

REVIEW

By **Assoc. Prof. Dr. Venelin Alexandrov Alexiev, Ph.D.**

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Regarding dissertation on the topic:

“ONE-STAGED LOCKED EXTERNALIZED PLATING FOR THE TREATMENT OF UNSTABLE PROXIMAL METADIAPHYSEAL TIBIAL FRACTURES” with thesis supervisor Prof. Dr. Dimitar Raykov, M.D., Ph.D., DSc.

presented for defence before a scientific jury formed by order № R-109-511/29.11.2021 of the Rector of MU - Varna. I was appointed as a member of the scientific jury and by the decision of the latter (Protocol №1 of 30.11. 2021) I have been appointed to submit a review for the awarding a scientific and educational degree of „Doctor“ on the dissertation of **Dr. Biser Aleksandrov Makelov**, an independent PhD - candidate in the scientific specialty "Orthopedics and Traumatology", at the Department of Orthopedics and Traumatology, Faculty of Medicine of Medical University ,Varna, professional field 7.1 "Medicine", 7. "Health and Sport".

Brief biographical information about the doctoral candidate

Dr Biser Aleksandrov Makelov is currently a teaching assistant professor since 2016 at the Department of Special Surgery of the Medical Faculty of Trakia University, Stara Zagora, and a specialist doctor and consultant at the Department of Orthopedics and Traumatology in University Hospital “Prof.dr.Stoyan Kirkovitch”, Stara Zagora.

Tibial fractures due to road traffic accidents are the most common fractures of the long tubular bones. The subcutaneous location of the anteromedial aspect of the tibia, together with the scanty skin-muscle coverage, are responsible for the higher incidence of injuries accompanied by significant soft tissue damage and/or open fractures They heal more slowly and may be accompanied by a number of complications such as non-unions, superficial or deep infections, leaving permanent sequelae or long-term disability. Unstable multifragmentary proximal tibial fractures (UMPTF) are a heterogeneous group of injuries and due to their high fracture diversity, it is difficult to apply the generally accepted and standard treatment algorithms. The therapeutic approach can be single or multi-stage

depending on the condition of the surrounding soft tissues and the general condition of the patient. The gold standard is a sequential, staged therapeutic management with initial emergency life-saving provisional fracture stabilization called "orthopedic trauma control" and subsequent multiple surgical interventions. In the late 1960s, the founding AO group developed the basic principles of modern operative traumatology for anatomic reduction, interfragmentary compression, and early mobilization. The exact anatomic reduction of the intra-articular component, achieved with open techniques is often frustrated by the subsequent complications of extended dissection through the primary injured soft tissues, which further impairs blood supply to the area of the ischemic bone fragments. In the last decade, the focus of surgical treatment has shifted to a soft tissue sparing approach, which is the essence of the concept of "biologic fixation". This is a combination of indirect reduction techniques and internal splinting with bridge plating with sufficient stability and optimal axial alignment. Modern innovative instrumentations allow minimally invasive percutaneous osteosynthesis based on the principle of a modern internal "external" fixator called the minimally invasive stabilization system for distal femoral metaphysis (LISS-DF), which can also be applied as a definitive external stabilizer in multifragmentary fractures in the proximal and distal tibial metadiaphyseal zones.

This dissertation describes the application of an innovative and sparing surgical approach of one-staged locked external stabilization (OLES) in the operative treatment of these fractures. The PhD candidate, has justified the proposed method following a previously generated three-dimensional biomechanical simulation model using the finite element method in AO Research Institute, Davos.

The scientific thesis presented by Dr. Makelov includes a prospective longitudinal clinical study with enrolled patients who meet the precise inclusion criteria and a follow-up visit with functional results evaluation at the 4th week after surgery and at the final patient check up.

The dissertation has 177 pages, of which 11 pages are taken up by the bibliography. The aim is on one page and the 4 tasks are set by the author to achieve it. The next 165 pages contain the necessary sections - introduction, literature review, purpose and tasks, participants and methodology, results and analysis, conclusion, summary points, contributions, bibliography. Thesis includes 20 tables and 83 high quality informative figures.

The bibliography comprises 179 titles, 8 of which are in Cyrillic. A limitations section is also included, and the adapted functional questionnaire used is attached; the structure of the work is consistent and logical. The literary sources, understandably the vast majority of which are in English, are 171.

The **literature review** focuses on the history of the problem and on the standard operative techniques and their complications and is extensive enough. All aspects of the problem are covered, presenting both classical works on the subject and contemporary publications in the literature from the year 2010 till 2020. The publications cited are from reputable scientific journals. The review is 46 pages, about ¼ of the total dissertation volume. Consistently presented are:

- Surgical anatomy of the tibia - the tibia has minimal anteromedial soft tissue coverage of skin and subcutaneous tissue only, which predisposes to damage to the soft tissues located immediately above the hard bony matrix,
- Biomechanics of the lower limb, coronally and sagittally - of particular importance in indirect reduction and external fixation with OLES is the restoration of the biomechanical axis of the lower limb before the final locking of the screws, because after that correction of the position cannot be made,
- Bone healing – with OLES, healing is secondary, under conditions of relative stability according to Perrin's strain theory, in the presence of optimal interfragmentary motion (IFM) ranging from a few microns to a few millimeters,
- The clinical diagnosis of UPMTF aims to exclude complications such as acute compartment syndrome (ACS) and includes orthogonal X-rays, CT and MRI.
- Classifications of proximal tibial fractures by AO/OTA - according to intra-articular involvement, severity of soft tissue injury and skin disruption,
- Treatment methods - Conservative ones are of almost historical value, and operative ones can be one-staged or staged, tailored to the "personality" of the fracture,
- Complications - infections; bone - union problems - delayed, mal or nonunion; ACS; deep vein thrombosis.

The literature review is well focused and relevant to the proposed hypotheses and presents the critical synthesis of Dr.Makelov's extensive knowledge of the problem.

The **aim** of the dissertation is formulated in Chapter III: " To investigate the feasibility and to evaluate the results of the application of one-stage externalized fixation with locked plates in the treatment of unstable proximal tibial fractures".

The four tasks are derived logically and clearly formulated from the aim: to perform a systematic review and critical analysis of the methods established for the treatment of unstable metadiaphyseal proximal tibial fractures; to investigate the biomechanical and biological aspects of locked external stabilization with LCP/LISS-DF plates by creating an

experimental computational three-dimensional finite element model; to report, systematize and analyze the final clinical and functional outcomes; to present a comprehensive evaluation of the therapeutic effect of the proposed method for the treatment of unstable proximal tibia injuries when applied in the clinical practice.

In **Chapter IV**, on 28 pages, the candidate presents the clinical material and methods used in the study. It presents patients with UPTFs treated with OLES between years 2013 – 2021, performed in the Department of orthopedics and traumatology at the University Hospital "Prof. Dr. Stoyan Kirkovich-AD", Stara Zagora. After a successful initial pilot study approved by the Ethics Committee of Medical Faculty of Trakia University a biomechanical virtual computational model by the finite element method was done at the AO Research Institute Davos.

The patients included were divided into groups according to: age - up to 50 and over 50; tibial locus - proximal or distal metadiaphysis; **simple** - multifragmentary metadiaphyseal without joint involvement and **complex**, compound with simple (without fragmentation and articular comminution) joint involvement and multifragmentary metadiaphyseal tibial separation; degree of soft tissue damage – from mild or severely injured soft tissue envelope.

The candidate examined the following variables for comparison across groups: time to bone union; operative time; functional assessment using the HSS scoring systems for the knee joint and the AOFAS for the ankle joint; and knee and ankle joint range of motion.

Over an eight-year period, 18 patients with a follow-up of up to 60 months were treated with one-staged locked external plating. The mean age of the studied subjects was 51 years, and 15 were male. The locus of fractures was proximal metadiaphysis in 12 patients, ten patients had grade II soft tissue injury, and according to the Gustillo classification for open fractures, 7 patients were grade II.

The surgical protocol includes preoperative planning based on orthogonal radiographs, closed indirect reduction combined with percutaneous screw fixation of the intra-articular component, which is followed by 3D alignment of the limb in coronal, sagittal and transverse planes and culminates in placement of a LEP along the anteromedial aspect of the tibia. In the presence of sufficient bone healing, full weight-bearing (FWB) of the limb is allowed for a month with the plate left "in situ". In the absence of patient complaints, 4 weeks after controlled-free walking with FWB - without crutches and after final orthogonal X-rays, the plate is removed without anesthesia in an outpatient setting. The candidate has inspired the creation of a computational simulation model with a scientific team at AO Research Institute Davos. Finite element analysis (FEA) is the simulation of a physical phenomenon or model

using a numerical technique called the finite element method (FEM). The method helps to find weak points and areas of stress and strain distribution. In the present work, a virtual model based on the CT scan data of a real patient from the pilot study was created to investigate the biomechanical parameters of interest: construct stiffness, interfragmentary motion and strain at fracture site - the degree of longitudinal deformation in three different implant configurations with different plate-bone offset corresponding to thick and thin soft tissue envelope. In the virtual model of UPTF externally fixed with LISS DF plate, the stiffness of the simulated structure decreases with increasing plate-bone offset. The interfragmentary motion was lowest in the simulated construct with 2 mm offset and was highest in the construct with 32 mm offset. In analyzing the results, we can assume that the construct with plate-offset bone in the range of 22-32 mm can provide conditions for secondary bone fusion with callus formation under partial limb loading. With full loading, a plate-to-bone distance of 22 mm to 32 mm does not provide the necessary optimal relative stability and there is a serious risk of nonunion. Based on computational model, Dr Makelov summarized that: "one-staged locked external stabilization in unstable proximal tibial fractures with simulated thin and thick soft tissue coverage, creates favorable biomechanical conditions for callus formation with values of longitudinal strain in the fracture zones that do not exceed 10% could provides optimal relative stability necessary for natural bone healing under controlled PWB in the early postoperative period.

The **statistical analyses** are well selected, comprehensive and correctly placed in a logical sequence. They provide an opportunity to illustrate the basic distribution, as well as to perform analyses and demonstrate separate groups/ mechanisms. **Chapter V** presents the statistical methods used to process and analyze the information related to this dissertation - variance descriptive analysis of all quantitative variables, parametric methods of investigation - Shapiro-Wilk test , non-parametric methods: Mann-Whitney Test, Kruskal-Wallis Test, Wilcoxon Signed-Rank Test, Friedman Test. The standard value of 0.05 was set as the cutoff value for the level of statistical significance.

The results of the study are correctly presented in **Chapter VI** in 48 pages and are supported by highly informative tabular and graphical material.

The HSS assessment performed both 4 weeks postoperatively and at the final examination showed a statistically significant increase in HSS regardless of age under or over 50 years, fracture proximity and complexity, and soft-tissue damage according to Gustulio.

The HSS assessment performed both 4 weeks after surgery and at the final examination showed a statistically significant increase in HSS regardless of age under or over 50 years, proximity and complexity of the fracture, and soft tissue damage according to Gustilo.

Final knee extension range of motion did not change statistically significantly with age under or over 50 years, fracture proximity and complexity, and soft tissue damage by Gustilo.

Final knee flexion range of motion was statistically significantly greater in patients under 50 years of age compared with patients over 50 years of age, and was also statistically significantly greater than that measured 4 weeks after surgery. While the knee flexion range of motion measured 4 weeks after surgery was statistically significantly smaller in patients with proximal fractures compared with patients with distal fractures, the final range of motion was not statistically different between these two groups but was statistically significantly larger than that measured 4 weeks after surgery.

Final knee flexion range of motion was not statistically significantly affected by fracture complexity and the degree of soft tissue damage as assessed by Gustilo.

The final AOFAS score of the ankle joint did not change statistically significantly with age less than or more than 50 years, proximity and complexity of fracture, and soft tissue damage by Gustilo.

Ankle joint plantar flexion range of motion measured 4 weeks after surgery was statistically significantly greater in patients under 50 years of age compared with patients over 50 years of age, but final ankle joint plantar flexion range of motion was not statistically different between the two age groups.

The final range of motion in plantar flexion of the ankle joint was not statistically dependent on the personality and complexity of the fracture and the degree of soft tissue damage.

Final range of motion in dorsal ankle joint flexion was not statistically dependent on patient age, localization and complexity of fracture, and the degree of soft tissue injury.

Fracture healing time was not statistically affected by age and localization of fracture. Fracture complexity was significant, where simple fractures heal significantly shorter than complex fractures.

The mean operative time was 33.2 minutes, and there was no statistically significant difference between the fixation times of proximal and distal fractures, or between simple and complex fractures. Compared with the mean operative time of 45.8 minutes in the other four studies, it is indicative of the operative experience of the present team and the consistency in the application of the WEVS.

The mean healing time was 21.1 weeks, and there was a statistically significant difference between the healing times of simple and complex fractures. Healing occurred in 100% of cases. The reason for the high rate of bone healing using WEVS is due to the provision of adequate IFA, and the fact that the method is sparing to the soft tissues, periosteum and blood supply in the injured area.

Operative time was not statistically different according to age under or over 50 years, fracture personality and complexity, and soft-tissue damage by Gustilo.

In the following **Chapter VII**, in a volume of 28 pages, a correct discussion of the own results is carried out, compared and supported by data from the literature. This chapter is the most creative part of the dissertation. It convincingly demonstrates Dr. Makelov's preparation of the issues presented and understanding of the shortcomings of his own research.

Although a similar technique of external plate fixation was first reported by Ramotowski in Poland several decades ago, no experimental study has been reported to clarify the biomechanical issues related to the size and magnitude of the fracture defect (gap), the distance (offset) of the plate-bone complex, and the values of the parameters that allow achieving a state of relative stability combined with early partial loading of the limb. This is what the author of the present study does - he investigates the degree of interfragmentary motion and the values of longitudinal strain in the fracture zone by computer simulation using the finite element method.

The limitations of the present study - small number of patients, relatively short follow-up period and lack of a control group of patients - are sincerely shared in **Chapter VIII**.

Chapter IX consists of 5 logical conclusions with which I absolutely agree. Here is also the conclusion regarding the OLES, which in a concise form synthesizes the thesis and gives a complete form to the development. The direction of evolution of healing methods is towards minimizing damage to soft tissue and bone from surgical accesses, and to periosteum of bone, from contact with the implant. Another major trend is the transition from absolute to relative biologic fracture stabilization and, consequently, from primary to secondary bone healing and the predominance of concern for soft tissue preservation and bone circulation over the achievement of "ideal" bone fracture reposition and allination.

The disadvantage of the OLES is the inability to adjust the position after locking the screws in the plate, but the advantages are predominant - minimum soft tissue damage; the low profile of the external fixation plate makes it more comfortable for the patient to tolerate; one-stage treatment without immobilization of adjacent joints with the possibility of early joint mobilization; and disassembly in the outpatient setting without anesthesia.

In **Chapter X**, the bibliography is arranged alphabetically and the references are listed uniformly.

On the dissertation topic, Dr. Makelov presented 3 publications (all of them met the criteria for real publications). They were published in peer-reviewed journals meeting the Minimum Requirements for Area 7. Health and Sport, according to the Regulations for the Implementation of the Law on the Development of Academic Staff in the Republic of Bulgaria of 2018. They contain individual parts of the developed material. Separately, the dissertation has also been published in a journal with an IF as required in Annexes 3 and 4 of the RMPNSWASMUS.

The 62-page abstract of the dissertation submitted to me is formatted as required in Appendix 8 of the RMPNSZAMUS.

The only critical remark is regarding the positioning of the explanation of the created three-dimensional virtual biomechanical model by the finite element method in the Results section and not in the Materials Methods section.

In conclusion, the dissertation submitted to me for review shows the ability of the dissertator to pose a scientific thesis, methodology for its solution, his ability to select and process material, as well as to make statistically reliable conclusions on a topical and specific topic - **“ONE-STAGED LOCKED EXTERNALIZED PLATING FOR THE TREATMENT OF UNSTABLE PROXIMAL METADIAPHYSEAL TIBIAL FRACTURES ”**. The dissertation fully complies with the qualitative and quantitative criteria set out in the requirements for a dissertation for the degree of Doctor of Education and Science of MU Varna. Due to this, and due to the fact that all the presented clinical material is almost entirely personally performed by Dr. Makelov surgical treatment, as well as the valuable scientific development of simulation software model, I believe that the dissertation Dr. Biser Alexandrov Makelov meets the requirements for awarding the scientific and educational degree "Doctor", field of *medicine*, scientific specialty *orthopaedics and traumatology*, which I offer to the esteemed jury formed by order R-109-511/29.11.2021 of the Rector of MU-Varna, to pronounce POSITIVE for his award.

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3 January 2022, Sofia



