ACUTE LIMB COMPARTMENT SYNDROME:
The Limb at Risk and Implications for Peri-Operative Analgesia

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INTRODUCTION

Acute limb compartment syndrome (ALCS) is a surgical emergency. Delay in diagnosis and management may result in disability, cosmetic and medico-legal complications as well as death. (1) ALCS is a relatively rare complication with an incidence around 3.1 per 100 000. (2)

Litigation in orthopaedic cases of ALCS are mainly due to delays in diagnosis and treatment. (3) While the diagnosis of ALCS is primarily dependent on the surgical team, anaesthetists are frequently involved in the operative management of this devastating complication. In addition, pain is an important symptom of ALCS with claims that perioperative analgesia may result in a delay in its diagnosis. The anaesthetist should be aware of the limb at risk as this has implications for post-operative pain management. We may also be relied upon to diagnose the condition or to alerting surgeons of developing ALCS in our interaction with patients as part of the post-operative pain service.

DEFINITION

A compartment syndrome occurs when an acute rise in pressures within a closed compartment compromises blood supply to tissues within the space. (4) In ALCS increased pressures within a closed osseo-facial compartments of the limb lead to local ischemia and tissue necrosis. (4) Most common compartments involved are the calf and forearm. (5) A chronic exertional compartment syndrome with muscle pain and elevated pressures within affected compartments is seen. It requires unique diagnosis and management which will not be described further. (5)

ANATOMICAL COMPARTMENTS

The musculo-skeletal structures of the limbs are enclosed within compartments surrounded by fascial layers with a limited ability to stretch. (6) The compartments enclose major muscle groups and neuro-vascular structures that pass through the compartment. Compromise of these structures leads to the symptoms and signs of compartment syndrome. The anatomy of the upper and lower limb compartments are briefly discussed below. (3)

Upper Limb

Arm

The arm consists of two compartments: anterior and posterior. The anterior compartment of the arm has mainly flexor functions while the posterior compartment has extensor functions. (6)
**Forearm**

The forearm consists of four compartments: the volar compartments (deep and superficial), the dorsal compartment and the lateral compartment (also known as the mobile wad).\(^6\) It has been shown that these compartments are interconnected. Consequently, decompression of the volar compartment alone may decrease the pressure in the other two compartments.\(^6\)

**Lower Limb: Thigh**

ALCS rarely develops in the thigh as it has three large anterior, posterior and medial compartments.\(^8\)
Lower Leg
The lower leg contains four compartments - anterior, deep and superficial posterior and lateral. Each compartment contains a major nerve. Signs of compartment syndrome affecting the anterior compartment include loss of sensation between the first two toes and weakness of dorsiflexion. Compartment syndrome of the lateral compartment includes weakness of dorsiflexion and foot inversion. Plantar hyperesthesia, weakness of toe flexion and pain with passive toe extension may be seen in deep posterior compartment syndrome. Inter-individual variability exists, which must be considered as both compartments especially the deep posterior compartment, are frequently involved in compartment syndrome.
PATHOPHYSIOLOGY

There are several hypotheses regarding the impairment of the circulation which occurs in ALCS - the arteriovenous pressure gradient theory described by Matsen and Krugmire is most commonly accepted. (10) As intra-compartmental pressure increases, the luminal venous pressures increase leading to a decrease in the arteriovenous pressure gradient. This results in a decrease in local perfusion. (1) Reduced venous drainage increases interstitial tissue pressure with resulting oedema. (1) The lymphatic drainage is then increased to protect against increasing interstitial fluid pressure. Once this has reached its threshold, further increases in intra-compartmental pressure cause collapse of the lymphatics. (10) In the late stages of a compartment syndrome arterial supply is compromised and continuing flow of blood into the compartment worsens swelling and oedema. (10) Critically low perfusion pressure results in tissue hypoxaemia. (10) Hypoxia and oxidative stress cause cell oedema due to impairment of the sodium–potassium ATPase channels. (10) The loss of cell-membrane potential results in chloride influx, which leads to swelling and cellular necrosis. A positive feedback loop is created with increasing in tissue swelling worsening the hypoxic state. (10)

Reperfusion injury is another cause of ALCS. (10) Once perfusion is restored, the production of oxygen free radicals and calcium influx results in an impairment of oxidative phosphorylation and destruction of cell membranes. (10) Hyperkalaemia and acidosis follow which may result in renal failure, arrhythmias and multi-organ damage and death.

TIMING TO FASCIOTOMY

The time from initiation to ALCS is variable, depending on the extent of injury and site. An ischaemic time of one hour in peripheral nerve tissue may lead to reversible neuropraxia, and with irreversible axonotmesis occurring as early as four hours. After six hours of ischaemia, irreversible changes are likely to result in contractures, nerve and vessel damage. (10) Improved outcomes have been reported when performing a fasciotomy within six hours after diagnosis (after onset of ALCS). This has been shown to have a lower amputation rate 3.2% compared to fasciotomy after 12 hours - with a 14% amputation rate. (11)

ALCS can be due to direct limb-related injury or non-limb-related injury. (10)

CAUSES OF ACUTE LIMB COMPARTMENT SYNDROME: (5)

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WHO IS AT RISK?

ADULT POPULATION

McQueen et al, have evaluated the risk factors for ALCS in adults patients over an 8 year period. Their study involved a 164 cases of ALCS, and categorised patients into fracture and non-fracture related groups.(12)

Age and Gender
High risk factors identified in McQueen’s study where young males, less than 35 years old.(12) The mean age for men was 30 years compared to 44 years for women.(12) This was postulated to be due to greater muscle mass and inelastic compartments and higher incidence of high velocity injuries in the male population group.(13)

Fractures
McQueen’s study showed that the primary condition causing ALCS was underlying fractures. This occurred in 69% of patients- just over half of these where fractures of the tibial diaphysis (36%).(12) This may be due to the high incidence of tibial fractures.(14) Only 5% of tibial plateau fractures developed a compartment syndrome.(12) These incidences were slightly highly than reported in other studies.(14) Fractures of the distal end of the radius where implicated in ALCS in 9.8% of adult cases.(12) The incidence of ALCS in patients with distal radius fractures was 0.25%. 7.9% of patients with ALCS occurred after diaphyseal fractures of the forearm.(12)

Soft tissue injury
Significant soft tissue injury without an associated fracture is also a cause of ALCS. Mainly due to direct blows to the affected compartment and the crush syndrome.(12) ACLS was related to soft tissue injuries without associated fractures in 23.2% of cases.(12) Crush syndrome was the underlying cause of ALCS in 7.9% of cases. Of this group 10.3% of patients where on anticoagulants or had a bleeding disorder.

McQueen’s study recommended intracompartmental pressure monitoring for (1) tibial diaphysis fractures, especially young men; (2) high-energy injury to the forearm diaphysis or distal radius; (3) high-energy fractures of the tibial metaphysis; and (4) following soft tissues injury in young men or those with a bleeding tendency.(12)

Other Risk factors
Other risk factors identified in the literature include the use of anticoagulants, vascular injuries, tourniquet use, tight casts and complications of intravenous and intraosseous infusions.(12) Other concerning factors include increased operating time and increased time spent on closed manipulation of fractures.(5)

PAEDIATRIC AND ADOLESCENT POPULATION

The incidence of ALCS in the paediatric population is lower than adult figures, although physiologically higher intra-compartment pressures (13-16mmHg) mean that children may be at greater risk of ALCS.(15)

Age and Gender
Grotkau and colleagues evaluated a total of 133 cases of ALCS- in children and adolescents. The study showed a predominance of cases of ALCS in male patients. The 10-14 year age group showed a peak incidence of ALCS.(16)
Fractures
Josef et al’s, small case series of 24 cases of ALCS in child and adolescent patients showed that in both groups fractures followed by soft tissue contusions was a cause of ALCS.(15) 85% of cases of ALCS where from fractures whereas 13% from soft tissue injuries. 78% of these fractures where of the lower extremity whereas 21% where of the upper extremity.(15)

In a review by Jozef et al, of all upper extremity ALCS- 74% where from forearm fractures, 15% from supracondylar and 11% from Carpal/metacarpal fractures.(11)

Supracondylar fractures
Supracondylar humerus fractures have been identified as one of the most frequently associated injuries in ACLS of the upper limbs in children.(11) ALCS is reported to occur in 0.1-0.3% of paediatric cases with supracondylar fracture. The required cast elbow flexion to 90 degrees and risk of vascular compromise result in an increased risk.(11)

Forearm fractures
Floating elbow-ipsilateral distal humerus fractures with forearm fractures place patients at increased risk of a compartment syndrome. Forearm fractures of the radius and ulnar- especially in cases undergoing prolonged operative times and intramedullary nailing are also implicated in ALCS.(11)

Lower Limb Fractures
The lower leg is also the most common site of ALCS in children.(17) Shore and colleagues showed that the incidence of ALCS was 11.6% in a study of 212 children with tibial fractures. Tibial tubercle fractures place children at increased risk of ALCS due to associated vascular injury.(17) High energy tibial shaft fractures also represent a group with increased risk. Josef et al showed that in children with ALCS of the lower limb 90% of cases where from leg fractures (tibia/fibula). The study showed a significant increased risk of ALCS in open leg fractures.

SCREENING AND DIAGNOSIS
Current diagnosis of ALCS relies on clinical examination and the ancillary use of special investigations. Commonly accepted signs of ALCS include the 5 P’s: pain, paraesthesia, paralysis, pulseless and pallor. However these signs are classically present with acute arterial ischaemia and maybe misleading in patients with developing ALCS. Of these important signs, pain is reported to be one of the first indicators of a developing compartment syndrome.(11) Specifically, the clinician should be alert to ALCS when pain that is progressive, requires increasing analgesia, is out of proportion to examination and occurs on passive stretch.(2) Loss of two point discrimination and paraesthesia in the affected extremity might be due to hypoxia of nerve tissue within a compartment.(18) Motor nerves may be resistant to ischaemia, and motor deficits might develop late therefore clinicians should be careful not to exclude ACLS based on absent neurological findings.(10) Compartment fullness may indicate a risk of ALCS. However subjective assessments of compartment tension have been shown to be unreliable and therefore, are insufficient to make a diagnosis.(19) .(18) Ulmer examined clinical signs in the diagnosis of ALCS and found a higher false-positive rate in relation to the true-positive rate.(18) Thus, clinical findings of ALCS were more likely to be present in patients without ALCS.(18) Clinical signs of ALCS therefore have a poor predictive value with a low sensitivity but high specificity for the diagnosis.(18) A combination of three or more signs in a patient at risk of ALCS may result in increasing sensitivity.(18) Therefore other diagnostic devices may be required to establish the diagnosis of ALCS, especially when diagnosis is in doubt.(18) While pain and paraesthesia are important clinical signs of developing compartment syndrome- pallor, paralysis, and absent pulses are very late signs.(10) An absent pulse only occurs after intra-compartmental pressure exceeds systolic blood pressure.(10)
Signs and symptoms of ALCS maybe difficult to assess in paediatric patients. (16) In children, clinicians should be alert to possible ALCS in patients with the 3A’s increasing analgesic requirements (difficulties with sedation), anxiety and agitation. (19) Difficulties in diagnosis may also be present in other patient groups, such as non-verbal patients, patients with developmental delay, anxiety, comatose patients, severe neurological injury, and patients with distracting injuries, the critically ill and patients who have undergone prolonged general anaesthesia.

A method for the accurate diagnosis of ALCS, especially in the difficult patient groups has yet to be developed. Some ancillary tests which may assist in the diagnosis are:

**INTRA-COMPARTMENTAL PRESSURE MEASUREMENT**
The normal intra-compartmental pressure range in adults is 4-8 mmHg while higher normal values occur in children (10–15 mm Hg). (10) Absolute intra-compartmental pressure greater than 30 mm Hg is reportedly associated with impaired tissue perfusion and is an indication for emergency fasciotomy. (3) Researchers have also explored the use of differential pressure (Δp=diastolic blood pressure – intra-compartmental pressure), with a threshold of less than 30 mmHg. (4) Differential pressure has been reported to be more sensitive minimizing the risk of unnecessary fasciotomies. (10) Various ways to measure intra-compartmental pressures exists:

**Needle Manometers**
Needle manometers are commonly employed for intra-compartmental pressure measurement but have been shown to have inaccuracies and cannot be used continuously. (4)

**Catheter technique systems**
These are more complex but can be used for continuous monitoring. (13) They require accurate placement of the transducer and are prone to obstruction. (13) Often arterial line transducer systems are used. (13) The accuracy is improved when placed within 5 cm of the fracture site in all compartments concerned. (10)

**Stryker Intra-compartmental Pressure Monitor system (STIC)**
This is the most validated method to measure limb ICP. (4) The system measures tissue fluid pressure, therefore it requires the injection of saline into the compartment concerned. (10) However less than 50 % of centres in the UK have access to this device to measure intra-compartmental pressures, the availability of this in the South African sector is significantly lower. Importantly studies have suggested that the use of continuous intra-compartmental pressure measurements may lead to unnecessary fasciotomies and increased complications such as prolonged hospitalization, infection and delayed healing. (4)

**NEAR INFRARED RED SPECTROSCOPY**
The principle behind near infrared spectroscopy (NIRS) is the use of differential light reflection and absorption to estimate the proportion of saturated oxyhaemoglobin 2–3 cm below the skin. (13) NIRS is non-invasive and can be used continuously. (13) Accuracy may be limited by skin pigmentation, subcutaneous fat and compartment depth. (13) Small studies have shown that lower oxygenation levels correlate with high intra-compartmental pressures and reduced perfusion pressure. (19) However threshold values have not yet been determined.

**CREATININE PHOSPHOKINASE MEASUREMENTS**
Serum creatinine phosphokinase (CPK) has been used as an indicator of compartment syndrome to indicate muscle necrosis. (13) Elevated CPK levels may be useful when diagnosis is in doubt and intra-compartmental pressure measurement is not available. (13) Severe rhabdomyolysis can lead to acute kidney dysfunction and failure. (3)
Other modalities under investigation include, ultrasound and magnetic resonance imaging, laser doppler flowmetry, scintigraphy, direct nerve stimulation and muscle hardness measurement.

CONCERNS OF ANALGESIC CHOICE FOR EXTREMITIES SURGERY IN PATIENTS AT RISK FOR ALCS?
Regional anaesthesia (epidural anaesthesia and peripheral nerve blocks), as well as systemic intravenous morphine patient-controlled analgesia (PCA) have been implicated in masking the early signs of compartment syndrome.(2, 11, 20) Regional anaesthesia has been implicated in masking ischemic pain in ALCS and resulting in a delay diagnosis.(2) Especially when longer acting peripheral nerve blocks are used or when blocks are associated with greater motor blockade. However regional anaesthesia provides several benefits in these patients groups, including better pain control, shorter hospital stays and avoidance of systemic opioids and general anaesthesia.(2) Similarly PCA- allows patients to control their analgesic requirements improving analgesia and avoiding opioid overdose and side effects.(2) It is also advantageous as it limits workload on nursing staff.(21) Morphine PCA has also been implicated in masking the symptoms of ALCS and delaying its diagnosis.(21) Some clinicians believe the use of regional anaesthesia in orthopaedic injuries poses a greater risk than PCA for masking the signs of ALCS.(2) Reports also suggest that when these methods of analgesia are used in high risk patients such as paediatric patients and severely obtunded patients there is an increased risk for delayed diagnosis due to their inability to communicate.(4)

WHAT IS THE IDEAL ANALGESIC CHOICE IN PATIENTS AT RISK FOR ALCS?
Currently the evidence based data considering the ideal analgesic modality in high risk patients is insufficient.(2) Analgesic modalities are commonly misattributed as the cause rather than an association with a delayed diagnosis of ALCS.(2)

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<td>• Systematic review</td>
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<td>• 28 articles -20 case reports and 8 case series.</td>
<td>• 34 relevant articles</td>
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<tr>
<td>•No evidence that PCA or regional analgesia delay the diagnosis of ALCS.</td>
<td>• 28 Case Reports</td>
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•No evidence to support the use of one modality of analgesia over the other with regard to lessening the risk of developing ALCS.

•Results did not show, that RA can be associated with higher risk in delay ALCS diagnosis compared to other analgesic modes.

Summary of literature: Effect of postoperative analgesia on diagnosis of ALCS. (11) (2) (20)

The finding of Mar and McGuirk, Driscoll et al and Jozef et al is summarised above. Driscoll et al, evaluated the effects of regional anaesthesia or PCA in orthopaedic surgical cases who developed ALCS. 23 articles focused on regional anaesthesia with 29 patient cases and five articles where related to PCA’s with 8 patient cases.
Of 23 regional anaesthesia articles, 13 authors (involving 19 cases) concluded that regional anaesthesia masked the symptoms of ALCS resulting in a delay in the diagnosis. However, of these 19 cases, 11 presented with breakthrough pain. In addition, eight cases who did not report pain, did present with other symptoms of ALCS, such as paraesthesia, oedema, tense and shiny skin, or paralysis. In the remaining ten regional anaesthesia articles, eight (80%) authors (eight cases) concluded that regional anaesthesia did not mask the symptoms of ALCS while two (20%) authors (two cases) were uncertain of the conclusion. Eight of the 23 regional anaesthesia articles were published between 2010 and 2013. The majority of the articles published between 2010 and 2013 did not conclude that regional anaesthesia masks symptoms of ALCS. When evaluating these articles, six (75%) concluded that regional anaesthesia or PCA does not mask symptoms of ALCS- which is more representative of current practise.

The PCA articles represented only eight total cases- three authors (six cases) concluded that PCA does mask signs of developing ALCS. In these 6 patients ALCS was diagnosed with a delay compared to regional anaesthesia. This suggests a slightly increased risk of delay with PCA however larger studies are required to draw definitive conclusions.

Overall, of the 37 cases (regional anaesthesia and PCA groups) who developed ALCS, 22 cases did present with breakthrough pain which was neglected. In the remaining 15 cases, patients where pain-free but did display other signs of ALCS.

They concluded that there are no clear recommendations regarding the use of regional anaesthesia or PCA in adult patients who are at increased risk of developing ALCS and there is no clear evidence to support the use of one modality over the other with regard to decreasing the risk of developing ALCS.

The French Society of Anaesthesia does not consider the risk of ALCS as a contraindication for regional anaesthesia. It is postulated that regional blockade can increase the blood flow through sympathetic blockade without blocking the warning signs of ALCS, therefore the society encourages the use of regional anaesthesia in patients in at risk of ALCS.

In 2010 British military leadership, also advocated for the use of regional anaesthesia in cases of limb trauma. This recommendation was based on a review of data that found that the majority of ALCS cases were identified without delay.

What about Paediatric patients?

Data specific to the paediatric population is lacking. Llewellyn and Moriarty conducted a prospective audit of paediatric patients with epidural anaesthesia. Four cases of ALCS where reported- with an incidence of 1: 1400. 1 patient had undergone an orthopaedic procedure and 3 patients’ general surgical procedures. In 2 cases the patients complained of persistent leg pain remote from the surgical site, in one patient the functioning of the epidural was questionable and breakthrough pain persisted despite the initiation of a PCA, and in the last patient leg pain persisted throughout the post-operative course with normal pressures on ICP monitoring. ALCS was diagnosed within 24 hours in all cases- and the audit concluded that the occurrence ALCS does not appear to be masked by the epidural analgesia.

The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anaesthesia and Pain Medicine regarding controversial topics in paediatric pain medicine in 2015 advocated for the use of regional anaesthetic techniques in paediatric orthopaedic procedures. They outlined best-practise rules and highlighted close follow-up by the acute pain service. They stressed that the root cause of delay in children is inadequate monitoring.
BEST PRACTISE RULES

1. A comprehensive discussion with the patient (or family) about the risks and benefits of the chosen technique. In reviews of lawsuits involving cases of ALCS amongst orthopaedic surgeons, the majority of cases won by the plaintiff cited poor surgeon-patient communication. (2) A record of patient counselling should be made in patient notes. (11)
2. Monitoring of high risk cases including instituting dedicated observation charts-monitoring pain and analgesic requirements and neurovascular assessments of the limb at risk. (22)
3. Communication with surgeons about the risks of ALCS in patients on an individual basis. (13)
4. Ultrasound guidance should be used for regional blocks. (13)
5. Single shot blocks are advocated-and if catheters are used, blocks should be titrated to the lowest motor and sensory blockade. (22)
6. Use low concentrations of local anaesthetics to avoid motor blockade and allow breakthrough pain detection. The volume of the local anaesthetic should also be reduced. (22)
7. Caution with additives to blocks such as adrenaline. (2)
8. Intra-compartmental pressure monitoring is recommended in (1) tibial diaphysis fractures, especially in young men; (2) high-energy injury to the forearm diaphysis or distal radius; (3) high-energy fractures of the tibial metaphysis (4) following severe soft tissues injury in young men or those with a bleeding tendency, young children, unconscious patients and when there is diagnostic uncertainty. (12, 19)
9. Constant review by the acute pain service and in patients at high risk for developing ALCS with a search for breakthrough pain, pain at a site remote from the operative site, increasing restlessness and increasing demands for analgesia. (2)
10. Epidural anaesthesia must be supervised by the acute pain service with an avoidance of dense sensory or motor blockade especially at remote sites. (19)
CONCLUSION

While ALCS remains primarily a surgical diagnosis, analgesic management post-operatively has important implications for the diagnosis of ALCS in the high risk patient. Currently the evidence based data considering the ideal analgesic modality in patients with a high risk of ALCS is insufficient and no clear recommendations exists regarding the use of regional anaesthesia or PCA in patients who are at increased risk of developing ALCS. Analgesic techniques should be individualised with diligent monitoring and implementation of the “best practise rules” described in high risk patients irrespective of the chosen analgesic technique.
REFERENCES