Acute compartment syndrome:
How long before muscle necrosis occurs?

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ABSTRACT
Objectives: Acute compartment syndrome (ACS) is a limb-threatening condition often first diagnosed by emergency physicians. Little is known about the rapidity with which permanent damage may occur. Our objective was to estimate the time to muscle necrosis in patients with ACS.

Methods: This historical cohort analysis of all patients who had a fasciotomy for ACS was conducted in 4 large teaching hospitals. Diagnosis was confirmed clinically or by needle measurement of compartment pressure. Muscle necrosis was determined using pathology reports and surgeons’ operative protocols. We used descriptive statistics and estimated tissue survival probability using the Vertex exchange method for interval-censored data.

Results: Between 1989 and 1997 there were 76 cases of ACS. Most cases occurred in young men (median age 32) as a result of a traumatic incident (82%). Forty-nine percent (37/76) of all patients suffered some level of muscle necrosis, and 30% (11/37) of those with necrosis lost more than 25% of the muscle belly. Necrosis occurred in 2 of 4 cases in which the patient had been operated on within 3 hours of the injury, and our exploratory survival analysis estimates that 37% (95% confidence interval, 13%–51%) of all cases of ACS may develop muscle necrosis within 3 hours of the injury.

Conclusions: This is the largest cohort of ACS and the first clinical estimation of time to muscle necrosis ever published. Ischemia from ACS can cause muscle necrosis before the 3-hour period post-trauma that is traditionally considered safe. Further research to identify risk factors associated with the development of early necrosis is necessary.

Key words: compartment syndromes; musculoskeletal diseases

RÉSUMÉ
Objectifs : Le syndrome de loge aigu est une atteinte menaçant l’intégrité des membres qui est souvent diagnostiqué par les médecins d’urgence. On sait peu de choses au sujet de la rapidité à laquelle des lésions permanentes peuvent subvenir. Notre objectif était d’estimer le délai d’instal-
Acute compartment syndrome (ACS) is a limb-threatening condition in which increased pressure within a closed tissue space compromises the nutrient blood flow to muscles and nerves. Patients usually present to the emergency department (ED) with a history of trauma-induced acute bleeding within a compartment, but ACS has also been associated with other circumstances, such as ischemia-reperfusion injuries, circumferential casts and illicit drug injections. Matson classified these etiologies of ACS into 2 main categories: increased compartment content and decreased compartment volume. The diagnosis is made clinically in half the cases, but intra-compartmental pressure measurements should be performed on patients with altered level of consciousness or when clinical signs and symptoms are equivocal. Scientists have different opinions on the pressure criteria for diagnosis of ACS but absolute pressures of 30 to 40 mm Hg are generally accepted. The only effective therapy for ACS is decompression of the affected compartments by a fasciotomy, and if this treatment is delayed, muscle necrosis and permanent disability may result. In a previous series of ACS cases presenting to the ED, the median injury-to-operation time interval was greater than 9 hours, suggesting that delays may be the rule rather than the exception.

Current opinion on how long muscles can tolerate ischemia is based solely on extrapolations from tourniquet models. According to these models, muscles can tolerate up to 3 hours of ischemia before developing necrosis, and some authors suggest that muscles can tolerate up to 6–8 hours of ischemia. However, tourniquet-induced ischemia may differ from compartment syndrome-induced ischemia. In animal research, ultra structural degeneration in canine skeletal muscle was more common and more severe in experimental ACS compared to that produced by tourniquet-induced ischemia. Although suggestive, this animal research requires supporting clinical evidence before it is generalized to the human condition. Such evidence is not yet available.

The objective of this study is to review a large cohort of ACS cases to determine muscle survival at the 3-hour injury-to-operation time interval currently accepted as safe. This information may help emergency physicians prioritize patients and determine the need for emergent or urgent management.

Methods

Study design

We conducted a multi-centre, historical cohort study of patients who had a fasciotomy for ACS. These subjects have already been a part of a published study looking at diagnostic and management delays. The Institutional Review Board in each of the participating hospitals gave their approval for the project.
Study setting and population
The study took place at all 4 McGill University teaching hospitals in Montréal, Canada, between 1989 and 1997. Using individual hospital medical record computerized databases, we obtained a list of all patients who underwent fasciotomy. Because fasciotomy is routinely performed prophylactically in patients undergoing vascular bypass surgery or thrombectomy/embolectomy,6,30 these cases were excluded from the initial search and were not reviewed. We defined our cohort as those patients who had a fasciotomy for ACS, regardless of body location. Looking for cases of ACS directly might seem more intuitive, but we felt that the diagnosis of ACS could sometimes be omitted in the discharge summary of polytrauma cases. However, surgeons always record operative procedures for medicolegal reasons and to ensure payment for the surgery performed. Because ACS is not a spontaneously reversible disease and the only current acceptable therapy is fasciotomy,9,12,13,15,18–20 we believe we identified all cases of ACS seen during the study period.

Patients were eligible for inclusion if absolute compartment pressure measurements were >30 mm Hg or if a clinical diagnosis of ACS was clearly mentioned in the chart by the treating physician or surgeon. In all cases, the diagnosis of ACS was clearly stated and retrieved from the chart. The time of injury for non-traumatic cases (in most cases exertional or drug overdose) was considered to be the time of the event leading to ACS. In cases where more than one time of injury was mentioned, the earliest time was selected. We considered the start of the anesthesia as the time of surgery because it was considered to be the most standardized time recorded in the chart.

Operative and pathology reports were reviewed for description of muscle damage (necrosis/resection). We expressed muscle necrosis in percentages of total muscle belly loss, with approximate 25% increments. If a small amount of muscle was excised and the patient did not require subsequent operations, we categorized the damage as minimal. This is because necrotic tissue usually acts as a foreign body and causes local reaction if not excised. In the absence of such a reaction, we considered that any possible necrotic tissue would probably be clinically irrelevant. In the cases where more than one compartment was involved, the compartment most severely injured was selected for the outcome measure.

Muscle damage was usually clearly recorded (e.g., “muscle did not twitch to electrical stimulation” or “three-quarters of the muscle was excised”). However, although the diagnosis of ACS was clear from the surgeon’s notes, documentation of muscle damage was vague in a few cases (e.g., “muscle appeared grayish”). To control for the variability of documentation in the chart, the data were recorded to be weak, moderate or strong depending on how clear the operative/pathological description of muscle damage was.

Study protocol and data collection
Two sport medicine physicians, one emergency medicine resident and one family medicine resident performed the chart review. The reviewers used a defined process, explicit definitions and specific data abstraction forms to increase reliability. Only one person reviewed each chart after having been trained by the senior author (I.S.) on how to use the data collection tool. A second data abstractor reviewed approximately 10% of charts (I.S. and C.V.). Although agreement was not measured formally, no systematic data discrepancy was found. In the few cases where interpretation of the notes was difficult, a consensus was reached between the original reviewer and the senior author (I.S.). All data were transcribed into an Excel database.

Measurement of outcome measures
Time of injury was obtained from the triage personnel, nursing, emergency physician, consultants, or ambulance dispatch notes. For traumatic events, it was always explicitly stated and retrieved from the chart. The time of injury for non-traumatic cases (in most cases exertional or drug overdose) was considered to be the time of the event leading to ACS. In cases where more than one time of injury was mentioned, the earliest time was selected. We considered the start of the anesthesia as the time of surgery because it was considered to be the most standardized time recorded in the chart.

Data analysis
We used a descriptive analysis for demographic data, to describe the location of ACS, to quantify the amount of muscle belly loss, to describe the reliability of information capture, and to determine if we observed cases of necrosis within the presumed 3-hour safe period post-injury.

We used the vertex exchange method (VEM) to estimate tissue survival probability using interval-censored data.32 Briefly, the time to necrosis of muscle that was alive at the time of fasciotomy was right-censored at that time. On the other hand, the time to necrosis of muscle that was necrotic at the time of fasciotomy was left-censored at that time, because necrosis could theoretically have occurred any time between the injury and the fasciotomy. Data consisting of both left- and right-censored times are called current status data, a special case of interval-censored data. The VEM algorithm estimated the survival time using all available data (i.e., necrotic and non-necrotic muscles). A con-
strained version of VEM was used to compute 95% confidence intervals (CIs), based on the asymptotic distribution of the empirical likelihood ratio with current status data. Calculations were performed using R software version 1.6.2 (The R Development Group). Other examples of current status interval-censored analysis can be found in the literature, such as the study of avalanche survivors. Readers wishing to learn more about VEM may review the excellent article by Böhning and colleagues.

**Results**

We reviewed 237 potential cases of ACS that occurred between 1989 and 1997 and excluded 151 patients who had fasciotomies for reasons other than ACS (e.g., to access fracture sites, for plantar fascia release of club-foot or plantar fasciitis). We also excluded 10 cases of ACS associated with necrotizing fasciitis because we could not attribute muscle damage solely to ACS in these cases. This left 76 surgically confirmed cases of ACS for analysis.

Table 1 summarizes characteristics of the study group and describes the events associated with the ACS. Overall, 7 patients were under 18 years of age, and the majority were young to middle-aged men involved in a traumatic event; approximately half of these had an associated fracture as a result of the initial trauma. Figure 1 shows the distribution of affected compartments, demonstrating that lower extremity injuries accounted for 79% (110/140) of cases. Of all the patients with ACS, 49% (37/76) suffered some level of muscle necrosis (Fig. 2). Among those with muscle necrosis, 30% (11/37) lost more than 25% of the muscle belly. Figure 2 shows that the level of certainty regarding the degree of muscle necrosis was highest in the group with the most damage.

Our data also demonstrated that ACS-induced necrosis can occur rapidly. Some necrosis was evident in 2 of 4 cases operated on within 3 hours, and 1 patient lost 100% of the compartment muscle within 4 hours of injury. On the other hand, 11 patients had an injury-to-fasciotomy time of greater than 24 hours and did not develop muscle necrosis. Among these, 9/11 were brought to the operating room less than 6 hours after the diagnosis of ACS was made, and 2/11 more than 24 hours later. Table 1 shows clinical characteristics of patients having early necrosis (within 6 hours post injury), and those without necrosis despite prolonged ACS (>24 hours).

### Table 1. Clinical characteristics and analysis of the 76 surgically confirmed cases of acute compartment syndrome (ACS)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study group N = 76</th>
<th>No. (and %)* of ACS patients who developed early necrosis (≤6 hours of injury) n = 11</th>
<th>No. (and %)* of ACS patients who did not develop necrosis despite prolonged ACS (&gt;24 hours post injury) n = 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yr (and range)</td>
<td>32 (1–80)</td>
<td>47 (20–78)</td>
<td>33 (9–74)</td>
</tr>
<tr>
<td>Men, no.</td>
<td>57</td>
<td>7 (64)</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic event</td>
<td>62</td>
<td>11 (100)</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Motor vehicle accident</td>
<td>19</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Crush injury or assault</td>
<td>18</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Fall from height</td>
<td>9</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Medical procedure</td>
<td>7</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stab or gunshot wound</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Winter sport</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Non-traumatic event</td>
<td>14</td>
<td>0 (0)</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Overdose</td>
<td>6</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Exertional</td>
<td>3</td>
<td>–</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Other features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated fracture</td>
<td>40</td>
<td>10 (91)</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Alcohol/drug intoxication</td>
<td>12</td>
<td>0 (0)</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Chronic vascular disease</td>
<td>11</td>
<td>1 (9)</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>7</td>
<td>0 (0)</td>
<td>3 (27)</td>
</tr>
</tbody>
</table>

* Unless otherwise indicated.
We used VEM methodology to develop a predictive model for time to necrosis after different durations of ischemia. VEM incorporates data from all patients in producing the estimate. At the 3-hour injury-to-operation time interval, our model estimates muscle survival to be 63% (95% confidence interval [CI], 49%–87%). In other words, we estimate that 37% (95% CI, 13%–51%) of patients with ACS develop necrosis within the 3-hour period previously presumed to be safe. The time-to-necrosis estimate remained unchanged when we limited our analysis to the 62 patients with traumatic events (63%; 95% CI 47%–87%), where time of injury is more accurate than for non-traumatic etiologies.

**Discussion**

This study is the largest cohort of ACS patients published to date. Although previous estimates of how long muscle can survive ACS-induced ischemia have been published, this is the first study to estimate the survival time based on actual clinical data. Our study confirmed the common clinical impression that the leg compartments, particularly the anterior compartment, are the most often involved. Importantly, we found that 2 of 4 patients operated on within the presumed 3-hour safe period post-injury developed muscle necrosis, and our survival analysis estimates that 37% (95% CI, 13%–51%) of patients with ACS will develop necrosis within the first 3 hours of injury — much sooner than the times suggested in experimental tourniquet-induced ischemia studies.

Our results show that necrosis can occur even before the 3-hour “safe-period” established by tourniquet-induced ischemia studies. This supports the results of animal studies showing that ACS-induced ischemia causes more damage than tourniquet-induced ischemia, and that the 2 conditions must be considered distinct. Similarly, a study of healthy volunteers concluded that 30 minutes of venous stasis (induced by casting the leg) led to a loss of sensation and muscle weakness, whereas 30 minutes of cylindrical air splint-induced ischemia (rapidly applied so that venous stasis did not occur before arterial ischemia) did not.

Some patients with ACS rapidly developed necrosis, and another subset of patients with a long injury-to-fasciotomy time interval did not. Of note, all of the subjects having early necrosis within 6 hours of the injury sustained a traumatic injury. Although it may make intuitive sense that their necrosis may be due in part to the initial mechanism of injury (e.g., crush injury), we also observed a number of patients without necrosis 24 hours after a similar crush injury or traumatic event. The 11 patients who did not develop necrosis despite a long injury-to-fasciotomy interval may have developed ACS many hours after their initial injury. In this retrospective review, it was impossible to determine whether this was the case, or if ACS was present from the beginning and the diagnosis was delayed. Delayed presentation of ACS, as long as 6 days, has been reported following progressive subcutaneous edema. Individual variability in muscular tolerance to ischemia, or differences in compartmental mechanical and biochemical fascia compliance could have played a role in these cases.

Almost half the patients with ACS developed some level of tissue necrosis. Furthermore, 30% of those with necrosis lost 25% or more of their muscle belly. We feel that most
people with this amount of tissue loss would suffer from permanent disability. Unfortunately, we were not able to contact our patients for follow-up information. The ethics committees required that the operating surgeon contact the patient first. We were concerned that this would lead to a selection bias because surgeons with poorer outcomes might not participate in the study. Existing literature already suggests that pain, discomfort and poor mobility may be long-term complications of ACS.

**Limitations**

Information obtained from retrospective studies may be less accurate than that obtained from prospective studies; however, prospective studies of rare diseases are difficult,
expensive and require many years to complete. We used an historical cohort design because it would be unethical to randomize patients to different amounts of “ischemia time” (longer ischemia time in ACS means more chance of necrosis), and a prospective cohort study would be hard to justify given the lack of clinical data, the expense and the recruitment time that would be necessary.

Study validity
We believe the current study represents the most valid data available for ACS, because current recommendations are based only on a disease-model that is known to underestimate the amount of damage that will occur.

Although some retrospective studies are limited by missing and inaccurate data, these were not significant problems with the charts we reviewed. For the current study, valid data interpretation is possible if 4 pieces of information are accurate. These include the diagnosis of ACS, the time of accident, time of surgery (time of accident and surgery are used to calculate ischemia time) and the presence or absence of muscle necrosis. While the pre-operative diagnosis of ACS was most often made on clinical grounds without compartment pressure measurements, we only included cases in which the diagnosis was confirmed at surgery and we excluded all cases where muscle necrosis may have been due to other causes (e.g., embolectomy, necrotizing fasciitis). If some patients were mistakenly diagnosed with ACS and had a fasciotomy, they would not have had any muscle necrosis. If this occurred in our study, the actual time before necrosis occurs in ACS would be even shorter than we report in the current study.

Second, the time of injury was always clearly recorded by the nurse, physician or registration desk. Although this time was usually an estimate with associated uncertainty (e.g., “the injury occurred 2 hours ago”), we believe it closely mimics the reality of patients presenting to EDs. Further, the uncertainty associated with the time of injury is least for patients with short delays between injury and hospital presentation and these are the patients of most interest in the current analysis. In 4 cases, a cast was applied before the diagnosis of ACS was made. Because the time of cast application was not known, we used the time of the initial injury for the survival analysis. If the cast was the insult leading to ACS, our analysis would have overestimated the amount of time a muscle can survive when ACS occurs, and the need for emergency treatment would be even greater than our results suggest. For all of these reasons, we feel that our data is valid for clinical decisions made on the basis of “time from injury” and if anything, underestimates the magnitude of the problem.

Third, we believe anesthetists accurately record the time of surgery within a couple of minutes. This degree of uncertainty (i.e., minutes) is not important given the objectives of the current study and therefore the time of surgery used in this study is a valid estimate.

Finally, the amount of damage recorded in the operative report may not be valid. We recognize that the amount of muscle damage (minimal, 25%, etc.) may be under-represented or over-represented. Acknowledging this limitation, we believe that when surgeons report necrotic muscle, it was present. First, most reports were confirmed by pathology reports. Second, muscle necrosis implies the operation was not done soon enough (e.g., delay due to OR availability, clinical priorities) and could result in malpractice suits (justified or not). Therefore, the unstated bias of the surgeon would be to under-report small amounts of muscle necrosis, which again would mean that necrosis would have occurred even earlier and more often than we report in the current study.

To summarize, although our analysis incorporates potential biases due to misclassification of exposure or outcome, all of these are in the direction such that time to necrosis would actually occur sooner than we report.

Conclusion
The etiology, progression and location of ACS are diverse. Contrary to what might be suggested by controlled studies of tourniquet occlusion, there does not appear to be any “safe-period” for cases of ACS seen in the ED. Victims of ACS are inhomogeneous, and clinical factors influencing outcomes are likely varied. Further studies are needed to help emergency physicians and other primary caregivers identify groups at risk for early necrosis at the time of initial presentation.

Competing interests: None declared.

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