

Case Scenario: Compartment Syndrome of the Forearm in Patient with an Infraclavicular Catheter

Breakthrough Pain as Indicator

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ACUTE compartment syndrome (ACS) represents a limb-threatening condition. Delaying diagnosis and therapy may lead to irreversible neuromuscular ischemic damages with subsequent functional deficits.¹ Diagnosis is primarily clinical and characterized by a pain level that quality exceeds the clinical situation. Diagnosis is assessed by invasive pressure monitoring within the suspected compartment. Once ACS has been confirmed it represents a surgical emergency with definitive treatment requiring immediate fasciotomy to relieve the pressure within the affected compartment. Irreversible tissue damage can occur within 4–6 h after the onset of symptoms. However, nerves are already seriously damaged after 2 h of increased compartment pressure.^{1,2} Concerns about masking pain as cardinal symptom and therefore leading to a delay in diagnosis and therapy have been raised in connection with regional anesthesia.^{3,4} Moreover, several case reports and case series have blamed different types of regional anesthesia^{4–11} and even the use of opioid patient-controlled analgesia¹² for delaying diagnosis of ACS. Therefore, the use

of regional anesthesia for trauma and orthopedic surgery remains controversial.^{4,6,13} A case involving continuous regional anesthesia of the upper extremity and the development of an ACS is presented.

Case Report

A 47-yr-old woman was scheduled for surgical treatment of a complex distal humerus fracture of her right dominant arm. Medical history was unremarkable except for obesity (body mass index 41.5), a metabolic syndrome (diabetes, obesity, and hyperlipidemia), and sulfazine treatment due to Crohn disease. The right arm showed classical signs of hematoma and swelling without any clinical sign for increased compartment pressure. All nerve functions were preserved. An open reposition of the fracture, osteosynthesis of the capitulum, trochlea humeri, and radial condylus were performed with postoperative placement of an open arm splint. The anesthetic management combined infraclavicular catheter, placed preoperatively but no local anesthetic was given until after the patient has been extubated, and general anesthesia performed with target-controlled infusion of propofol (Disoprivan®, AstraZeneca, Zug, Switzerland) and remifentanyl (Ultiva®, GlaxoSmithKline, Münchenbuchsee, Switzerland). Infraclavicular catheter placement and general anesthesia were uneventful including stable patient's hemodynamic parameters during the 150 min lasting surgical intervention. After extubation, the sensomotor function of the operated arm was checked by the surgeons and the infraclavicular catheter was started thereafter. An initial bolus of 30 ml ropivacaine 0.5% (Naropin®, AstraZeneca) was applied with intermittent aspiration, and block assessment indicated a successful block. The patient was transferred to the postoperative care unit for further observation and a patient-controlled regional analgesia infusion with ropivacaine 0.3% (Naropin®) was started with a continuous rate of 6 ml/h, an additional bolus of 5 ml with a lockout time of 20 min. Additionally, acetaminophen (Perfalgan®,

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Bristol-Myers Squibb, Baar, Switzerland) 4 × 1 g/day was prescribed.

During the first 2 h in the postoperative care unit, the patient did not complain about pain, hemodynamic parameters remained within normal range, and peripheral pulses were present. The wound drainage showed 70 ml blood loss before discharge to ward and assessment of the infraclavicular catheter revealed a good function.

Patient's pain assessed on the visual analog scale was 10/100 during the first postoperative night without the need for additional analgesics. Fourteen hours after surgery she developed severe forearm pain (visual analog scale 90/100). The anesthesia resident on call found a sensory and motor block of all target territories/muscles in the hand but a preserved contraction of the biceps and coracobrachial muscles. Suspecting a not blocked musculocutaneous nerve being responsible for the increasing pain she administered an additional bolus of 20 ml ropivacaine 0.5%. The severe pain was still present 20 min after its administration despite the occurrence of a new complete motor and sensory block of all territories. The characteristics of the breakthrough pain alarmed the anesthesiologist who suspected an incipient ACS. The orthopedic surgeons were informed and observed an intense pain on the dorsolateral part of the right forearm in the area of the extensor compartment with a significant increase in pain with stretching of these muscles. The intracompartmental pressure was measured using the Stryker Intra-Compartmental Pressure Monitor System (Stryker®, Kalamazoo, MI). The pressure in this compartment was 40 mmHg. Emergency fasciotomy of the extensor compartment of the forearm was performed under general anesthesia within 1 h after assessment of intracompartmental pressure. Intraoperatively, the extensor compartment of the forearm was greatly swollen and very tense. Upon decompression, the muscles were edematous but viable. Further exploration of the wound revealed two hematomas which were evacuated but no other compartments (of the forearm or arm) were under tension. The fascia of the extensor compartment was left open but the skin could be closed without any problem. Therefore, primary wound closure was performed. The infraclavicular catheter was removed. The motor and sensory function returned to normal after 4 h. The patient made an uneventful recovery and was discharged 3 days later. The follow up at 3 months showed no sensory or motor disabilities of the operated arm.

Discussion

Basic Science

ACS is defined as an increase of pressure within a fixed osteofascial anatomic space, leading due to decreased local tissue perfusion to an impairment of cellular function and, when sustained, to irreversible changes like infarction of muscles and nerves in the compartment. Important variables affecting the outcome are the amount and the duration of pressurization and the extent and severity of soft tissue injury.¹⁴

The different symptoms and signs describing ACS are reported in table 1. Although previous studies have reported that resting interstitial tissue pressures in the healthy vary between 0 and 8 mmHg for the dorsal and volar forearm compartments and less than 15 mmHg in the interosseous muscles of the hand¹⁵ pressure measurement is considered to be accurate. Interstitial tissue pressure measurement is measure point dependent in noninjured¹⁵ and injured extremities with higher pressures within 5 cm of the fracture.¹⁶

Different absolute compartment pressures or calculated pressures (difference between systolic or mean arterial pressure and the compartment pressure) have been described in the literature.^{17,18} Although the mean arterial pressure for the difference calculation (mean arterial pressure—compartmental pressure) seems to be more accurate comparative, clinical trials are lacking. It must be emphasized that much of above work exclude children and was mainly carried out studying ACS of the lower extremity. Upper extremities might have other pressure thresholds but due to lacking evidence the established threshold of ΔP 30mmHg is retained. In children, the mean arterial pressure rather than the diastolic pressure has been suggested to calculate the ΔP as the diastolic blood pressure is often lower in children.¹⁹

I. Incidence

Data from the Royal Infirmary of Edinburgh show an average annual incidence of 3.1 per 100,000 people (7.3 per 100,000 men and 0.7 per 100,000 women).¹⁷

II. Pathophysiology of Compartment Syndrome

The key element is the elevation of tissue pressure within encapsulated muscles. In the ACS, fluid shifts between the blood and the extra- and intracellular space due to an increased tissue pressure of the compartment leading to an

Table 1. Accuracy of Clinical Signs for the Diagnosis of Acute Compartment Syndrome

	Pain	Passive Stretch	Pain	Paresis	Paresthesia	%
Specificity, %	97	97		97	98	
Sensitivity, %	19	19		13	13	
PPV, %	14	14		11	15	
NPV, %	98	98		98	98	
Probability of ACS if one clinical syndrome present						25
Probability of ACS if three clinical syndromes present						93

ACS = acute compartment syndrome; NPV = negative predictive value; PPV = positive predictive value.

increased extravascular venous pressure. Further pressure leads to a decrease of capillary blood flow and decrease in tissue P_{O_2} ending in a metabolic deficit. The end stage is deficit muscle ischemia and necrosis. Tissue metabolism requires an oxygen tension of 5–7 mmHg. This tension is maintained by capillary perfusion pressure of 25 mmHg which is above the normal interstitial tissue pressure of 4–6 mmHg. The tissue perfusion pressure equals capillary perfusion pressure minus interstitial pressure. When tissue pressures reach 30–40 mmHg,²⁰ the extraluminal pressure causes progressive arteriole collapse due to direct pressure effects and to interferences with critical closing pressures leading to local tissue hypoxia with secondary shunting to areas with less vascular resistance. Moreover, local tissue perfusion ceases when the interstitial tissue pressure equals the diastolic blood pressure. The rising tissue pressure causes collapse of the veins. Arterial flow increases the venous pressure reestablishing the flow, but the increased venous pressure adversely affects the arteriovenous gradient with consecutive ischemia²¹ (fig. 1).

Two pathophysiology theories are the “arteriovenous gradient theory” and the “ischemia–reperfusion syndrome.”²² Both theories share the increasing tissue pressure, the consequently decreasing capillary blood flow, and the decrease of tissue P_{O_2} resulting in a metabolic deficit. If the ACS is caused either by external pressure or by an increased internal pressure, first the arteriovenous gradient theory explains the reduced capillary blood flow with increasing venous pressure or increasing capillary resistance. In the case of additional injuries leading to hypovolemic shock, the “arteriovenous gradient theory” explains the diminished arterial pressure resulting in reduced capillary blood flow. In

the case of reperfusion after revascularization or tourniquet release, the “ischemia–reperfusion mechanism” explains how different factors such as the release of oxygen-free radicals, massive accumulation of calcium in the ischemic muscles, and the infiltration of neutrophils into the reperfused vessels lead to an increase in compartment pressure. The hypoxic injury releases vasoactive substances, which increase the endothelial permeability. Subsequently, this mechanism leads capillary leakage into the extravascular space provoking additional edema and additional rise in compartment pressure. The falling pH and the degradation products contribute to a further increase in the tissue pressure, thereby reducing microperfusion as explained by the “arteriovenous gradient theory” leading to a self-perpetuating vicious circle. As a result of ischemia nerve conduction slows down.

However, several authors have demonstrated that early decompression leads to a drop in extraluminal pressure, restoration of local blood flow, removal of anaerobic metabolites, and return of normal cellular function.²³ Cells may become edematous and demonstrate histological evidence of injury after decompression, but the morphology and function of most of them will return to normal within some days.

III. Diagnosis of ACS

Pain is considered to be the main clinical symptom of a developing ACS. Pain exceeding clinical expectance, pain not responding to analgesics, palpable tenseness in the affected compartment and pain worsening with passive stretching of the muscles in the according compartment are the most accurate early indicators. Paresthesia, paresis, and pulselessness are in most circumstances late signs of an ACS

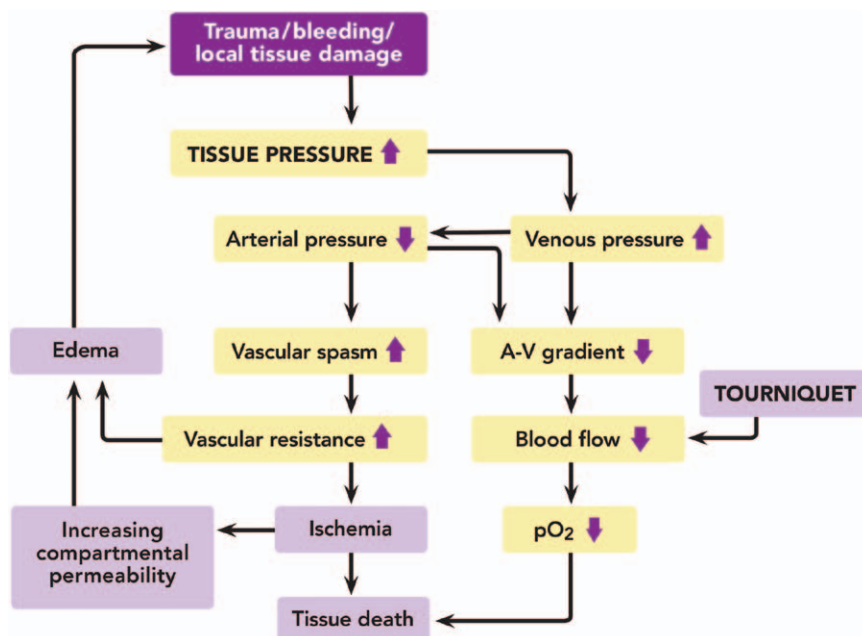


Fig. 1. Pathophysiology and the vicious circle of the acute compartment syndrome. Modified according to Janzing *et al.*²² Adapted with permission from Janzing H: Epidemiology, etiology, pathophysiology, and diagnosis of the acute compartment syndrome of the extremity. *Eur J Trauma Emerg Surg* 2007; 33:576–83.

and already indicating a potentially irreversible compartment and muscle damage. However, pain may not be useful in children or in adults with an altered level of consciousness.¹

Commonly used signs in clinical practice are neither reliable nor sufficiently specific or sensitive if there are not at least three signs.²⁴ Pulselessness in fact is considered to be a late sign and is associated with bad prognosis.^{4,18} Even pain is unreliable if there is no breakthrough pain or increasing analgesic demand.⁴ In fact, the simple presence of pain was insufficient to prevent from delaying ACS diagnosis.²⁵⁻²⁷ Even the clinical palpation of the tense and swollen extremity has been shown to be strongly assessor dependent and unreliable with a sensitivity of 24% and specificity of 55%.²⁸ Paresthesia and other altered sensations are also of questionable diagnostic value due to many confounders like central acting analgesics, alcohol, brain and spine injuries, altered level of sensation, other distracting injuries, extremes of age, language, and ethnical barriers.¹ Despite these limitations arguments against regional anesthesia or even opioid patient-controlled analgesia focus on the possible interference of these techniques with the classical signs of ACS.^{2,3}

The reference method for diagnosis of ACS remains the measurement of interstitial tissue pressures. Different methods for measuring intracompartmental pressure have been described to directly, indirectly, or continuously measure compartment pressure²⁹ (table 2). There are less invasive new technologies like laser doppler flowmetry and ⁹⁹Tcmethoxy-isobutryl isonitril scintigraphy. However, it is unclear how practical and cost-effective these methods are in clinical practice. An interesting development in the field of noninvasive measurement techniques was introduced by the near-infrared spectroscopy which detects changes and trends

in relative oxygen saturation of hemoglobin. In the setting of ongoing ACS, near-infrared spectroscopy has been described to have a high sensitivity and specificity detecting and providing continuous monitoring of intracompartmental ischemia and hypoxia.³⁰ However, more studies are warranted to define the correlation with critical pressure thresholds. Magnetic resonance imaging and scintigraphy are not sensitive enough to be recommended for ACS diagnosis.

Treatment and Outcome

In the case of an incipient compartment syndrome, frequent clinical reevaluation must be completed and accurately documented.¹⁴ Casts and circumferential dressings must be removed and positioning with tension or distortion must be avoided to not further compromise blood flow. Fluid therapy must be carefully evaluated, electrolytes, renal function, coagulation, and hemodynamic parameters must be monitored. Once the diagnosis of ACS has been established, surgical decompression of the affected osseofascial compartments is warranted.³¹

The most outcome relevant factors are fasciotomy, timing of diagnosis and fasciotomy performance, and the concomitant injuries. However, for the ACS of the upper extremities controversial opinions exist. Good results are reported after early diagnosis and quick fasciotomy, poor results with delayed treatment. However, there is no prospective study documenting the benefit of early fasciotomy for upper extremity ACS.³²

Delaying fasciotomy for more than 12 h has been shown to significantly worsen outcome.¹⁶ According to Hayakawa *et al.*³³ fasciotomy performed by 6 h after diagnosis of ACS led to a satisfactory outcome in 88% of cases with an

Table 2. Pros and Cons of Different Clinically Used Techniques for Intracompartmental Pressure Monitoring in ACS

Techniques	Pros	Cons
Needle manometer	Cheap Simple	Invasive, poor accuracy, indirect measure, no continuous measurement possible, fluid infusion can worsen ACS, needle obstruction, false positive and false negative results
Slit catheter	Continuous monitoring Large surface area Good accuracy	Invasive, indirect measure, obstruction of the catheter possible, false low reading due to air bubbles, transducer must be at level of catheter to avoid incorrect measurement
Wick catheter	Continuous monitoring Large surface area Good accuracy Seldom obstruction of catheter	Invasive, indirect measure, retention of wick material, blockage at fluid/air junction, transducer must be at level of catheter to avoid incorrect measurement
Solid state transducer intracompartmental catheter	Continuous monitoring Good accuracy Transducer level not dependent on catheter level	Invasive, indirect measure, expensive, heparinized saline and resterilization required
Near-infrared spectroscopy	Noninvasive Continuous monitoring Good accuracy and correlation	Validation compared to golden standard still lacking, expensive, depth of measurement unclear

ACS = acute compartment syndrome.

amputation rate of 3.2% and 2% deaths, whereas fasciotomy after 12 h showed satisfactory outcome in only 15% of cases with 14% amputations and 4.3% deaths. There is sparse data about the timeframe >6 h but <12 h, as residual deficits happen also if fasciotomy is performed only 2 h after ACS diagnosis.³⁴

IV. Implication of Regional Anesthesia in the Diagnosis of Compartment Syndrome

Regional anesthesia in patients at risk for developing an ACS is a highly controversial topic discussed.^{2,3,35} However, there is no randomized trial comparing outcome after different anesthesia managements. Actual clinical practice is based only on case reports, retrospective case series, recommendations and reviews, and the belief that regional anesthesia completely blocks pain and alters sensory-motor response to impede diagnosis of ACS.⁴ Advances in regional anesthesia techniques, drugs, and concentrations which allow a goal-directed therapy of pain with spare of sensory-motor functions are ignored.

This patient presents an ACS of the upper extremity involving regional anesthesia. Interestingly, some of the published case reports blame a peripheral nerve block (PNB) for masking an ACS in a territory not covered by the block. This challenges the sole responsibility of the PNB in masking the ACS.^{7,10} There is one recent case report blaming continuous perineural blocks for delaying diagnosis of ACS after distal femur and proximal tibia osteotomy.⁵ Additional to general anesthesia continuous sciatic and femoral nerve blocks were run with ropivacaine 0.2% after an initial bolus of 30 ml ropivacaine 0.5% through each catheter. Due to persistent breakthrough pain on postoperative day 2 the surgeon performed a clinical evaluation (dense swollen gastrocnemius muscle, excruciating upon passive plantar flexion, and dorsiflexion of the foot) and a compartment pressure measurement (30 mmHg). Despite these findings, a reevaluation was performed 2 h later showing the same findings. Finally, an emergent decompressive fasciotomy was performed. Once again, the breakthrough pain was ignored. This delay had serious consequences: tissue loss and functional deficits resulted. A second case report using continuous popliteal nerve block describes a patient who was sent home on postoperative day 1 with a popliteal catheter after foot surgery despite a dense motor and sensory block.¹¹ Pain became worse overnight and presented to the emergency department on postoperative day 2. The cast was splinted but not removed, no compartment pressures were measured. Patient refused to have the continuous PNB removed and was managed through the telephone. On postoperative day 4 the catheter was removed uneventfully. Probably, this is not a case of ACS but of pressure pain induced by tight cast which could have led to an ACS. However, patient management in this case report is not according to common standard. The case described by Noorpuri *et al.*⁹ describes an ACS after an ankle block for a revisional forefoot arthroplasty.

The patient developed increasing pain despite receiving supplementary analgesia, paresthesia, motor weakness and showed a tense swollen forefoot with a delayed capillary refill. No compartment pressure monitoring was performed and fasciotomy was performed due to increment clinical signs. Despite the neglect of typical clinical signs the authors blamed the ankle block for masking the ACS and delaying its diagnosis.

None of the five currently published case reports blaming peripheral regional analgesia for delaying diagnosis or therapy of ACS can stand a thorough study of the case. Ignored increasing pain and typical clinical signs are present in all cases and in one regional anesthesia did not even block the area of interest.

V. Lessons Learned from This Case

Our case shows the development of an ACS in a patient treated for analgesia using an infraclavicular catheter. As reported in section IV and in table 3 we suggest not to activate the perineural catheters in patients the surgeons consider to be at risk for either surgery associated nerve damage or compartment syndrome. This allows an immediate testing after surgery without delay in diagnosis. In the case of high risk for an ACS a delay in starting the catheter can be wise or the application of a very low concentration of local anesthetics preventing motor block might be suggested.

In this case the ACS developed slowly and breakthrough pain was a symptom. The resident evaluated the pain as postsurgical due to the motor function of the biceps and coracobrachial muscles. The fingers were according to her first description not swollen. Interesting is the fact that despite 20 ml 0.5% ropivacaine after 20 min the pain was still present despite the occurrence of a new complete motor block. This and the measured compartment pressure were the only clinical signs. The swelling was only appreciated after removal of the splint. This further suggests, that at least for PNB, regional anesthesia does not mask the cardinal symptom of ACS: breakthrough pain. However, the typically used 0.5% concentration for the top up of the catheters should be reconsidered in patients at risk for ACS. What would happen with our patient if pain had improved by 50%? Moreover, the communication between anesthesiologist and surgeons remains to be of pivotal importance. ACS is a surgical diagnosis and therefore patients with unclear pain must be evaluated by both, anesthesiologist and surgeon.

There is no single case report showing a delay in ACS diagnosis due to peripheral regional anesthesia, even considering continuous regional anesthesia. Almost all published cases including epidural analgesia (EDA) showed that patient complained of increasing pain despite regional anesthesia,¹⁰ loss of motor function despite reduction of local anesthetic concentration³⁶ or increasing analgesic demand.^{4,5,11} Only in two cases was a dense motor block noted after EDA at time point of ACS diagnosis.^{26,37} Other cases even blamed a continuous PNB for an ACS in a territory the block did

Table 3. Recommendation for Anesthesia and Postoperative Analgesia for Patients at High Risk for Postoperative ACS

Anesthesia Techniques	Drugs to Be Used	Comments
General anesthesia	Propofol/gas Low dose long-acting opioids (fentanyl); remifentanyl target controlled infusion until CPNB	Avoid central blocks if there is no need to avoid general anesthesia and if surgery extends short-/medium-acting local anesthetics for neuraxial blocks. Combine GA with CPNB if possible for postoperative pain.
Single shot spinal	Bupivacaine 0.5% hyperbaric/isobaric low dose (7.5 mg- max 10 mg) Mepivacaine 1% (30 mg) Chlorocaine 1% 50 mg Prilocaine 2% hyper/isobaric 30–60 mg	No case report correlated to ACS. Consider unilateral SSPA for shorter duration. Avoid combination with CEDA.
Continuous spinal	Surgery: Bupivacaine hyperbaric 0.5% Analgesia: Bupivacaine isobaric 0.125–0.2% for 0.5–1 ml/h	No case report correlated to ACS. Start the analgesia with the lowest concentration and rise the sensory level just to cover the site of surgery. Close documented monitoring (every hour) during infusion.
Single shot epidural	Lidocaine 1.5% Chlorporcaine 3%	No case report correlated to ACS. Avoid combination with CEDA.
Continuous epidural	Ropivacaine 0.1% (–0.2%)	Avoid EDA whenever possible. Many case reports also if only two with dense motor block associated with ACS. Close documented monitoring (every hour) during infusion. Consider wash out. No patient controlled epidural analgesia.
Single shot PNB	Lidocaine 1.5% Mepivacaine 1% Chlorporcaine 3%	Case reports for the lower extremity (but ACS signs ignored). For a better postoperative pain control CPNB is the better choice, otherwise combine SPNB with multimodal systemic analgesia.
Continuous PNB	Ropivacaine: bolus with 10–20 ml of 0.1–0.2% PCRA: ropivacaine 0.1–0.2% (0.3%) 4–6 ml/h, bolus 3–4 ml, lock out 20–30 min	Case reports for the lower extremity (but ACS signs ignored). If possible avoid initial bolus, or perform it with the lowest concentration. PCRA or CPNB possible. 0.3% only if pain problem after exclusion of ACS. Avoid for top up of catheters high concentrations like 0.5% in patients at risk of ACS.
Continuous wound/intraarticular infusion	Ropivacaine 0.2–0.3% Bupivacaine 0.25%	For lower extremity not inferior to PNB, for upper extremity unclear data, PNB probably more effective.

ACS = acute compartment syndrome; CEDA = continuous epidural analgesia; CPNB = continuous perineural block; CSPA = continuous spinal anesthesia; EDA = epidural anesthesia; GA = general anesthesia; PCRA = patient-controlled regional anesthesia; PNB = perineural block; SPNB = Single shot perineural block; SSPA = single shot spinal anesthesia.

not cover.^{7,10} The other case reports did not give any details about documentation or patient management before start of symptoms/clinical signs.⁴ Therefore, regional anesthesia can only be considered to be associated but not the cause of the delay in diagnosis. Excluding both cases with dense motor block after EDA^{26,37} there was no evidence that regional anesthesia masked important symptoms of compartment syndrome.

Despite this evidence, the use of regional anesthesia for patients at risk for ACS remains a topic of dispute between anesthetists and surgeons.³ As reported by Cascio *et al.*³⁸ a good, standardized documentation improved the awareness of this complex diagnosis. However, in a retrospective study of preoperative medical records of 30 consecutive patients who underwent fasciotomies for ACS, documentation was inadequate in 21 (70%) patient records.³⁴

A proper documentation, a high level of suspicion with postoperative repeated clinical and if needed invasive monitoring are of utmost importance.^{34,39} Data must be recorded at

least in a 2-h interval, in the case of new or pathological findings, the frequency of assessment must be adapted. The classical “5 P’s” are of unreliable value²⁴ particularly in the presence of regional anesthesia and should therefore be complemented by the clinical signs “breakthrough pain” and “increasing demand of analgesia.”⁶ As described by Bae *et al.*²⁷ increasing analgesia demand preceded neurovascular changes by an average of 7.3 h (range 0–30). However, in 36 cases of compartment syndrome the average time to surgical decompression from the increase in analgesia requirement was 25.2 h.

The proposed concepts which were elaborated in our clinic together with the orthopedic surgeons are presented in table 3. The choice of regional anesthesia is justified if there are clear advantages over general anesthesia or over morphine analgesia. For central blocks like spinal anesthesia, short-acting drugs adapted to surgery time should be used. The advantage of avoiding spinal anesthesia consists in the possibility of testing motor and sensory function directly after surgery and therefore to stabilize a baseline for further

clinical measurements. Patients at high risk for general anesthesia and with a surgery time extending the duration time of short- and medium-acting local anesthetics can benefit from a continuous spinal anesthesia which avoids long blocks, as the volume of the local anesthetic can be tailored to the surgery time. Epidural drug as compared to spinal application should not be used preferentially for analgesia because the level of the surgical block is more difficult to control. If general anesthesia is contraindicated a combination of EDA with spinal anesthesia considering the reflections described above are possible. EDA should not be started until the surgeon has made the above-described baseline clinical assessment. Thereafter, low concentration of ropivacaine can be used, as the effect on motor function is minimal. Additives must be considered from case to case. Low dose (levo-) bupivacaine with or without additives is possible but not considered as a first choice. As EDA is the most blamed technique in literature for delaying diagnosis of ACS its use should be restricted and (continuous-) PNBs should be favored. However, with EDA dense motor blocks must be avoided and if needed wash-out techniques are recommended.⁴⁰

Single shot PNB are only recommended if postoperative pain is not a major issue. Short-acting drugs with low impact on motor function after surgery are needed. Continuous PNBs are the best choice to our mind. In cases of high risk for an ACS, general anesthesia is combined with a continuous PNB which is placed but not started (nonactivated continuous PNB) before general anesthesia until postoperative evaluation is performed. Pain therapy is performed with low doses of fentanyl in combination with remifentanyl target controlled infusion or even remifentanyl alone until start of continuous PNB. This allows a perfect timing with the surgeon but requires that catheters are placed without injecting first local anesthetic through the needle. The catheter should be started with a low concentration bolus of 10–20 ml ropivacaine 0.1–0.2% to avoid initial motor function loss and followed with a continuous infusion (or patient-controlled infusion) using ropivacaine 0.2% (e.g., 4–6 ml/h, bolus 3–4 ml, lock out 20–30 min). Ropivacaine 0.3% has been shown not to influence motor strength compared to 0.2% for interscalene block and could be used in an experienced team for extremely painful surgery under continuous infusion.⁴¹ However, according to our experience using a bolus of ropivacaine might lead to a weak motor block and should therefore, for safety reasons, be avoided in this setting. Continuous wound infusion or intraarticular infusions are not contraindicated, even using ropivacaine 0.3%.⁴²

VI. Knowledge Gap and Research Perspectives

The pathophysiology of ischemic muscular pain is highly complex and is mediated by chemical and inflammatory markers acting on nociceptors. During ischemia it is postulated that bradykinin, acetylcholine, serotonin, adenosine, hydrogen ions, and potassium ions are some of the substances leading to ischemic pain. Tissue acidosis

initiates the pain pathway acting on skeletal muscle nociceptors resulting in pain impulse transmission and leading to a nonadapting activation of nociceptors. We agree with Cometa *et al.*⁵ who postulated that compartment ischemia activated nociceptors via hydrogen ion excitation can lead to an ineffective regional anesthesia with 0.2% ropivacaine. In our case, ropivacaine 0.3% was infused and breakthrough pain was still present even after a bolus with 0.5% ropivacaine. It would be interesting to evaluate the optimal concentration and volume for bolus application and continuous infusion to use regional anesthesia as an indirect and early indicator of increased muscle ischemia.

Local anesthetics act on the voltage-gated sodium channels. The $Na_{v1.7}$ is the main channel for pain transmission in the peripheral nerves. Selective blocking of this channel for the postoperative period could be of special interest for patients at risk for ACS and for ambulant continuous PNB avoiding motor block.

Further long-term outcome studies dealing with the usefulness and effect of intracompartmental pressure monitoring and data on the diagnostic performance characteristics of intracompartmental pressure monitoring are needed. Moreover, the critical ΔP for other regions of the body and for children must be defined.

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