Pulmonary Embolism Secondary To Para-Inflammatory Thrombosis Of The Iliac Veins
M Hoffmann, S Limmer, E Schloericke, H Bruch, P Kujath

Abstract
Background: Acute inflammatory diseases are known risk factors for the development of deep vein thrombosis and consecutive venous thrombembolic disease. Virchow described a triad of changes in the blood viscosity, alterations of the vascular endothelium and changes of the laminar blood flow as causative for the manifestation of DVT. Methods: Here we present a retrospective analysis of 8 patient cases with thrombosis of the entire inferior Vena cava and pulmonary embolism originating from DVT of the internal iliac veins that were in imminite proximity to abscess formations in the ilio-psosatic muscles. Results: The abscesses seem to originate from injections into the ileo-sacral joints and spondylodiscitis. All patients were suffering from spondylarthrosis and degenerative disease of bones and cartilage. Conclusions: As a rare complication following the injection of analgetic drugs or corticosteroids into the gluteus muscles or the ileo-sacral joint devastating infections in the retroperitoneal space may occur. The initial presentation of these abscesses can be difficult to interprete. Buttock claudicatio must lead to the suspicion of abnormalities in the vascular inflow/outflow from the (internal) iliac arteries and veins.

INTRODUCTION
VTE is a feared complication of operative procedures and interventions. Moreover acute inflammatory diseases as e.g. pneumonia or sepsis are also primary order risk factors for developing thrombosis of the deep veins of the lower extremities. Proximal thrombosis of the veins superior to the cooper ligament bears a substantially higher risk of pulmonary embolism compared to peripheral thrombosis [1].

Degeneration of cartilage and bone stuctures is a common disease entity in the older population. The prevalence is on a continuous rise following the changes in demography [2].

Part of the multimodal analgesic therapy in these diseases is sometimes injections into muscles or even joints. These injections might lead to devastating infections of superficial and deep compartiments of the human body [3].

This is a retrospective analysis of the patients’ data of eight patients, that were treated in the Clinic for Surgery of the University Clinic Schleswig-Holstein Campus Luebeck, between 1994 and 2008. The aim of the analysis was to evaluate possible connections between local or systemic analgesic therapy by recurrent injections and the development of venous thrombembolic disease secondary to phlegmonous infections in the retroperitoneal space.

MATERIALS AND METHODS
A database search was done with the key-search words pulmonary embolism, vena-cava thrombosis and abscess retroperitoneal. We were able to identify eight patients that were admitted to our surgical university clinic with the simultaneous presentation of an abscess and VTE. The patients were treated in our clinic between 1994 and 2008.

THE PATIENT DATA WAS ANALYZED FOR THE FOLLOWING PARAMETERS:
age, sex, underlying immunosupression, history of degenerative disease of the lumbar spine or ileo-sacral joint, co-medications, prior antibiotic treatment, history of injections into joints or muscle, time between injection and development of symptoms, extent of pulmonary embolism (unilateral or bilateral), need for ICU management, anticoagulant drug for treatment of pulmonary embolism and cava-thrombosis.

Because of the small number of patients and the inexistence of a matched control group a statistical analysis was not done. The results of the analyses of the patients´ data are presented descriptively.

RESULTS
Our database search identified eight patients with pulmonary
embolism secondary to parainflammatory thrombosis of the iliac veins. The patient cohort comprises four male and four female patients. The median age of our patient cohort was 72.6 years.

Underlying immunosuppressive therapy was prevalent in all patients. In 3 patients a systemic immunosuppressive therapy was administered. One of these three patients received methotrexat due to rheumatoid arthritis. Two patients received systemic oral therapy with corticosteroids. All patients received local injections into the gluteal muscles or the ileo-sacral joints with corticosteroids.

Relevant co-medications were non-steroidal antirheumatic drugs (NSAR) in six patients, all of these patients were also on therapy with es-omeprazole.

Three patients were on antibiotic therapy with different penicillins.

Beside these drugs several other medications were given to the patients without relative cumulation of substance class or individual drug.

All patients had a history of degenerative disease of the lumbal spine (6 patients) and/or the ileo-sacral joint (5 patients). Two patients had a lumbar spondylodiscitis.

The average time between the last injection and the development of symptoms was two weeks with a range of one to four weeks.

The clinical presentation of the patients was inconsistent. Six patients complained about pain in the gluteal muscles that was dependent from exercise. Seven patients were suffering from fever of unknown origin and in four patients the pain in the gluteal muscles led to an almost complete immobilisation leading to the induction of medical treatment.

Very interestingly only one patient complained about shortness of breath as a leading symptom. All of the other patients of our cohort suffered from silent pulmonary embolism. None of the commonly known clinical signs of pulmonary embolism (e.g. shortness of breath, dyspnea on exercise, hemoptoe, tachycardia) were apparent in these patients.

**DISCUSSION**

Factors leading to deep vein thrombosis are known since the days of Virchow, they comprise alterations of either the velocity of blood flow, the composition of the blood or
endothelial damage [4]. Most common a DVT originates from the deep veins of the lower extremities. A lot of risk factors are known that put patients at a higher risk to develop DVT. Primary order risk factors attributable to our patient cohort were inflammatory disease, age, relative immobilization and obesity. Any inherited coagulation abnormalities were unknown before admission and weren’t detected during the hemostaseological laboratory check up.

It has to be pointed out that the study does reflect an aspect of clinical reality in treatment of degenerative diseases of the bone and cartilage. The patients are not selected in the sense that they present as emergencies admitted through the emergency admissions office without having been previously been known to our clinic.

The development of VTE is special in these patients because of the direct initiation of the thrombosis by an inflammatory process directly adjacent to the iliac veins. Parainflammatory occlusions of large veins are known from the portal vein in chronic pancreatitis [5].

The patients’ risk factors mentioned above might have perpetuated the gravity of the disease but the initial absence of a thrombosis of the external iliac vein consecutively to a DVT of the leg clearly exclude the „classic” way of thrombosis development in 6 of 8 patients.

The primary manifestation in the internal iliac vein is supported by the patients initially complaining about buttock or thigh claudicatio - a symptom known from patients with occlusive disease of the internal iliac artery. Profound venous stasis in the same region should result in a similar clinical presentation [6].

A thorough research in the international medical databases was not able to retrieve a study comparable to this retrospective analysis.

The etiology of the development of the abscess structures in the ilio-psatic muscles is subject to speculation. All patients suffered from degenerative diseases of the lumbar spine or the ileo-sacral joints. All but one patients received injections of NSAR and corticosteroids into the gluteal muscles and even more important into the ileo-sacral joints. Five patients suffered from degeneration of the ileo-sacral joints while two had spondylodiscitis. The microbiological examination of the abscess material detected exclusively gram-positive bacteria (Staphylococcus spp. and Streptococcus spp.) typical for the skin surface in 5 of 8 cases in the remaining three cases Staphylococci and Streptococci were part of a polymicrobial infection.

A triad of possible causes for the development of DVT and pulmonary embolism therefore seems highly probable:

In patients with multiple injections into the ileo-sacral joints and the detection of gram-positive bacteria in the abscesses inadequate anti-sepsis during the injection procedure seems to be most likely. Cutaneous injection abscesses are a known complication following injections that are described and evaluated in many case-reports and reviews. Abscesses of small or large joints after diagnostic or therapeutic puncture are also a known and feared complication in orthopedic surgery [7].

All studies demonstrate the need for adequate anti-sepsis. A similar case with thrombosis development nevertheless can not be found in the international literature.

In one case the abscess formation was directly adjacent to an acute sacro-ileitis of the right ileo-sacral joint. This patient received injections into the gluteal muscle but not into the joint itself. This raises suspicion for a direct activation of coagulation and consecutive thrombosis in the internal-iliac vein secondary to the inflammatory process in imminite proximity.

A similar mode of the activation of coagulation is known from acute and chronic pancreatitis. In this disease entity thrombosis of the portal or the large intestinal veins is common [5].

Development of retroperitoneal abscesses in the psoatic-muscles secondary to a spondylodiscitis in the lumbar spine. A lot of publications deal with the development and operative (+ interventional) or conservative treatment of these abscesses [8]. None of the publications evaluated the incidence of thrombosis of the iliac veins. A combination of coagulation activation and local compression might be causative.

All cases had a history of corticosteroid-injections. If the immunosuppressant effect of this drug class might have perpetuated the infection is subject to speculation. Several trials demonstrate a higher probability of abscess formation during treatment with local or systemic corticosteroids [9].

The therapy comprised of a combination of local abscess treatment and an adequate anticoagulation. Abscess treatment was accomplished by open retroperitoneal or CT-guided abscess-drainage combined with antibiotic therapy in
five cases, three patients were treated with intravenous antibiotics alone. All patients were under initial surveillance at the intensive care unit due to pulmonary embolism in all cases. Anticoagulation was obtained by administration of i.v.-Heparin, low-molecular-weight heparin and fondaparinux. All treatment options resulted in complete recanalisation of the inferior vena cava and the central pulmonary arteries. A superiority of one anticoagulant can not be derived from the accessible data.

All but one patient presented with silent pulmonary embolism although the extent of the occlusion of the pulmonary arteries was remarkable. The leading clinical sign was claudicatio of the buttocks/the thigh that was progredient after mobilization or exercises. Physicians should keep in mind that in the absence of arterial occlusions venous occlusions might have the same clinical presentation.

CONCLUSIONS
Apart from the known activation of coagulation by acute inflammatory diseases a direct induction of thrombosis by phlegmonous infections adjacent to large vessels must be kept in mind. A rare differential diagnosis of chronic pain and claudicatio of the gluteal muscles in patients without occlusive disease of the peripheral arteries is thrombosis of the internal iliac vein.

Injections into the gluteal muscles and even more into the ileo-sacral joints bear the potential risk of developing deep injection abscesses. Therefore oral analgesics should be given to the patient if possible. If injections can’t be omitted adequate antiseptic is of crucial importance.

In our view therapy of pulmonary embolism should be done with low-molecular weight heparins under initial intensive-care surveillance due to the better predictablility of the anticoagulant effect in comparison to unfracionated heparin.

References
Author Information

Martin Hoffmann, MD
Surgical Clinic, University Clinic Schleswig-Holstein Campus Luebeck

Stefan Limmer, MD
Surgical Clinic, University Clinic Schleswig-Holstein Campus Luebeck

Erik Schloericke, MD
Surgical Clinic, University Clinic Schleswig-Holstein Campus Luebeck

Hans-Peter Bruch, MD
Surgical Clinic, University Clinic Schleswig-Holstein Campus Luebeck

Peter Kujath, MD
Surgical Clinic, University Clinic Schleswig-Holstein Campus Luebeck