus injections in areas at risk of vascular occlusion[25].

7) Avoid using adrenaline, or products containing adrenaline, as this may mask the blanching produced by an occlusion[1,8].

8) Injection of local anaesthetic or pre-mixed with a soft tissue filler may mask any pain experienced by the patient in the event of a vascular occlusion and

the practitioner should not rely on this warning sign alone.

9) Do not inject into the tip of the nose as this is a highly vascular area with restricted tissue space.

10) Use caution when injecting into the glabellar region[13]. Injections should be placed superficially (intradermal) and medially[17]. Practitioners should be encouraged to use botulinum toxin first in the glabella to reduce severity of wrinkle before injecting soft tissue filler. This area should only be injected by experienced injectors.

11) The use of blunt ended cannulas of 25G or larger bore diameters are less likely to penetrate vessels and lead to an inadvertent intravascular injection[1,15]. The risk of penetration of a vessel wall with a blunt tipped cannular increases with the force used and the age of the patient.

12) Patient selection is paramount, be cautious when treating patients who have undergone rhinoplasty[10] or other surgical procedures as the anatomy and vasculature may be altered.

13) Pay attention when injecting – look for warning signs and listen to your patient!

14) The risk of vascular occlusion is higher when using fillers of a greater density (higher G prime) as these have the potential to create a greater extrinsic pressure on a vessel.

15) Practitioners, particularly less experienced practitioners, should consider using only reversible hyaluronic acid fillers as this may make the management of a vascular occlusion easier due to its hydrolysis by hyaluronidase[1].

Treatment of vascular occlusion:

A vascular occlusion may result from arterial occlusion by direct injection into an artery or embolisation of product, typically presenting immediately with acute pain and blanching. It may also occur due to venous occlusion from external compression of a vessel by soft tissue filler or subsequent oedema and compression, more often with hyaluronic acid fillers. Venous occlusion usually presents later with a less severe dull pain or no pain at all[14] and dark discolouration of the skin[13].

In some cases, it may be possible to resolve the occlusion with conservative measures, such as massage, tapping and or heat applied to the area. However, if conservative methods fail, hyaluronidase should be administered without delay when a hyaluronic acid dermal filler has been used.

1. **Immediately stop treatment**[7,8,10,11,13,14,17,18]

   As soon as the practitioner suspects the blood supply has been compromised (typically pain and blanching in the injected area), the most important step is to immediately discontinue injecting any further product and if possible, aspirate any product when withdrawing the needle or cannula[23].

   Inform the patient of the problem. If the practitioner is not confident or is inexperienced in the management of a vascular occlusion, they should seek the immediate advice of a more experienced practitioner. However, a vascular occlusion needs prompt management as the risk of tissue

damage and skin necrosis increases over time.

Assess Capillary Refill Time (CRT):

The capillary refill time should be assessed on the affected and unaffected sides. Capillary refill time (CRT) is defined as the time needed by a distal body region, such as the fingertip, to regain the original colour after having been compressed. Sansone, 2017[24] considers a normal physiological capillary refill time of 2 and 3 seconds under 65 years of age, for males and females respectively, as well as 4 seconds in both genders for elderly persons. CRT greater than 3 seconds may be suggestive of a vascular compromise. A fast capillary refill time on a background of a bluish skin discolouration may indicate venous insufficiency[15].

It is prudent to observe and assess skin colour and capillary refill prior to treatment as a benchmark for post treatment assessment.

To test capillary refill time, moderate pressure with either a finger or small, firm, flat object should be applied to the area being assessed for 5 seconds and then released. The time for the skin to return to its normal colour should be observed and recorded. The test should be conducted over the entire area and on both the affected and unaffected sides for comparison.

If capillary refill time is sluggish but not less than 3 seconds, an initial attempt using conservative measures, such as massage, tapping and heat, should be used.

If capillary refill time is not improved by conservative measures or CRT is greater than 3 seconds, practitioners should employ the ACE Group high dose pulsed hyaluronidase protocol[25].

2. **Firmly massage the area**[7,8,10,11,13,14,17,26]

   Firm and prolonged massage may help to encourage blood flow and may remove any obstruction caused by a foreign body occluding a vessel. Massage may be required for several minutes.

3. **Apply heat**[7,8,10,11,13,14,17,18,19,23,26]

   Heat will encourage vasodilatation and increase blood flow to an area.

4. **Tap the area**[14,19]

   Tapping over an area may dislodge intra-arterial emboli either at the site or further up in the vessel.

5. **Inject with hyaluronidase**[1,7,10,11,13,14,18,19,23,26]

   Where hyaluronic acid fillers are the culprit, injecting with hyaluronidase may relieve the problem before complications even occur[25]. Practitioners must remember that this is a time critical event and that test patching is not required if hyaluronidase is used for a vascular occlusion as the risk of tissue damage is generally greater than the risk of anaphylaxis. As with any aesthetic treatments, it is important to have appropriate resuscitation equipment available to deal with any potential complication[15]. There is some evidence to suggest that using hyaluronidase when a non-hyaluronic acid soft tissue filler has been injected may lessen the

subsequent tissue damage[11] due to dissolving native hyaluronic acid and decreasing pressure on the blood supply[23].

Practitioners should employ the ACE Group high dose pulsed hyaluronidase protocol[25]. Despite the simplicity of the intervention, it has prevented necrosis in virtually all cases since it has been implemented and even up to 48 hours after the initial treatment. The protocol involves repeated administration of relatively high doses of hyaluronidase into the whole area of compromised tissue and not just where the filler was injected[14], repeated hourly until clinical resolution (improvements in capillary refill, skin colour and pain). This technique has also led to successful and complete recovery without any adjunctive treatment required[2].

There is contradictory evidence to suggest that hyaluronidase diffuses into the lumen of blood vessels even when injected external to it. However, when treating a vascular occlusion, it is not necessarily essential to inject directly into the vessel, but the surrounding area is also likely to result in dissolution of the product. Indeed, the injection of hyaluronidase into the subcutaneous plane rather than attempting intra-arterial injection has shown more favourable outcomes[27].

6. **Aspirin**[1,15]

Following the evidence for the use of aspirin in cardiovascular disease, in order to limit platelet aggregation, clot formation and further vascular compromise, a stat dose of 300mg should be given immediately, followed by 75mg a day[28] until the vascular occlusion has resolved where there are no contra-indications. Concomitant use of gastric protection medication may be recommended in some patients.

If treatment of a vascular occlusion has failed, necrosis may ensue. The patient should be monitored regularly and if tissue breakdown occurs, a referral for specialist management and care may be appropriate (Refer to ACE Guidelines on Necrosis).

7. **Antibiotics**[1,10,13,23]

Necrosis consists of dead cells and dead tissue and is prone to secondary opportunistic infection. Depending on the extent of necrosis, topical and/or oral antibiotics may be required to promote healing and to prevent further complications developing.

Anti-herpetic medication may be advised if necrosis occurs in a susceptible patient in a perioral distribution[1,11].

In the case of a treated vascular occlusion without any signs of skin damage, antibiotics should not be given for prophylaxis.

8. **Superficial debridement**[7,10,13,17,18]

Referral to a plastic surgeon may be required for removal of dead tissue to promote healing.

9. **Wound care management**[1,10,17]

Appropriate dressings and wound care to encourage healing.

10. **Pain management**

Pain management needs considering in cases of necrosis, as although over

the counter medication may be all that is required, necrosis can cause severe pain requiring opioid analgesia.

11. Refer

It is always sensible to involve other practitioners experienced in the management of vascular occlusion for further advice and/or treatment.

12. Speak to your medical defence organisation

A vascular event can be a distressing ordeal for both patient and practitioner. Whether or not it is managed well and resolved, a claim may ensue.

Other treatment options:

Hyperbaric oxygen therapy (HBOT) has been successfully used in nasal tip grafting following cases of cancer or trauma with positive results on revascularisation although there is limited evidence to recommend this for necrosis secondary to aesthetic procedures[10,13,29]. Several case reports have described an improvement in aesthetic outcome using HBOT[1] but some authors do not feel that the costs, risks and inconvenience is warranted[30]. HBOT increases the supply of oxygen to the compromised tissue and helps to remove toxic free radicals[23,29].

The use of low molecular weight heparin[1,11] has been used to prevent thrombosis and embolisation in one case report[31] although there is not enough evidence to recommend this as a standard treatment.

Oral vasodilators including PDE5 (cGMP-specific phosphodiesterase type 5) inhibitors or Prostaglandin E1 (PGE1)[1] have also been advised for the treatment of vascular occlusion but evidence is lacking for their wider use for this indication[11].

No longer recommended: Nitroglycerin paste

2% Nitroglycerin (glyceryl trinitrate) paste induces vasodilatation and increases blood flow to the area. It has been recommended to be used topically in the event of a vascular occlusion to encourage reperfusion[1,7,8,10,11,13,17,19,26,32]. Dayan et al[32] reported a series of 9 patients whose vascular occlusion was successfully healed with a protocol of hyaluronidase and nitroglycerine paste 2cm applied daily with massage in clinic plus a daily dose of aspirin 325mg with antacid until capillary refill was less than 2 seconds. Nitroglycerin paste (Rectogesic®, used off label) is applied under an occlusive dressing and used for several days, it was recommend applying for 12 hours and then removing for 12 hours until clinical improvement was seen[17] or until it was no longer tolerated. Nitroglycerin can lead to skin reactions, irritation and erythema as well as systemic effects including dizziness and hypotension.

However, a study by Hwang et al, 2016[34] failed to show any improvement in outcome using topical nitroglycerin ointment 2% in induced arterial occlusion in an animal model using rabbit ears. In fact, it tended to cause a more congested appearance and worsen perfusion by allowing filler material to diffuse from capillaries into larger arterioles thereby further compromising the circulation.

The authors do not recommend the use of topical nitroglycerin for vascular occlusion following soft tissue augmentation.

Follow-up:

All patients presenting with a vascular occlusion need follow up until the problem has completely resolved, this may be on a day by day basis initially. Immediate follow up is required when a patient contacts the practitioner and a delayed onset of vascular occlusion is suspected. All practitioners carrying out soft tissue augmentation should provide patients with an emergency out of hours number and if a patient reports symptoms that may be consistent with a vascular occlusion, an immediate face to face review should be arranged. It is not acceptable to do this via electronic media. Good follow up, on-going support and full explanations to the patient is the best approach to stop a complication turning into a litigious medical malpractice claim.

Table 1 (Adapted from De Lorenzi, 2017[3])

SIGNS/SYPMTOMS	TIME OF ONSET	CONSIDERATIONS
Pain	Immediate or seconds.	May be absent in the presence of local anaesthetics
Blanching	Immediate, may be transient.	Phenomenon of blanching may be fleeting in nature due to assistance in perfusion from collateral vessels. Adrenaline in local anaesthetics may mimic and even disguise blanching associated with intravascular injection of soft tissue filler.
Livedo pattern	Minutes to tens of minutes.	Skin colour may be affected by ambient temperature, poor circulation or from pre-existing medical conditions.
Delayed capillary refill time	Minutes.	Greater than three seconds suggestive of vascular compromise.
Blue/Grey appearance	Tens of minutes to hours.	Due to the build-up of deoxygenated blood in the affected tissue.
Skin breakdown	Days.	Opportunistic anaerobic bacteria predominate due to the lack of oxygen in the tissues and choice of antibiotic needs to be considered.
Repair	Days/weeks.	After epithelial integrity has been lost, repair begins via the method of secondary intention.

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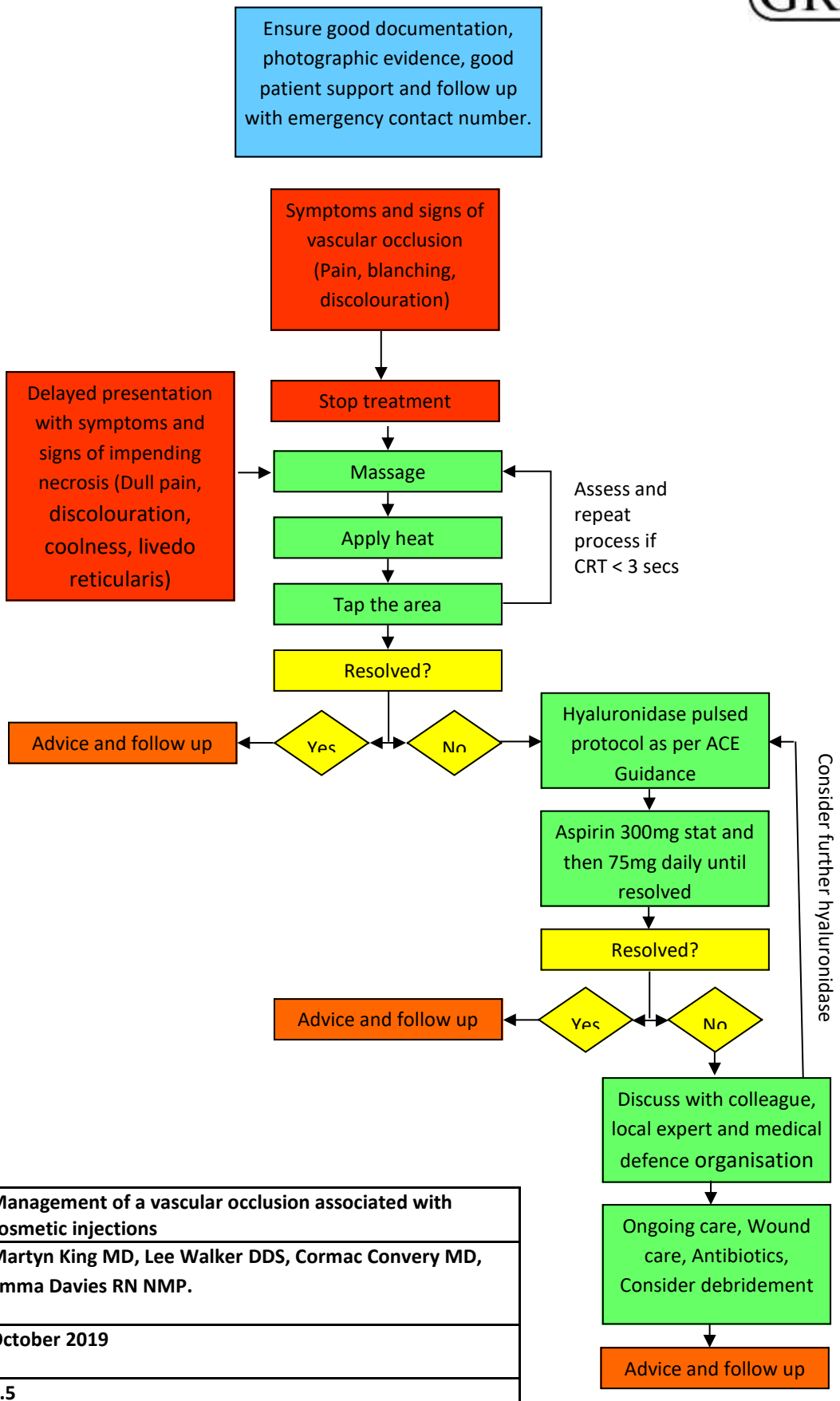

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Management of a vascular occlusion and the prevention of skin necrosis associated with cosmetic injections

The ACE Group have produced a series of evidence based and peer reviewed guidelines to help practitioners prevent and manage complications that can occur in aesthetic practice. These guidelines are not intended to replace clinical judgement and it is important the practitioner makes the correct diagnosis and works within their scope of competency. Some complications may require prescription medicines to help in their management and if the practitioner is not familiar with the medication, the patient should be appropriately referred. Informing the patient's General Practitioner is considered good medical practice and patient consent should be sought. It may be appropriate to involve the General Practitioner or other Specialist for shared care management when the treating practitioner is not able or lacks experience to manage the complication themselves. Practitioners have a duty of care and are accountable to their professional bodies and must act honestly, ethically and professionally.

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