Clinical aspects of lower leg compartment syndrome

J.G.H. van den Brand

Clinical aspects of lower leg compartment syndrome

J.G.H. van den Brand

Clinical Aspects of lower leg compartment syndrome
van den Brand, Johan Gerard Henric

Thesis, University Utrecht, with a summary in English and Dutch

ISBN: 90-393-3865-5
Printed by: Ponsen & Looijen
Design & Lay-out: Multimedia, UMC Utrecht
Cover: Detail of the pump control panel of a 1951 Bickle-Seagrave fire engine. Photograph by Dr. Will Brooks, Ottawa, Canada. (www.seagraveowners.org)

Clinical aspects of lower leg compartment syndrome

Klinische aspecten van het compartiment syndroom van het onderbeen

(With a summary in English)
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de Rector Magnificus, Prof. Dr W.H. Gispen, ingevolge het besluit van het College voor Promoties in het openbaar te verdedigen op

vrijdag 26 november 2004 des middags te 16.15 uur

door
Johan Gerard Henric van den Brand
Geboren op 13 juni 1968, te Someren

Promotor: Prof. Dr Chr. van der Werken

Copromotor: Dr E.J.M.M. Verleisdonk

Financial support for this thesis was provided by:

Hutchinson Technology
Biomet
Synthes
Huntleigh Healthcare
Sanofi-Synthelabo
ConvaTec Nederland
Tyco Healthcare
Stryker
AstraZeneca
B.Braun Medical
KCI Medical
Zimmer Netherlands
dePuy
Nutricia
Nederlandse Vereniging voor Traumatologie
Chirurgisch fonds, UMC Utrecht

Contents

Lower leg compartment syndromes

Introduction, overview and questions

I

Introduction

A compartment syndrome is a condition in which increased pressure within a limited space compromises the circulation and function of tissues within that space.[1] Two manifestations of compartment syndrome in the lower leg can be distinguished, the acute and the chronic form. Although pathofysiology may be roughly similar in both forms the clinical presentation and functional outcome are completely different.[3] Acute Compartment Syndrome (ACS) is an extremely aggressive form of pressure induced leg pain. It is a complication that is usually related to trauma, - to lower leg fractures in 40% of all acute compartment syndromes[2]-, but it may also follow revascularisation after prolonged critical ischemia of a limb. In ACS high intra-compartmental pressures can lead to serious, limb- and even life-threatening conditions, and emergency decompression of the affected compartments through complete fasciotomies is absolutely indicated to prevent permanent damage.

The chronic version is always exercise related and is therefore generally referred to as Chronic Exertional Compartment Syndrome (CECS). The clinical picture is usually rather mild in its presentation with disabling pain while walking or running as the characteristic presentation. Although these complaints are generally reversible and don't need emergency treatment, they can cause considerable morbidity and serious limitation of activity.

Although both lower leg compartment syndromes have been the subject of numerous investigations and publications, several questions still remain.

Anatomy of the lower leg

Compartment syndromes can occur in any part of the body, but are by far most often seen in the lower leg. Not only is the lower leg frequently exposed to trauma, it has a typical predisposing anatomy and it is almost continuously loaded during gait. Everywhere in the body, muscles are surrounded by tight fascial envelopes. This is particularly true in the extremities, and even more so in the lower leg, where fascias, membranes, tibia and fibula enclose four compartments. These compartments are generally referred to as the anterior, lateral (or peroneal), deep- and superficial posterior compartment, each with specific muscles, vascular structures and nerves, providing to the lower leg and foot. The strong osteofascial structures around the compartments prohibit and limit large volume increases of its contents. If a swelling of the tissue within one of these compartments occurs, the tight surrounding envelope can not yield and even small increases in volume can lead to a significant increase in pressure.[3]

Acute compartment Syndrome (ACS)

Pathophysiology

Blunt or penetrating trauma, infection, burns or vascular injury can cause ACS.[2-6] Swelling of tissues within a compartment decreases the transmural pressure in capillaries and venules, diminishes local blood flow and causes tissue hypoxia, thus ultimately leading to cellular death.[7] High elevation of a limb also reduces the arteriovenous pressure gradient. This makes the tissue more susceptible to ischaemic injury and may explain why an iatrogenic form of ACS is seen after lengthy surgery in the (hemi-)lithotomy position. Sustained endothelial cell damage will lead to increased vessel permeability and plasma leakage into the interstitium. This initiates the vicious circle of swelling, high pressure, ischemia, cell death and even more swelling, etc. Time plays an important role in the equation, high ICP's will cause damage sooner, but lower pressure maintained for a longer period can also result in severe tissue damage[8], that is irreversible after four to six hours of ischemia.[4,9] The only rational way to halt the problem is to create room for tissue expansion through rigorous decompressive fasciotomies.

Clinical presentation and diagnostic procedures

After every injury and also after lengthy surgery in the lithotomy-position one should be at guard to recognise developing ACS. The clinical picture is characterized by intense pain - disproportional to the sustained injury - and tenseness of the affected compartment on palpation. Paraesthesia of the foot, ankle joint stiffness and pain on passive muscle stretch are often found. Distal pulses are still present, because ICP never raises above systolic arterial blood pressure. The consequences of an untreated compartment syndrome are catastrophic. They include permanent neurological deficits, muscle necrosis, secondary infection, ischaemic contracture and acute renal failure, when myoglobin precipitates in the kidneys.[1] These complications can easily lead to loss of the affected limb or even life.[1]

The confirmation of the clinical diagnosis remains controversial. Measuring "delta"- or differential-pressure (DP) - the difference between ICP and diastolic blood pressure - is an accepted diagnostic tool, though somewhat controversial.[10-13] It takes into account that local tissue perfusion depends on the relation between intra-compartmental pressure and systemic blood pressure. A DP less than 30 mm Hg is arbitrarily considered pathognomonic for compartment syndrome. Although routine continuous monitoring of all patients at risk for compartment syndrome may seem rational and reassuring[14], it might well

result in overtreatment[15], and is unreliable if a catheter is not placed close to the fracture site.[16]
In our surgical department we don't perform ICP measurements routinely. We prefer a prophylactic fasciotomy on strict indication in a limited number of patients, when the chances of a developing compartment syndrome are high and/or the risk of delayed diagnosis is considerable. Victims of high-energy trauma, with comminuted lower leg fractures and extensive soft tissue damage, who are multiply injured, comatose or sedated qualify for this procedure. In other patients we perform fasciotomy on clinical grounds, using an ICP measurement only for confirmation when in doubt. This intervention should preferably be done as an "early" therapeutic procedure, when only the very first symptoms of an imminent compartment syndrome are present. If the fasciotomy is done "too late", compartment syndrome can be fully established and the ischemic damage might already be irreversible.

Prophylaxis and treatment
Once an acute compartment syndrome of the lower leg is suspected or has actually been diagnosed immediate dermato-fasciotomy of all four compartments is the only rational approach. It gives the injured tissue room to expand, so that pressures will drop dramatically and adequate perfusion will return. Although many advocate the combined medial and lateral incision, we prefer the parafibular approach.[3] The single incision provides good access to all four compartments and is relatively easy. To prevent the skin becoming the limiting envelope after all compartments have been opened, the skin incision must be long enough.[17] This will also reduce the risk of iatrogenic superficial peroneal nerve lesion and allow adequate inspection of the underlying tissues, with direct excision of necrosis, if indicated. Although a fasciotomy in itself will lead to a certain amount of morbidity, it must be preferred over the eventually disastrous outcome of an acute compartment syndrome that was missed or treated with delay.

There are a number of questions concerning Acute Compartment Syndrome that still need to be answered.

- Can risk factors for development of iatrogenic compartment syndrome during or after surgery in the lithotomy position be identified? What preventive measures can be taken to prevent this complication?
- What is the morbidity of a purely prophylactic or timely performed fasciotomy for imminent acute compartment syndrome?

- Is it acceptable to wait until the first symptoms of an imminent acute compartment syndrome are present before performing a fasciotomy or should a prophylactic fasciotomy be performed in (selected) high risk patients?

Chronic Exertional Compartment Syndrome (CECS)

Pathophysiology

During exercise muscle has been shown to increase in volume from 8 up to 20%.[18,19] This leads to an increase in pressure because of the restricting envelope around the muscles. The anterior compartment of the lower leg is most often involved. This is a consequence of the function of the anterior tibial and extensor digitorum muscles during the gait cycle and of the form of the compartment. Increased pressure within the compartment is translated to the intracompartmental vascular structures. Especially capillary and venous structures will be affected because of their thin walls and low perfusion pressure. As the transmural arterio-venous pressure gradient drops, local blood flow can be seriously decreased and therewith fail to meet the metabolic demands of the tissues. This leads to ischemia of structures within the compartment. Deterioration of neuromuscular function can lead to pain, muscle weakness or dysaesthesia. Because this cascade is exercise induced, it can be halted again by the cessation of activities. After exercise, the volume and pressure gradually return to their normal values. Complaints will subside accordingly, seldom acutely, but generally within minutes or hours. If exercise is not stopped on the appearance of symptoms and the patient "pushes through", eventually a critical pressure limit will be passed. From that point on the patient will enter the vicious circle of an acute compartment syndrome, bringing on the need for immediate treatment.

Clinical presentation and diagnostic procedures

In CECS, complaints are typically exercise related. The amount of activity after which pain develops in the affected compartment is usually rather consistent in each individual. Besides pain, patients may complain of muscle weakness and disaesthesia distal of the affected compartment, due to loss of sensory nerve function. Those who participate in exercise with repetitive loading, like military marching, running or soccer, are particularly at risk. Physical examination at rest is generally unremarkable, with the exception that fascial hernias are more often encountered in those diagnosed with CECS.[20,21] Pain on pal-

pation of the tibial shaft should prompt the attending physician towards other diagnoses like medial tibial stress syndrome or stress fractures.[22,23] Other (rare) differential diagnoses should be peroneal nerve entrapment, deep venous thrombosis, tendonitis and intermittent vascular claudication. In order to come to a reliable diagnosis, the patient should be observed during and directly after the activity that provokes the complaints. Usually this examination can be performed on a treadmill, but sometimes other circumstances must be found, for example in long distance ice skaters. During and after exercise, the pain can be localised in or over the affected compartment, muscle weakness and sensory deficits may become evident and diagnostic tests can be obtained. The most broadly used test to confirm diagnosis is the measurement of intra compartmental pressure (ICP). This can be done through an indwelling needle or catheter, during or after exercise.[24,25] Although there is still an ongoing debate on how and when to record ICP, we have settled on doing a single measurement technique of the affected compartment(s), with a side-ported needle[26], directly after exercise with the patient in supine position. This method has proven to be rather reliable in confirming CECS, showing a sensitivity of 93% and a 74% specificity when an ICP of 35 mmHg or higher is considered pathognomic for CECS.[27] Disadvantages are that results are hard to reproduce and that no generally accepted cut-off point has been established. In this respect our current diagnostic method is arbitrary too. Recent publications revealed promising abilities for non-invasive tests like Magnetic Resonance Imaging (MRI) and Near InfraRed Spectroscopy (NIRS).[28-32]

Treatment

Various conservative treatment options have been recommended in the past, varying from passive stretching and physiotherapy to non-steroidal anti-inflammatory drugs and footwear adaptations, but none of these methods has ever proven to enable the affected individual to return to his previous level of activity.[33] Only resolute cessation of all provoking activities makes complaints dissapear. If treatment is indicated to maintain activities on the same level, a fasciotomy of the affected compartment is the only rational approach. Fasciotomy of the anterior compartment of the lower leg can be performed through a small incision in a half open manner, under regional or general anaesthesia.[21,34] Postoperative rehabilitation is very important and patients must be encouraged to regain activity from the first day after operation, in order to prevent the formation of restrictive scar tissue in the newly created gap in the fascia. With this protocol, good results can be obtained, with a very low recurrence rate.[21,35]

A number of questions concerning CECS need to be answered:

- What is the natural history of CECS? If left untreated, will complaints eventually subside, stabilise or worsen in time?
- Is increased intra-compartmental pressure really the pivotal origin of Chronic Exertional Compartment Syndrome and if so, can one critical pressure threshold causing complaints be identified?
- Should we explore ischemia as a parameter for diagnosing Chronic Exertional Compartment Syndrome?
- Are non-invasive diagnostic tests, like MRI and NIRS, capable of replacing invasive ICP measurements for diagnosing Chronic Exertional Compartment Syndrome?

References

1 Matsen FA, III, Winquist RA, Krugmire RB, Jr. Diagnosis and management of compartmental syndromes. J Bone Joint Surg [Am] 1980; 62: 286-91.

2 Elliott KG, Johnstone AJ Diagnosing acute compartment syndrome. J Bone Joint Surg Br. 2003 Jul;85(5):625-32. Review.

3 Matsen FA 3rd, Rorabeck CH.Compartment syndromes. Instr Course Lect. 1989;38:463-72. Review

4 Mubarak SJ, Hargens AR. Acute compartment syndromes. Surg Clin North Am. 1983 63(3):539-65

5 Georgiadis GM. Tibial shaft fractures complicated by compartment syndrome: Treatment with immediate fasciotomy and locked unreamed nailing. J Trauma 1995;38(3):448-52

6 Tiwari A, Haq AI, Myint F, Hamilton G.: Acute compartment syndromes. Br J Surg. 2002 89(4):397-412

7 van der Elst M, van der Werken Chr. Fasciotomy for compartment syndrome of the lower leg. Surgical Techniques in Orthopaedics and Traumatology, Paris, Editions Scientifiques et Médicales Elsevier SAS 2000; 55-610-D-10

8 Hargens AR, Romine JS, Sipe JC, Evans KL, Mubarak SJ, Akeson WH. Peripheral nerve-conduction block by high muscle-compartment pressure. J Bone Joint Surg Am. 1979 Mar;61(2):192-200.

9 Williams AB, Luchette FA, Papaconstantinou HT,Lim E, Hurst JM, Johannigman JA, Davis K Jr. The effect of early versus late fasciotomy in the management of extremity trauma. Surgery 1997 122(4):861-6

10 Whitesides TE, Haney TC, Morimoto K, Harada H. Tissue pressure measurements as a determinant for the need of fasciotomy. Clin Orthop. 1975 Nov-Dec;(113):43-51

11 McQueen MM, Christie J, Court-Brown CM. Acute compartment syndrome in tibial diaphyseal fractures. J Bone Joint Surg Br. 1996 Jan;78(1):95-8

12 McQueen MM, Court-Brown CM. Compartment monitoring in tibial fractures. The pressure threshold for decompression. J Bone Joint Surg Br. 1996 Jan;78(1):99-104.

13 White TO, Howell GE, Will EM, Court-Brown CM, McQueen MM. Elevated intramuscular compartment pressures do not influence outcome after tibial fracture. J Trauma. 2003 Dec;55(6):1133-8

14 McQueen MM, Gaston P, Court-Brown CM Acute compartment syndrome. Who is at risk? J Bone Joint Surg Br. 2000 Mar;82(2):200-3.

15 Janzing HM, Broos PL. Routine monitoring of compartment pressure in patients with tibial fractures: Beware of overtreatment! Injury. 2001 Jun;32(5):415-21.

16 Heckman MM, Whitesides TE Jr, Grewe SR, Rooks MD. Compartment pressure in association with closed tibial fractures. The relationship between tissue pressure, compartment, and the distance from the site of the fracture. J Bone Joint Surg Am. 1994 Sep;76(9):1285-92.

17 Cohen MS, Garfin SR, Hargens AR, Mubarak SJ. Acute compartment syndrome. Effect of dermotomy on fascial decompression in the leg. J Bone Joint Surg Br. 1991 Mar;73(2):287-90

18 Ashton H. The effect of increased tissue pressure on blood flow. Clin Orthop 1975;(113):15-26..

19 Rorabeck CH, Macnab I. The pathofysiology of the anterior tibial compartmental syndrome. Clin Orthop 1975; 113: 52-7.

20 Styf JR, Korner LM. Chronic anterior-compartment syndrome of the leg. Results of treatment by fasciotomy. J Bone Joint Surg [Am] 1986; 68: 1338-47.

21 Verleisdonk EJ, van den Helder C, Hoogendoorn HA, van der Werken C. The chronic compartment syndrome of the lower leg: Results of fasciotomy. In; Hefte zu der "Unfallchirurg", Heft 267: "Das Kompartiment Syndrom" SpringerVerlag 1997; 363-367
22 Styf J. Diagnosis of exercise-induced pain in the anterior aspect of the lower leg. Am J Sports Med. 1988 Mar-Apr;16(2):165-9.
23 Touliopolous S, Hershman EB. Lower leg pain. Diagnosis and treatment of compartment syndromes and other pain syndromes of the leg. Sports Med. 1999 Mar;27(3):193-204. Review.
24 Moed BR, Thorderson PK. Measurement of intracompartmental pressure: a comparison of the slit catheter, side-ported needle, and simple needle. J Bone Joint Surg Am. 1993, 75(2):231-5.
25 Hargens AR, Ballard RE. Basic principles for measurement of intramuscular pressure. Oper Tech Sports Med. 1995 Oct;3(4):237-42. Review.
26 Awbrey BJ, Sienkiewicz PS, Mankin HJ. Chronic exercise-induced compartment pressure elevation measured with a miniaturized fluid pressure monitor. A laboratory and clinical study. Am J Sports Med. 1988, 16(6):610-5.
27 Verleisdonk EJ. [At what tissue pressure, measured immediately after exercise should the diagnosis of chronic exertional compartment syndrome of the lower leg be made]. [The exertional compartment syndrome]. Utrecht, the Netherlands: University Medical Center, 2000: 111-127.
28 Verleisdonk EJ, van Gils A, van der Werken C. The diagnostic value of MRI scans for the diagnosis of chronic exertional compartment syndrome of the lower leg. Skeletal Radiol 2001; 30: 321-5.
29 Amendola A, Rorabeck CH, Vellett D, Vezina W, Rutt B, Nott L. The use of magnetic resonance imaging in exertional compartment syndromes. Am J Sports Med. 1990 Jan-Feb;18(1):29-34.
30 Kiuru MJ, Mantysaari MJ, Pihlajamaki HK, Ahovuo JA. Evaluation of stress-related anterior lower leg pain with magnetic resonance imaging and intracompartmental pressure measurement. Mil Med. 2003 Jan;168(1):48-52.
31 Mohler LR, Styf JR, Pedowitz RA, Hargens AR, Gershuni DH. Intramuscular deoxygenation during exercise in patients who have chronic anterior compartment syndrome of the leg. J Bone Joint Surg Am 1997; 79: 844-9.
32 Breit GA, Gross JH, Watenpaugh DE, Chance B, Hargens AR. Near-Infrared spectroscopy for monitoring of tissue oxygenation of exercising skeletal muscle in a chronic compartment syndrome model. J Bone Joint Surg Am 1997; 79: 838-43.
33 Hutchinson MR, Ireland ML.Common compartment syndromes in athletes. Treatment and rehabilitation. Sports Med. 1994 Mar;17(3):200-8. Review.
34 Fronek J, Mubarak SJ, Hargens AR, Lee YF, Gershuni DH, Garfin SR, Akeson WH. Management of chronic exertional anterior compartment syndrome of the lower extremity. Clin Orthop. 1987 Jul;(220):217-27.
35 Detmer DE, Sharpe K, Sufit RL, Girdley FM. Chronic compartment syndrome: diagnosis, management, and outcomes. Am J Sports Med. 1985 May-Jun;13(3):162-70.

Near infrared spectroscopy in the diagnosis of chronic exertional compartment syndrome

a feasibility study

2

JGH van den Brand, EJMM Verleisdonk, Chr van der Werken
American Journal of Sports Medicine, Vol 32, No. 2, 2004: 452-456

Abstract

Introduction

Patients with chronic exertional compartment syndrome (CECS) experience pain during exercise. An abnormal increase in intra-compartmental pressure (ICP) leads to impaired local tissue perfusion resulting in ischemia and pain. At cessation of exercise, pain subsides. Diagnosis is confirmed through post-exercise ICP. Near infrared spectroscopy (NIRS) can measure tissue oxygen saturation (StO_2) non-invasively. This study was performed to see if NIRS could diagnose CECS by showing tissue deoxygenation.

Methods

In this prospective nonrandomized clinical trial volunteers completed a standardized exercise protocol. Those suspected of CECS did so pre- and post-operatively. StO_2 and ICP were monitored. Data were compaired between volunteers and patients and pre- and post-fasciotomy.

Results

Significant differences between the StO_2 values of volunteers and patients with CECS were found. The average peak exercise StO_2 value for those with CECS was lower than for the healthy (27 vs 56, $p<0.05$), Patients showed more absolute and percent change between baseline and peak exercise StO_2 (absolute: 60 vs 35, $p<0.05$, percent: 67 vs 38, $p<0.05$). StO_2 values in legs with confirmed CECS returned to the normal range post-fasciotomy. All changes differed significantly with pre-operative values.

Conclusion

StO2 can distinguish healthy from diseased legs. This study provides compelling evidence supporting NIRS as a non-invasive, painless alternative to ICP in the diagnosis of CECS

Introduction

Patients with chronic exertional compartment syndrome (CECS) experience recurrent episodes of pain during exercise. After cessation of exercise, the pain generally subsides within minutes. Although the aetiology of this syndrome is incompletely understood, the general agreement is that exercise causes abnormal increases in intramuscular pressure, thus impairing local tissue perfusion causing ischemia and pain.[1-3] Although history and physical examination findings may be suggestive of an existing CECS, they cannot fully exclude other causes of exertional lower leg pain. Therefore, the diagnosis must be confirmed by measurement of intra-compartmental pressure (ICP). An elevated pressure (>=35 mmHg) recorded after exercise is diagnostic for CECS.[4-7] This ICP measurement is an invasive technique, therefore it imposes some pain and certain risks.

Through near infrared spectroscopy (NIRS), it is possible to measure haemoglobin saturation of deep tissues in a non-invasive manner. Ischemia results in an increased extraction of oxygen by muscular tissue and, therewith, a decrease in venous oxyhaemoglobin. Since more than 80% of blood in tissues is in the venous compartment, tissue oxygen saturation (StO_2) reflects in most part the venous saturation and thus the level of local ischemia. Previous studies have shown that patients with typical complaints and elevated ICP show greater relative deoxygenation than those without pressure elevation or healthy controls do.[8,9] These studies used isokinetic models and relative oxygenation values. Our study is the first to test patients in a dynamic exercise model on the treadmill, measuring absolute StO_2 values between 0 and 100.

Study methods

This was a single-center, prospective, non-randomized feasibility study to determine if a difference in StO_2 between healthy volunteers and patients with CECS was observed during rest, treadmill exercise and recovery from exercise. The protocol was approved by the institutional ethical commitee and all participants gave written informed consent.

Adult caucasian males and females with intact skin, free of birthmarks or tattoos, over the anterior tibial muscles to accommodate placement of the near infra red spectrometer shields were enrolled as volunteers. Patients suspected of CECS had a typical history and an ICP of 35 mmHg or higher immediately after completing a standardized exercise protocol. All consecutive out-patients meeting inclusion criteria were admitted to the study until the diagnosis was confirmed in at least eight subjects.

For analytic purposes three groups were created. The healthy volunteers constituted group A. After confirmation of the diagnosis the patients' pre-operative results were analysed as group B and as group C post-operatively. ICP and StO_2 measurements were compared between group A and B and between B and C (figure 1).

Both groups completed a standardized exercise protocol: they walked on a treadmill at 6.0 km/h against a slope of 5 degrees for at least 10 minutes, or until symptoms occurred.[7] They rated their leg pain once a minute during the exercise protocol using a validated pain scale.[10]

ICP was measured with a pressure monitor (Quick Pressure Monitor System, Stryker Instruments, Kalamazoo, Michigan, USA) fitted with a side-ported needle. Prospective studies have shown it to be a reliable and reproducible way to record intra-muscular pressure, especially in the hands of the more experienced.[11,12] For a single measurement we considered it to be sufficient. The needle was inserted in the middle of the anterior compartment at a 45 degree angle. ICP was measured immediately after exercise in both legs in all subjects (within 30 seconds), additional ICP measurements were obtained from the patients with suspected CECS one minute prior to exercise and following completion of the exercise protocol after 10 minutes of rest.

StO_2 measurements were collected continuously every 3.5 seconds throughout the entire protocol in both legs with two InSpectraTM tissue spectrometers (Hutchinson Technology Inc., Hutchinson, MN USA). A 25 mm probe was placed on the skin over the tibialis anterior muscle. The measurement point was approximately 10 cm distal to the tibial tuberosity and 2 cm lateral of the tibial crest. The probe was connected to a cable containing transmitting and receiving optical fibres. This cable was linked to the photo-sentisitive detector in the spectrometer. The detector signal was processed and displayed as per cent hemoglobin oxygen saturation in tissue (StO_2). Effects of myoglobin are mitigated by its lower tissue concentration and its reluctance to release oxygen until hemoglobin is significantly deoxygenated.[13]

To enable continuous measurement before, during and after exercise the StO_2 monitors were positioned between the treadmill and an examination table, so patients could move eitherway without having to be dis- and re-connected. Both StO_2 monitors were linked to a computer, therewith enabling the recording of StO_2 data in text-files for later analysis.

All patients with ICP >=35 mmHg immediately after exercise (group B) underwent subcutaneous fasciotomy in a halfopen manner with a fasciotome inserted through a small incision.[14] They returned for a second visit at least six weeks after fasciotomy (group C), when the exercise protocol and measure-

ments were repeated. The diagnosis of CECS was confirmed by relieve of symptoms and normal ICP's post-operatively.

Analysis Methods

Each StO_2 data file contained marks to indicate the end of baseline, start and stop of treadmill exercise, and end of the post-exercise rest period. The StO_2 data file for each leg of each patient was processed to obtain specific endpoints. Definitions of the endpoints are shown in Table 1. The choice of endpoints was based on clinical observations and on results of previous studies in the literature.[8,9] A logistic growth curve was fit to the data collected after the stop exercise mark. The Logistic Growth Curve Equation was expressed as: StO_2 = a/(1+b*ctime) where a, b, and c are estimated from the data and time is the number of seconds since the end of the treadmill exercise.[15] The equation that

Table 1
Definition of Endpoint Calculations

Endpoint	Definition
Baseline StO_2	An average of 15 StO_2 registration-points prior to the baseline mark
Peak Exercise StO_2	An average of 15 StO_2 registration-points prior to the stop exercise mark
Absolute Change StO_2	Baseline StO_2 minus Peak Exercise StO_2
Percent Change StO_2	((Baseline StO_2 minus Peak Exercise StO_2)/ Baseline StO_2)*100
T-half	The time in seconds required for the StO_2 to recover by half of its exercise induced fall. The following equation was solved for time: T-half StO_2 =a/(1 + b*ctime) =0.5*(baseline StO_2 – peak exercise StO_2) + peak exercise StO_2. Where a, b, and c are estimated for each StO_2 data file
T-baseline	The time in seconds required for the StO_2 to recover to its baseline value. The following equation was solved for time: Baseline StO_2 = a/(1 + b*ctime), where a, b, and c are estimated for each StO_2 data file
Recovery-percentage	Level of StO_2 reached during recovery as a percentage of the baseline value The "a" parameter from the logistic growth curve equation is the estimated recovery StO_2: Recovery-percentage = (Recovery StO_2/ Baseline StO_2)*100

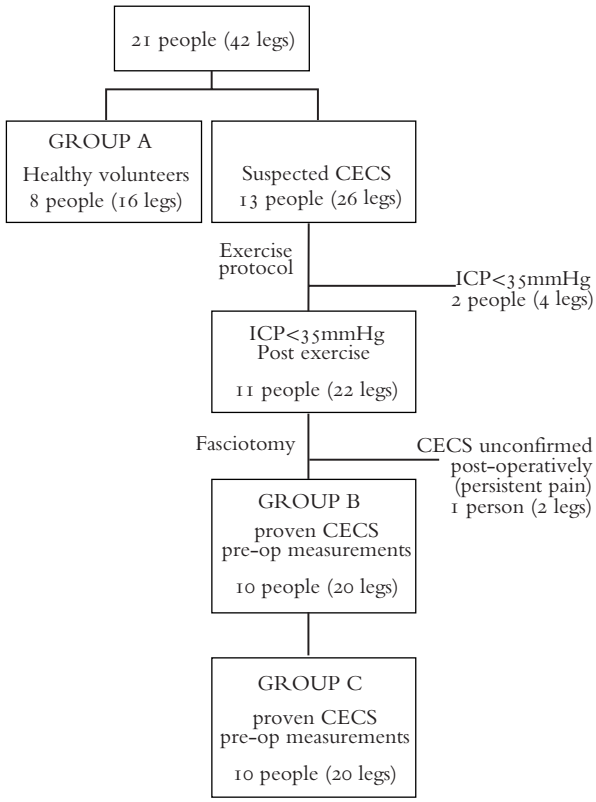
resulted from the fit to the data was used to estimate T-half, T-baseline and Recovery-percentage.

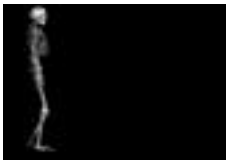
Testing for a statistical difference between group A and B was done using a repeated measures model. P-values were compared to an alpha value of 0.05 to assess statistical significance.The comparison of group B and C was done using the Wilcoxon Signed Rank Test.

Results

Eight healthy volunteers and 13 patients with suspected CECS were included in the study between September 2001 and January 2002. All participating patients had bilateral complaints and were analysed for both legs. Figure 1 shows details of enrolment and follow-up.

Figure 1





Included patients were predominantly from the military population: young adult Caucasian males in their twenties. The age and gender distribution were comparable between the volunteer and patient group (31.3 ± 7.6 yrs vs. 22.9 ± 5.6 yrs; 88% male vs. 80 %).

Table 2 shows the outcome of the various endpoints for the three groups. As could be expected ICP values differed significantly between volunteers (A) and pre-operative values (B) and between pre- (B) and post-operative (C) values ($p<0.0005$). Most of the StO_2 endpoints also showed a highly significant difference between the healthy volunteers (A) and those with CECS (B) and between the pre- (B) and post-operative (C) values. This was found for: Peak exercise StO_2, Absolute change StO_2, Percent change StO_2 (all $p\leq0.005$) and Recovery percentage StO_2 ($p\leq0.053$). The slower recovery of tissue saturation in CECS patients in comparison to healthy volunteers as reported in earlier publications wasn't found.[8,9]

In this population an ICP of 35 mm Hg had a diagnostic power that was comparable to the sensitivity and specificity of results in the literature (Table 3). When tested for their sensitivity and specificity different cut-off values for various StO_2 parameters or combinations of parameters proved to be very comparable to those found for ICP (table 3).

Table 2

Outcome results per group

	A **Healthy Volunteers** **(16 legs)**	**B** **CECS Patients** **(20 legs)**	**C** **Post-op Patients** **(20 legs)**
Parameter	Mean + SD	Mean + SD	Mean + SD
ICP after exercise (mmHg)	28 + 9	61 + 27#	30 + 8★
Baseline StO_2 (%)	91 + 5	87 + 11	88 + 12
Peak Exercise StO_2 (%)	56 + 16	27 + 19#	54 + 19★
Absolute Change StO_2 (%)	35 + 19	60 + 25#	34 + 14★
Percent Change StO_2 (%)	38 + 19	67 + 24#	39 + 17★
T-half (sec)	44 + 19	37 + 23	42 +18
T-baseline (sec)	119 + 39 (N=6)^	98 + 58 (N=17)^	107 + 42 (N=15)^
Recovery percentage (%)	101 + 4	107 + 9#	104 + 9†

\# $p<0.05$ (Group comparison within repeated measures model, i.e. comparing Group A to B)

★ $p<0.05$ (Wilcoxon Signed Rank Test comparing Group B to Group C)

^ Not all StO_2 curves returned to the actual baseline value.

† $p=0.053$ (Wilcoxon Signed Rank Test comparing Group B to Group C)

Table 3
Sensitivity and Specificity per parameter

Parameter	Sensitivity N=20 legs (95% CI)*	Specificity N=16 legs (95% CI)*
ICP directly after exercise		
>= 35 mmHg	90% (77%, 100%)	63% (39%, 86%)
Peak Exercise StO_2		
StO_2 <=50%	85% (69%, 100%)	69% (46%, 92%)
StO_2 <=55%	95% (85%, 100%)	63% (39%, 86%)
Percent Change StO_2		
>= 40%	85% (69%, 100%)	63% (39%, 86%)
>= 35%	90% (77%, 100%)	63% (39%, 86%)
Peak Exercise StO_2 and Percent Change StO_2		
StO_2 <= 60%; % Change >= 30%	95% (85%, 100%)	56% (32%, 81%)
StO_2 <= 60%; % Change >= 35%	90% (77%, 100%)	63% (39%, 86%)
StO_2 <= 55%; % Change >= 30%	90% (77%, 100%)	63% (39%, 86%)
StO_2 <= 55%; % Change >= 35%	90% (77%, 100%)	69% (46%, 92%)

* 95% Confidence interval

Discussion

The objective of this study was to determine the diagnostic value of NIRS in patients with suspected CECS. This study did not include patients with leg pain who did not have CECS as a second control group. They were omitted because this was a feasibility study. We chose to measure groups at both ends of the spectrum: healthy and those with a proven CECS. In future work this critical reference population must and will be assessed to really prove the discriminating, diagnostic utility of the technique.
Since this patient sample only contained Caucasian patients, we can not comment on the diagnostic ability of the technique on individuals from other races. Prior to exercise, at baseline, we found no difference in StO2 measurements between groups. During exercise StO_2 parameters of patients with proven CECS differed significantly from those of healthy volunteers and from the same parameters after surgery. The StO_2 curves of patients who were asymptomatic after surgery were equivalent to those of healthy volunteers. (Figure 2)

Sensitivity and specificity of various StO_2 cut-off values are comparable with those of ICP. The ICP cut-off point of 35 mm Hg in this study was based on references in the literature and on previous research in our clinic in 156 patients.[4-7] The critical ICP value for confirming CECS is still under discussion.

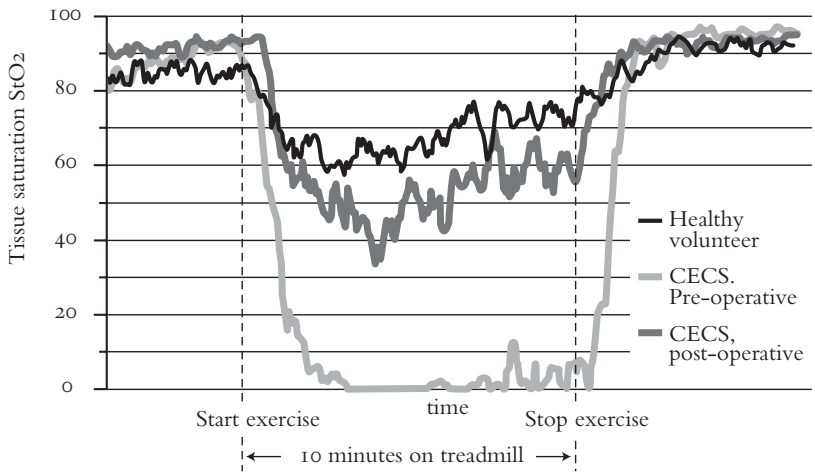
We tried to be pragmatic by choosing a method that is easy to use-measuring immediately after rather than during exercise- with proven good reliability in our hands (sensitivity 93%, specificity 74%, positive predictive value 85%).[7] The 90% sensitivity and 63% specificity we found for NIRS in this feasibility study are almost equal.

Our results provide compelling preliminary evidence for the diagnostic ability of StO_2 in CECS patients. A statistically significant difference in StO_2 measurements was noted between the healthy and those with CECS and between pre- and post-fasciotomy values. The post-fasciotomy ICP and StO_2 measurements in the surgically treated CECS patients were similar to those of healthy volunteers. Patients with CECS demonstrated a greater deoxygenation in the anterior compartment during exercise than volunteers. Our results, particularly the magnitude of deoxygenation during exercise, are consistent with findings in previous studies.[8,9]

Conclusion

StO_2 measured through Near InfraRed Spectroscopy (NIRS) is a non-invasive, painless, easy to use alternative to Intra-Compartmental Pressure (ICP) in the diagnosis of Chronic Exertional Compartment Syndrome.

Figure 2
Typical NIRS curves



References

1. Ashton H. The effect of increased tissue pressure on blood flow. Clin Orthop 1975;(113):15-26.
2. Rorabeck CH, Macnab I. The pathophysiology of the anterior tibial compartmental syndrome. Clin Orthop 1975;(113):52-57.
3. Sheridan GW, Matsen FA, III, Krugmire RB, Jr. Further investigations on the pathophysiology of the compartmental syndrome. Clin Orthop 1977;(123):266-270.
4. Qvarfordt P, Christenson JT, Eklof B, et al. Intramuscular pressure, muscle blood flow, and skeletal muscle metabolism in chronic anterior tibial compartment syndrome. Clin Orthop 1983;(179):284-290.
5. Styf J. Diagnosis of Chronic Compartment Syndrome in the Leg by History, Signs and Intramuscular Pressure Recordings. In: Willy C, Sterk J, Gerngross H, editors. Das Kompartment Syndrom. Berlin, Heidelberg: Springer Verlag, 1998: 277-281.
6. Styf JR, Korner LM. Chronic anterior-compartment syndrome of the leg. Results of treatment by fasciotomy. J Bone Joint Surg Am 1986; 68(9):1338-1347.
7. Verleisdonk EJ. [At what tissue pressure, measured immediately after exercise should the diagnosis of chronic exertional compartment syndrome of the lower leg be made]. [The exertional compartment syndrome]. Utrecht, the Netherlands: University Medical Center, 2000: 111-127.
8. Breit GA, Gross JH, Watenpaugh DE, et al. Near-infrared spectroscopy for monitoring of tissue oxygenation of exercising skeletal muscle in a chronic compartment syndrome model. J Bone Joint Surg Am 1997; 79(6):838-843.
9. Mohler LR, Styf JR, Pedowitz RA, et al. Intramuscular deoxygenation during exercise in patients who have chronic anterior compartment syndrome of the leg J Bone Joint Surg Am 1997; 79(6):844-849.
10. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain 1986; 27(1):117-126.
11. Awbrey BJ, Sienkiewicz PS, Mankin HJ. Chronic exercise-induced compartment pressure elevation measured with a miniaturized fluid pressure monitor. A laboratory and clinical study. Am J Sports Med. 1988, 16(6):610-5.
12. Moed BR, Thorderson PK. Measurement of intracompartmental pressure: a comparison of the slit catheter, side-ported needle, and simple needle. J Bone Joint Surg Am. 1993, 75(2):231-5.
13. Mancini DM, Bolinger L, Li H, Kendrick K, et al. Validation of near-infrared spectroscopy in humans. J Appl Physiol 1994; 77(6):2740-2747.
14. Verleisdonk EJ, van den Helder CJ, Hoogendoorn HA, van der WC. [Good results of fasciotomy in chronic compartment syndrome of the lower leg]. Ned Tijdschr Geneeskd 1996; 140(50):2513-2517.
15. Snedecor G, Cochran W. Statistical Methods. Ames, Iowa: Iowa State University Press; 1981.

The diagnostic value of intra compartmental pressure measurement, magnetic resonance imaging and near infrared spectroscopy in the chronic exertional compartment syndrome

A prospective study in 50 patients

3

JGH van den Brand, T Nelson, EJMM Verleisdonk, Chr van der Werken
American Journal of Sports Medicine, in press (accepted july 2004)

Abstract

Introduction

Patients with chronic exertional compartment syndrome (CECS) have recurrent pain during exercise that usually subsides at rest. History and physical examination may raise the suspicion of CECS but diagnosis is usually confirmed by Intra Compartmental Pressure measurement (ICP) after exercise. Recent studies have shown that Magnetic Resonance Imaging (MRI) and Near Infrared Spectroscopy (NIRS) also have diagnostic ability in CECS, this study seeks validation for both methods in a larger series of patients.

Methods

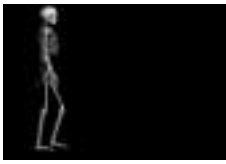
In this prospective non-randomized clinical trial patients were enrolled if there was a clinical suspicion of CECS and a fasciotomy was performed based solely on this suspicion. Prior to fasciotomy ICP, NIRS and MRI data were collected during and after a treadmill-exercise. NIRS and ICP values were recorded in the same manner after fasciotomy. The retrospective proof that the diagnosis CECS had been correct was when the exertional complaints from visit # 1 were gone during exercise at the post-fasciotomy visit.

Results

50 patients (100 legs) participated in the pre-fasciotomy visit, 3 patients refused fasciotomy, 2 were lost to follow-up. Of the 45 patients (90 legs) that completed the post-fasciotomy visit, the diagnosis CECS was retrospectively confirmed in 42 patients (84 legs) and discarded in 3 patients (6 legs). The sensitivity for ICP (cut-off point ICP > 35 mmHg) found in this study was 77% (67%, 86%, Exact 95% CI), lower than comparator estimates from literature (93%). The sensitivity (cut-off: percent change in StO_2 > 35%) found in this study for NIRS was 84% (74%, 91%, Exact 95% CI) which validates the estimate found in the literature (85%). The sensitivity of MRI was found to be comparable to that of ICP and NIRS. However, the associated specificity at a given sensitivity appeared to be lower with MRI.

Conclusion

This study validates the sensitivity of NIRS and provides initial estimates for the sensitivity and specificity of MRI in Chronic Exertional Compartment Syndrome in a large group of patients. The sensitivity of Near InfraRed Spectroscopy -a non-invasive technique- is clinically equivalent to that of invasive intra compartmental pressure measurements.



Introduction

Patients with chronic exertional compartment syndrome suffer from recurrent episodes of pain during exercise. After exercise, complaints generally subside within several minutes. Although the aetiology of this syndrome is incompletely understood, the general agreement is, that exercise causes abnormal elevation of intramuscular pressure. The raised intra-compartmental pressure impairs local tissue perfusion and thereby results in ischemic pain.[1-4] Although history and physical examination may rise the suspicion of a chronic compartment syndrome, it's generally very difficult to exclude other causes of lower leg pain during exercise even for those who are highly experienced in this field.[5-7] Therefore an intra-muscular pressure measurement, preferably after exercise is usually performed to verify the diagnosis.[8-10] To measure the pressure within a muscle compartment a needle or catheter is introduced through the skin and fascia. With the finding of elevated pressures after exercise the diagnosis Chronic Exertional Compartment Syndrome (CECS) is confirmed. This technique however is invasive, painful and carries the hypothetical risk of bleeding or infection. In spite of these disadvantages, pressure measurements were the only available, practical, objective parameter. Although Intra-Compartmental Pressure (ICP) is the best-documented parameter, it has always been the subject of debate.[11] The best sensitivity and specificity found in a large clinical study is 93% and 74% respectively (at a cut off point of 35 mm Hg).[12] This explains the search for other – probably non ivasive - diagnostic methods.

MRI scans have proven to show an increase in T2 weighted signal in legs affected with CECS after exercise.[13-17] The results in some -small quantity- studies published thus far seem promising and MRI could be an alternative in confirming the diagnosis of CECS.

With Near InfraRed Spectroscopy (NIRS) it is possible to measure the haemoglobin saturation of tissues in a non-invasive manner. Ischemia causes an increased extraction of oxygen by muscular tissue and therefore a decrease in venous oxyhaemoglobin. Since more than 80% of the blood in tissue is in the venous compartment, tissue saturation (StO_2) reflects more or less the venous saturation and therewith the level of local ischemia. Previous studies have shown that patients with typical complaints and elevated intra-compartmental pressures show a larger decrease in StO_2 after exercise than those without pressure elevation or healthy controls.[18-20]

Neither MRI nor NIRS have been proven completely reliable in a large

prospective study. All three methods, intra-compartmental pressure measurement, MRI and NIRS have previously proven that they can help in confirming the diagnosis of chronic exertional compartment syndrome of the leg. The aim of this study is to compare the performance of these tests within one study and to validate the diagnostic values that were found for both non-invasive methods in previous pilot studies in a limited number of patients.[13,20]

Study methods

Patients

Patients were recruited from the military population in the Central Military Hospital (CMH) in Utrecht. All patients with complaints of exertional lower leg pain were seen by a single surgeon (JvdB). If history and examination led to a clinical suspicion of uni- or bilateral chronic exertional compartment syndrome, the patient was included in the study. In case of doubt a short treadmill test was done to clarify clinical diagnosis. (no pressure measurements were done at that time). All of the included patients went on to have a fasciotomy of the affected compartment of the leg. The decision to operate was made on clinical grounds alone, before all three pre-operative tests were performed and was not influenced by the test results. Patients with prior musculoskeletal surgery to the affected leg, aberrant skin over the anterior compartment of the affected leg (wounds, tattoos or birthmarks) or pregnancy and those who refused to sign informed consent were excluded from the study. Patients with contra indications for MRI (e.g. pacemaker) could not participate in the MRI portion of the study.

Pre-operative procedures

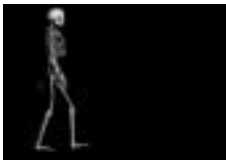
- Exercise: After inclusion, patients were submitted to a standardised exercise protocol on a treadmill: They walked with a speed of 6 kilometres/hour against a slope of 5 degrees for at least ten minutes or until pain symptoms caused the test to be stopped. If typical pain complaints had not developed during the first 6 minutes of exercise, walking speed was increased to a maximum of 8 kilometres/hour and/or the slope was increased to 8 degrees.
- ICP: Intramuscular pressure of the affected compartments was assessed immediately after exercise. These single measurements were done with the patient in supine position with a digital intramuscular pressure registration device, fitted with a side-ported needle (Stryker instruments, Kalamazoo, Michigan, USA). The needle was inserted in the middle of the anterior

compartment at an angle of 45°. This method has been tested and validated in clinical settings.[21,22] For analysis of the diagnostic value we used a cut-off point of 35 mm Hg as previously defined in the literature.[12]

- MRI: Magnetic Resonance Images were obtained with the patient at rest and the leg positioned in a specially designed mould to standardise MR images. A cross-section in the axial plane was taken midway through the lower leg - 10-15 cm below the knee joint - and marked on the skin. In a cross-sectional slice of 10 mm thickness 3 regions of interest (ROI) with a total surface area of 2 cm^2 were chosen in both the anterior and superficial posterior compartment of the affected legs. The ROI's were chosen in identical locations in different patients, as much as was possible. Vascular structures were kept outside of the ROI's. In each ROI, the average T2 weighted signal intensity was calculated, after which the average value of the three ROI's was arbitrarily accepted as the average T2 signal intensity in the entire cross-section of the compartment (= AvT2). After this examination at rest, patients were submitted to the same treadmill-test described before, with the treadmill positioned next to the scanner. Within one minute after the exercise a new AvT2 was determined, enabling the assessment of differences with resting condition in both the anterior and posterior compartment. The signal intensity ratio, comparing the anterior to the superficial posterior compartment was determined for each symptomatic extremity before and after exercise. The percentage increase in this ratio after exercise was calculated. (Table 1)
- NIRS: During and after exercise tissue oxygen saturation (StO_2) in the affected compartment was continuously registered using two In Spectra™ Tissue Spectrometers and a 25 mm optical cable (Hutchinson Technology, Hutchinson, Minnesota USA). A probe was placed directly on the skin over the middle one third of the anterior compartment. The incorporated emitting and receiving optical fibre units use wavelength signals between 650 and 810 nm. Light in the near infrared spectrum passes relatively easily through tissue, but haemoglobin and oxyhaemoglobin differentially absorb the different wavelengths. Thus, the reflected recollected near-infrared light can be used to provide the StO_2 value of the underlying part of the body.
  Each NIRS data file contained marks to indicate the start and stop of treadmill exercise. The NIRS data file for each leg of each patient was processed to obtain specific endpoints, based on results as published in earlier studies (Table 1).[18-20] The analysis was performed in the same manner as published previously.[20]

Table 1
Definition of Endpoint Calculations for study parameters

Endpoint	Definition
MRI	
Percent increase in ratio during exercise	The increase in T2 weighted signal for the ratio between the anterior and posterior compartment after exercise Calculated as (post exercise ratio – pre exercise ratio)/ (pre exercise ratio); pre exercise ratio = (AvT2 anterior compartment)/ (AvT2 superficial posterior compartment) prior to exercise; post exercise ratio = same calculation for post exercise values.
Percent increase in anterior compartment	The increase in T2 weighted signal in the anterior compartment after exercise Calculated as: (post exercise AvT2– pre exercise AvT2)/ (pre exercise AvT2). (all values from the anterior compartment)
Percent increase in superficial posterior compartment[5]	The increase in T2 weighted signal in the superficial posterior compartment after exercise Calculated as: (post exercise AvT2– pre exercise AvT2)/ (pre exercise AvT2). (all values from the superficial posterior compartment)
NIRS	
Baseline StO_2	An average of 15 StO_2 registration-points prior to the baseline mark
Peak exercise StO_2	An average of 15 StO_2 registration-points prior to the stop exercise mark
Absolute change StO_2	Baseline StO_2 minus Peak Exercise StO_2
Percent change StO_2	(Baseline StO_2 minus Peak Exercise StO_2)/ Baseline StO_2)*100



Fasciotomy
Fasciotomy of the affected compartment (it was anterior compartment in all included patients) was performed under general anaesthesia, in a half open manner with a fasciotome through a small incision.[6,23] Patients received strict instructions considering their after-treatment: they were to start mobilisation on the first postoperative day and had to go walking at least three sessions of 30-minutes a day.

Follow up
Minimally six weeks after operation all patients were examined in the out-patient department for recurrent or persisting complaints. They were resubmitted to the exercise-test with ICP measurement and StO_2 registration in the manner previously described. No post-operative MRI investigations were done. Absence of typical exercise related complaints post-operatively was considered the gold standard for diagnosis: if patients were symptom free and without exertional complaints, the diagnosis of a chronic exertional compartment syndrome was consequently retrospectively confirmed.

Statistical anaysis
The results of the different tests were compared between those in whom CECS was confirmed and those in whom it was not. Pre- and postoperative results were compared within each group using the Wilcoxon Two-Sample Test. We then calculated the estimated sensitivity and specificity with exact 95% confidence intervals for each of the three tests.

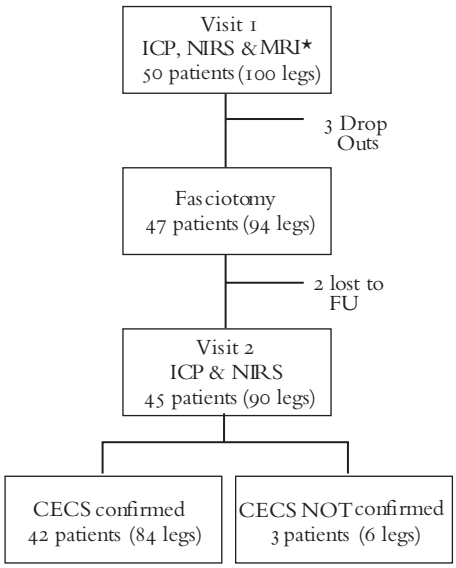
Results

From April 2002 until January 2003, ninety-seven (97) consecutive patients with lower leg pain reported to the surgical clinic of the Central Military Hospital. The clinical diagnosis of 52 persons in this group was compatible with CECS. Two of them withdrew from the study prior to any data collection. The remaining fifty each had bilateral complaints in the anterior compartment, none of the other compartment was affected. Thus a total of 100 legs was analysed according to the protocol. All patients enrolled in this study were enlisted in the Dutch army, so the sample of participants was predominantly young and male (male:female 42:8, median age 21, range 17-30). After the pre-operative visit three patients refused operation for miscellaneous reasons (as patients were blinded to the outcomes of tests the results cannot have influenced their decision). After surgery two patients were lost to follow up,

the complete follow up is schematically shown in Figure 1.
Postoperatively only a small number of the study subjects were found to have persistent, unaltered complaints, therewith proving the diagnosis CECS wrong. Subsequently, this compromised estimates of specificity and precluded an analysis using ROC curve methodology. Given this the analysis was limited to the estimation of sensitivity values for NIRS and ICP at previously defined cut-offs. In addition, pilot estimates of sensitivity and specificity were prepared for various cutoff vaues of the MRI parameters.
The mean results and 95% confidence intervals for the diagnostic parameters collected in this study are given in table 2.

- ICP & NIRS: Based on the distinct 95% confidence intervals as well as the mean values, these data clearly show the same trend as in previous research: ICP and NIRS values were significantly different in legs in which CECS had been diagnosed in comparison to those without (Wilcoxon Two-Sample Test, $p<0.05$). Table 3 provides the study estimates for the sensitivity and specificity of the pre-operative ICP and StO_2 values. Our current results are quite comparable to those from the aforementioned smaller studies, there-

Figure 1
Flow chart of patient follow up



*Two patients failed to undergo the MRI examination.

Table 2

The mean results and 95% confidence intervals for the diagnostic parameters ICP, MRI and StO_2 Pre- & Postfasciotomy.

	Pre-fasciotomy		Post-fasciotomy	
	CECS confirmed	CECS Not confirmed	CECS confirmed	CECS Not confirmed
Parameter	N=84 42 subjects Mean ± SD (95% CI)	N=6 3 subjects Mean ± SD (95% CI)	N=82 41 subjects Mean ± SD (95% CI)	N=6 3 subjects Mean ± SD (95% CI)
ICP directly after exercise (mmHg)	59 ± 30 (53, 65)	28 ± 4 (23, 32)	28 ± 12 (26, 31)	23 ± 4 (19, 27)
MRI Percent increase in ratio during exercise	8 ± 12 (5, 11) [1]	-0 ± 5 (-5, 5)		
Percent increase in anterior compartment	19 ± 12 (16, 22) [1]	11 ± 7 (4, 19)		
Percent increase in superficial posterior compartment	11 ± 6 (9, 12) [1]	11 ± 4 (7, 16)		
NIRS Baseline StO_2 (%)	86 ± 9 (84, 88)	83 ± 9 (74, 92)	85 ± 9 (83, 87)	70 ± 21 (48, 91)
Peak exercise StO_2 (%)	25 ± 25 (20, 31) [2]	48 ± 11 (37, 60)	53 ± 21 (49, 58)	52 ± 20 (31, 73)
Absolute change between baseline and peak exercise StO_2	61 ± 25 (55, 66) [2]	35 ± 17 (17, 53)	32 ± 19 (28, 36)	18 ± 7 (10, 25)
Percent change between baseline and peak exercise StO_2 (%)	71 ± 28 (65, 77) [2]	41 ± 17 (23, 58)	38 ± 23 (33, 43)	26 ± 11 (15, 38)

Table shows mean values ± Standard deviation and 95% Confidence interval (in brackets)

1 n=80: Two patients failed to undergo the MRI examination.
2 n=82: Both InSpectra devices ceased to provide StO_2 values shortly after exercise began in one coloured patient.

with validating the methods and cut-off points. The sensitivity for ICP found in this study was 77% (67%, 86%, Exact 95% CI), lower than the comparator estimate from the literature (93%). The best estimate of sensitivity for NIRS found in this study was 85% (76%, 92%, Exact 95% CI), which validates the previous estimate of 90%. Post-fasciotomy the values for ICP and StO_2 parameters of patients with CECS returned to values that were similar to the pre-fasciotomy values of patients without CECS or normal controls.[20] Of note, StO2 could not be registered in one patient with a very dark skintone.

- MRI: The percent increase in AvT2 ratio during exercise (anterior compartment / superficial posterior compartment) was higher, albeit not statistically significant (Wilcoxon Two-Sample Test, p-value not significant), in those with CECS as was the percent increase in the anterior compartment (table 3). No clear cut-off point was established previously for MRI when diagnosing CECS. We analysed the change in pre and post-exercise ratios for all legs and calculated the sensitivity and specificity for some different

Table 3

Sensitivity and Specificity for pre-fasciotomy ICP & NIRS Measurements

	Sensitivity (95% CI)[1] N=84 legs	Specificity (95% CI) [1] N=6 legs
ICP		
directly after exercise (>= 35 mmHg indicates a leg with CECS)	77% (67%, 86%)	83% (36%, 100%)
NIRS		
Peak exercise StO_2 (StO_2 <=50% indicates a leg with CECS)	78% (68%, 86%)[2]	67% (22%, 96%)
(StO_2 <=55% indicates a leg with CECS)	78% (68%, 86%)[2]	67% (22%, 96%)
Percent change between Peak exercise StO_2 and Baseline StO_2 (>= 40% indicates a leg with CECS)	84% (74%, 91%)[2]	67% (22%, 96%)
(>= 35% indicates a leg with CECS)	85% (76%, 92%)[2]	67% (22%, 96%)

1 Exact 95% Confidence Interval

2 n=82: Both InSpectra devices ceased to provide StO_2 values shortly after exercise began in one coloured patient.

cut-offs (percent change in ratio). As can be seen in table 4, the diagnostic ability of MRI appears to be relatively poor in comparison to StO_2 and ICP (table 3). The sensitivity of MRI was found to be comparable to that of ICP and StO_2, but, the associated specificity at a comparable sensitivity appeared to be lower with MRI. Of note, two patients failed to undergo MRI measurements, due to logistical reasons.

Table 4
Sensitivity and Specificity for pre-fasciotomy MRI Measurements (Percent Increase in Ratio During Exercise) for Various Cut-offs.

	Sensitivity	Specificity
MRI	(95% CI)[1] N=80 Legs[2]	(95% CI)[1] N=6 Legs
Cut-off, percent change in ratio		
(> 10% indicates a leg with CECS)	40% (29%, 52%)	100% (54%, 100%)
(> 5% indicates a leg with CECS)	53% (41%, 64%)	83% (36%, 100%)
(> 0% indicates a leg with CECS)	70% (59%, 80%)	50% (12%, 88%)
(> -5% indicates a leg with CECS)	86% (77%, 93%)	17% (0%, 64%)

1 Exact 95% Confidence Interval
2 Two patients failed to undergo the MRI examination.

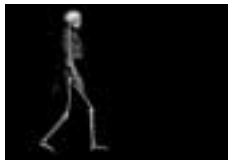
Discussion

This study reconfirms the diagnostic value of a 35 mm Hg cut off point of intra compartmental pressure (ICP) measurements in chronic exertional compartment syndrome (CECS). It is however the first study to show a clinically equivalent validated sensitivity associated with Near Infrared Spectroscopy in a larger group of patients, after earlier studies have shown promising results in a small series. These results prove that NIRS is a very reasonable, reliable - non-invasive - alternative to invasive pressure measurements when percent change in StO_2 > 35% is used as a cut off.

The diagnostic value of MRI is somewhat disappointing when compared to ICP and NIRS, as it is when compared to the results of earlier studies. The trend was the same as described previously: i.e. there was a larger increase in the average T2 weighed signal in the affected anterior compartments than there was in the superficial posterior compartment in patients with CECS. Also, the percentage AvT2 increase in the anterior compartment after exercise was larger in patients with CECS. Finally there is a clear increase in the anterior/posterior ratio when the post-exercise values are compared to those pre-exercise. The magnitude of this change in ratio - the most obvious parameter in other studies -, however, is smaller in this study. A possible explanation is that the patients in previous studies had more pronounced and advanced complaints of CECS due to the different patient selection.
Of course the small number of legs in which CECS was not diagnosed and the subsequent wide confidence intervals make the reliability of the specificity estimates in this study questionable, so that comparison of this part of the results to the literature is difficult. The fact that so little patients without CECS were included was somewhat surprising to us, as the study protocol was set up - based on literature and personal experience - with the expectation that including patients solely on clinical grounds would result in a relatively large group of patients with lower leg complaints that weren't caused by CECS. In this way we hoped to be able to make more reliable calculations of specificity and ROC curve analysis, to establish cut-off points for future reference.
Although we agree that it is generally recommended to confirm the clinical diagnosis through ICP or StO_2 measurements, these results show that a physician with a special interest in this field can make a fairly reliable clinical diagnosis. The accuracy in this study was 93% (84 out of 90 legs were confirmed CECS) Of course one has to bear in mind that this was a selected group of patients of enlisted military personnel, visiting a military hospital, therewith raising the incidence of CECS.

Conclusion

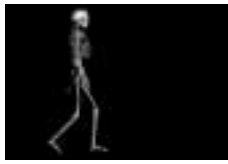
The diagnostic ability of Intra Compartmental Pressure measurements and Tissue saturation measurements through Near Infrared Spectroscopy for chronic exertional compartment syndrome are confirmed and validated in this study, MRI is clearly less suitable to confirm this diagnosis.



References

1. Matsen FA, III, Winquist RA, Krugmire RB, Jr. Diagnosis and management of compartmental syndromes. J Bone Joint Surg [Am] 1980; 62: 286-91.
2. Ashton H. The effect of increased tissue pressure on blood flow. Clin Orthop 1975; 113: 15-26.
3. Rorabeck CH, Macnab I. The pathofysiology of the anterior tibial compartmental syndrome. Clin Orthop 1975; 113: 52-7.
4. Sheridan GW, Matsen FA, III, Krugmire RB, Jr. Further investigations on the pathofysiology of the compartmental syndrome. Clin Orthop 1977; 123: 266-70.
5. Willy C, Sterk J, Volker HU, Benesch S, Gerngross H. The significance of intracompartmental pressure values for the diagnosis of chronic functional compartment syndrome. A meta-analysis of research studies of pressures in anterior M. tibialis during exercise stress. Unfallchirurg. 1999 Apr;102(4):267-77
6. Fronek J, Mubarak SJ, Hargens AR, Lee YF, Gershuni DH, Garfin SR, Akeson WH. Management of chronic exertional anterior compartment syndrome of the lower extremity. Clin Orthop. 1987 Jul;(220):217-27.
7. Puranen J, Alavaikko A Intracompartmental pressure increase on exertion in patients with chronic compartment syndrome in the leg. J Bone Joint Surg Am. 1981 Oct;63(8):1304-9.
8. Styf JR, Korner LM. Chronic anterior-compartment syndrome of the leg. Results of treatment by fasciotomy. J Bone Joint Surg [Am] 1986; 68: 1338-47.
9. Qvarfordt P, Christenson JT, Eklof B, Ohlin P, Saltin B. Intramuscular pressure, muscle blood flow, and skeletal muscle metabolism in chronic anterior tibial compartment syndrome. Clin Orthop 1983; 284-90.
10. Styf J. Diagnosis of chronic compartment syndrome in the leg by history, signs and intramuscular pressure recordings. Heft 267: "das Kompartimentsyndrom" Springer Verlag 1997; hefte zu "der Unfallchirurg": 277-81.
11. Mannarino F, Sexson S. The significance of intracompartmental pressures in the diagnosis of chronic exertional compartment syndrome. Orthopedics. 1989 Nov;12(11):1415-
12. Verleisdonk EJ. [At what tissue pressure, measured immediately after exercise should the diagnosis of chronic exertional compartment syndrome of the lower leg be made]. [The exertional compartment syndrome]. Utrecht, the Netherlands: University Medical Center, 2000: 111-127.
13. Verleisdonk EJ, van Gils A, van der Werken C. The diagnostic value of MRI scans for the diagnosis of chronic exertional compartment syndrome of the lower leg. Skeletal Radiol 2001; 30: 321-5.
14. Amendola A, Rorabeck CH, Vellett D, Vezina W, Rutt B, Nott L. The use of magnetic resonance imaging in exertional compartment syndromes. Am J Sports Med. 1990 Jan-Feb;18(1):29-34.
15. Kiuru MJ, Mantysaari MJ, Pihlajamaki HK, Ahovuo JA. Evaluation of stress-related anterior lower leg pain with magnetic resonance imaging and intracompartmental pressure measurement. Mil Med. 2003 Jan;168(1):48-52.
16. Eskelin MK, Lotjonen JM, Mantysaari MJ. Chronic exertional compartment syndrome: MR imaging at 0.1 T compared with tissue pressure measurement. Radiology. 1998 Feb;206(2):333-7.
17. Lauder TD, Stuart MJ, Amrami KK, Felmlee JP. Exertional compartment syndrome and the role of magnetic resonance imaging. Am J Phys Med Rehabil. 2002 Apr;81(4):315-9.

18. Mohler LR, Styf JR, Pedowitz RA, Hargens AR, Gershuni DH. Intramuscular deoxygenation during exercise in patients who have chronic anterior compartment syndrome of the leg. J Bone Joint Surg Am 1997; 79: 844-9.
19. Breit GA, Gross JH, Watenpaugh DE, Chance B, Hargens AR. Near-Infrared spectroscopy for monitoring of tissue oxygenation of exercising skeletal muscle in a chronic compartment syndrome model. J Bone Joint Surg Am 1997; 79: 838-43.
20. Van den Brand JGH, Verleisdonk EJMM, van der Werken C. Near infrared spectroscopy in the diagnoses of chronic exertional compartment syndrome. Am J Sports Med. 2004 Mar-Apr;32(2):452-6.
21. Awbrey BJ, Sienkiewicz PS, Mankin HJ. Chronic exercise-induced compartment pressure elevation measured with a miniaturized fluid pressure monitor. A laboratory and clinical study. Am J Sports Med. 1988, 16(6):610-5.
22. Moed BR, Thorderson PK. Measurement of intracompartmental pressure: a comparison of the slit catheter, side-ported needle, and simple needle. J Bone Joint Surg Am. 1993, 75(2):231-5.
23. Verleisdonk EJ, van den Helder C, Hoogendoorn HA, van der Werken C. The chronic compartment syndrome of the lower leg: Results of fasciotomy. In; Hefte zu der "Unfallchirurg", Heft 267: "Das Kompartiment Syndrom" SpringerVerlag 1997; 363-367



Near-infrared spectroscopy in heavily pigmented persons

Reliability affected by melanin

4

EB Wassenaar, JGH van den Brand
Submitted

Abstract

Introduction

Near-infrared spectroscopy (NIRS) is a promising non-invasive technique for the continuous monitoring of tissue oxygen delivery. NIRS detects light absorbance of hemoglobin chromophores to determine tissue oxygen saturation (StO_2). As skin colour is also determined by the presence of chromophores, it is plausible that NIRS signal quality may be affected by dark skin pigmentation.

Methods

Tissue saturation in the anterior compartment of the lower leg during isometric contraction was measured using NIRS in 17 volunteers with dark skin pigmentation. Measurements were continued until StO_2 was zero percent or until the signal disappeared.

Results

The NIRS device failed to register tissue saturation values at some point in nine of seventeen volunteers. This occurred more often in individuals with darker skin.

Conclusions

In patients with a dark pigmented skin, NIRS StO_2 measurements should be interpreted with caution, as melanin clearly interferes with the quality of the reflected NIRS signal.

Introduction

Near-infrared spectroscopy (NIRS) is a promising non-invasive technique for continuously monitoring tissue oxygen delivery (HbO_2 saturation).[1] The technique was simultaneously developed in several centres between 1977 and 1991.[2-4] Value has been demonstrated in several investigational settings, e.g. in the ICU[5], for continuous monitoring of the lower extremity for acute and chronic compartmental syndrome[6-12], for monitoring of local oxygen pressure in white brain matter[13,14], for measuring regional tissue oxygenation in hemorrhagic shock[15], for training measurements in sports medicine[16,17,] and for diagnosis of abdominal compartment syndrome.[18]

NIRS uses light at wavelengths e.g. 650-1000 nm that pass readily through skin and subcutaneous tissue, but are absorbed by chromophores such as melanin, carotenoids, and haemoglobin. The combination of these chromophores determines the colour of skin.[19] Tissue oxygen saturation can be determined by the amount of light that is absorbed or reflected by haemoglobin and oxyhaemoglobin at multiple wavelengths. The near-infrared light may also be influenced by chromophores other than haemoglobin such as, myoglobin, melanin and cytochrome aa3.

When we used NIRS for detecting chronic exertional compartment syndrome in a patient with a very dark skin we observed the loss of signal, when tissue oxygen saturation (StO_2) dropped.[20] The relationship between the patient's dark skin colour and the loss of signal was obvious. Shortly after we had a similar observation in another patient with very dark pigmented skin. A PubMed search on the relationship between skin colour or melanin in human beings and NIRS resulted in no publications on this subject. Therefore, we designed a study to test NIRS system reliability in people with dark skin pigment.

Patients and Methods

Healthy volunteers with skin colour III – VI (on a I to VI scale[21]) were recruited. Skin colour IV to VI is described as black, very black and incredibly black respectively.[21]

All individuals went through a standardized protocol. Their weight and height were recorded to calculate Body Mass Index (BMI = weight/length^2 (kg/m^2)). Blood pressure was measured and the dominant leg was determined. The skin colour of the lower leg was measured using a mexameter-18 (CK-electronic, Köln, Germany), a device that determines melanin content and erythema level in a range of 0 – 999 through absorption and reflection.[22] Melanin is measured by specific wavelengths chosen to correspond to different absorption rates by

the pigments. Other wavelengths that correspond to the spectral absorption peak of haemoglobin and avoid other colour influences (e.g. bilirubin) are used for the erythema measurement.

The subjects were placed in the supine position with their dominant lower leg slightly elevated and their heel in a fixed position with a weight attached to the foot through a pulley. In this way isometric contraction of the anterior compartment muscles was accomplished. Tissue haemoglobin oxygen saturation (StO_2) was measured by applying two probes of NIRS devices (InSpectra, Hutchinson technology, USA) on the skin over the anterior compartment. The signals were registered on two laptops each connected to a tissue spectrometer. Both devices used a pre-determined calibration table that relates each possible StO_2 value (0–99% at 1% resolution) to a scaled 720 nm second derivative attenuation measurement (scaled $2D_{720}$).[23] One device used an older version of software which would not display StO_2 when a measured scaled $2D_{720}$ value was below the lowest value (zero StO_2) in the calibration table. The second device incorporated a newer software version, which allowed an extrapolated StO_2 value to be displayed when a measured scaled $2D_{720}$ value was below the calibration table zero value.

The device was also able to measure tissue haemoglobin index (THI), a measure of all haemoglobin in a specific tissue volume independent of the oxygenation status. This method requires measurement of both StO_2 and the second derivative attenuation value at 760 nm ($2D_{760}$) which specifically corresponds to deoxyhemoglobin concentration.[24] The product of $2D_{760}$ and a StO_2 specific multiplying coefficient provided the THI signal.[25]

During measurements the InSpectra device emits and simultaneously detects light at wavelengths of 680, 720, 760 and 800 nm. The amount of detected signal depends on how much light has been absorbed by chromophores, tissue light scattering properties and the distance separating the probe emission and detection optical fibres (send and receive spacing). A 25 mm reflectance probe was used for all StO_2 and THI measurements. Prior to tissue measurements the probe is placed on a polyethylene foam reference media (representative of tissue scattering without absorption) and then the device detector gain (photomultiplier tube control voltage) is adjusted to obtain a detection signal that is near 80% saturation (2 million counts). The sample signal is limited to a 2.5 optical density (OD) change relative to the polyethylene foam reference media (OD = - log [sample intensity/reference intensity]). Once the sample signal drops below 5000 counts (OD > 2.5) a low signal condition is indicated by no display of StO_2 or THI signals ("- -" where StO_2 digits are normally displayed).

A blood pressure cuff was applied to the upper dominant leg and inflated when StO_2 values stabilised. Cuff-pressure was gradually increased from 50% of patients' systolic blood pressure, through 100% up to 150%. Each experiment ended when the StO_2 reached zero % or when the monitor ceased to give a reading.
For statistical analysis the Wilcoxon signed ranks was used with SPSS 12.0 for Windows. Differences were accepted as statistically significant with $p < 0.05$.

Results

Seventeen healthy volunteers with dark skin pigmentation participated in the study. Table 1 shows their characteristics. In six cases only the new software-version was used and in eleven both the old and new software were used simultaneously, so that 28 logs from 17 volunteers were available for analysis. The NIRS signal loss occurred in nine individuals, totalling 14 logs: three on

Table 1
Volunteer Characteristics

sex	Melanin	Erythema	BMI kg/m2	NIRS Signal Loss old software	new software
F	301	281	21.6	--	no
M	364	341	25.2	0%	0%
M	412	339	24.0	--	no
M	427	312	20.8	0%	no
F	444	293	21.3	no	no
M	501	375	20.8	no	no
F	511	331	38.4	no	no
M	519	343	28.4	0%	31%
M	544	343	23.9	no	0%
M	546	341	26.3	--	36%
F	546	441	21.5	--	no
F	568	348	24.9	40%	20%
M	587	383	25.5	--	no
M	625	382	21.9	20%	80%
M	633	355	42.3	no	no
M	725	391	23.8	--	82%
M	820	371	28.4	28%	0%

Melanin and Erythema as measured with a mexameter-18 (CK-electronic, Köln, Germany);
BMI=Body-mass Index (=mass /length^2 =kg/mtr^2);
NIRS Signal loss: No: signal never disappeared;
X %: last recorded StO_2 percentage before signal loss;
-- : no measurement performed

Table 2

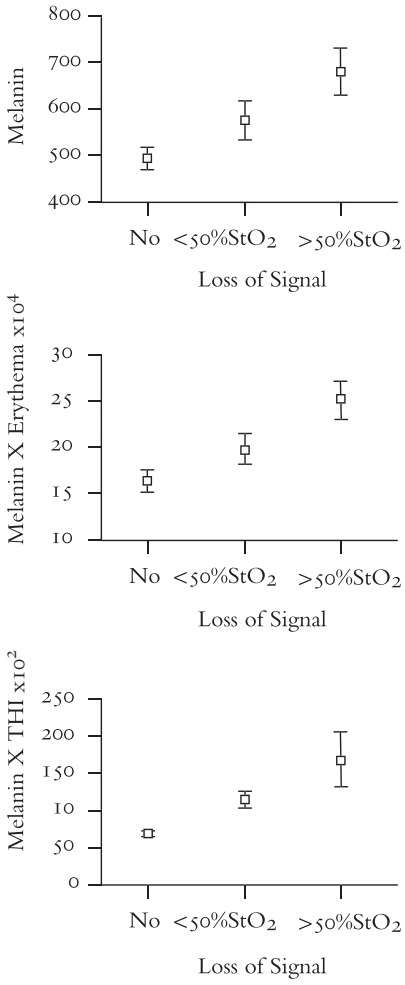
	All subjects n = 17 MEAN (SD)	Signal Loss n = 9 MEAN (SD)	No Signal Loss n = 8 MEAN (SD)	Wilcoxon signed ranks test P-VALUE (Z)
melanin level	534 (128)	571 (140)	492 (105)	0.012 * (-2.52)
erythema level	351 (38)	352 (24)	350 (51)	0.78 (-0.28)
BMI (kg/m^2)	26 (6.0)	25 (2.6)	27 (8.5)	0.62 (-0.49)

The mean level (and standard deviation (SD)) of Melanin and Erythema (as measured with a mexameter-18 (CK-electronic, Köln, Germany)) and Body-Mass Index (BMI = mass/length^2 = kg/m^2). First column represents all subjects; signal loss represents only those in whom NIRS signal loss occurred during the measurements, third column shows values of those on whom signal loss did not occur. Last column shows results of Wilcoxon test on signal loss versus no signal loss.
* Melanin level is significantly higher in those individuals in whom signal loss occurred.

the device using the newest software only, one on the device using older software only and in five individuals on both devices. In all cases the OD values were steadily increasing and the last registered value before signal disappearance was just below 2.5, meaning that the returned signal had dropped below 5000 counts.

Mean melanin levels were significantly higher in those volunteers in whom the signal disappeared ($Z = -2.51$, $p = 0.012$), while the erythema levels and BMI were not different between those with or without signal loss (table 2). Although limited statistical significance is shown in this small sample, the trend was clearly recognisable when the recorded values for melanin, erythema and Total Hemoglobin Index (THI) in individuals were plotted versus the moment of signal loss (graph 1-3). For this the recorded patient data files were arbitrarily divided into three groups: a group without loss of StO_2 signal (No signal loss: n=14); a group with loss of StO_2 signal only after StO_2 had dropped below 50 % (<50 % StO_2 n=12); and a group with signal loss before StO_2 dropped under 50% (>50 % StO_2 n=2). The relationship between signal loss and a high melanin concentration is obvious from these graphics (graph 1). This becomes even more distinct when the products of melanin and erythema (graph 2) or melanin and THI (graph 3) are plotted against the moment of signal loss.

Graph 1 – 3



melanin (graph 1), melanin x erythema (graph 2) and melanin x THI (=tissue haemoglobin index) (graph 3) are plotted against three groups: No (loss of signal); Loss of signal with StO_2 under 50; Loss of signal with StO_2 above 50 %. means +/- SEM (standard error of the mean) are displayed. These graphs show that early loss of signal (>50% StO_2) occurs in combination with high levels of scattering particles (values on the Y-axis), where No loss of signal is combined with much lower levels of melanin, erythema and THI.

Discussion

Quantified analysis of reflectance spectra is known to be complicated by the fact that skin has a complex multilayered non-homogeneous structure with a spatially varying absorption coefficients, mainly determined by melanin pigmentation, oxygen saturation of cutaneous blood, index of erythema, bilirubin, beta-carotene and other chromophores.[26] NIRS is a haemoglobin oxygen saturation measuring system using wavelengths of light (680 to 800 nm) to target tissue oxyhemoglobin and deoxyhemoglobin concentration.[23] It has proven its value in a wide range of fields.[5–18]

No research has been published on the effect of skin colour on the reliability of NIRS signals and on the phenomenon of signal disappearance in darkly pigmented people. Pringle et al. measured the effect of calf skull skin colour at NIRS measurements but did not find a difference between white and black skin.[13] A possible explanation might be that other studies were not designed to reach tissue saturations below normal physiological levels. The fact that the optical density (OD) exceeded 2.5 in all cases where signal disappered means that strong attenuation of the signal had occurred, resulting in a minimal return of near infrared light to the detection optical fibres. This attenuation is caused amongst others by melanin. The effect of melanin is further enforced by a high total haemoglobin or by strong erythema, because both also scatter and absorb light, therewith causing a decreased reflection. Although the disappearance of the signal is the result of a threshold (OD >2.5 (= returned signal < 5000 counts)) that has been defined by the manufacturer of this specific NIRS device, the attenuation that causes the diminished returned signal is a factor that needs serious consideration. NIRS devices without a threshold for a minimal returned signal can be dependent on relatively few counts, therefore having a higher change of an unreliable outcome.

Conclusion

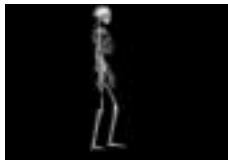
A clear relationship exists between dark skin pigmentation and attenuation of the NIRS signal, leading to signal loss. However, this study is too small to quantify this effect.

Current and future developments in the software of NIRS equipment may be able to decrease the likelihood of signal loss. Stronger light sources, higher detector sensitivity and narrower probe spacing may be used to minimize the effect of attenuation from melanin and THI (blood volume) and to prevent signal loss. In patients with a dark skin pigmentation, NIRS signals should be interpreted with caution, because melanin affects the quality of the returned near infrared light and may result in signal loss.

References

1. Mancini DM, Bolinger L, Li H, Kendrick K, Chance B, Wilson JR. Validation of near-infrared spectroscopy in humans. J Appl Physiol 1994; 77(6):2740-7.
2. Jöbsis FF. Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science 1977; 198(4323):1264-7.
3. McCormick PW, Stewart M et all. Noninvasive cerebral optical spectroscopy for monitoring cerebral oxygen delivery and hemodynamics. Crit Care Med 1991; 19:89-97.
4. McCormick PW, Stewart M, Goetting MG, Balakrishnan G. Regional cerebrovascular oxygen saturation measured by optical spectroscopy in humans. Stroke 1991; 22(5):596-602.
5. Simonson SG, Piantadosi CA. Near-infrared spectroscopy. Clinical applications. Crit Care Clin 1996; 12(4):1019-29.
6. Breit GA, Gross JH, Watenpaugh DE, Chance B, Hargens AR. Near-infrared spectroscopy for monitoring of tissue oxygenation of exercising skeletal muscle in a chronic compartment syndrome model. JBJS Am 1997; 79:838-43.
7. Mohler LR, Styf JR, Pedowitz RA, Hargens AR, Gershuni DH. Intramuscular deoxygenation during exercise in patients who have chronic anterior compartment syndrome of the leg. JBJS Am 1997; 79:844-9.
8. Garr JL, Gentilello LM, Cole PA, Mock CN, Matsen FA. Monitoring for compartmental syndrome using near-infrared spectroscopy: a non-invasive, continuous, transcutaneous monitoring technique. J Trauma 1999; 46(4):613-6.
9. Arbabi S, Brundage SI, Gentilello LM. Near-infrared spectroscopy : a potential method for continuous transcutaneous monitoring for compartmental syndrome in the critically injured patients. J Trauma 1999; 47(5):829-33.
10. Gianotti G, Cohn SM, Brown M, Varela JE, McKenney MG, Wiseberg JA. Utility of near-infrared spectroscopy in the diagnosis of lower extremity compartment syndrome. J Trauma 2000; 48(3):396-9.
11. Svendsen LB, Flink P, Wojdemann M, Riber C, Mogensen T, Secher NH. Muscle oxygen saturation during surgery in the lithotomy position. Clin Physiol 1997; 17(5):433-8.
12. Gentilello LM, Sanzone A, Wang L, Liu PY, Robinson L. Near-infrared spectroscopy versus compartment pressure for the diagnosis of lower extremity compartmental syndrome using electromyography-determined measurements of neuromuscular function. J Trauma 2001; 51(1):1-8.
13. Pringle J, Art T, Lekeux P. Near infrared spectroscopy for non-invasive assessment of intracranial haemoglobin oxygenation in an in vitro model of the calf head. Res Vet Sci 1998; 65(2):103-9.
14. Brawanski A, Faltermeier R, Rothoerl RD, Woertgen C. Comparison of near-infrared spectroscopy and tissue p(O2) time series in patients after severe head injury and aneurismal subarachnoid hemorrhage. J Cereb Blood Flow Metab 2002; 22(5):605-11.
15. Beilman GJ, Groehler KE, Lazaron V, Ortner JP. Near-infrared spectroscopy measurement of regional tissue oxyhemoglobin saturation during hemorrhagic shock. Shock 1999; 12(3):196-200.
16. Quaresima V, Lepanto R, Ferrari M. The use of near-infrared spectroscopy in sports medicine. J Sports Med Phys Fitness 2003; 43(1):1-13.
17. Boushel R, Piantadosi CA. Near-infrared spectroscopy for monitoring muscle oxygenation. Acta Physiol Scand 2000; 168(4):615-22.

18. Varela JE, Cohn SM, Gianotti GD, Dolich MO, Ramon H, Wiseberg JA, McKenney M. Near-infrared spectroscopy reflects changes in mesenteric and systemic perfusion during abdominal compartment syndrome. Surgery 2001; 129(3):363-70.
19. Bleehen SS. Disorders of skin colour. In: Champion RH, ed. Textbook of Dermatology. Oxford: Rook, Wilkinson and Ebling, 1998: 1753-5.
20. Van den Brand JG, Verleisdonk EJ, Van der Werken C. Near infrared spectroscopy in the diagnosis of chronic exertional compartment syndrome. Am J Sports Med 2004; 32:452-6.
21. Young AR. Chromophores in human skin. Phys Med Biol 1997; 42:789-802.
22. Clarys P, Alewaeters K, Lambrecht R, Barel AO. Skin color measurements: comparison between three instruments: the Chromameter, the DermaSpectrometer and the Mexameter. Skin Research and Technology 2000; 6:230-8.
23. Anderson DL, Houk GL, Lewandowski MS, Myers DE, Ortner JP. Tissue chromophore measurement system. U.S. Patent No. 5,879,294 March 1999.
24. Matcher SJ, Cooper CE. Absolute quantification of deoxyhaemoglobin concentration in tissue near infrared spectroscopy. Phys Med Biol 1994; 39:1295-12.
25. Myers DE. Total Hemoglobin Concentration Measurement. U.S. Patent No. 6,473,632 October 2002.
26. Meglinski IV, Matcher SJ. Computer simulation of the skin reflectance spectra. Computer Methods and Programs in Biomedicine 2003; 70:179-86.



The natural history of chronic exertional compartment syndrome

5

JGH van den Brand, PJCM Schure, EJMM Verleisdonk, Chr van der Werken
Submitted

Abstract

Introduction

Patients with chronic exertional compartment syndrome (CECS) suffer from pain during exercise, most commonly in the lower leg. The only rational therapy is a fasciotomy of the affected compartment. Little is known about natural history or success rate of conservative therapy of CECS. Goal of this study was to describe this natural history and determine the effect of fasciotomy in patients with long existing typical complaints.

Methods

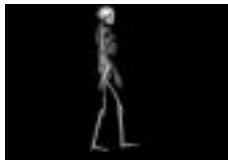
Patients with typical complaints for CECS, who underwent Intra Compartmental Pressure-measurements (ICP) in the years 1997- 1999 and did not have a fasciotomy, were studied for current complaints. Information was collected on past and present activity, tissue saturation (StO_2) during and ICP immediately after exercise were registered. A subcutaneous fasciotomy was offered to all patients with persistent typical complaints, independent of their test-results. After operation all measurements were repeated.

Results

39 patients participated. Follow-up was at least 4 years, 36 patients had persistent complaints, with which most of them had learned to cope through an adaptation of their daily behaviour. ICP after exercise had significantly increased in the entire patient group. The overall activity-level in the group had decreased
significantly. Sixteen subjects opted for surgical therapy. Postoperatively 14 patients had responded well to surgery. Pre-operative ICP was significantly lower in legs that did not respond well to fasciotomy. But even low pre-operative ICP values gave a very reasonable chance of success of fasciotomy in this group of patients. StO_2 did not proof to be of use in predicting the success of a fasciotomy.

Conclusion

CECS does not heal spontaneously and the natural history is perseverance of complaints with an increase of ICP. Many learn to live with their complaints. The reaction to fasciotomy is excellent in most cases. Measuring ICP can help to give some prediction of the chance of success of fasciotomy.



Introduction

Patients with chronic exertional compartment syndrome (CECS) suffer from recurrent episodes of pain during physical exercise in the affected limb. The lower leg is the most common site of complaints. The pain generally wears off within minutes after cessation of exercise.[1-4] Although the etiology of this syndrome is incompletely understood, it is thought that an increase of intramuscular pressure during exercise causes impairment of local perfusion and leads to local ischemia and pain in the affected muscle compartment.[1-4]

Besides a typical history and non-specific findings at physical examination, an intra-compartmental pressure measurement (ICP) immediately after exercise can be done to confirm the diagnosis. Over the last few years ICP threshold value to confirm CECS in our institution was reduced from 50 to 35 mm Hg. Even so the diagnostic reliability of the test remains limited, with a sensitivity and specificity of only 93 and 74 %.[3,5] Recently Near Infrared Spectroscopy (NIRS) has proven its value as a new tool to confirm CECS.[5] It measures haemoglobin saturation of deep tissue layers (StO_2) in a non-invasive manner, but has the same diagnostic flaws as ICP measurements, with a sensitivity and specificity of 85 and 67 %.[5,9]

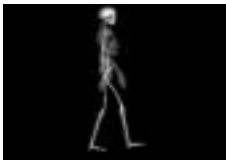
After confirmation of the diagnosis the only rational therapy is a fasciotomy of the affected compartment, creating more space for the (muscular) tissue to expand. Very little is known about the natural history of CECS or the success rate of conservative (or "wait and see") therapy, although those studies that do mention it label it as not successful.[4,6]

To find out more about this natural history of chronic exertional compartment syndrome we reviewed the patients who had been analysed 4-5 years ago and who were turned down for fasciotomy at the time, because their ICP after exercise was slightly below the threshold value of 35 mm Hg. We also looked at those who refused operation, to find out how their complaints had developed. The goal of this study is to describe the natural history of CECS and to determine the place of fasciotomy in patients with –long existing - typical complaints in the anterior compartment of the lower leg and a low ICP after exercise. Can the regular cut off points be used for this specific group or should the indications to proceed to operation be more liberal?

Patients and Methods

In this prospective study the charts of all consecutive patients with typical complaints compatible with chronic exertional compartment syndrome (CECS) of the lower leg, who underwent ICP measurements in our surgical

department at the Central Military Hospital Utrecht in the years 1997, 1998 and 1999, (the index visit) were studied. Patients were invited for follow up examination (visit A) if they had had an ICP of ≥ 20 mm Hg post exercise in the anterior compartment of at least one lower leg and did not undergo fasciotomy (for whatever reason). If pressure was under 20 mm Hg in one of the legs at the time of the index visit, this leg was not included in the analysis
Additional information was collected during an interview and physical examination. Activity scores of 1997-1999 and present activity were obtained, using a Short Questionnaire to Assess Health enhancing physical activity, or SQUASH.[7] This is a validated scale that converts the level of physical activity of an individual to a number, thus allowing intra- and inter-individual comparison. Activities during work, leisure time, household or transportation are all awarded a level of intensity and are subsequently multiplied by the number of minutes spent on it per week. Adding up all items leads to the SQUASH score. This score can vary enormously: a person with a very low habitual activity level (white collar job, evenings on the couch, no sports) could well stay under 1000 points, while someone very active (hard labour at daytime, sports in the evening) can score up to 30.000 points or even more.
Patients marched on a treadmill during 10 minutes with a speed of 6 km/h and an incline of 5 degrees. Before, during and after exercise the StO_2 values in the anterior compartment of each leg were collected by Near Infrared Spectroscopy (NIRS) using two InSpectra™ tissue spectrometers (Hutchinson Technology Inc., Hutchinson, Minnesota, USA). Two 25 mm probes were fixed to the skin approximately 10 cm distal to the tibial tuberosity and 2 cm lateral of the tibial crest of each leg, so that they were over the muscles of the anterior compartment. Data were collected continuously every 3,5 seconds. The StO_2 monitors each were linked to a laptop computer, recording the data. For analytic purposes we calculated the percent change in StO_2 ($PCStO_2$) between baseline and peak exercise: a difference of more than 35% indicates a strong decrease in tissue saturation during exercise and is highly predictive of CECS, as was shown in previous studies.[5,9]
Immediately after exercise the ICP was measured in the anterior compartment of the affected leg(s) with the patient in supine position. ICP was measured using a side-ported needle fixed to a pressure monitor (Quick Pressure Monitor System, Stryker Instruments, Kalamazoo, Michigan, USA). The needle was inserted in the centre of the anterior compartment at an angle of 45°. Surgical treatment was offered to all the patients who had had persistent typical complaints over the previous years, independent of the outcome of their test results. Those patients who agreed, proceeded to a subcutaneous fasciotomy of



the anterior compartment with a special fasciotome.[2,8] Six weeks after operation these patients came in for follow up evaluation (visit B). The treadmill exercise - with NIRS data registration and ICP measurements immediately afterwards - was repeated at this time.
The effect of the performed fasciotomy was assessed and initial ICP values (index visit) were compared with those of visits A and B. NIRS data were analysed for diagnostic reliability in this patient group. For statistical analysis SPSS 12.0 for Windows was used. Paired data were analysed using a paired T-test, the students T-test was used for unpaired data. Differences were accepted as statistically significant when p was < 0.05.

Results

From 1997 until 1999 292 patients, who experienced recurrent episodes of pain in at least one lower leg during exercise, highly suspect for CECS, underwent ICP measurements. Sixty-one patients were found to have had an Intra Compartmental Pressure of 20 mm Hg or more, immediately after exercise in at least one leg and had not proceeded to fasciotomy after ICP measurement, so they were eligible for the current study. Of these 61 patients, 45 were turned down for surgery because their ICP was lower than the threshold

Table 1

	index visit	**visit A**			**visit B**
		all patients	did not proceed to fasciotomy	proceeded to fasciotomy	
	n=39 (70 legs) MEAN (±SD)	n=39 (70 legs) MEAN (±SD)	n=23 (41 legs) MEAN (±SD)	n=16 (29 legs) MEAN (±SD)	n=16 (29 legs) MEAN (±SD)
ICP	33 (±14)	37[1] ★ (±15)	35[2] (±16)	40[o] (±15)	26[¶] (±8)
$PCStO_2$	--	47 (±26)	45 (±15)	49[o] (±26)	32[¶] (±18)
Squash	10055 (±4995)	8292 ★ (±3203)	8408 (±3186)	8124[o] (±3324)	-

1 n = 68 legs ; 2 n = 39 legs (1 patient refused ICP measurements at visit A) ;
★: Significantly different when compared to index visit (paired T-test p<0,05); o: No statistical differences compared to the subjects that did not proceed to fasciotomy (Students T test); ¶ Significantly different from pre-operative values. (paired T-test p<0,05)

Mean values found for ICP (intracompartmental pressure), $PCStO_2$ (percent change in StO_2), and SQUASH (Short Questionnaire to Assess Health enhancing physical activity) at the different visits. At visit A results are shown for the entire group and separately for those who refused surgery and those who chose to proceed to fasciotomy. No real differences can be found between these groups. The post operative tests (visit B), measured 6 weeks after fasciotomy show values that have returned to normal.

Table 2

		ICP at visit A Mean FU 59 months (+ 7,8)					
ICP at index visit	n (=legs)	< 20 mm Hg	20-24 mm Hg	25-29 mm Hg	30-34 mm Hg	≥ 35 mm Hg	Median ICP (mm Hg)
20-24 (mm Hg)	22	2 ⋆	4	4	4	6	28.5 (13-63)
25-29 (mm Hg)	14	1 ⋆	3 ⋆	2	6	2	31 (19-67)
30-34 (mm Hg)	18		2 ⋆	4 ⋆	2	10	36 (20-72)
≥ 35 (mm Hg)	16		3 ⋆	1 ⋆	2 ⋆	10	41 (20-83)
Total	70	3	12	11	14	28	32 (13-83)

Course of ICP (intracompartmental pressure) over the period from the index visit to visit A. Numbers in the table represent the number of legs with an ICP result in that category. The mean ICP had increased in each separate group during the follow up period of almost 5 years. ICP after exercise was lower at visit A than it had been at the index visit in 18 legs (marked ⋆ in table), it had increased in 40 legs.
(One patient (index visit 20-24 mm Hg) refused ICP measurements at visit A)

value of 35 mm Hg being used at that time. Sixteen patients did have an ICP higher than the cut off point, but refused an operation for various personal reasons. Eventually 39 patients participated. They had a median age of 28 years (range: 23-51) at visit A and 11 of them were female. Twenty-two subjects did not take part in this study, because they were unwilling to co-operate (11), could not be traced (6), or because they already had a fasciotomy performed (5). The 11 individuals, who didn't want to cooperate, were all interviewed by telephone, revealing that complaints had resolved spontaneously in only four of them.

According to their charts all 39 participants had had both a history and an examination typical for CECS at the index visit. One patient suffered from exertional pain in one leg and seven had an ICP in one leg that was lower than 20 mm Hg, so 70 limbs were available for analysis. Mean ICP was 33 mm Hg (± 14) and the mean SQUASH score was 10055 (table 1). Thirty-five subjects were enlisted in the Dutch army at that time.

Visit A: The follow-up period was at least 4 years (mean FU 59 months ± 7,8). Only three patients had spontaneously become symptom free in the meantime. The remaining patients had persistent complaints, with which most of them had learned to cope through an adaptation of their daily behaviour. Twenty patients could easily accept their current lifestyle with restricted activities. Sixteen subjects considered themselves impeded by their complaints and opted for surgical therapy. Eleven of these 16 were still in the army, compared to only nine in the group of 23 patients who refused surgery. In the period from the index visit until visit A, the mean ICP after exercise in the anterior com-

Table 3

	visit A (pre fasciotomy)		visit B (post fasciotomy)	
	non-responders n=2 (4 legs) MEAN (±SD)	Responders n=14 (25 legs) MEAN (±SD)	non-responders n=2 (4 legs) MEAN (±SD)	Responders n=14 (25 legs) MEAN (±SD)
ICP	26# (±4,8)	43# (±15,5)	21° (±6,4)	27° (±8,5)
PCStO2	42%° (±16,9)	50%° (±31,1)	30%° (±9,7)	32%° (±19,7)

#: Significantly different values. (p<0,05);
o: No statistical difference between non-responders and responders (Students T test)

Mean ICP (intracompartmental pressure) and PCStO$_2$ (percent change in StO$_2$) for those subjects who proceeded to fasciotomy. Pre and post-operative results are shown, separated into those who did and those who did not respond to fasciotomy. Non-responders are those subjects that were not relieved of complaints after fasciotomy. Note that non-responders had a significantly lower ICP pre-operatively. PCStO2 didn't differ between groups. A pre-operative high ICP immediately post-exercise seems to be the best predictor of success in this group of patients.

partment had significantly increased in the entire patient group (paired T-test, p<0,05); from 33 mm Hg at the index visit, to a mean of 37 mm Hg (± 15,9) at visit A. (table 1 & 2). The mean PCStO$_2$ (percent change in StO$_2$) for the whole group was 47 percent (± 26). The mean SQUASH score now was 8292 (± 3203), while at the index visit it had been 10055. This indicates that the overall level of activity in the whole group had decreased significantly (paired T-test, p<0.05) (Table 1). This fall in activity level was even more clearly in those patients who refused fasciotomy (10421 (index) vs. 8408 (visit A), mean difference 2013, 95% CI −294-4320, p-value=0,08). Through the years the mean Squash scores of the 16 patients who went on to have a fasciotomy had also decreased, but their mean reduction in activity was considerably smaller (9530 (index) vs. 8124 (visit A), mean difference 1406, 95% CI −1173-3984, p-value=0,26).

Fasciotomy: Sixteen patients (with 29 symptomatic legs) chose to proceed to surgery. The others were either free of complaints(3), or had learned to cope with the pain, by avoiding provoking activity (20). No significant differences in ICP, PCStO2 or SQUASH were found between legs of persons who proceeded to fasciotomy and legs of those that didn't (table 1). (students T-test: n.s.)

Visit B: Of the 16 operated patients (29 legs), two (4 legs) had not noticed any improvement six weeks after operation. Two patients (4 legs) had experienced a marked relieve of complaints postoperatively, but weren't completely pain

free. The remaining 12 patients (21 legs) were completely free of symptoms and complaints. The mean postoperative ICP value was 26 mm Hg (± 8). This is significantly lower than it had been before operation (40 mm Hg; paired T-test, p<0,05). Mean $PCStO_2$ postoperatively was 32% (± 18) (49% pre-operative; paired T-test, p<0,005).
All four legs that did not respond well to fasciotomy had a pre-operative ICP beneath 35 mm Hg. This was significantly lower than the 25 legs with a good response (students T-test: p<0,05) (table 3). From 16 legs with an ICP under 35 mm Hg, no less than 12 responded well to surgery. All legs with a preoperative ICP of 35 mm Hg or more (n=13) were free of all pain postoperatively. This means that even with a low pre-operative ICP value (<35 mm Hg) there was a very reasonable (75%) chance of success of a fasciotomy in this specific group of patients. In other words, even when a preoperative ICP lower than 35 mm Hg was found, only one of four patients did not benefit from fasciotomy. A statistical difference in preoperative $PCStO_2$ between the legs that did or did not respond well to fasciotomy could not be found (table 3). $PCStO_2$ was higher than 35% (considered pathognomonic for CECS) in 19 legs pre-operatively, 16 of which were free of complaints after fasciotomy, but nine of the ten legs with a $PCStO_2$ value lower then 35% also improved post operatively.

Discussion

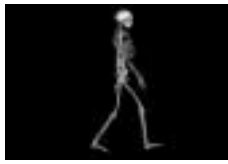
This study shows that CECS does not heal spontaneously and that the natural history is perseverance of exertional complaints with a gradual increase of ICP over the years. Many patients learn to live with their complaints by reducing their professional (mostly military) and/or recreational activities, as demonstrated by the activity scores (SQUASH). Even though complaints hadn't really changed in time in 90% of our study population, 60% refused to proceed to a simple and potentially curative fasciotomy. The group that didn't opt for surgery had had a bigger reduction in their activities over the years. Of course one has to bear in mind that we examined a selected group of patients, all with long lasting complaints, while a quarter of those who were eligible for inclusion in the study did not participate.
Still, patients with chronical complaints, characteristic for CECS will often benefit from a fasciotomy, even with ICP's below 35 mm Hg directly after exercise or with a $PCStO_2$ that is below 35%. In our series moderately elevated ICP's certainly reduced the success chance of surgery, with a 25% failure rate when pressure was below 35 mm Hg. The results of NIRS measurements showed no correlation with the post-operative results, therewith showing that

the measurement of $PCStO_2$ is of no value in predicting the outcome of fasciotomy in this particular group of patients. The explanation of the poor performance of both tests might well be in the combination of their relatively low sensitivity and specificity and in the selection of the patient group that was studied. Since most of these patients had typical complaints and "normal test results" at a previous occasion, they might well be statistical "outliers". This could explain why so many benefit from a fasciotomy, despite relatively "normal" test results.

Probably, the most important reason for measuring ICP in patients with a long-standing and "classic" history of exertional lower leg pain that is typical for CECS, is to give the patient at least some prediction of the chance of success of fasciotomy.

References

1. Matsen F A, Winquist R A, Krugmire R B. Diagnosis and management of compartment syndromes. Journal of bone and joint surgery. March 1980; vol 62-a: no. 2: 286-291.
2. Fronek J, Mubarak SJ, Hargens AR, Lee YF, Gershuni DH, Garfin SR, Akeson WH. Management of chronic exertional anterior compartment syndrome of the lower extremity. Clin Orthop. 1987 Jul;(220):217-27.
3. Verleisdonk EJ, van den Helder C, Hoogendoorn HA, van der Werken C. The chronic compartment syndrome of the lower leg: Results of fasciotomy. In; Hefte zu der "Unfallchirurg", Heft 267: "Das Kompartiment Syndrom" SpringerVerlag 1997; 363-367
4. Reneman R S, Wieberdink J, Strackee J. Chronic anterior and chronic lateral compartment syndrome of the lower leg; a frequently not recognized syndrome. Ned Tijdschr Geneeskd. 1971 Mar 27;115(13):543-51.
5. Brand, van den J G H, Verleisdonk E J M M, Werken van der Chr. Near Infrared Spectroscopy in the Diagnosis of Chronic Exertional Compartment Syndrome. The American Journal of Sports Medicine. 2004; vol 32, No. 2: 452-456.
6. Hutchinson MR, Ireland ML. Common compartment syndromes in athletes. Treatment and rehabilitation. Sports Med. 1994 Mar;17(3):200-8.
7. Wendel-Vos W, Schuit J. Short Questionnaire to Assess Health Enhancing Physical Activity. RIVM. April 2002.
8. Verleisdonk E J, van den Helder C, Hoogendoorn H A, van der Werken C. Good results of fasciotomy in chronic compartment syndome of the lower leg. Ned Tijdschr Geneeskd. 1996;140(50):2513-2517.
9. Brand, van den J G H, Nelson T, Verleisdonk E J M M, Werken van der Chr. The diagnostic value of Intra Compartmental Pressure Measurement, Magnetic Resonance Imaging and Near Infrared Spectroscopy in the Chronic Exertional Compartment Syndrome; A prospective study in 50 patients.Unpublished data/The American Journal of Sports Medicine. In press



Acute compartment syndrome after lower leg fracture

Long term results of prophylactic and therapeutic fasciotomy

6

JGH van den Brand, NL Sosef, EJMM Verleisdonk, Chr van der Werken.
European Journal of Trauma, Vol. 30, No. 3, 93-97

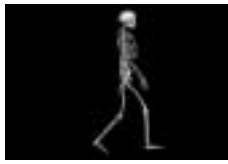
Abstract

Introduction
Fasciotomy in acute situations can be done prophylactically or as an early therapeutic decompression, the latter being performed as soon as the first symptoms of compartment syndrome (CS) are present.

Patients and methods
Results of fasciotomy after lower leg fracture from 1992 to 2001 were reviewed with emphasis on the efficacy of treatment and morbidity of the procedure sec. Patients - divided into a prophylactic (A) and a therapeutic fasciotomy group (B) - were interviewed and examined, focusing on late sequelae of CS and of the fasciotomy sec.

results
52 patients, were followed up, after a median period of 40 months, 18 fasciotomies in group A, 34 in B. All fractures in group A were operated within 24 hours, one third of patients in B was operated later. In group A, one short-foot syndrome was found. In group B five amputations were done for ischemic muscle necrosis, two short-foot syndromes were found and five legs showed other late compelling signs of manifest CS. In the 31 legs without
sustained CS only seven had no fasciotomy related abnormalities besides a scar: reduced endurance and swelling were most frequently found. An iatrogenic superficial peroneal nerve lesion was diagnosed in seven legs.

Conclusions
Outcome after prophylactic fasciotomy seems to be superior to that after early therapeutic decompression. Though prophylactic fasciotomy is effective, its morbidity is quite high, with long-term consequences in three-quarters of patients.



Introduction

Acute compartment syndrome occurs when fluid accumulates within a muscle compartment enclosed by tight osteofascial envelopes. This results in elevated tissue pressures with reduced capillary circulation leading to ischemia and irreversible damage to muscles and nerves.[1] Early decompressive fasciotomy prevents this neuromuscular damage.[2] Ischemia tolerance of muscle tissue without irreversible damage is generally agreed to be four to six hours.[2,3] Most compartment syndromes occur in the lower leg generally after a tibial fracture.[3-5] Fasciotomies in acute situations can be divided into two groups; early prophylactic decompression and therapeutic fasciotomy, which is performed when the first symptoms of compartment syndrome are present. The generally accepted clinical signs are: Tenseness on Palpation; Disproportional Pain; Paraesthesia; Present Pulses; Decreased range of motion at the ankle joint; Pain on Passive muscle stretch.

In this study we retrospectively reviewed the results of patients after lower leg fracture with either prophylactic or early therapeutic fasciotomy with emphasis on the efficacy of early treatment and the morbidity of the fasciotomy sec.

Patients and methods

All patients with lower leg fracture who underwent fasciotomy from 1992 to 2001 were included in this study. The compartment syndrome was diagnosed by the consulting surgeon. As this is a retrospective study no strictly defined set of signs for compartment syndrome was made available or used. The consulting surgeon was free to use intracompartmental pressure measurements to confirm his diagnosis. Immediately after diagnosis fasciotomy was performed: all four compartments were opened by a perifibular approach via one lateral incision.[1,5] The skin was left open, preferred method of secondary wound closure was the vesselloop shoelace technique.[6]

Personal data were extracted from the medical records, e.g. trauma mechanism, fracture type (classified according to the A.O.) and severity of soft tissue injury.[7-9] Initial treatment, related complications and subsequent operations were scored. If a patient had a bilateral lower leg fracture and fasciotomy, they were only analyzed for the leg that had been operated first. At follow-up patients were interviewed on social functioning and satisfaction. The affected limb was examined, focusing on the possible sequelae of compartment syndrome or fasciotomy.

For analytic purposes patients were divided into two groups.

Group A, the prophylactic fasciotomy group. Patients were allocated to this

group if early decompression was performed immediately as part of the initial fracture treatment before clinical signs of a compartment syndrome were present. Group B, the therapeutic fasciotomy group, including those in whom decompression was carried out as soon as first signs of a compartment syndrome were observed by the attending medical staff.
If amputation because of ischemic muscle necrosis had been performed or a short foot syndrome was seen at follow-up patients were considered to have had a compartment syndrome that was treated too late. Other sequelae of a fasciotomy that was performed too late were defined as: equines position of the foot, sensory deficit at the foot sole or at the first web-space or discrete claw toes (without short foot syndrome). If patients had two or more of these minor signs at physical examination they were arbitrarily considered to have had compartment syndrome.

All non amputated patients were invited for long term follow up examination. They were asked to appoint a final score to their fasciotomy scar and to the "overall function" of their leg on a Visual Analogue Scale (VAS): 100 points was the optimal and 0 the worst outcome.
Finally Group C was constituted with patients from both groups A and B who had no sequelae of compartment syndrome at follow up, in other words in whom fasciotomy had been timely performed. This group was studied for possible side effects of the fasciotomy sec: lower muscle strength, an anamnestic reduction in endurance, swelling of the lower leg (≥ 10 mm increased circumference in comparison to the non-affected side, measured 15 cm. distally of the knee joint) or iatrogenic lesion of the superficial peroneal nerve.

Results

Patient-characteristics
In the period 1992-2001 64 patients had had fasciotomies to prevent or treat compartment syndrome after lower leg fracture. Four persons were treated for both legs and in those cases only the first leg to be operated was analysed. Fifty-two patients acquired their fractures in road traffic accidents.
Twenty-one fasciotomies qualified for the 'prophylactic' group (A), the other 43 cases were carried out after first signs of a compartment syndrome were present and hence were 'therapeutic' (group B). Fifty-two patients (81%) were available for follow-up after a median period of 40 months (range 8-117), 18 in group A, 34 in group B. Eight patients could not be traced or lived abroad

and four patients had died (three due to the trauma). (Diagram 1)
Groups A and B were comparable for age and gender distribution (table 1). The rate of multiply injured patients in group A was significantly lower than that in group B (7/18 vs. 25/34 p=0,019 Chi square test). Almost 60 % of all fractures were open, with the highest percentage of compound fractures and the most severe soft tissue injuries in group A (n.s. Chi square test). All fractures in group A were operated within 24 hours, in group B one third of patients was operated more than a day after their accident. Methods of fracture treatment and peri-operative complications are shown per group (table 1).

Diagram 1

Patient enrolment

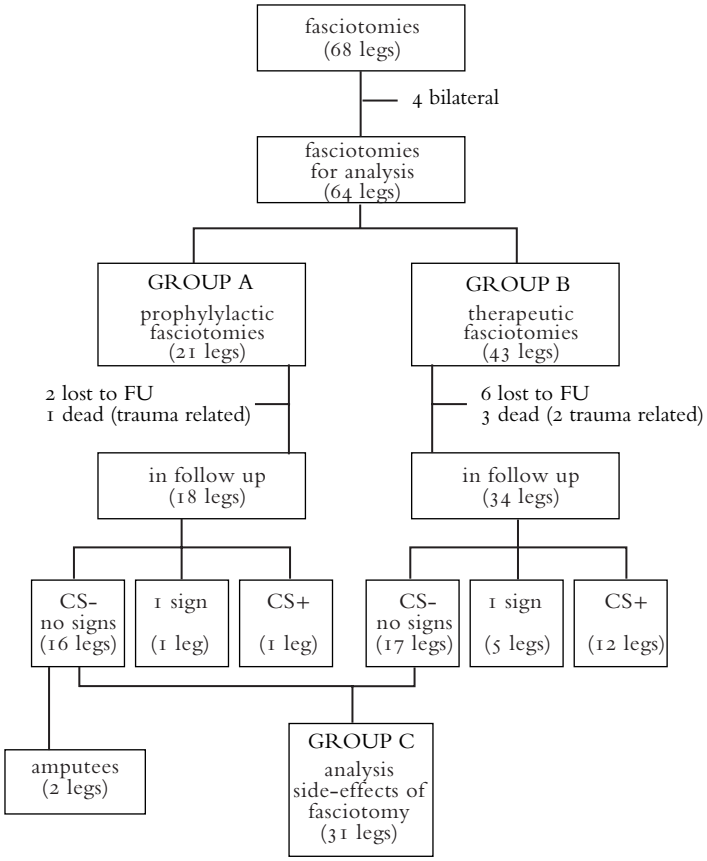


Table 1

Patient characteristics per fasciotomy-group.

Variable	GROUP A Prophylactic fasciotomy (18 legs)	GROUP B Therapeutic fasciotomy (34 legs)
Gustilo-classification		
O	6	17
I	2	8
II & III	10	9
A.O. fracture classification		
A: Simple	3	6
B: With separate fragment	5	11
C: Multifragmentary	10	13
Unknown	0	4
Fracture treatment		
Intramedullary nailing	7	18
External fixation	6	9
Plating	5	5
Plaster of Paris	-	2
Time between trauma and fasciotomy in hours		
≤ 6	10	6
> 6-≤12	6	7
> 12-≤24	2	8
> 24	0	12
Unknown	0	1
Peri-operative reported complications of fasciotomy		
Haematoma	0	1
Lesion of the supf. per. n.	0	2
Inadequate fasciotomy	0	2
Wound-infection	2	4

A.O. = Arbeitsgemeinschaft für Osteosynthesefragen.
supf per.n. = superficial peroneal nerve.

Fracture treatment

Initial fracture treatment was by intramedullary nailing in 25, by external fixation in 15 and by plating in 10 cases. Two fractures were treated non-operatively. Distribution between groups is shown in table 1.

Fasciotomy skinwound management

The vesselloop-shoelace technique was used 36 times, in 13 cases the wound was left to heal by secondary intention. Thirty-one patients required a second operation for wound closure: split-skin grafting (18) or delayed "primary" closure (13 times).

Sequelae of compartment syndrome

In group A, (the prophylactic-group) a short foot syndrome as a proof of compartment syndrome was found in one leg, one leg showed one minor sign and 16 had none (table 2). Two secondary amputations were performed for traumatic tissue damage, not because of ischemic muscle necrosis.
In group B five lower legs were amputated, all because of ischemic muscle necrosis. A short foot syndrome was found in two legs, five legs showed at least two late signs of compartment syndrome, five one and 17 legs were symptom free. This means that no less than 12 out of 34 legs in this group showed late compelling signs of manifest compartment syndrome, which means that the decompressive fasciotomy had been performed too late.

When interviewed for social consequences 11 out of 16 patients in group A experienced no complaints whatsoever. Five kept their scars covered out of embarrassment. No one experienced functional impairment. In group B 17 of

Table 2

Late sequelae of compartment syndrome per fasciotomy-group

Variable	A (18 legs)	B (34 legs)
Amputation due to comp.syndr.	0	5
Short Foot syndrome	1	2
Claw-toes (no short foot syndr)	0	6
Equines position of the foot	0	4
Sensory deficits foot sole	0	2
Sensory deficits 1st web-space	1	7
Patients with ≥ 2 late signs	0	5
Sustained compartment syndrome	**1/18**	**12/34**

Table 3

Late effects of fasciotomy sec

Variable	31 legs
reduced muscle strength	3
reduced endurance	17
swelling	12
lesion supf. peroneal nerve	7
legs with sequelae of fasciotomy sec	**24**

Two legs were still being treated for pseudoarthrosis, they could not be judged for endurance.

29 patients were symptomfree, 11 had a scar that caused serious embarrassement. In this group three patients had to give up their work or hobby because of fasciotomy related complaints, like pain or stiffness. One had to wear an orthopaedic shoe. The final score for the affected leg on a VAS was 72 in group A (median) and 50 in group B.

Side-effects of the fasciotomy sec

14 legs from group A and 17 from group B, without late signs of a sustained compartment syndrome, were combined in group C (diagram 1). Of these 31 legs only seven had no fasciotomy related abnormalities besides the scar: reduced endurance and swelling were most frequently found. At follow-up a lesion of the superficial peroneal nerve was diagnosed in seven legs. Only two of these lesions had actually been reported in the medical record as intra-operative complication. (table 3)

Discussion

Compartment syndrome is a dramatic complication and only early fasciotomy can prevent substantial consequences such as contractures, amputation or even death. Outcome of prophylactic fasciotomy (group A) appears to be better than that of therapeutic decompression (group B). However, statistical analysis of the data was not performed. Because of the retrospective character of this study confounding factors were not identified and groups were not stratified. Differences between groups seem to be too big to allow for comparison (e.g. amount of multiply injured patients). Nevertheless our long-term results seem to proof that a therapeutic fasciotomy is often too late to be of value, even if performed immediately after first symptoms have emerged. In our series only just over 50 % was free of sequelae while compelling evidence for compartment syndrome was found in about one third of the legs after therapeutic fasciotomy. The favourable results of prophylactic fasciotomy stand out even more if one takes the severity of injuries in both groups into account, with a higher percentage compound (Gustilo 2 & 3) and multi-fragmentary fractures (AO type C) in group A. It was just because of this injury severity that fasciotomies were performed earlier. A reason for delay in group B might be the fact that it holds more patients who are multiply injured, comatous or sedated, thus masking diagnostic signs. Although (continuous) pressure measurements might seem appealing in this group, we don't use or advocate routine pressure monitoring. We found that the results show a high intra-individual variation, highly dependent on the position where the needle is inserted. This has also been

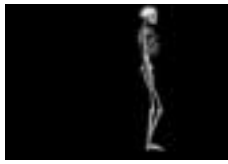
proven in a study that investigated the relation between tissue pressure and the distance to the fracture site and found major variances at an increasing distance from the fracture.[10] The consequence of this variation is that the measurement shows many false positive and false negative results, leading to either unnessecary operations or irresponsible postponement of fasciotomy.
In the light of the good results in prevention of compartment syndrome, one could be tempted to perform a prophylactic fasciotomy liberally. The fasciotomy however does not only leave a scar, in our patients it left a disabling mark in more than 75 %. Almost one of every four patients paid a price in the form of an iatrogenic lesion of the superficial peroneal nerve.
When interpreting our results one has to take in to account that we treated relatively many multiply injured patients with high energy fracture patterns. Associated traumatic lesions might distract attention from the lower limb, causing treatment delay.

Conclusion

The outcome after prophylactic fasciotomy seems to be superior to that of early therapeutic decompression. Though prophylactic fasciotomy is effective indeed, the morbidity of such an intervention in itself is quite high, with some long term consequences in three quarters of patients.

References:

1. van der Elst M, van der Werken Chr. Fasciotomy for compartment syndrome of the lower leg. Surgical Techniques in Orthopaedics and Traumatology, Paris, Editions Scientifiques et Médicales Elsevier SAS 2000; 55-610-D-10
2. Williams AB, Luchette FA, Papaconstantinou HT,Lim E, Hurst JM, Johannigman JA, Davis K Jr. The effect of early versus late fasciotomy in the management of extremity trauma. Surgery 1997 122(4):861-6
3. Mubarak SJ, Hargens AR. Acute compartment syndromes. Surg Clin North Am. 1983 63(3):539-65
4. Georgiadis GM. Tibial shaft fractures complicated by compartment syndrome: Treatment with immediate fasciotomy and locked unreamed nailing. J Trauma 1995;38(3):448-52
5. Tiwari A, Haq AI, Myint F, Hamilton G.: Acute compartment syndromes. Br J Surg. 2002 89(4):397-412
6. Berman SS, Schilling JD, McIntyre KE, Hunter GC, Bernhard VM. Shoelace technique for delayed primary closure of fasciotomies. Am J Surg 1994 167(4):435-6.
7. Müller ME, Nazarian S, Koch P. The comprehensive classification of fractures of long bones. Berlin, Springer-verslag, 1990
8. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J. Bone Joint Surg [Am]. 1976;58A:453-458
9. Gustilo RB, Mendoza RB, Williams DN.: Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984;24:742-746.
10. Heckman MM, Whitesides TE Jr, Grewe SR, Rooks MD. Compartment pressure in association with closed tibial fractures. The relationship between tissue pressure, compartment, and the distance from the site of the fracture. J Bone Joint Surg Am. 1994 Sep;76(9):1285-92



Compartment syndrome of the leg after surgery in the modified lithotomy position

7

EB Wassenaar, JGH van den Brand, Chr van der Werken,
Diseases of Colon and Rectum, in press (accepted september 2004)

Abstract

Introduction

Acute compartment syndrome is known to develop after trauma or revascularisation after ischemia. It can also occur when a patient has been lying in the lithotomy position during prolonged surgery. Methods were searched for the prevention of this iatrogenic complication after a series of 7 patients who developed compartment syndrome after surgery at our hospital.

Methods

A series of seven consecutive patients who developed compartment syndrome of the lower leg(s) after abdomino-perineal surgical procedures from 1997 - 2002 is presented and so are the lessons learned to prevent this problem.

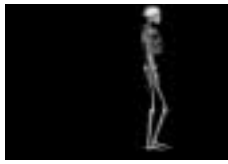
Results

When comparing our experiences with data from literature, the seven patients had the usual risk factors for development of a compartment syndrome: a lengthy procedure (over 5 hours); decreased perfusion of the lower leg due to Trendelenburg positioning combined with the lithotomy position and external compression of the lower legs (due to positioning, stirrups or anti-embolism stockings).

Measures have been taken to prevent compartment syndrome from developing after prolonged surgery in the lithotomy position. This complication has not occurred again following the introduction of these measures two years ago.

Conclusions

Acute compartment syndrome can be prevented if adequate measures are taken, but after lengthy surgery maximum alertness for emerging acute compartment syndrome remains indicated. Early diagnosis and treatment by four-compartment fasciotomy is still the only way to prevent irreversible damage.



Introduction

Acute compartment syndrome of the lower leg can have serious consequences, including renal failure, sepsis or death.[1-14] This syndrome is well known to develop after trauma or revascularisation after ischemia. Swelling inside a confined compartment enclosed by fascia and bone causes an increase in intra-compartimental tissue pressure. If this pressure exceeds capillary venular pressure, outflow impairment and oedema occur. The thin-walled venules collapse through compression and the arterio-venous pressure gradient falls, impairing microcirculation. This leads to hypoxia of muscles with local acidosis and further oedema, causing the intracompartimental pressure to rise even further. If this self propagating cycle keeps progressing, eventually arteriolar compression can occur and ischemia will lead to neuromuscular damage within several hours.[12,14]

Compartment syndrome can also occur when a patient has been lying in a non-physiological position, such as the lithotomy position, during prolonged surgery. Elevation of the legs leads to a reduction in the arteriovenous pressure gradient, making tissue more susceptible to ischaemic injury. If this position is sustained during a long period of time it can lead to the above-mentioned vicious circle.

The modified lithotomy position is used during general, orthopaedic, urologic and gynaecologic surgery. Numerous risk factors for developing compartment syndrome in the lower leg after surgery in this position are found in the literature: a decreased perfusion due to elevation of the legs above heart level as occurs in the lithotomy and Trendelenburg position[2,4-6,8,11,15-17]; intra-operative low blood pressure; chronic or acute arterial or venous insufficiency (e.g. by hyperflexia of the hip- or knee joint causing compression of iliac, femoral or popliteal vessels[5,6,8,12]); external compression of the lower legs due to bad positioning in the leg supports or leaning on the patient by a member of the operating team[6,11,15,18-20]; decreased compartmental size through anti-embolism stockings or stirrups[21]; and duration of the operation of more than 5 hours.[1-5,7-10,12,13,16] Additionally strongly developed calf muscles in young men also seem to be a risk for the development of compartment syndrome.[22]

In this article a series of seven consecutive patients is presented who developed compartment syndrome of the lower leg(s) after abdomino-perineal surgical procedures and the lessons learned from these cases.

Patients and Methods

The records of all patients who needed a fasciotomy of the lower leg in the period 1997 – 2002 for acute compartment syndrome were examined retrospectively. If the compartment syndrome had developed after surgery in the modified lithotomy position patients were included in this study. Through a literature search accepted risk factors for compartment syndrome after surgery in the lithotomy position were identified. These risk factors were then compared with those found in our patient group.

Patients and Operations

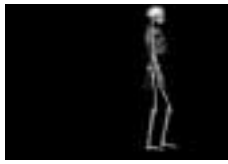
Some 200 cases with patients in the leg supports for 90 minutes or more are performed annually in the surgical and gynaecological department of our institution. This amount has been reasonably stable over the past ten years. In the period 1997 – 2002 acute lower leg compartment syndrome was diagnosed nine times in seven patients, operated on in the lithotomy position. Two patients developed compartment syndrome of both lower legs, three of the right leg and two of the left leg. Duration of surgery, derived from the anaesthesia form, ranged from 5 h. 15 min. to 8 h. 30 min.; median 7 h. Patient characteristics are shown in table 1. Surgery was for benign urological, gynaecological and colorectal conditions, with exception of one man with a prostate carcinoma. Four of our patients were young men (median age 30.5 yr., range 23 39 yr.) with a median Body Mass Index of 26.4, range 22.1 – 31.4 kg/m^2. Two were

Table 1

Sex	Age (yrs)	BMI (kg/m^2)	Diagnosis	Procedure	Operating time	lowest MAP (mmHg)	Blood loss (cc)
M	34	24.2	FAP	IPAA	7 hours	57	1400
F	30	21.9	Mayer Rokitansky	neovaginal plasty	6 hours 30 min	55	1000
F	41	27.6	FAP	INRA	5 hours 15 min	64	1100
M	39	31.4	ulcerative colitis	INRA	8 hours 30 min	?	4000
M	23	22.1	ulcerative colitis	INRA	8 hours	60	1400
M	27	28.6	urethra stricture	urethraplasty	5 hours 30 min	71	1000
M	65	21.1	prostate carcinoma	lap. radical prostatectomy	7 hours	65	50

Legend

Table 1: Patient characteristics.
BMI: body mass index
FAP: familial adenomatous polyposis
IPAA: Proctocolectomy and ileal pouch anal anastomosis
INRA: ileo-neorectal anastomosis[23]
MAP: mean arterial pressure



women (age 30 and 41 yr., BMI 21.9 and 27.6 kg/m^2). One patient (M, 65 yr., 21.1 kg/m^2) had peripheral arterial disease. All patients were in the lithotomy position throughout their operation. No specific measures were taken at this time to prevent compartment syndrome. Although hypotension was prevented diligently, Mean Arterial Pressure (MAP) dipped under 65 mmHg for a median of 22.5 minutes (0 – 120 minutes) in four patients. Median blood loss was 1100 cc (50 – 4000 cc). No vasoconstrictor drugs were used during any of the operations. Most patients were in the Trendelenburg position during some part of the operation for better access to the inner pelvis. Five patients wore elastic stockings during operation for thromboembolism prophylaxis. Three patients had post-operative epidural analgesia as well as intravenous morphine.

Symptoms

In six patients the main symptom was pain in the lower leg. Other common symptoms were tense calves, loss of foot sensation (especially in the first web space) and muscle weakness.

In all seven patients the diagnosis was made on clinical grounds. Compartment pressures were measured for confirmation of the diagnosis in four patients using a a pressure monitor (Quick Pressure Monitor System, Stryker Instruments, Kalamazoo, Michigan, USA) fitted with a side ported needle (65 to 84 mmHg; normal <35-40).

Treatment

Time from the end of operation untill diagnosis differed considerably: range 2 – 45 hours (median 10 hours). In one case (M, 27 yr., BMI 28.6 kg/m^2, no epidural analgesia) it took the attending urologist almost two days to diagnose the pain in this patients leg as caused by a compartment syndrome. Post-operative epidural analgesia did not result in extra delay. The median time to diagnosis was 10 hours (2 – 22 hrs) in the three patients with epidural analgesia versus 13.5 hours (4 – 45 hrs) in the four patients without epidural.

All patients were treated immediately after diagnosis of the compartment syndrome with four-compartment fasciotomy of the lower leg. Obvious bulging of muscle after decompression was encountered in all legs. No muscle ischemia was found. A vessel loop shoelace system was applied at the final stage of the operation in all patients: An elastic cord was weaved through skin staples positioned on both sides of the incision. By tightening the vessel loops every other day, starting on the fifth day post-operatively, secondary wound closure was obtained in all patients.

In four patients both creatinine kinase (CK) and myoglobin in serum were

raised (15424 – 78471 u/litre; normal 15 -180 and 1360 – 11100 ug/litre; normal < 80 respectively). Elevated CK blood levels neccesitated treatment with sodium carbonate infusion, volume resuscitation and induced diuresis, preventing the development of renal failure in all four patients.

Follow up

All patients were interviewed 1 – 4 years after surgery. Only one patient (M, 28 yr.) experienced no late consequences of the sustained compartment syndrome, complaining only of the scars that remained. He had no restrictions in daily activities or work. Four patients had to change jobs because of lower leg problems. They suffered mainly of pain in the legs, obstructing their professional activities, especially standing or walking. One patient (M, 65 yr., peripheral arterial disease, loss of sensation over dorsum of the foot) complained of loss of normal sensation, his feet feeling cold continuously. Oedema occurs when his foot is hanging down, it subsides when he is walking or after raising the foot.

Discussion

Compartment syndrome can lead to serious complications and life-threatening situations (rhabdomyolysis, kidney failure, and sepsis). It's a continuing cycle that starts with tissue damage, leading to oedema and venous-outflow obstruction, in a confined anatomical space, which leads to an increase in the intra-compartmental pressure. This results in a low arteriovenous gradient with a reduction in perfusion, ischemia and irreversible tissue damage.

Compartment syndrome after surgery has been reported before. Leff and Shapiro1 were the first to describe a 38 year old man with bilateral compartment syndrome after a 6.5 hour urological operation in the lithotomy position. Since then, compartment syndrome after prolonged orthopaedic, gynaecologic, urologic and surgical procedures in the modified lithotomy position has been described in an array of case reports.[2-5,7-10,12,13] One patient (35 yrs, proctocolectomy) from our current study has been described in a case report (in Dutch) before.[12] That article and the follow up of this particular patient have been the matrix on which the current study has expanded.

When comparing our experiences with data from the literature, our seven patients had all the regular risk factors for development of a compartment syndrome: a lengthy procedure (over 5 hours), decreased perfusion of the lower leg due to Trendelenburg positioning combined with the lithotomy position and external compression of the lower legs (due to positioning, stirrups or anti-embolism stockings).

In spite of all these well known risk factors, no real measures were taken to prevent the development of an acute compartment syndrome in these patients. After the first cases measures were initiated to try to prevent the development of compartment syndrome.
Our new leg supports (YelloFins, Allen Medical Systems, Acton, Massachusets, USA) can be operated through the surgical drapings, so the legs can be lowered during the major part of the surgery and raised only when strictly necessary. The leg supports do not compress the calves and are padded with gel pads. If these adjustable stirrups are not available there is a very feasible alternative: The legs can be taken out of the stirrups and extended when the indication for modified lithotomy position is no longer in effect, which is typically after the anastomosis, before placing of drains, closing and / or ostomy construction. (If the foot of the operating table is raised or re-attached the legs can be taken out of the supports and placed in a horizontal position at this time.) Extra care is taken during positioning and during surgery so as not to compress any tissue or artery. Intermittent external compression can be used as an alternative for anti-embolism stockings, to cause a decrease in compartment pressure.[20]
No new manifestation of acute compartment syndrome after surgery in leg supports has been encountered since these preventive measures were initiated more than two years ago.
However, even with maximum preventive measures and alertness there is a possibility of an emerging acute compartment syndrome after lengthy surgery. Early diagnosis and treatment by four-compartment fasciotomy are still the only way to prevent irreversible damage.

References

1. Leff RG, Shapiro SR. Lower extremity complications of the lithotomy position: prevention and management. J Urol. 1979;122:138-9.
2. Reddy PK, Kaye KW. Deep posterior compartmental syndrome: a serious complication of the lithotomy position. J Urol. 1984;132:144-5.
3. Dugdale TW, Schutzer SF, Deafenbaugh MK, Bartosh RA. Compartment syndrome complicating use of the hemi-lithotomy position during femoral nailing. J Bone Joint Surg Am. 1989;71:1556-7.
4. Adler LM, Loughlin JS, Morin CJ, Haning Jr RV. Bilateral compartment syndrome after a long gynecologic operation in the lithotomy position. Am J Obstet Gynecol. 1990;162:1271-2.
5. Bergqvist D, Bohe M, Ekelund G et al. Compartment syndrome after prolonged surgery with leg supports. Int J Colorect Dis. 1990;5:1-5.
6. Martin JT. Compartment syndromes: concepts and perspectives for the anesthesiologist. Anesth Analg. 1992;75:275-83.
7. Moses TA, Kreder KJ, Branley Thrasher J. Compartment syndrome: an unusual complication of the lithotomy position. Urology 1994;43:746-7.
8. Goldsmith AL, McCallum MID. Compartment syndrome as a complication of the prolonged use of the Lloyd-Davies position. Anaesthesia. 1996;51:1048-52.
9. Tuckey J. Bilateral compartment syndrome complicating prolonged lithotomy position. Br J Anaesthesia. 1996;77:546-9.
10. Scott JR, Daneker G, Lumsden AB. Prevention of compartment syndrome associated with dorsal lithotomy position. Am Surg. 1997;63:801-6.
11. Svendsen LB, Flink P, Wojdemann M et al. Muscle oxygen saturation during surgery in the lithotomy position. Clinical Physiology. 1997;17:433-8.
12. Ho GH, Laarhoven van CJHM, Ottow RT. Compartimentsyndroom van beide onderbenen na langdurige chirurgie in steensnedenligging. Ned Tijdschr Geneeskd. 1998;142:1210-2.
13. Mathews PV, Perry JJ, Murray PC. Compartment syndrome of the well leg as a result of the hemilithotomy position: a report of two cases and review of literature. J Orthop Trauma 2001;15:580-3.
14. Tiwari A, Haq AI, Myint F, Hamilton G. Acute compartment syndromes. Br J Surg. 2002;89:397-412.
15. Halliwill JR, Hewitt SA, Joyner MJ, Warner MA. Effect of various lithotomy positions on lower-extremity blood pressure. Anesthesiology. 1998;89:1373-6.
16. Peters P, Baker SR, Leopold PW et al. Compartment syndrome following prolonged pelvic surgery. Br J Surg. 1994;81:1128-31.
17. Turnbull D, Farid A, Hutchinson S et al. Calf compartment pressures in the Lloyd-Davies position: a cause for concern? Anaesthesia. 2002;57:905-8.
18. Chase J, Harford F, Pinzur MS, Zussman M. Intraoperative lower extremity compartment pressures in lithotomy-positioned patients. Dis Colon Rectum. 2000;43:678-80.
19. Meyer RS, White KK, Smith JM et al. Intramuscular and blood pressures in legs positioned in the hemilithotomy position. J Bone Joint Surg A. 2002;84:1829-35.
20. Pfeffer SD, Halliwill JR, Warner MA. Effects of lithotomy position and external compression on lower leg muscle compartment pressure. Anesthesiology 2001;95:632-6.
21. Proctor MC, Greenfield LJ. Thromboprophylaxis in an academic medical center. Cardiovasc Surg. 2001;9:426-30.

22. McQueen MM, Gaston P, Court-Brown CM. Acute Compartment Syndrome. Who is at risk? J Bone Joint Surg Br. 2000;82:200-3.
23. Laarhoven van CJHM, Andriesse GI, Schipper MEI et al. Ileoneorectal anastomosis. Early clinical results of a restorative procedure for ulcerative colitis and familial adenomatous polyposis without formation of an iloeanal pouch. Ann Surg. 1999;6:750-8.

Summary, Discussion and Conclusions

8

Compartment syndrome of the lower leg occurs in two different presentations: the acute and the chronic (exertional) form. The pathophysiological key similarity between both forms is increased tissue pressure in one or more of the four anatomical compartments of the lower leg. Acute compartment syndrome is the most commonly known. It can occur after trauma to the leg, critical ischemia of the limb or after prolonged surgery in the (hemi-) lithotomy position. Characteristic feature is severe pain, probably due to hypocirculation with subsequent ischemia of the affected tissues. If the diagnosis is made (too) late, it can lead to limb- or even life-threatening situations, thus creating large morbidity. Therapy consists of emergency dermato-fasciotomy of all four compartments of the lower leg.
Chronic exertional compartment syndrome (CECS) can occur in any muscle group in the body, but is most often seen in the lower leg. It is provoked by exercise, like marching or running. Those who suffer from it experience recurrent pain over or in the affected compartment - almost exclusively the anterior -, after lengthy and specific exercise. After stopping this exercise the pain generally subsides quickly. Although patients can be severely limited in their activities by these complaints, its presentation is nowhere near as dramatic of that of acute compartment syndrome and diagnostic procedures and treatment can be performed in an elective setting. After diagnosis has been confirmed – usually by an intra-compartmental pressure measurement after exercise – treatment consists of a subcutaneous fasciotomy of the affected compartment.

Chapters 2 through 5 focus on chronic exertional compartment syndrome. Because intra-compartmental pressure measurements have not established themselves beyond discussion and – as an invasive technique – pose certain risks on the patient, we looked for a new diagnostic method for Chronic Exertional Compartment syndrome (CECS). Near Infrared Spectroscopy (NIRS) is a technique that uses light in wavelengths between 680 and 800 nm to quantify tissue saturation. This non-invasive technique uses the reflection of near infrared light by chromophores like haemoglobin, therewith determining the percentage of saturated haemoglobin. **Chapter 2** describes a feasibility study, to asses the ability of NIRS to distinguish between a healthy leg and a leg with CECS in 8 healthy volunteers and 10 individuals with (proven) CECS. The results show that tissue saturation (StO_2) measurements with NIRS can distinguish healthy from diseased legs and present NIRS as a non-invasive painless alternative for invasive pressure measurements.

After this a larger study was initiated to confirm the diagnostic ability of NIRS in CECS and to compare it to the other two possible diagnostic modalities, intra-compartmental pressure measurements (ICP) and magnetic resonance imaging (MRI). This study is described in **chapter 3**. Fifty consecutive patients presenting to the outpatient department who were clinically diagnosed with bilateral CECS were included, after informed consent. They all proceeded to fasciotomy, solely on the clinical diagnosis, independent of the outcome of the additional tests. Pre-operatively they were submitted to a treadmill test with an ICP measurement directly post exercise, registration of tissue saturation (StO_2) with NIRS during and after exercise and a MRI scan of the lower leg immediately before and after exertion. Thereafter a fasciotomy of the anterior compartment (which was the site of complaints in all 100 legs) was performed in a half open manner. Minimally 6 weeks after operation the ICP measurement and StO2 measurements were repeated. Freedom of complaints at this point was the gold standard for confirmation of the diagnosis CECS. This study confirmed and validated the diagnostic ability of ICP and tissue saturation measurements through NIRS for chronic exertional compartment syndrome in a larger group of patients. MRI was found to be a less reliable diagnostic test.

During the experiments that were described in chapter 3 a problem developed while registering StO_2 in a patient with a very dark skin-tone. The NIRS device ceased to give a StO_2 reading below a certain value. Because melanin is a chromophore, like haemoglobin and myoglobin, we postulated that its higher contents in the skin might compromise the NIRS technique and influence the StO_2 measurements. A study was designed to test the performance of NIRS in persons with a (very) dark skin, who were exercised, with a tourniquet around the thigh until they reached a StO_2 of zero, or until signal disappeared. Their skin-tone was registered using a Mexameter, a device that measures melanin and haemoglobin content of the skin, the two main components determining skin colour. The study design and results are given in **chapter 4**. The phenomenon was observed again in 11 out of 17 tested individuals. After evaluation of the data it was concluded that the combination of high melanin content and high tissue haemoglobin values caused increased scattering of near infrared light (meaning more signal attenuation), thus not reflecting enough signal for an adequate reading. This limitation of NIRS hasn't been described before.

The natural history of CECS was assessed in **chapter 5**. Patients who had been evaluated between 1997 and 1999 for a probable chronic exertional

compartment syndrome, but were found to have an ICP over 20 mm Hg and weren't treated with a fasciotomy were identified and invited for a follow up visit. This group consisted of those with an ICP between 20 and 35 mm Hg – not eligible for fasciotomy because of low ICP, according to our original protocol at that time – and those with an ICP over 35 mm Hg who had refused surgery for personal reasons. Their current complaints and sports activities were evaluated and ICP after a treadmill exercise and StO_2 during and after exertion were obtained. All these individuals were offered a fasciotomy, if their complaints were persistently disabling over the last years. Thirty-six of 39 patients had persistent complaints after a follow–up of at least 4 years (mean 5 years). Since the index visit, ICP values had significantly increased. Fifty percent of the patients with persisting exertional pain had by now adapted their lifestyle to avoid their complaints and they did not opt for fasciotomy. Sixteen subjects (29 legs) were operated, 12 (21 legs) were completely relieved of complaints postoperatively, two (4 legs) partially and two patients (4 legs) experienced no improvement whatsoever. The four legs that remained symptomatic after fasciotomy all had a pre-operative ICP below the threshold of 35 mm Hg. But in the 14 patients who clearly experience relief of their pain, 12 legs had a low ICP (<35 mm Hg) and 13 had an increased ICP above the threshold. NIRS measurements did not prove to be of diagnostic value in this selected group.
Patients with a long-standing history of exertional lower leg pain that clearly resembles CECS often learn to live with their complaints. If not, they should be treated with a fasciotomy. If post-exercise ICP values are not increased over 35 mm Hg, the chance of a successful operation is clearly reduced, but certainly not precluded. If the post exercise ICP value is not increased, the chance of a successful operation is somewhat reduced, but it is certainly not without prospect.

In the following chapters questions concerning acute compartment syndrome (ACS) were answered. **Chapter 6** shows the result of a retrospective study, which was designed to assess the timing of fasciotomies in relation to outcome and the morbidity of this procedure in itself. All patients with lower leg fractures who had undergone fasciotomies in a nine-year time-span were identified and analysed. They were divided in two groups: A: the prophylactic fasciotomy group, with those patients in whom fasciotomy was performed as part of the initial treatment, before clinical signs of a compartment syndrome were present. B: the therapeutic fasciotomy group, with those in whom the decompression was carried out directly after the diagnosis of compartment syndrome was

made. Patients were invited for a long term follow up examination and analysed for the presence of sequelae of compartment syndrome. Those patients in whom no sequelae of ACS were found - and therefore must have had a fasciotomy that was performed in time or purely prophylactic - were studied separately for morbity caused by the fasciotomies sec. The results show that profylactic fasciotomy is by far superior to therapeutic fasciotomy, leaving the patient with significantly less sequelae. The morbidity of the fasciotomy itself must however not be underestimated: it led to some permanent, disabling problem in three-quarters of patients.

Development of acute compartment syndrome after surgery in the (hemi-) lithotomy position is a serious iatrogenic complication. We saw seven consecutive patients with this complication in our hospital, in a relatively short period, all after undergoing lengthy operative procedures, mostly major, advanced, "new", open or laparoscopic surgical procedures. This led to the retrospective study that is described in **chapter 7**. We analysed these cases and did a literature search for risk factors, to be able to come up with guidelines for prevention. Numerous risk factors for development of ACS were identified. Duration of the operation seems to be the most important, together with the amount of time that the legs are elevated above the heart level. Others are: intra-operative low blood pressure; arterial or venous insufficiency and external compression of the leg. This analysis led to a number of preventive measures, which are now standard in our department when we embark on a lengthy operation with the patient in the leg supports. We have encountered no new cases of this complication since these measures were introduced two and a half year ago.

The questions that were formulated in the introduction are answered through the research described in the chapters of this thesis.

- **Is increased intra-compartmental pressure really the pivotal origin of Chronic Exertional Compartment Syndrome and if so, can one critical pressure threshold causing complaints be identified?**
  Although increased intra compartmental pressure plays a pivotal role in the aetiology of CECS, it remains difficult - if not impossible - to define a critical pressure threshold that can indisputably distinguish a "normal" leg from one with CECS. This supports the theory that onset of complaints is caused by more parameters than by increased pressure alone, factors like systemic blood pressure and general fitness probably play an important role as well.

- **Should we explore ischemia as a parameter for diagnosing Chronic Exertional Compartment Syndrome?**
  The results of tissue saturation measurements clearly show that Near Infrared Spectroscopy can reliably diagnose CECS. This proves that ischemia indeed plays a major role in the pathophysiology of this syndrome and can be used to confirm diagnosis.

- **Are non-invasive diagnostic tests, like MRI and NIRS, capable of replacing invasive ICP measurements for diagnosing Chronic Exertional Compartment Syndrome?**
  Although MRI can diagnose CECS, results are not good enough to make it a standard diagnostic tool. NIRS is a good, easy to use, non-invasive alternative to ICP measurements and is probably capable of replacing it.

- **What is the natural history of CECS? If left untreated, will complaints eventually subside, stabilise or worsen in time?**
  Complaints will stabilise or worsen, with a gradually increasing ICP. Most patients will adapt their lifestyle, so that they are no longer debilitated by their limitations. Those who do not adapt and are continuously hindered by exertional pain, respond very well to fasciotomy, even when "all" test results are "normal".

- **Is it acceptable to wait until the first symptoms of an imminent acute compartment syndrome are present before performing a fasciotomy or should a prophylactic fasciotomy be performed in (selected) high risk patients?**
  The catastrophic consequences of an acute compartment syndrome that is treated with delay are displayed in chapter 6. This provides strong arguments to perform a prophylactic fasciotomy liberally in patients with a high risk of ACS, although this might lead to over-treatment in a small number of cases. The fasciotomy itself can lead to certain morbidity as well. The consequence therefore is that prophylactic fasciotomy can only be recommended as a standard procedure in patients with a very high risk for development of ACS: After a high energy injury to the lower limb, with extensive soft tissue damage and a comminuted fracture, especially in combination with a coma or sedation (for ventilation). Because the results of therapeutic fasciotomy are disappointing, one will have to remain at very close guard in all those who are at (some) risk for ACS, because of the disastrous consequences of delayed diagnosis.

- **What is the morbidity of a purely prophylactic or timely performed fasciotomy for imminent acute compartment syndrome?**
  This morbidity is rather high. Three-quarters of the patients in whom a fasciotomy was performed timely, without any sign of a sustained compartment syndrome in the long term, experience some debilitating late consequence, like superficial peroneal nerve lesion or reduced endurance and muscular strength of the operated leg.

- **Can risk factors for development of iatrogenic compartment syndrome during or after surgery in the lithotomy position be identified? What preventive measures can be taken to prevent this complication?**
  The most important risk factors are duration of the operation and the time that the legs are in the stirrups (and thus above heart level). With adequate attention it should be possible to prevent this complication in most cases. Leg supports can usually be lowered during the major part of the surgery and raised only during the phase in which it is strictly necessary. The supports should not compress the calves. Special care should be taken during positioning and surgery not to compress any tissue, especially vascular structures. Intermittent external compression can be used to lower the intra-compartmental pressure.

Klinische aspecten van compartiment syndromen van het onderbeen;

Een samenvatting in het Nederlands voor niet ingewijden en leken

9

"Een compartiment syndroom is een toestand waarbij de doorbloeding en functie van de weefsels binnen een beperkte ruimte bedreigd worden door verhoogde druk binnen die ruimte. " (FA Matsen III, 1980)
Een compartiment syndroom kan overal in het lichaam voorkomen, maar het onderbeen is het vaakst aangedaan. Dit heeft te maken met de bouw, de functie en de positie van het onderbeen aan het lichaam. Mede door de kwetsbaarheid van het onderbeen loopt het een hoog risico op een verwonding tijdens ongevallen. Bij een ongeluk in het verkeer - als automobilist, als fietser of als voetganger -, maar ook bij sportongevallen, komen letsels van het onderbeen vaak voor. Een breuk van het scheenbeen (de tibia) of kneuzing van de spieren zal in zo'n geval snel leiden tot een bloeduitstorting met zwelling van weefsels.

De bouw van het onderbeen
Als we kijken naar de anatomie dan valt op dat het onderbeen in vier spier compartimenten verdeeld is, ook wel loges genoemd, die van elkaar gescheiden zijn door de twee botten van het onderbeen - de tibia en de fibula – enerzijds en stugge pees- of bindweefsel-platen, fascies genoemd anderzijds. De omgevende fascies om deze compartimenten zijn zodanig stijf dat ze bij uitzetten van de weefsels binnen het compartiment niet kunnen meegeven, waardoor er verhoogde druk ontstaat. De vier compartimenten bevatten ieder eigen spieren, bloedvaten en zenuwen, die de bewegingen en kracht, de doorbloeding en het gevoel en coördinatie van het onderbeen en de voet verzorgen. Als er een verhoogde druk ontstaat binnen de beperkte ruimte waarin ze liggen komt de doorbloeding van deze weefsels in gevaar, dit leidt tot hevige pijn en als deze toestand te lang duurt, komt zelfs de levensvatbaarheid in gevaar.
De functie van het onderbeen. Tijdens lopen, sporten maar vooral marcheren worden de spieren in het onderbeen volop gebruikt. Het intensieve gebruik van spieren kan leiden tot een volumetoename van 8 tot 20%. Als deze spieren zich in een beperkte ruimte bevinden en niet kunnen uitzetten, zal dit dus leiden tot een drukverhoging.

Acute & chronische vorm
Een compartiment syndroom (van het onderbeen) kent twee varianten, een acute en een chronische vorm. Hoewel beide door een vergelijkbaar mechanisme veroorzaakt worden - een verhoogde druk in het aangedane compartiment – zijn de presentatie en het verloop totaal verschillend.
De meest voorkomende vorm, **het acute compartiment syndroom**, wordt vooral gezien na ongevallen, waarbij drukverhoging optreedt via het hierboven omschreven mechanisme van zwelling zonder mogelijkheid tot expansie.

Deze verhoogde druk leidt tot verminderde doorbloeding van de weefsels met zeer hevige pijn als gevolg. De aangedane weefsels reageren op het zuurstofgebrek met verzuring en verdere zwelling. Zo ontstaat een vicieuze cirkel, die resulteert in de afsluiting van de (micro-) bloedtoevoer die binnen enkele (4-6) uren het onomkeerbare versterf van de spieren en zenuwen in het been tot gevolg heeft. Bij het te laat uitvoeren of uitblijven van de juiste behandeling leidt dit tot het verlies van het aangedane been of zelfs tot het overlijden van de patiënt, die wordt vergiftigd door afvalstoffen die door de avitale spieren worden afgescheiden. Een acuut compartiment syndroom kan ook ontstaan als een been langere tijd niet of zeer slecht doorbloed geweest is, zoals voorkomt bij sommige vaatpatienten en bij ingrepen aan de bekkenbodem en het laatste deel van het maag-darm kanaal (anus en rectum), hierbij liggen de benen tijdens de operatie vaak langere tijd in steunen omhoog. Ook in deze gevallen leidt het gebrek aan zuurstof in de spieren tot verzuring en dus tot zwelling, waarmee de eerder genoemde vicieuze cirkel in gang gezet kan worden. Na het opheffen van de verminderde doorbloeding – door openmaken van het bloedvat of het aanleggen van een bypass of door de benen uit de beensteunen te halen – wordt dit effect nog extra versterkt. De herstelde, nu goede doorbloeding, via inmiddels "beschadigde" (en dus) vocht doorlatende bloedvaten leidt tot lekkage van bloed en vocht, en dus tot een toename van volume en een stijging van de druk in het compartiment. De enige juiste behandeling van een acuut compartiment syndroom van het onderbeen is het direct verrichten van een '4-loge-fasciotomie'. Bij deze operatie worden de huid en de membranen / fascies om alle compartimenten via een grote snee aan de zijkant van het been volledig geopend, van de knie tot de enkel. Zo krijgt de inhoud weer ruimte en kan de druk dalen. Bij patiënten die letsels van het onderbeen hebben die zo ernstig zijn dat er een zeer grote kans is op de ontwikkeling van een compartiment syndroom wordt de 4-loge-fasciotomie ook wel preventief verricht. Als het risico vooraf als minder groot wordt geschat kan tijdens nauwkeurige observatie het beloop afgewacht worden. Op het moment dat de eerste verschijnselen van een compartiment syndroom zich openbaren wordt dan alsnog een 4-loge-fasciotomie verricht, in zo'n geval wordt deze ingreep omschreven als (vroeg) therapeutisch. Als er twijfel is over de diagnose dan kan deze eventueel bevestigd worden door een weefsel drukmeting waarbij het "verdachte" compartiment aangeprikt wordt met een speciale naald waaraan een drukmodule gekoppeld is. Deze meting gebeurt echter niet altijd, omdat eerdere onderzoekingen al aantoonden dat de meting niet altijd een betrouwbare waarde geeft, zodat er bij herhaalde metingen wisselende waarden gevonden worden.

Het chronische compartiment syndroom verloopt veel milder dan de acute vorm. Ook hier leidt zwelling van de spieren in het onderbeen (meestal tijdens sportbeoefening of marcheren) tot verhoogde druk binnen het compartiment en dus verminderde doorbloeding, resulterend in pijn. Het stoppen van de provocerende activiteiten doet de zwelling geleidelijk weer afnemen en daarmee de pijn verdwijnen. Bij herhaling van dezelfde activiteiten komen de klachten over het algemeen weer terug. Dit ziektebeeld wordt het chronisch inspanningsgebonden compartiment syndroom genoemd. Als hier op basis van het klachten patroon van de patiënt en de bevindingen bij onderzoek een verdenking op is, is het - tot nu toe -, gebruikelijk om de diagnose te bevestigen door een drukmeting. Onmiddellijk nadat de patiënt op een lopende band gelopen heeft wordt een naald ingebracht in de spieren van het onderbeen, om zo te kijken of er een verhoogde druk in het compartiment is. Is de gemeten druk sterk verhoogd dan is daarmee de diagnose bevestigd. De enige rationele behandeling van een chronisch inspanningsgebonden compartiment syndroom bestaat uit een fasciotomie: het over de gehele lengte klieven van de fascie om het aangedane compartiment – meestal het voorste – via een kleine huidincisie van 2 centimeter. Dit gebeurt in het algemeen in narcose of na een ruggenprik. Hiermee wordt ruimte gecreëerd voor de spieren, zodat deze de volgende keer dat de patiënt inspanning verricht wel kunnen uitzetten zonder in de knel te komen.

Dit proefschrift beschrijft onderzoeken naar een aantal aspecten van chronisch en acuut compartiment syndroom, met de nadruk op methoden om de diagnose te stellen en manieren om weefselbeschadiging door een weefseldrukverhoging te voorkomen.

In **hoofdstuk 2** worden de resultaten beschreven van onderzoek naar een nieuwe methode om de diagnose chronisch inspanningsgebonden compartiment syndroom te stellen. In plaats van de gebruikelijke drukmeting met een naald wordt het zuurstofgehalte in de spier (weefselsaturatie of StO_2) gemeten met een sensor die op de huid geplaatst wordt. Het hiervoor gebruikte apparaat maakt gebruik van licht met golflengtes die in de buurt liggen van die van infrarood licht, vandaar de naam Near Infrared Spectroscopy (NIRS).
Dit licht wordt weerkaatst door het haemoglobine in de rode bloedcellen en het apparaat rekent aan de hand van het terugontvangen licht uit hoe hoog de zuurstof verzadiging in het bloed is. Deze methode werd eerst getest bij 8 gezonde vrijwilligers en 10 patiënten met een (achteraf bewezen) chronisch compartiment syndroom. De vóór de operatie gemeten waarden bij patiënten

waren duidelijk (significant) verschillend van die van gezonde vrijwilligers. De controle van de patiënten na de fasciotomie leverde een extra aanwijzing voor de toepasbaarheid van deze methode. De postoperatieve weefselsaturatie waarden (en spierdrukken) waren vrijwel hetzelfde geworden als die van gezonde vrijwilligers.

Vervolgens werd de toepasbaarheid van Near Infrared Spectroscopy getest bij een grotere groep van 50 patiënten met een verdenking op een chronisch inspanningsgebonden compartiment syndroom – allen met dubbelzijdige klachten – en werden de resultaten vergeleken met die van een spierdrukmeting en een MRI scan. De resultaten van dit onderzoek worden beschreven in **hoofdstuk 3**. Het diagnostisch vermogen van NIRS – een meting middels een sensor op de huid - bleek even groot als die van een spierdrukmeting – een pijnlijke prik in de spieren van het onderbeen. Het stellen van de diagnose door een MRI scan direct na inspanning bleek minder betrouwbaar dan de andere twee methoden.

Tijdens het uitvoeren van de bovenbeschreven experimenten gaf de NIRS apparatuur geen zuurstof verzadigingswaarde weer bij een patiënt met een zeer donkere huidskleur. Dit fenomeen werd vervolgens nader onderzocht. De resultaten van de daarvoor verrichte studie worden in **hoofdstuk 4** beschreven. Tijdens de studie – bij 17 proefpersonen, allen met een (zeer) donkere huidskleur – deed hetzelfde fenomeen zich bij 11 van hen opnieuw voor. Een grote hoeveelheid pigment in de huid blijkt het "near infrared" licht extra te verstrooien, waardoor de hoeveelheid licht die wordt weerkaatst onder een - tevoren door de producent ingestelde - kritische waarde kan komen, waardoor de apparatuur geen verzadigings waarde meer berekent en dus ook niet weergeeft. Dit onderzoek toont aan dat ook deze nieuwe techniek dus zijn beperkingen kent.

Hoofdstuk 5 beschrijft een onderzoek dat gedaan werd naar het natuurlijk beloop van een chronisch inspanningsgebonden compartiment syndroom. Hiertoe werden patiënten opgeroepen die in het verleden een drukmeting van de spierloge ondergaan hadden omdat ze verdacht werden van een compartimentsyndroom, maar destijds niet geopereerd werden, omdat de druk niet hoog genoeg was volgens het destijds geldende protocol, of omdat ze zelf niet geopereerd wilden worden. Alle patiënten werden onderzocht middels een drukmeting en NIRS meting. Na gemiddeld 5 jaar bleken 36 van de 39 onderzochte patiënten nog steeds – in meerdere of mindere mate – dezelfde klachten te hebben. Van hen had de helft de levensstijl zodanig aangepast dat

de klachten zich nog maar zelden voordeden. Slechts 16 mensen kozen ervoor om alsnog een fasciotomie te ondergaan, terwijl deze ingreep aan allen aangeboden werd. Na deze operatie waren 12 patiënten (met 21 pijnlijke benen) volledig klachtenvrij, twee (met 4 benen) meldden een duidelijke verbetering van de klachten en twee patiënten (eveneens 4 benen) beschouwden de operatie als mislukt. NIRS bleek in deze zeer specifieke groep van patiënten niet goed in staat te voorspellen wie er baat bij een operatie zouden hebben. Ook weefsel drukmeting kon de succeskans van de ingreep niet nauwkeurig voorspellen, hoewel het wel duidelijk werd dat de kans op succes kleiner was bij een lage weefseldruk.
Deze studie leert dat een chronisch inspanningsgebonden compartiment syndroom niet spontaan geneest. Het natuurlijk beloop is het persisteren van de pijn tijdens inspanning. Als er langdurig typische klachten bestaan, dan hebben patiënten een zeer grote kans op een gunstig resultaat van een fasciotomie, zelfs als "alle" test uitslagen "normaal" zijn.

Het volgende deel van het proefschrift richt zich op het acute compartiment syndroom. Om een uitspraak te kunnen doen over het gunstigste tijdstip voor het verrichten van een fasciotomie werden alle patiënten die tussen 1992 en 2002 een 4-loge fasciotomie ondergingen bij een fractuur van het onderbeen geanalyseerd. De resultaten van dit onderzoek worden besproken in **hoofdstuk 6**. Aan de hand van de gegevens in de medische status werden patiënten ingedeeld in twee groepen, een profylactische (=preventieve) groep, met die patiënten bij wie de fasciotomie onderdeel was van de eerste behandeling van het onderbeensletsel, om zo een compartiment syndroom te voorkomen en een (vroeg) therapeutische groep, met diegenen die een fasciotomie ondergaan hadden nadat de eerste verschijnselen van een acuut compartiment syndroom zich geopenbaard hadden. Verder werd er gekeken naar laattijdige gevolgen van de fasciotomie sec. De patiënten werden daartoe opgeroepen voor poliklinisch onderzoek. Uit de resultaten blijkt dat de kans op ernstige gevolgen van een compartiment syndroom vele malen hoger is als een fasciotomie pas verricht wordt zodra de eerste klinische symptomen zich al geopenbaard hebben. In de (vroeg) therapeutische groep werden deze ernstige gevolgen vastgesteld bij 13 van de 36 patiënten, zo waren er in deze groep niet minder dan 5 amputaties van het onderbeen, terwijl er in de profylactische groep maar bij één van de 20 patiënten een ernstig gevolg van een compartiment syndroom gevonden werd. Een fasciotomie op zich blijkt echter ook niet zonder risico en gevolgen. Dit onderzoek toonde dat driekwart van de patiënten op lange termijn hinderlijke gevolgen overhoudt van de fasciotomie sec.

Het ontstaan van een acuut compartiment syndroom bij een patiënt die een lange operatie - gelegen met de benen omhoog in zgn. beensteunen - heeft ondergaan is een ernstige complicatie, die kan ontstaan als gevolg van een tijdelijke kritische doorbloedingsstoornis. Naar aanleiding van zeven patiënten bij wie zich in de afgelopen jaren deze complicatie voordeed en aan de hand van een literatuur onderzoek maakten wij een analyse van risicofactoren en stelden richtlijnen op ter preventie van deze complicatie. De uitkomsten worden besproken in **hoofdstuk 7**. De duur van de operatie blijkt de belangrijkste risicofactor, samen met de tijd dat de benen omhoog en dus boven hartniveau liggen. Ook lage bloeddruk en afwijkingen aan de (slag-)aderen en druk op het been van buitenaf geven een verhoogde kans op het ontstaan van een compartiment syndroom. Aan de hand van deze studie werden richtlijnen opgesteld voor de dagelijkse praktijk, ter preventie van dit probleem. Sinds de maatregelen ruim twee jaar geleden ingevoerd werden deden zich geen nieuwe gevallen meer voor.

De onderzoeken die in dit proefschrift beschreven zijn geven ieder voor zich antwoord op een aantal vragen over het chronische en het acute compartiment syndroom van het onderbeen. Meerdere hoofdstukken zijn inmiddels als wetenschappelijk artikel gepubliceerd in de medische vakliteratuur. Zowel op het gebied van het chronische als van het acute compartiment syndroom resteren echter ook nu nog vele vragen, met name op het gebied van de diagnostiek en de selectie van patiënten voor de operatieve behandeling.

Dankwoord

Curriculum Vitae

Dankwoord

Deze rubriek is gemiddeld een van de meest gelezen hoofdstukken uit ieder proefschrift en de vaste lezers weten het dus al lang: een proefschrift schrijf je nooit alleen. Ook mij past het een aantal mensen te bedanken.

Prof. Dr Chr. van der Werken, promotor, beste Chris, zoals al vele malen eerder gememoreerd zijn je tempo en energie van een ongekend niveau. Correcties liggen steevast binnen een dag weer in het postvak. Ook op klinisch gebied is je niveau ongeëvenaard en ik ben trots dat ik je mijn leermeester in de traumatologie mag noemen. Dank voor het vertrouwen en de geïnvesteerde tijd en energie, zowel in de kliniek als op wetenschappelijk gebied. Ik ben blij dat we ons over de "valse start" heen hebben kunnen zetten.

Dr E.J.M.M. Verleisdonk, co-promotor, beste Egbert, ruim 4 jaar geleden vroeg je me of ik mee wilde doen aan "een onderzoekje". Omdat jij eigenwijs genoeg bleek om de kritiek op die keuze te weerstaan hebben we ondertussen dit project kunnen afronden. Het volgende gezamenlijke project staat ondertussen al op stapel. Dank voor je introductie in de wereld van het compartimentsyndroom, maar ook voor je begeleiding in de kliniek, je collegialiteit en je vriendschap. Zullen we binnenkort een keer gaan golfen zonder Joop?

Prof. Dr I.H.M. Borel Rinkes, beste Inne, ik vind het een eer dat jouw handtekening onder mijn chirurgenbul staat, je bent niet alleen een opleider, maar ook een vriend. Vier jaar geleden vertelde je me dat je tussen je gealfabetiseerde proefschriften (?) iets miste bij de B. Hopelijk is dat bij deze opgelost.

Prof. Dr Th.J.M.V. van Vroonhoven, u stond aan de basis van mijn carrière in de Heelkunde. Altijd heb ik uw klinische kwaliteiten en niveau van patiëntenzorg als een voorbeeld beschouwd. Ik ben blij en trots dat ook uw naam onder mijn bul staat.

Prof. Dr R.M. Castelein, Prof. Dr L.P.H. Leenen, Prof.dr. E. Lindeman, Prof. Dr R.K. Marti, Prof. Dr W.L. Mosterd, leden van de leescommissie. Dank voor uw tijd en uw interesse voor mijn proefschrift.

Mijn co-auteurs: Nico Sosef, Pascale Schure en Eelco Wassenaar. Dank voor jullie hulp bij de in dit boek beschreven onderzoeken. Helaas is het jullie niet alle drie gelukt om in opleiding te komen, maar twee van de drie is toch zeker

niet slecht. Ik hoop dat we elkaar nog geregeld zullen treffen in de toekomst.
Teresa Nelson, thank you for your help with the statistical analysis of chapters 2 and 3. It was good to see how simple difficult statistics can be.
Dean Myers, thank you for explaining two typical ignorant surgeons how that machine really works.

De dames van de polikliniek chirurgie in het CMH: Ria, Sandra, Chris, maar vooral Mini, dank voor jullie steun in de afgelopen jaren. Extra poli's, 150 polikaarten binnen 3 dagen klaarleggen, honderden extra drukmetingen doen, bij jullie was niets een probleem en bovendien was het ook nog altijd gezellig, bedankt.

Romy en Mariëlle, secretaresses van de heelkundige staf, dank voor al jullie hand- en spandiensten en de gezelligheid.

Hutchinson Technology, Joop, Rini, Heleen en Eric (in volgorde van binnenkomst), dank voor het beschikbaar stellen van de apparatuur en de mentale en wetenschappelijke ondersteuning. De samenwerking was altijd prettig en de begeleiding op reis adequaat. Dit project was een mooi voorbeeld van hoe het kan en hoort tussen medici en industrie. Goede wijn behoeft overigens inderdaad geen krans.

De MRI laboranten van het UMC, met name Brendan Bakker, dank voor het werk op al die zaterdagen. Het resultaat - hoofdstuk 3 - mag er zijn.

Zonder patiënten en vrijwilligers is het onmogelijk dit soort onderzoeken te doen. Zij die meewerkten waren essentieel voor het welslagen. Daarvoor wil ik hen hartelijk danken.

Mike Liem en Frank de Beun, mijn paranimphen, dank voor het accepteren van deze niet lichte taak. Met deze Indo-Chinees-Surinaamse combine achter me weet ik me gesterkt. Ik kijk ernaar uit om weer gezamenlijk een biertje te drinken, met een slap verhaal van Frank en Mike die van zijn kruk afvalt.

Mijn ouders, aan jullie draag ik dit proefschrift op. Dank voor de geweldige gezamenlijke tijd, voor de warmte en voor jullie stimulerende opvoeding.
Meer dan jullie je kunnen realiseren staan jullie aan de basis van dit proefschrift.
Leo, ik ben trots en blij dat je erbij bent, realiseer je dat Möp altijd een beetje aanwezig is, waar Leon, Mijke en ik ook zijn.

Dan tot slot, mijn gezin: Charlotte, Puck & ?? Dank voor jullie vermogen om altijd weer afleiding te brengen tijdens de soms wel erg lange avond- en weekend-sessies achter de computer. Charlotte, na je geduld in de afgelopen jaren is er vanaf nu weer ruim voldoende tijd voor jou, Puck en wie of wat er verder volgt….

Curriculum Vitae

Han van den Brand, the author of this thesis, was born in Someren on june 13, 1968. His childhood was happy and uncomplicated and so was secondary school at the St.-Willibrord Gymnasium in Deurne, where he graduated in 1986 at the age of 17. He chose to study medicine at the University of Utrecht. He quite liked life as a student and took plenty of time for social activities. The doctoral exam was passed in 1992 and after a short waiting period the internships were commenced, with foreign electives in Guildford (England) and Kingston (Jamaica). The medical degree was obtained in July 1995.
His working life started as a resident (agnio) in the University Hospital in Utrecht (head: ThJMV van Vroonhoven). A year and a half later in 1997 he commenced his surgical training at the Groot ZiekenGasthuis in 's Hertogenbosch (head: J Wever). In 2000 he returned to his beloved Utrecht, where his final three years of surgical training took place at the University Medical Center (heads: ThJMV van Vroonhoven, IHM Borel Rinkes). The research for this thesis was started in this period, when Egbert Verleisdonk asked Han to conduct "a small study with a new device". Upon finishing his residencies at the end of 2002 he remained in Utrecht, as a fellow in traumatology (head: Chr van der Werken), for a two year period. In February and March 2004 he did an AO-fellowship traumatology in the Kantonsspital Chur, Switserland (heads: A Leutenegger and Ch Sommer). In the year 2005 he will finally spread his wings and leave Utrecht.
The author currently lives in Bilthoven with his wife Charlotte and his daughter Puck.