

S.O.L.V.E.D

A Study of Locked Plates versus Intramedullary Nails in Distal Femur Fractures:
A Multicenter Randomized Trial Comparing IM Nails and Plate Fixation

Revised October 15, 2007

Summary of Study Design

We propose a randomized controlled multicenter trial in which individuals sustaining a fracture of the supracondylar (metaphyseal) region of the distal femur will be operatively managed by one of two strategies. The first strategy involves fixation of the fracture with a reamed, interlocking intramedullary nail (Nail Group). The second treatment strategy involves open reduction and internal fixation of the fracture with a locking periarticular plate (Plate Group). The null hypothesis of the study is that there will be no difference in the two groups with respect to the primary and secondary outcome measures. To the degree possible, patients in the two groups will receive post-operative care according to the same standards and protocols. We will monitor critical aspects of pre-operative and post-operative care and provide immediate feedback to the participating surgeons when any important deviation from the following protocol occurs.

Primary Outcomes: General outcome will be determined by both the SF-36 and EuroQol 5D. Disease-specific outcomes will be assessed by the Musculoskeletal Functional Assessment measure (MFA) and a knee score.

Secondary outcomes: Rate of re-operation (secondary procedures), nonunion*, superficial infection rates, deep infection, malunion (>5 degrees varus/valgus, >10 malrotation degrees, 1 cm translation in frontal or sagittal plane, and >1cm shortening) and knee range of motion. The treatment provided will be obvious because of differences in surgical incisions and radiographic appearance of the injured limbs; therefore it will not be possible to blind all the patients, surgeons, and some evaluators to treatment allocation. When possible, outcome assessment will be done by independent, blinded parties. We will follow and monitor primary outcome as described on the **Data Collection Grid** (attached), as well as secondary outcomes, complications and adverse events continually.

Background

Distal femur fractures are unstable injuries that are generally treated with surgical fixation to maintain alignment of the extremity during the healing process. The two most common methods of fixation are intramedullary nailing and plate fixation. Both techniques are considered the standard of care. Each method has risks associated with it, and some surgeons prefer one method over the other. However, no comparison between the two techniques has been performed. We plan a randomized trial comparing these two fixation methods using standardized validated general and disease specific measures as well as standard radiographic and clinical outcomes.

Patient Recruitment

For this study, we anticipate recruiting 160 patients with closed or open distal femur fractures. For our primary outcome, we consider an important difference in SR-12 to correspond to a moderate effect as reported by Cohen as well as a minimally important difference in the SF-12 as reported by Ware. In both cases, the value is at least ½ the standard deviation, equivalent to a 6-point difference in score. Specifying an alpha-level=0.05, a beta=0.20 (study power=80), we require a sample of least 126 patients (63 per group) to ensure detection of a ½ standard deviation improvement. We will enroll 160 patients to account for loss to follow-up and errors in randomization.

Inclusion Criteria:

1. Skeletally mature,
2. Fracture of the metaphyseal distal femur with or without intra-articular extension and with or without a TKA,
3. Fracture requiring operative treatment amenable to either IM nail or plate,
4. Surgeon agreed to randomize patient
5. Informed consent obtained,
6. Patient is English speaking.

Patients may have undergone previous surgical interventions either for placement of a spanning external fixator and/or debridement of open fracture wounds. This may have been done at the eventual treating institution or not. That is, the patient could represent a referral of a distal femur fracture, which had undergone previous debridement and spanning external fixator placement.

Exclusion Criteria:

We exclude individuals from the study if they have the following characteristics:

1. Fracture of the metaphyseal distal femur with intraarticular comminution
2. Fracture with vascular injury (Gustillo Type IIIC injury) requiring repair
3. Pathological fracture
4. Known metabolic bone disease
5. Retained hardware or existing deformity in the affected limb that would complicate IM nailing or plating
6. Symptomatic knee arthritis
7. Soft tissue injuries compromising either treatment method with nail or plate
8. Surgical delay greater than 3 weeks for closed fractures or 24 hours for open fractures
9. Contralateral distal femur fractures (bilateral injury) or ipsilateral lower extremity injury that would compromise function of the knee
10. Immunocompromised
11. Unable to comply with postoperative rehabilitation protocols or instructions (i.e. head injured or mentally impaired)
12. Current or impending incarceration
13. Unlikely to follow-up in surgeon's estimation

Inclusion of Children, Women and Members of Minority Groups

We include all individuals who are skeletally mature. Skeletal maturity is typically achieved by age 18 in males and age 16 in females. We are not including individuals with open growth plates (i.e. skeletally immature patients) for two reasons: 1) these individuals are most often treated by non-operative means due to their better healing potential, and 2) the insertion of rigid intramedullary nails has the potential to damage the growth plate resulting in growth arrest and deformity. We are also collecting information on gender and race/ethnicity in our baseline evaluation forms. A semi-annual report will detail patients (males, females, unknown) enrolled in the study by the following categories: American Indian or Alaskan Native, Asian or Pacific Islander, Black-not Hispanic origin, White-not Hispanic origin, Other or unknown.

Eligibility Review and Central Adjudication Committee

We register all patients who meet the inclusion criteria and document reasons for failure to randomize. An independent Central Adjudication Committee (CAC) blinded to allocation will review the initial radiographs and eligibility forms from all randomized patients to ensure that they met eligibility criteria. Patients will only be ruled ineligible if the grounds for ineligibility were known at the time of randomization. The CAC will include the Study Biostatistician, the Principal Investigator, the Co-Principal Investigator, and two orthopaedic surgeons.

Patient Enrollment

When a patient presents with a distal femur metaphyseal fracture he or she will be screened for possible enrollment in the study using criteria on the ***Inclusion /Exclusion Criteria Form***. If the patient is deemed appropriate by the treating surgeon, meaning that they meet all the inclusion criteria and do not meet any exclusion criteria, the patient will be given the consent form to read and reviewed with the patient with time allowed to answer all questions. If the patient agrees to enter the study he or she will sign the consent form. After consent is given, the surgeon or designee will login to the web-based randomizer to obtain the procedure (see Patient Randomization for more details). The surgeon or designee will complete the ***Patient Information Form*** in its entirety. Of great importance is obtaining two alternate contacts to aid in maintaining access to the patient's location and access to the patient throughout the course of the study. All other data points on the study form will be completed including specifics regarding the site of injury, the mechanism of injury, the Abbreviated Injury Scores (AIS) and the Injury Study Score (ISS). Additionally, information will be gathered on the patient's prior social history, medication history, and surgical history. Finally, the current medications that the patient is taking will be reviewed and confirmed. Upon completion of this data, the fracture itself will be evaluated.

Fracture Evaluation

The patient's fracture will be evaluated as per the ***Fracture Characteristics Form***. Information to be taken includes whether or not the fracture is open, the size of the wound if it is open, and the Tcherne grade if it is closed and the location of the fracture with respect to specific measurements as outlined on the form. The classification of the fracture using, the Orthopaedic Trauma Association (OTA) classification, will be marked on the ***Fracture Characteristics Form***. These forms can be completed before or after the patient enters the operating room.

Patient Randomization

We have chosen the patient as the unit of randomization. The PI or designee will randomize all patients who sign consent and are eligible through a secure, HIPAA compliant online randomization system. Each site will receive a unique password and user-id for the randomizer. Patients with a distal femur fracture but do not fit eligibility criteria can be saved as a "screen failure" and will not be randomized or identifiable in anyway. All randomized participants will be assigned individual study numbers in consecutive order. All information will be secured in a database and will not be accessible by any of the co-investigator sites. All inclusion/exclusion data will be kept in confidence per HIPAA guidelines. Once this information is entered, the treatment allocation is revealed. Randomization should lead to approximately the same number of such patients in the two groups

Clinical centers receive complete sets of all data forms prior to joining the study. Each randomization package contains the following data forms: ***Inclusion / Exclusion Criteria Form***, ***Patient Information Form***, ***Fracture Characteristic Form***, ***SF-12v Form***, ***EQ-5D Form***, ***Short Musculoskeletal Assessment Form***, ***Surgical Summary form***, ***Adverse Event Form***, ***Follow-up Clinical Assessment Form*** (for each visit), ***Knee Society Form***. The research coordinator for each participating center ensures that all forms are properly completed and submitted in the HIPAA compliant Electronic Data Capture system developed by Synergos, Inc. The data gathered and the time frame is demonstrated in the attached ***Data Collection Grid***.

Intervention

Previous Provisional Stabilization in Splint or with External Fixation

Not all fractures will be internally fixed acutely. In the setting of an open fracture, the fracture may undergo irrigation and debridement and placement in a splint or spanning external fixation for later definitive fixation. This may also be the case in a closed fracture with swelling. In both cases, various factors may influence the timing of definitive fixation including the stability of the patient, soft tissue wound, contamination of the wound, availability of the surgeon, etc. We will define the “Fixation Procedure” as that surgery in which definitive fixation of the distal femur fracture is carried out. The number of previous surgeries (and their purpose) prior to the “Fixation Procedure” will be noted. Details of the “Fixation Procedure” ensue:

Debridement of Open Wounds:

Open wound size and location will be recorded. After appropriate preparation and draping, the open fracture wound will be treated with debridement of the skin, subcutaneous tissue, and bone. The traumatic wound will be extended, with the extent of the wound also recorded. After debridement, the open wound will be irrigated with at least 6 liters of fluid. A new preparation and draping will be performed prior to definitive fixation. All personnel will put on new gowns and gloves and new instruments will be used.

Patient Positioning:

The patient will be positioned supine on a conventional operating table with a radiolucent extension or a completely radiolucent table. A tourniquet may be used during surgical exposure but should not be used during nailing or reaming of the femur. Triangular leg supports or bumps may be utilized.

Articular Fracture Reduction:

If the patient has a fracture with articular involvement, the articular injury will be reduced and fixed before the nail or plate is applied. If the patient has been randomized to NAIL treatment, a parapatellar, paratendinous, or transpatellar tendon approach will be utilized for placement of the nail. If necessary, the articular surface may be visualized and manipulated through this incision. Screws may then be placed either from medial to lateral or lateral to medial in positions not interfering with the nail. The number and diameter of the lag screws will be recorded on the surgical report form. If the patient has been randomized to PLATE treatment, either an anterolateral approach or lateral parapatellar approach may be utilized for placement of the plate. If necessary, the articular surface may be visualized and manipulated through this incision. As

with the NAIL group, articular surface screws may then be placed either from medial to lateral or lateral to medial in positions not interfering with plate or locked screw positions. The number and diameter of the lag screws will be noted on the surgical report form.

Surgical Approach

For the NAIL group, a paratendinous or transpatellar tendon approach may be utilized. With the PLATE group, either a lateral peripatellar approach or anterolateral approach may be utilized.

For both groups, certain characteristics of the approach will be documented:

- Type of approach,
- Length of skin incision,
- Visualization of articular surface or not,
- Modification of traumatic wound or not (open fractures),
- Wound separate from open wound or not (open fractures).

Within the PLATE group, differentiation between *open* or *submuscular* approaches will be made. All information will be detailed and reported on the ***Surgical Summary Form***

Distal Femoral Nailing

If necessary, the articular surface will first be reduced and internally fixed as described in the previous section. A guide wire/cannulated reamer or awl will then be utilized to establish the starting point/canal entrance for the nail. The starting point will be anterior to the origin of the Posterior Cruciate Ligament. Fluoroscopy will be utilized to confirm that the reaming/nail path is in line with the intramedullary canal in both the AP and lateral planes. Reaming will be performed with the fracture reduced and the canal will be reamed until “chatter”. Reaming should be conducted over the guide wire with cannulated power reamers. The choice of reamer is left to the operating surgeon. To avoid inconsistencies in the degree of reaming, surgeons are to adhere to the following protocol 1) Surgeons will ream the intramedullary canal until the first detection of “cortical chatter” (i.e. the reamer just begins to contact the cortical bone of the femur), or to the point at which the surgeon has reamed to 1-1.5 mm larger than the largest intramedullary nail available. 2) The size of the nail (diameter) will correspond to the point of “cortical chatter” (e.g., if chatter occurs with an 10mm reamer, then the nail size will be 10mm.) If the canal is capacious, a size 11mm or 12mm nail will be used. 3) Following the presence of “cortical chatter”, surgeons will ream 1-1.5 mm larger than the chosen nail's diameter to facilitate its insertion. It is intended for the length of the nail to come to at least the level of the lesser trochanter. The choice of intramedullary nail (i.e. Company) and material (titanium or stainless steel) is at the discretion of the operating surgeon. The nail will then be inserted and interlocking screws placed both proximally and distally. All nails will be statically locked. One or two screws may be utilized proximally and at least 2 must be used distally. For all cases in the NAIL group, the following will be documented:

- Type of nail,
- Size of nail,
- Number of proximal and distal interlocking screws,
- Number of transverse and off axis screws,
- Presence of an end cap or not, and
- Number of “locked” fixed angle interlocking screws (those through threaded holes or otherwise secured to the nail)

Distal Femoral Plating

If necessary, the articular surface will first be reduced and internally fixed. As noted above, the surgeon will choose between one of three surgical approaches for plate fixation:

1. Lateral peripatellar approach with submuscular placement of the plate,
2. Anterolateral approach with open placement of the plate (i.e., elevation of the vastus lateralis anteriorly),
3. Anterolateral approach with submuscular placement of the plate

Plates with the ability of placing distal fixed angled screws will be utilized. The type of implant utilized, length of the plate, use of locked or unlocked screws, use of unicortical or bicortical screws, and number of screws utilized are all left to the judgment of the operative surgeon. The distal screws should be fixed angle (locking) with exceptions as needed. The plate should allow at least 6 holes proximal to the fracture. Longer plates are encouraged, although left to the discretion of the surgeon. Diaphyseal fixation will generally be in every other or every third hole.

There are essentially three methods of reduction and fixation for the metaphyseal / diaphyseal component of the distal femoral fracture when plate fixation is utilized. They are:

1. Direct clamp application either done openly or in a percutaneous manner (e.g., simple spiral metaphyseal fracture),
2. Utilization of the plate to help afford the reduction, and
3. Closed reduction of the metaphyseal /diaphyseal component of the fracture with reliance on modalities such as manual traction, bumps, femoral distractors, etc.

All surgical variables will be reported on the ***Surgical Summary Form.***

Ensuring Standardization of Surgical Techniques

To ensure that all participating surgeons perform both procedures in a similar manner, a practical technique-oriented session is conducted prior to the commencement of each new center's enrollment. Experts in both techniques will prepare a video highlighting the critical aspects of both procedures. The principal investigator at every site is responsible for the educational process as they are experts in both techniques.

Bone Grafting

No primary bone grafting will be performed. Bone grafting may be performed within the first six months of the primary fixation surgery in the setting of an open fracture and bone loss.

Antibiotic beads or spacers may be provisionally placed in such cases. In general, bone grafting in the first six months should be reserved for severe bone loss (which is considered a critical defect), if planned at the time of the initial procedure and recorded on the ***Surgical Summary Form.***

Other surgery

Including fixation of additional fractures, abdominal procedures or any other surgery are recorded on the ***Surgical Summary Form.***

Planned secondary re-operations

Any anticipated secondary procedure(s), such as bone grafting, flap coverage, wound V.A.C. changes, etc. is recorded on the ***Surgical Summary Form***.

Radiographic Alignment

Radiographic Evaluation will be done on AP radiograph of the knee and femur and lateral radiograph of the knee and femur. A centered line drawn directly in the middle of the femoral shaft will determine varus and valgus and it intersects with a line parallel with the joint surface of the distal femur. Normal will be considered seven (7) degrees of valgus unless the other side is available and can be compared. On the lateral radiograph angulation will be determined by the appearance of the fracture site or a line drawn parallel to the axis the femoral condyles as it intersects with a line centered in the femoral shaft. Normal will be considered ninety degrees (90). The amount of varus, valgus, anterior, posterior angulation are recorded on the ***Surgical Summary Form***. Leg length discrepancy is determined by clinical examination and radiographic appearance in uncomminuted fractures and recorded on the ***Surgical Summary Form***.

Rotational Alignment

The physical exam will include rotational alignment by determining the arc of rotation as compared with the normal leg and by the position of the knee/foot while the patient is supine at rest.

Peri-operative Treatment Common to Both Groups

To ensure similar peri-operative regimens, key aspects of pre- and post-operative care have been standardized among participating centers.

Postoperative Rehabilitation

There will be two (2) optional postoperative protocol arms, one with Continuous Passive Motion (CPM) and one without CPM. If CPM is used, it will begin on on post-operative day number one and will be initiated with a range of motion 0-30° and advanced as tolerated, generally 5°-10° /shift reaching 90° within the first two weeks. CPM may be discontinued when 90° of flexion is sustained. In the second arm, patients will not receive CPM but will initiate range of motion exercises with a physical therapist while in the hospital. Both groups will be seen by physical therapy as inpatients and will be instructed regarding range of motion exercises. Cold therapy (ice) will be used as long as the patient has a knee effusion. Patients will not be sent to a physical therapist unless they are unable to achieve 90° of passive flexion and full extension at the time of their two (2) week follow-up. Isometric exercises will begin immediately and minimal weight (3-5 pounds) resistance exercises may be initiated six (6) weeks following surgery if callus is present on radiographs. Increased resistance exercises may be initiated when full weight bearing is started.

Weight Bearing

All patients will be treated with the same postoperative protocol for mobilization. Immediately after surgery, patients will be allowed foot flat weight bearing. Once callus is seen on x-rays, partial weight bearing will be allowed. Patients will be allowed full weight bearing once bridging callus is seen on two orthogonal radiographic views.

Antibiotics

In Closed Fractures 1) Peri-operative antibiotic administration is continued for 24 hours post-operatively (specific antibiotic regimens at the discretion of the operating surgeon: gram positive coverage).

In Open Fractures 1) Peri-operative intravenous antibiotic administration includes a cephalosporin and an aminoglycoside which will be continued for 48-72 hours post-operatively (specific antibiotics used at the discretion of the attending surgeon. The recommended guidelines include: intravenous (iv) Ancef for Type I-II injuries, iv Zosyn for Type III injuries, and iv Zosyn plus penicillin for grossly contaminated injuries). 2) Primary versus delayed wound closure is at the discretion of the surgeon, 3) For wounds left open, repeat irrigation and debridement of soft tissues and contaminated bone repeated as necessary: usually every 48 hours until tissues are clean and all non-viable tissue has been removed). 4) Definitive wound closure by delayed primary closure, split thickness skin grafting, or flaps (for grade IIIB only) should occur by 7 days following the initial surgery. The time from injury to debridement (in hours) and time from injury to definitive fixation (in days), as well as the method of provisional stabilization (if any), is recorded on the ***Surgical Summary Form***.

Follow-up Evaluation

Surgical follow-up visits are outlined on the attached ***Data Collection Grid***. All outcome forms will be completed at the time indicated on the grid. Radiographs will be obtained as displayed on the ***Data Collection Grid*** and taken according to standard of care.

History:

The surgeon, at the time of each follow-up visit, will make sure that at some point questions one through three (1-3) on the form are completed. These include the times of definitive surgery, definitive closure and the type of closure. During each visit the surgeon or designee will enter additional information regarding whether CPM is in use, any further surgical procedures performed and if any complications have occurred. If any complication is recognized an ***Adverse Event Form*** (AE) must be completed. The local Institutional Review Board (IRB) at the patient's medical institution must be made aware any Serious Adverse Event (SAE).

Physical Exam:

The physical exam will include rotational alignment by determining the arc of rotation as compared with the normal leg and by the position of the knee/foot while the patient is supine at rest. A clinical leg length evaluation will be measured from the ASIS to the medial joint line of the knee or by block testing. Knee flexion and extension and ankle dorsiflexion and plantar flexion will be measured for active and passive range of motion. This must be done using a large goniometer and not by subjective evaluations. Sensation will be documented as normal, diminished or absent in the superficial and deep peroneal nerve distributions as well as the post tibial nerve distribution. Manual muscle testing of the quadriceps and ankle dorsiflexors will be made using standard muscle strength grading (0-5). Other questions regarding the patient's weight bearing status will be answered as they appear on the form including the amount of weight the patient has been bearing the two weeks prior to the visit and what the recommended weight bearing status and ambulatory support are immediately following the visit. Two pain scales will be completed. These are visual and numerical scales for both the fracture site and for

generalized pain. The frequency of pain medication and the type of medication will be documented. The workers compensation status and litigation status will be documented.

Assurance of Protocol Adherence

Given the inherent variability in practice patterns among orthopaedic surgeons, it will be important to ensure that surgeons adhere as closely as possible to the surgical management protocol. The Research Coordinator (RC) reviews all surgical reports and makes periodic checks of charts during the rehabilitation process. If the RC finds apparent protocol violations, the site investigators and the methods center receive photocopies of the relevant information from the charts and, if they confirm the problem, take appropriate action. The site investigator receives a random sample of chart documentation from the RC to review for protocol adherence and take appropriate action if problems are detected. In addition, study forms include documentation of fundamental technical aspects that the study coordinator reviews on all patients and inform the Principal Investigator and site investigator if problems are noted.

Contamination and Cointervention

In general, crossovers (switching treatment groups) should not occur. However, if this occurs (for example due to unrecognized distal extension of the fracture, lack of availability of a needed implant) patients will be analyzed in an *intention to treat* manner.

Co-intervention with drugs that alter bone turnover (bisphosphonates, estrogens, and steroids) during the course of the study may act as potential confounders to fracture healing. Moreover, surgical co-intervention, such as a general, neurosurgical or other orthopaedic procedures, may confound outcomes. Standardization of management protocols should limit co-intervention, and we will document the use of drugs that affect the bone, as well as major additional procedures that patients undergo. Additionally, no form of bone stimulator may be used prior to 6 months after the “fixation procedure”.

Measurement of Outcome

Follow up will continue for a period of two (2) years following randomization. Clinical and radiologic assessments will occur at the time of admission to hospital (baseline), preoperatively, 3, 6, 12 and 24 months (see grid). Follow up assessment forms will include major complications (see ***Adverse Event Form***), subsequent operative procedures and functional status.

Outcomes

Functional Outcome:

Patient functional outcome will be assessed by a self-administered questionnaire, which the research coordinator supervises at the preoperative, 3, 6, 12, and 24 month visits. Functional assessment includes a generic health status measurement instrument, the ***SF-12v2***, a generic utility measure, the ***EQ-5D***, a disease-specific functional measure targeted to patients with lower extremity fractures (***Short Musculoskeletal Functional Assessment***), and a knee score (***Knee Society Form***). All measures have been extensively used and validated.

Ethics, Safety and Confidentiality

The patient’s physician and the study investigators will share responsibility for patient safety. The CAC, comprised of two orthopaedic surgeons, a statistician and an epidemiologist will have

primary responsibility for the monitoring and accumulating of study data for adverse events following treatment. Both surgical techniques (nailing and plating) are currently being used in different centers worldwide. Orthopaedic surgeons, each with their own preference, will generally acknowledge the other technique as a treatment option.

Data Management

Patient Classification and Randomization

We document all patients presenting to participating surgeons with a diagnosed distal femur fracture amenable to intramedullary nailing or plating. Such patients are classified as 1) excluded (if they subsequently do not meet the eligibility criteria), 2) missed (due to error), or 3) eligible and randomized. Participating surgeons who identify an eligible patient who consents to randomization will use the web-based randomization to obtain the treatment procedure (NAIL or PLATE).

Data Entry

Data collection forms will be collected by a trained research associate from the patient at the clinic or before the patient reaches the clinic as part of hospital admission. Upon completion, the research coordinator will enter the data collected in the forms through an Electronic Data Capture (EDC) website. The site PI and coordinator will be given the website address, a unique user name and password to login. Training, a user-id, and a password will be provided to investigators and coordinators prior to implementation. All data will be kept in compliance with HIPAA. Forms can be faxed to Boston Medical Center as a backup if necessary. A report of missing data, implausible data, and inconsistencies will be generated and the research coordinators from each clinical center are contacted by phone to ensure problems are corrected.

Completeness of Data Collection

Each center will receive a monthly study status report, showing, for each center, the number of: 1) subjects entered into the trial, 2) completed follow ups, 3) outstanding data clarification requests, and 4) overdue assessments. Centers are identified by number to preserve their anonymity. The Data Safety Monitoring Board (DSMB) will meet twice a year to ensure the validity of the data.

REFERENCES

1. Miclau T, Holmes W, Martin RE, Krettek C, Schandelmaier P. Plate osteosynthesis of the distal femur: surgical techniques and results. *J South Orthop Assoc.* 1998;7:161-170.
2. Schatzker J. Fractures of the distal femur revisited. *Clin Orthop.* 1998;347:43-56.
3. Siliski JM, Mahring M, Hofer HP. Supracondylar-intercondylar fractures of the femur. Treatment by internal fixation. *J Bone Joint Surg Am.* 1989;71-A:95-104.
4. Neer CS, Grantham SA, Shelton ML. Supracondylar fracture of the adult femur. A study of one hundred and ten cases. *J Bone Joint Surg Am.* 1967;49-A:591-613.
5. Stewart MJ, Sisk TD, Wallace Jr SH. Fractures of the distal third of the femur. A comparison of methods of treatment. *J Bone Joint Surg Am.* 1966;48-A:784-807.
6. Olerud S. Supracondylar, intraarticular fracture of the femur. Results of operative reconstruction. *Acta Orthop Scand.* 1971;42:435-437.
7. Wenzl H. [Results in 112 surgically treated distal femoral fractures]. *Hefte Unfallheilkd.* 1975;120:15-24.
8. Schatzker J, Home G, Waddell J. The Toronto experience with the supracondylar fracture of the femur, 1966-72. *Injury.* 1974;6:113-128.
9. Schatzker J, Lambert DC. Supracondylar fractures of the femur. *Clin Orthop.* 1979;138:77-83.
10. Mast JW, Jakob R, Ganz R. In: Planning and Reduction Technique in Fracture Surgery. Berlin Heidelberg New York: Springer-Verlag; 1989

11. Gerber C, Mast JW, Ganz R. Biological internal fixation of fractures. *Arch Orthop Trauma Surg.* 1990;109:295-303.
12. Bolhofner BR, Carmen B, Clifford P. The results of open reduction and Internal fixation of distal femur fractures using a biologic (indirect) reduction technique. *J Orthop Trauma.* 1996;10:372-377.
13. Kregor PJ, Stannard JA, Zlowodzki M, Cole PA. Treatment of distal femur fractures using the less invasive stabilization system: surgical experience and early clinical results in 103 fractures. *J Orthop Trauma.* 2004;18:509-520.
14. Schütz M, Muller M, Regazzoni P, et al. Use of the less invasive stabilization system (LISS) in patients with distal femoral (AO33) fractures: a prospective multicenter study. *Arch Orthop Trauma Surg.* 2005;125:102-108.
15. Fankhauser F, Gruber G, Schippinger G, et al. Minimal-invasive treatment of distal femoral fractures with the LISS (Less Invasive Stabilization System): a prospective study of 30 fractures with a follow up of 20 months. *Acta Orthop Scand.* 2004;75:56-60.
16. Markmiller M, Konrad G, Sudkamp N. Femur-LISS and distal femoral nail for fixation of distal femoral fractures: are there differences in outcome and complications? *Clin Orthop.* 2004;426:252-257.
17. Weight M, Collinge C. Early results of the less invasive stabilization system for mechanically unstable fractures of the distal femur (AO/OTA types A2, A3, C2, and C3). *J Orthop Trauma.* 2004;18:503-508.
18. Syed AA, Agarwal M, Giannoudis PV, Matthews SJ, Smith RM. Distal femoral fractures: long-term outcome following stabilisation with the LISS. *Injury.* 2004;35:599-607.

19. Ricci AR, Yue JJ, Taffet R, Catalano JB, De Falco RA, Wilkens KJ. Less Invasive Stabilization System for treatment of distal femur fractures. *Am J Orthop*. 2004;33:250-255.
20. Lucas SE, Seligson D, Henry SL. Intramedullary supracondylar nailing of femoral fractures. A preliminary report of the GSH supracondylar nail. *Clin Orthop*. 1993;296:200-206.
21. Iannacone WM, Bennett FS, DeLong WG Jr, Born CT, Dalsey RM. Initial experience with the treatment of supracondylar femoral fractures using the supracondylar intramedullary nail: a preliminary report. *J Orthop Trauma*. 1994;8:322-327.
22. Gellman RE, Paiement GD, Green HD, Coughlin RR. Treatment of supracondylar femoral fractures with a retrograde intramedullary nail. *Clin Orthop*. 1996;332:90-97.
23. Janzing HM, Stockman B, Van Damme G, Rommens P, Broos PL. The retrograde intramedullary nail: prospective experience in patients older than sixty-five years. *J Orthop Trauma*. 1998;12:330-333.
24. Janzing HM, Stockman B, Van Damme G, Rommens P, Broos PL. The retrograde intramedullary supracondylar nail: an alternative in the treatment of distal femoral fractures in the elderly? *Arch Orthop Trauma Surg*. 1998b;118:92-95.
25. Danziger MB, Caucci D, Zecher SB, Segal D, Covall DJ. Treatment of intercondylar and supracondylar distal femur fractures using the GSH supracondylar nail. *Am J Orthop*. 1995;24:684-690.
26. Gynning JB, Hansen D. Treatment of distal femoral fractures with intramedullary supracondylar nails in elderly patients. *Injury*. 1999;30:43-46.

27. Ostermann PA, Hahn MP, Ekkernkamp A, David A, Muhr G. [Retrograde interlocking nailing of distal femoral fractures with the intramedullary supracondylar nail]. *Chirurg.* 1996;67:1135-1140.
28. Krettek C, Schandelmaier P, Miclau T, Tscherne H. Minimally invasive percutaneous plate osteosynthesis (MIPPO) using the DCS in proximal and distal femoral fractures. *Injury.* 1997;28 Suppl 1:A20-30.
29. Farouk O, Krettek C, Miclau T, Schandelmaier P, Tscherne H. Effects of percutaneous and conventional plating techniques on the blood supply to the femur. *Arch Orthop Trauma Surg.* 1998;117:438-441.
30. Farouk O, Krettek C, Miclau T, Schandelmaier P, Guy P, Tscherne H. Minimally invasive plate osteosynthesis: does percutaneous plating disrupt femoral blood supply less than the traditional technique? *J Orthop Trauma.* 1999;13:401-406.
31. Kregor PJ, Stannard J, Zlowodzki M, Cole PA, Alonso J. Distal femoral fracture fixation utilizing the Less Invasive Stabilization System (L.I.S.S.): the technique and early results. *Injury.* 2001;32 Suppl 3:SC32-47.
32. Schutz M, Muller M, Krettek C, et al. Minimally invasive fracture stabilization of distal femoral fractures with the LISS: a prospective multicenter study. Results of a clinical study with special emphasis on difficult cases. *Injury.* 2001;32:SC48-54.
33. Kassab SS, Mast JW, Mayo KA. Patients treated for nonunions with plate and screw fixation and adjunctive locking nuts. *Clin Orthop.* 1998;347:86-92.
34. Haas N, Hauke C, Schutz M, Kaab M, Perren SM. Treatment of diaphyseal fractures of the forearm using the Point Contact Fixator (PC-Fix): results of 387 fractures of a prospective multicentric study (PC-Fix II). *Injury.* 2001;32 Suppl 2:B51-62.

35. Zlowodzki M, Williamson S, Cole PA, Zardiackas LD, Kregor PJ. Biomechanical evaluation of the less invasive stabilization system, angled blade plate, and retrograde intramedullary nail for the internal fixation of distal femur fractures. *J Orthop Trauma*. 2004;18:494-502.
36. Wong MK, Leung F, Chow SP. Treatment of distal femoral fractures in the elderly using a less-invasive plating technique. *Int Orthop*. 2005;29:117-120.
37. Kregor PJ, Hughes JL, Cole PA. Fixation of distal femoral fractures above total knee arthroplasty utilizing the Less Invasive Stabilization System (L.I.S.S.). *Injury*. 2001b;32 Suppl 3:SC64-75.
38. Müller ME, Allgower M, Schneider R, Willenegger H. In: Manual of Internal Fixation. Techniques Recommended by the AO-ASIF Group. Berlin, Heidelberg, New York: Springer-Verlag; 1991;750
39. Nork SE, Segina DN, Aflatoon K, et al. The association between supracondylar-intercondylar distal femoral fractures and coronal plane fractures. *J Bone Joint Surg Am*. 2005;87:564-569.
40. Ostrum RF, Geel C. Indirect reduction and internal fixation of supracondylar femur fractures without bone graft. *J Orthop Trauma*. 1995;9:278-284.
41. Leung KS, Shen WY, So WS, Mui LT, Grosse A. Interlocking intramedullary nailing for supracondylar and intercondylar fractures of the distal part of the femur. *J Bone Joint Surg Am*. 1991;73-A:332-340.
42. Krettek C, Schandelmaier P, Miclau T, Bertram R, Holmes W, Tscherne H. Transarticular joint reconstruction and indirect plate osteosynthesis for complex distal supracondylar femoral fractures. *Injury*. 1997b;28 Suppl 1:A31-41.

46. Butt MS, Krikler SJ, Ali MS. Displaced fractures of the distal femur in elderly patients. Operative versus non-operative treatment. *J Bone Joint Surg Br.* 1996;78-B:110-114.
47. Jeon IH, Oh CW, Kim SJ, Park BC, Kyung HS, Ihn JC. Minimally invasive percutaneous plating of distal femoral fractures using the dynamic condylar screw. *J Trauma.* 2004;57:1048-1052.
48. Huang HT, Huang PJ, Su JY, Lin SY. Indirect reduction and bridge plating of supracondylar fractures of the femur. *Injury.* 2003;34:135-140.
51. Ziran BH, Rohde RH, Wharton AR. Lateral and anterior plating of intra-articular distal femoral fractures treated via an anterior approach. *Int Orthop.* 2002;26:370-373.
53. Zehntner MK, Marchesi DG, Burch H, Ganz R. Alignment of supracondylar/intercondylar fractures of the femur after internal fixation by AO/ASIF technique. *J Orthop Trauma.* 1992;6:318-326.
55. Dominguez I, Moro Rodriguez E, De Pedro Moro JA, Cebrian Parra JL, Lopez-Duran Stern L. Antegrade nailing for fractures of the distal femur. *Clin Orthop.* 1998;350:74-79.
57. Armstrong R, Milliren A, Schrantz W, Zeliger K. Retrograde interlocked intramedullary nailing of supracondylar distal femur fractures in an average 76-year-old patient population. *Orthopedics.* 2003;26:627-629.

58. Seifert J, Stengel D, Matthes G, Hinz P, Ekkernkamp A, Ostermann PA. Retrograde fixation of distal femoral fractures: results using a new nail system. *J Orthop Trauma*. 2003;17:488-495.
59. Watanabe Y, Takai S, Yamashita F, Kusakabe T, Kim W, Hirasawa Y. Second-generation intramedullary supracondylar nail for distal femoral fractures. *Int Orthop*. 2002;26:85-88.
60. Saw A, Lau C P. Supracondylar nailing for difficult distal femur fractures. *J Orthop Surg*. 2003;11:141-147.
61. Kumar A, Jasani V, Butt MS. Management of distal femoral fractures in elderly patients using retrograde titanium supracondylar nails. *Injury*. 2000;31:169-173.
62. Henry SL. Supracondylar femur fractures treated percutaneously. *Clin Orthop*. 2000;375:51-59.
63. Handolin L, Pajarinen J, Lindahl J, Hirvensalo E. Retrograde intramedullary nailing in distal femoral fractures--results in a series of 46 consecutive operations. *Injury*. 2004;35:517-522.
64. Manfredini M, Gildone A, Ferrante R, Bernasconi S, Massari L. Unicondylar femoral fractures: therapeutic strategy and long-term results. A review of 23 patients. *Acta Orthop Belg*. 2001;67:132-138.
65. Ostermann PA, Neumann K, Ekkernkamp A, Muhr G. Long term results of unicondylar fractures of the femur. *J Orthop Trauma*. 1994;8:142-146.
66. Davison BL. Varus collapse of comminuted distal femur fractures after open reduction and internal fixation with a lateral condylar buttress plate. *Am J Orthop*. 2003;32:27-30.

67. Rademakers MV, Kerkhoffs GM, Sierevelt IN, Raaymakers EL, Marti RK. Intra-articular fractures of the distal femur: a long-term follow-up study of surgically treated patients. *J Orthop Trauma*. 2004;18:213-219.
68. Krettek C, Miclau T, Grun O, Schandelmaier P, Tscherne H. Intraoperative control of axes, rotation and length in femoral and tibial fractures. Technical note. *Injury*. 1998;29 Suppl 3:C29-39.
69. Bezwada HP, Neubauer P, Baker J, Israelite CL, Johanson N A. Periprosthetic supracondylar femur fractures following total knee arthroplasty. *J Arthroplasty*. 2004;19:453-458.
70. Althausen PL, Lee M A, Finkemeier CG,, Meehan JP, Rodrigo JJ. Operative stabilization of supracondylar femur fractures above total knee arthroplasty: a comparison of four treatment methods. *J Arthroplasty*. 2003;18:834-839.
71. Chen F, Mont MA, Bachner RS. Management of ipsilateral supracondylar femur fractures following total knee arthroplasty. *J Arthroplasty*. 1994;9:521-526.
72. Zehntner MK, Ganz R. Internal fixation of supracondylar fractures after condylar total knee arthroplasty. *Clin Orthop*. 1993;293:219-224.
73. Gliatis J, Megas P, Panagiotopoulos E, Lambiris E. Midterm results of treatment with a retrograde nail for supracondylar periprosthetic fractures of the femur following total knee arthroplasty. *J Orthop Trauma*. 2005;19:164-170.
74. Wick M, Muller EJ, Kutscha-Lissberg F, Hopf F, Muhr G. [Periprosthetic supracondylar femoral fractures: LISS or retrograde intramedullary nailing? Problems with the use of minimally invasive technique]. *Unfallchirurg*. 2004;107:181-188.

75. Levy BA, Zlowodzki MP, Graves M, Cole PA. Screening for extremity arterial injury with the arterial pressure index. *Am J Emerg Med.* 2005;23:689-695.
76. Johansen K, Lynch K, Paun M, Copass M. Non-invasive vascular tests reliably exclude occult arterial trauma in injured extremities. *J Trauma.* 1991;31:515-519.
77. Lynch K, Johansen K. Can Doppler pressure measurement replace "exclusion" arteriography in the diagnosis of occult extremity arterial trauma? *Ann Surg.* 1991;214:737-741.
78. Zlowodzki M, Bhandari M, Marek DJ, Cole PA, Kregor PJ. Operative treatment of acute distal femur fractures: Systematic review of two comparative studies and 45 case series (1989-2005). *J Orthop Trauma.* 2006.