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Compression sonography for non-invasive measurement of lower leg compartment pressure in an animal model

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ABSTRACT

Introduction: Cowcl"a"1mpression ultrasound is a non-invasive technique allowing for qualitative visualization and quantitative measurements of mechanical tissue properties. In acute compartment syndrome (ACS), cadaver studies have proven that the intra-compartmental pressure (ICP) measured by compression sonography correlates with the ICP measured invasively. This study aimed to evaluate compression sonography for compartment pressure measurements in an animal model.

Material and methods: The pressure in the anterior tibial compartment of 6 domestic pig legs was increased from baseline to 40 mmHg in 5 mmHg steps. Using compression sonography, the compartment diameter was measured without external pressure and during manual application of five levels of external pressure. The elasticity ratio (ER) was computed as the ratio of the compartment diameter with and without external pressure.

At 40 mmHg of external pressure the ERs at different ICP levels were compared using repeated ANOVA measurements. Post-hoc comparisons evaluated the lowest detectable ICP fulfilling the definition of ACS (ICP $\geq$ 30 mmHg) by starting from each pressure below 30 mmHg (baseline, 20 mmHg and 25 mmHg, respectively). Receiver operator characteristic analyses defined ER limits with appropriate sensitivity and specificity to detect ACS.

Results: The ER increased from 79.0% at baseline ICP to 89.3% at 40 mmHg ICP. The ER at baseline and at 20 mmHg ICP significantly differed from the ER at 30 mmHg ICP ($p = 0.007$ and 0.002, respectively); the ER at 25 mmHg ICP significantly differed from the ER at 40 mmHg ICP ($p = 0.001$).

An ER less than 87.1% had a sensitivity of 94.4% and a specificity of 88.9% to proper diagnosis of ACS.

Conclusion: Compression sonography might offer a non-invasive technique to guide treatment in cases of uncertain acute compartment syndrome. Further studies are needed to collect elasticity ratio data in humans and to clinically validate compression sonography for compartment pressure measurements.

Introduction

The acute compartment syndrome (ACS) is defined as an increase in intra-compartmental pressure (ICP) leading to decreased perfusion pressure and finally tissue hypoxemia [1]. Trauma and reperfusion injury are the most common causes for the acute compartment syndrome of the lower leg [2]. Timely diagnosis and early fasciotomy of the affected compartments are essential for restoration of function as delay in treatment is associated with poor outcome [3].

Clinical symptoms were shown to exhibit high negative predictive values and helped in excluding an ACS, but their positive predictive values were 15% or less, rendering them of little help for confirmation of the diagnosis [4]. Obviously, pain and loss of function cannot be tested in unconscious or uncooperative patients, thus reducing the probability of early diagnosis. Thus, many authors recommend invasive ICP measurements with an ICP of more than 30 mmHg or a tissue perfusion pressure (mean arterial pressure – ICP) of less than 30 to 40 mmHg indicating the need for fasciotomy [5–7].

Most invasive ICP measurement systems like needle manometer, Wick, slit, and solid-state transducer catheters require saline injections or a pool of heparinized saline around the tip to avoid

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blockade by soft tissue herniation [8–12]. The saline injections evoked concerns about possible worsening of an impending compartment syndrome or false pressure readings due to bubbles in the saline lines [11]. Falsely high or low readings with saline injection [8] can be avoided with transducer-tipped probes using the piezo-resistive principle [13].

Nevertheless, every invasive ICP measurement is painful and yields the risk of complications including bleeding [14], breakage of the catheter leaving parts in the muscle, and infections. Accordingly, attempts have been made to establish non-invasive means for ICP-monitoring including ultrasonic pulsed phase-locked loop analysis of fascial displacement [15–17], observation of muscle oxygenation with Near-Infrared Spectroscopy [18], and quantitative hardness measurement using a piston probe [19].

Compression sonography was introduced in the early 1990s and allows for qualitative visualization and quantitative measurements of mechanical tissue properties [20–22]. Previous laboratory studies have proven the feasibility of the principle and have shown a good correlation between the elasticity of the muscle compartment as measured by compression sonography and the invasively measured ICP. So far, these measurements have only been performed in cadaver legs or plastic models but not in living tissue [23–25].

The aim of this study was to evaluate the feasibility and reproducibility of non-invasive ICP measurement using compression ultrasound in an animal model.

Methods

This study complied with the Swiss national guidelines for the Care and Use of Laboratory Animals, National Academy of Sciences, 1996, and approval of the Commission of Animal Experimentation of Canton Bern, Switzerland (approval number BE 40/16) was obtained.

8 domestic pigs (weight 40 ± 1 kg (mean $\pm$ SD)) were admitted to the local animal hospital and examined by a veterinarian. Prior to the experiment they fasted overnight but had free access to water all the time. During pilot testing several technical problems regarding stable ICP increments and proper invasive ICP measurements were encountered as described below. The first 5 pigs were used to solve these problems. Finally, the data of 3 pigs (6 legs) were available for analysis.

Anaesthesia and monitoring

The animals were premedicated with ketamine and xylazine intramuscularly, followed by cannulation of an ear vein. Oral intubation was performed after administration of midazolam and atropine. The animals were ventilated with a volume-controlled mode (Servo-I, Maquet Critical Care, Solna, Sweden) with a positive end-expiratory pressure of 5 mmHg and a FiO2 of 30% aiming for a normal oxygenation (PaO2 above 90 mmHg). The respiratory rate was adjusted to maintain a pH between 7.35 and 7.45.

Following intubation, the animals received 1.5 g of cefuroxime as an antibiotic prophylaxis prior to surgery. The anaesthesia was maintained using propofol (4–8 mg/kg/h) and fentanyl (5–10 mcg/kg/h). Continuous BIS-measurement (Aspect Medical, Nantucket, USA) with a goal of 40–60 and hourly nose pinch testing was used to ascertain proper anaesthesia depth and analgesia. Additional injections of fentanyl (25 μg) were given as needed.

Electrocardiogram (ECG) and pulse oximetry (attached to the tail) were continuously monitored. A central venous and an arterial catheter were inserted into the left jugular vein, and carotid artery, respectively, via cervicotomy. Arterial pressure (MAP) and central venous pressure (CVP) were recorded with pressure transducers (xtrans®, Codan Medical, Germany), which were calibrated using a water scale, and zeroed at atrium level before the measurements. All pressure tracings were continuously displayed on a multimodular monitor (S/5 Critical Care Monitor®; Datex-Ohmeda, GE Healthcare, Helsinki, Finland) and subsequently recorded as two-minute median values. Body temperature was recorded using nasally placed temperature probe (a-line, Anandic Medical Systems AG, Feuerthalen, Switzerland). Tidal volume, respiratory rate, PEEP, end-inspiratory plateau pressure and inspired oxygen concentration were monitored continuously.

Induction of compartment syndrome

The skin at the proximal part of the anterior tibial compartment was incised, but the fascia was left intact. A single lumen catheter with multiple perforations at the tip (Arrow International, Inc, 2400 Bernville Road, PA 19605, USA) was placed into the compartment using Seldinger technique. This catheter was used to increase the intra-compartmental pressure (ICP). During pilot testing hydroxyethyl starch (HES/HAES) 6% solution was used to increase the ICP. However, this led to unstable pressure levels, possibly due to small leakages in the fascia allowing for drainage of the liquid. We therefore used blood taken from the central venous catheter expecting that clotting of the blood would prevent such drainage and this finally resulted in stable pressure levels throughout the testing. The ICP of the anterior tibial compartment was increased stepwise beginning from baseline, i.e. the prevalent pressure at the beginning of the experiments to 20, 25, 30, 35, and 40 mmHg, respectively.

An air-pouch probe (parenchymal probe 3PN, Spiegelberg GmbH & Co. KG Tempowerkring 4, 21079 Hamburg, Germany) was placed into the compartment and connected to a monitor (ICP-monitor HDM26.1, Spiegelberg GmbH & Co. KG Tempowerkring 4, 21079 Hamburg, Germany) to display the ICP. During pilot testing a single catheter for liquid installation and ICP monitoring was used. However, this led to unstable ICP measurements most likely because of muscle tissue occluding the catheter during pressure measurements. Using an air-pouch probe eliminated this problem. Proper placement of the two catheters in the middle of the compartment at the level of the largest diameter was confirmed by ultrasound.

Ultrasound examination

To estimate intra-compartmental pressure the elasticity ratio (ER) of the compartment was measured using compression sonography. A linear ultrasound probe (5.5–10 MHz) was placed at the level of the largest calf diameter in such way that the lateral tibia cortex was exposed horizontally. The compartment diameter was measured between the tibia cortex and the fascia on a line perpendicular to the tibia cortex, first without externally applied pressure and then while applying external pressure by pushing the US probe onto the skin. The ERs were computed as the ratio of the compartment diameters with and without application of external pressure; the resulting ERs were reported in percent (Fig. 1).

The applied external pressure was monitored using the Veinpress® system which consists of a translucent silicon membrane connected to a pressure meter (VeinPress 2014, VeinPress GmbH, 3110 Muensingen, Switzerland). It is mounted onto an US transducer and continuously monitors the manually applied pressure onto the tissue by the examiner during an US examination. The Veinpress® System was developed for non-invasive measurement of the central venous pressure [26–28]. It is not commercially available but only for research purposes (Fig. 2).

As we expected the ER to be dependent on the amount of externally applied pressure, the following five levels of external pressure were applied: 15, 30, 40, 50, and 100 mmHg. The ICP was increased stepwise and at every single ICP level the US measurements were performed with the aforementioned five different

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