Dissertations

Fibrinolysis and blood loss in major arhtroplasty—the effect of tranexamic acid

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Blood loss in major arthroplasty may be abundant and often necessitates blood transfusions. These may transmit disease and entail an immunological burden to the recipient.

After trauma and surgery, the fibrinolytic system reacts with a short period of increased activity, followed by a fibroinolytic shut-down.

In this thesis we investigated the impact of the early fibroinolytic activation on blood loss in total hip (THR) and knee arthroplasty (TKA), and the effect of a fibrinolytic inhibitor, tranexamic acid (TA), on posterpartive blood loss and blood transfusions in these operations. A retrospective analysis of 179 TKA indicated that the use of TA decreased blood loss by a mean of 340 ml. The effect was confirmed in a double-blind randomised study of 86 TKA. Tranexamic acid (10 mg/kg) was given shortly before the release of tourniquet and three hours postoperatively. The blood loss (mean ± SD) in patients receiving TA was 730 ± 280 ml versus 1410 ± 480 ml in the placebo group ($p<0.001$). The number of blood tranfusions were reduced by 2/3.

In a randomised, double-blind study of 39 THR, TA was given after the cementing of the femoral component in order to avoid fibrinolytic inhibition during the pulmonary embolisation that often occurs during this procedure. The administration was repeted after three hours. There was no significant effect of TA on blood loss in THR, possibly because the drug was administered too late.

Analyses of blood specimens of the wounds and peripheral veins during the operations showed an activation of coagulation and fibrinolysis, most pronounced in the wounds. TA significantly decreased D-dimers in the wounds in TKA, but not in peripheral blood. We found no significant effect of TA on oxygen saturation, measured by pulse oxymetry.

In a separate study we investigated the pharmacokinetics of TA in THR and found that 10 mg/kg body weight i.v. resulted in therapeutic plasma concentrations during surgery,

In conclusions we have thus found a profound local activation of fibrinolysis in THA and THR. The prophylactic administration of TA significantly reduces blood loss and the need of blood transfusions in TKA. We found, however, no such effect when TA was given at the end of the operation in THR.

Radiographic assessment of cup migration and wear after hip replacement

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Methods are needed for accurate measurement of acetabular cup migration and wear after hip replacement. The EBRA (Ein Bild Röntgen Analyse) method was recently introduced as a computerized method for radiographic assessment of acetabular cup migation.

In this study, various standard methods for measuring migration were evaluated and compared to radiostereometry (RSA), which has proved to be highly accurate. A subroutine for wear measurement was developed and added to the EBRA method.

Of the standard methods, Nunn's method was the best for migration measurement and Livermore's the best for wear measurement. Measurements with EBRA were better than the standard methods.

Pelvic tilt seemed to be the main source of error in measurements. The effect of pelvic tilt was evaluated experimentally. EBRA detected and excluded tilted radiographs, the errors of measurement beeing smaller with EBRA than with standard methods.

The precision of the input procedure, repeated radiographic examination, the intra- and interobserver errors were assessed. Apart from the digital input of the data, EBRA was better than the standard methods.

Normal values concerning acetabular cup migration and wear was obtained from long-term surviving hip replacements, without radiographic signs of loosening. No method of measurement detected evidence of changes in the wear-rate and in migration over time. EBRA showed cold-flow in some cups, but did not provide additional information in the long-term.

Nunn's method of migration measurements and Livermore's method for wear are recommended in clinical practice. EBRA is more accurate and should be used for studies of new implant designs that have passed the preclinical and, preferably, radiostereometric anlaysis. RSA is unsurpassed and is recommended for early clinical follow-up in a limited number of patients.

Segmental kinematics of the lumbar spine

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Stability and mobility of the lumbar spine are governed by a complex neuromuscular system, involving passive (intervertebral disc, ligament, passive muscle, tendon, vertebra, zygopophysial joint), active (muscle), and neural (peripheral and central nervous system) structures. Interactions between these structures, under normal or degenrative conditions, are not well understood. Injury or pathology to a spinal structure disrupts the intricate balance within the system, and can lead do dysfunction and/or pain. Segmental instability in the lumbar spine is believed to be manifested as abnormal segmental kinematics. The purpose of this work was to elucidate mechanisms which alter the kinematic behavior of a lumbar motion segment and to investigate the contribution of the lumbar musculature toward spinal stability.

An in vivo technique which could dynamically quantify sagittal plane motion in a lumbar motion segment was developed and applied in experimental and clinical studies for measuring spinal kinematics during flexion-extension. Experimental models of acute segmental instability, and chronic intervertebral disc and zygapophysial joint lesions were created in vivo in porcine lumbar motion segments via surgical interventions to passive spinal structures. Segmental kinematic behavior was detrimentally altered by the acute injuries to the passive structures, i.e. greater motion and hysteresis. Stimulation of the paraspinal musculature added stability to the acutely injured motion segment. However, the musculature was overall less efficient at providing stability when the intervertebral disc or zygapophysical joint were afflicated with chronic lesions. In a porcine model, activation of neural elements in the annulus fibrosus of the intervetrebral disc and in the zygapophysial joint capsule elicited contractions in the paraspinal muscles, while stretching of zygapophysical joint sapsule inhibited the muscular response. These studies demonstrated different neural interactions between the passive and active structures, where both nociceptors and proprioceptors are known to exist. In the clinical study, chronic low back pain patients with segmental instability had significantly restricted intervertebral motion, which was insufficient to trigger, stretch reflexes which could allow flexion relaxation. In the control subjects, however, intervertebral motion reached adequate levels, such that flexion relaxation of the lumbar erector spinae muscles occurred.

Persistent muscle activation is a mechanism by which the neuromuscular system provides stabilization to guard diseased passive structures from abnormal motions which may cause pain and/or further tissue damage.

The Swedish Knee Arthroplasty study, with special reference to unicompartmental prostheses

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The Swedish Knee Arthroplasty study has prospectively followed knee arthroplasties done in Sweden since 1976. Demography, epidemiology and general knee prosthetic biofunction is given for 30,003 primary knee arthoplasties and their revisions through 1992. The annual of knee arthoplasties increased fourth fold while the relative use of Unicompartmental knee arthroplasty (UKA) decreased as Tricompartmental knee arthroplasty (TKA) increased. The 5-year Cumulative revision rate (CRR) decreased for each 5-year period studied for TKA in osteoarthrosis (OA) but for UKA no change was seen. The annual percentage of revisions has diminished from 10% to 5%. In OA, modern TKA have a lower CRR than UKA, with a 5-year CRR of 3% and 8%, respectively. Change of prosthetic design has led to new failure modes as is shown for the PCA Uni prosthesis (femoral loosening and excessive HDPE wear) and the Oxford Meniscal knee (dislocating meniscus and femoral loosening) with 5-year CRR of 16% and 10% respectively, compared to 5% for the Marmor. Two relatively unchanged prostheses, Marmor and Total Condylar, were used from 1975–1986 with continuous improvement in CRR over time. This indicates that factors other than prosthetic design affect the CRR.

In failed UKA for OA, revision with exchange using new unicompartmental components gave a 5-year Cumulative rerevision rate (CRRR) of 26% while conversion to TKA gave 7%. Also addition of components in the contralateral compartment gave.an inferior 5-year CRRR of 17%. Failed UKA should be converted to TKA. In comparison modern primary TKA had a CRR of 3%.

A cohort of 14,551 patients followed for 66,622 patient years was matched with the Swedish National Cancer Registry. The cancer incidence was not increased after knee arthroplasty.

Wear, particles and physical factors in loosening of hip prostheses

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The cellular responses to the presence of various particles (UHMwPE, HDPE, Co-Cr alloy, Ti alloy, zirconium oxide and polystyrene) in sizes less than 2 μm in vital synovial (knee joints) and bone (distal femoral intramedullar spaces) environments in rats have been evaluated. In presence of HDPE and UHMwPE only a slight thickening of the synovium was observed in the knee joints, mainly caused by fibroblast proliferation. A massive recuitment of macrophages was never observed; all types of prticles were observed; all types of particles were observed to be mainly ingested by fibroblasts. In intramedullary spaces, with use of a preformed PMMA cylinder as a reference point, no increased osteoclast activity nor evidence of bone resorption was observed with all types of particles. Only in the presence of HDPE or UHMwPE significant inhibition of bone formation was seen. It may be concluded that the presence of wear particles alone is not sufficient to initiate bone resorption in vivo.

A new experimental implant model is presented to study whether high fluid pressure can induce osteolysis at a bone implant interface. Twelve nature rabbits received a titanium implant which was allowed to osseointegrate before a fluid pressure of 150 mmHg was applied to a specific area of the titanium bone interface in 6 of the animals. In all 6 implants exposed to the fluid pressure, osteolysis occurred. In some speciments with extensive osteolysis the microscopic appearance was similar to that of prosthetic loosening: high numbers of macrophages were observed containing intracellular bone particles. In none of the 6 control animals one resorption was found. These results point at the possibility that all features of prosthetic loosening that are ascribed to particle activation can be alternatively explained by fluid pressure.

The experimental implant model previously described was used to study whether oscillating fluid pressure, applied during 2 hours per day, can lead to osteolysis at a bone implant interface. The pressure was applied during 2 hours per day for 14 days and oscillating between 70 and 150 mmHg with a frequency of 0.1 Hz. Bone resorption was not found in any of the control animals. A small localised osteolytic lesion had developed under 4 implants exposed to fluid pressure with evidence of osteocyte death in the direct surrounding cortical bone. In 4 specimens (3 with and 1 without osteolysis) bone formation was observed at the endosteal side opposite to the pressure zone. In the controls bone formation did not occur. Our results indicate that oscillating fluid pressure can lead to osteolysis, even when present only during short periods of time.

A new experimental implant model is presented to evaluate the tissue response to a compressive force with micromovements but without sliding or skewing movements. In the tibia of 12 mature rabbits a titanium implant was placed over a vital cortical bone bridge of 2x7 mm and allowed to osseointegrate. The implant contained a device to digitally apply a compressive force upon the bone with a maximum displacement of 100 μm. A cyclic compressive force yielding a pressure of approximately 30–40 MPa was applied on the bone with a frequency of 0.5 Hz during 2 minutes per day for 14 days in 6 of the rabbits. The 6 non-loaded control animals showed vital cortical bone with evidence of apposition of new bone up to the titanium implant, practically without interveining fibrous tissue. In all manipulated animals, areas of necrotic bone was observed to a depth exceeding the amplitude of the displacement. This necrotic bone was being replaced by fibrous tissue. Within this fibrous tissue, areas of cartilage were observed, especially at the locations where the highest compressive force was exerted. Remodeling processes of vital cortical bone were seen throughout the cortical bone bridge. The histological appearance of the tissue along well fixed and well functioning prosthetic components is in many aspects similar to the results of the present study. It seems therefore that the presence of fibrous tissue, fibrocartilage, areas of bone necrosis and bone remodeling may reflect only the mechanical situation and that e.g. wear debris is unnecessary for this tissue response to develop.

Radiographic measurements of the polyethylene socket were performed of 34 hip prostheses with an 32 Al_2O_3-ceramic head with rotating bearing and 37 prostheses with a taper "fixed" ceramic head. There was a mean follow up of twelve years in both groups. The mean annual linear wear of the polyethylene was 0.034 and 0.069 mm (Mann-Whitney U-test: $p < 0.0001$), respectively, in the "rotation" and the "fixed" group. We concluded that use of a rotating bearing leads to a significant reduction of socket wear as compared to fixed taper junctions.

The results of a retrival study of a rotating joint between the head and neck in 13 Weber Rotation modular total hip prostheses are presented after 11 years (range 9.5 to 17 years) of use. This rotating "secondary" head-neck joint was designed to reduce friction and wear of the "primary" head-socket joint. At revisionary surgery rotating and telescoping movements could be visualised. Of 13 explanted stems wear of the cylindrical trunnion of this metal on metal "secondary" joint was measured and wear of both components together was calculated to be a few microns (mean 2.4 ìm; SD 1.4) per year. Macroscopic and microscopic (light microscopy and EM) metallosis of the pseudocapsule was not observed, suggesting a low production of metal wear debris.

A preliminary survivalship analysis is presented of the Weber Rotation THR with a mean follow up of 9.2 years. After 20 years a total of 30 hips had been revisioned: 24 because of aseptic loosening, 5 because of infection and 1 because of a femoral fracture. Survivorship analysis with revision as endpoint for a total of 297 hips showed 93% and 78% survival after 10 and 15 years, respectively. For the socket alone the survival after 10 and 15 years was 99% and 89%, respectively, and for the stem 94% and 81%, respectively. Survival at 15 years with radiological evidence of loosening as endpoint, was 85% for the socket and 72% for the stem. Compared to the Charnley THR; "the gold standard", the results of the Weber Roation THR are approximately equal at 10 years but not as good at 15 years. Clearly, the decline of survival of the stem was responsible for the decline in survival of the Weber Rotaion THR after 10 years.

Renal dysfunction in orthopaedic surgery—with special reference to drug effects in the elderly

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Total hip replacement (THR) is a common procedure, generally performed in elderly persons. Previous studies indicated that the use of isoxazolyl pencillins could induce a transient post-operative renal dysfunction in these patients.

By measuring urinary levels of markers for glomerular (albumin, IgG) and tubular (protein HC) function we studied the influence of systemic cloxacillin, the gentamicin in bone cement and the bone cement itself on renal function following THR or total knee replacement (TKR). We studied peroperative pharmacokinetics of cloxacillin in THR and TKR patients. In healthy elderly we studied the influence of diclofenac on cloxacillin pharmacokinetics, and also investigated exercise-induced proteinuria, and the possible effect of prostacyclin on it.

Patients underdoing THR or TKR developed a transient increase in glomerular and tubular markers. This was not primarily caused by cloxacillin, gentamicin or bone cement. THR patients had lower creatinine, and lower clearance for cloxacillin than TKR patients, and lower than healthy elderly. Diclofenac did not alter the pharmacokinetics for cloxacillin in healthy, unstressed, elderly. Exercise induced a transient glomerular and proximal, but not distal tubular impairment in the volunteers. The exercise-induced proteinuria was not altered by prostacyclin.

Present surgical and anesthetic techniques have partly overcome the risk for developing postoperative renal failure, but THR patients probably still are at an increased risk. Proteinuria following surgery or exercise is suggested to share, in part, common pathways.

Articular distension in arthroscopy—an experimental study on intra- and extraarticular effects of pressure

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The purpose of this thesis was to analyse the effects of various intra-articular pressures (IAP) on soft tissues and to provide guidelines for the choice of safe infusion pressures during arthroscopy.

Ten tensile properties of the knee-joint capsule were recorded from stress-strain-relaxation tests whitin 170 mmHg IAP. During stepwise infusion, there was a linear increase in stiffness without signs of plastic deformation. The mean volume increase after 15 min of stress-relaxation was 7.4%, which was attributed to capsular adaptation. Extra-articular fluid loss had little significance for the pressure fall during stress-relaxation. Short-term pressures below 170 mmHg can be used during knee arthroscopy without harming the joint capsule.

The IAP in three different knee joint compartments was recorded during arthroscopy at 75 mmHg or 100 mmHg resting IAP. During a standardised ROM between 45–0–90–45° with and without external rotation of the lower leg, there were pressure peaks at 350 mmHg in flexion and extension in the 100 mmHg group. In all joints there was a pressure equilibrium between the anteromedial, posteromedial and suprapatellar compartments. Intra-articular flow obstruction during arthroscopy is not a risk factor for the development of the capsular rupture.

Using the duplex ultrasound technique, the flow velocity and cross sectional area of the great saphenous vein and one of the posterior tibial veins of the lower leg were recorded during knee arthroscopy at 0, 100 and 180 mmHg IAP. At all pressure levels, recordinugs were made with the thigh supported and unsupported by a leg holder. Thigh compression caused a significant blood flow redistribution from the deep system to the superficial system—an affect that was pronounced at 180 mmHg. The thigh should be compressed in the leg holder for as short periods as possible and the IAP should no be raised above 100 mmHg.

The intramuscular pressure (IMP) of the supraspinatus and the deltoid muscles, and the intravascular absorption of ethano-labeled irrigation fluid, was recorded during arthroscopic acromiosplasty at 100 or 150 mmHg of bursa fluid pressure. The IMP in the subacromial procedure averaged 60 mmHg while pressure peaks were recorded at 120 mmHg IMP. Fluid absorption amounted to 100 ml in the 100 mmHg group and 37 mL in the 150 mmHg group. Arthroscopic acromioplasty at 150 mmHg procduces IMP levels that may affect the muscular blood flow, while the fluid absorption is negligeble.

The capsular elasticity and joint volume in post-traumatic anteriorly unstable shoulders were measured from stress-strain infusion curves obtained from infusion at 100 mL/min during arthroscopy. In all patients, the contralateral stable shoulder was examined using the same technique. The capsular elasticity was the same in the stable and the unstable shoulder. The joint volume was 27 ml at 100 mmHg and 33 ml at 180 mmHg in the stable and the unstable shoulder in the same patient. Recurrent dislocation cause neither a permanent capsular distension nor an increased joint volume that maintains the instability.

On the nature and etiology of chronic achilles tendinopathy

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The present studiec included 362 consecutive patients and 147 healthy controls and were conducted to provide a rational basis for treatment and future research.

The major lesion was a focal non-inflammatory tendon degeneration (tendinosis). Twenty per cent of the cases were complicated by a secondary partrial rupture. The paratenon was normal.

A study of tendon blood flow, using laser Doppler flowmetry, refuted the popular theory of the mid-tendon hypovascular zone as a cause of ruptures and chronic lesions. Symptomatic tendons had an increased blood flow of uncertain origin corresponding to the lesion.

There was little difference between patients and controls with regard to alignment and joint motion in the foot. Biomechanical abnormalities, often incriminated in overuse injuries, are not important in chronic achilles tendionopathy and the virtue of orthotics is questionable.

Previous steorid injections were associated with a doubled rate of partial ruptures in surgical cases and have no logical place in treatment of a degenerative lesion.

Abnormal imaging with ultrasonography and MRI was associated with more servere histopathology and could indicate a poor prognosis but neither method afforded any advantages over clinical evaluation in preoperative assessment and decision making.

Men prevailed and had an increased rate of abnormal biopsies and an increased risk of acquiring a partial rupture wich is mainly due to higher participation in sports as compared with women. Old age was related to servere histoparthology, and a decrease in physical activity, blood flow and flexibility of tendon. Most patients were athletes but physical activity was not correlated to histopathology and could be more important in provoking symptoms than in the evaluation of the actual lesion.