

REVIEW

On dissertation written by **Dr. Stoyan Zhelyazkov Hristov, MD**

For acquiring the educational and scientific degree PhD / `Doctorate`

Dissertation topic: **Operative treatment of proximal humeral fractures by locking plate with or without augmentation- comparative analysis**

Reviewer: **Prof. Dr. Nedelcho Tzachev, MD**

Head of Department for Orthopedics, Traumatology, Reconstructive Surgery and Rehabilitation at Military Medical Academy Sofia

By order of the Executive Director of University Multi-disciplinary Hospital for Active Treatment and Emergency Medicine "N. Pirogov" EAD No. RD 523 of 14 February 2022, I was appointed as a member of the Scientific Jury and by decision of the latter (Minutes No. 1), I was appointed to present the review on the dissertation paper of Stoyan Zhelyazkov Hristov, MD, free doctoral student at the Scientific Council of University Multi-disciplinary Hospital for Active Treatment and Emergency Medicine "N. Pirogov" EAD, in the field of higher education 7. "Health and Sports" in professional field 7.1 "Medicine" and doctoral program "Orthopaedics and Traumatology".

Dr. Stoyan Hristov was born on 28.07.1971 in Burgas. He has acquired his secondary education at Academic Nicola Obreshkov high school for Natural sciences and Mathematics in Burgas. In 1995 he graduated Human Medicine at Medical university in Varna. After a competition in 1997 he was enrolled as a resident in Orthopedics and Traumatology at UMHATEM Pirogov, in former 4th Traumatology clinic. In 2002 he mastered his specialty exam. He started work at Department for Orthopaedics and Traumatology at Multiprofile hospital for active treatment in Burgas, where he has been working since then. During this time -frame he got one year working experience in Germany / 11.2003- 10.2004/ and two years in UK / NHS 6.2014- 5.2016/.

Dr. Stoyan Hristov has participated in a great number of courses in Bulgaria and abroad as well and has obtained certificates in specialized activity in ultrasound diagnostic of musculoskeletal system, joint replacement surgery and arthroscopy. During his stay in Germany he attended a Course in open and arthroscopic shoulder surgery (Ludwig-Maximilians Universitaet-Muenchen, Germany) and in UK - Arthroscopy Course and Primary and revision hip and knee replacement course (Royal College of Surgeons - London, UK). Dr. Hristov has undergone a four module education - in 2007 and 2009 at EPOS - Instructional Courses on Paediatric Orthopaedics - Speising Hospital/ Vienna, Orton Hospital/ Helsinki, Timone Hospital/ Marseille, Dana Hospital/ Israel. Dr. Hristov has attended

The topic in the area of surgical treatment of proximal humeral fractures has undergone serious discussions and corrections in the last twenty years. That's related to the changes in fracture pathology, increasing of patients' age as well with the applying of technologically new models of osteosynthesis tools such as the locking plates /LP/. Indications for operative treatment of such fractures have significantly increased. However, results show a high percentage of complications, up to 49% according some authors. Some of them are improper bone healing (mal-union), avascular necrosis, screw penetration, subacromial impingement and infection. This indicates that a stable fixation of proximal humeral fracture (PHFx) in cases with complicated morphology is hardly achievable. The augmentation of LP osteosynthesis in proximal humeral fractures is a reasonable alternative, providing better mechanic stability of the construction. This theory has developed through practical experience. **Gardner et al.** is the first to promote the strengthening of the medial support via screws. **Ponce et al.** prove that medial comminution reduces by 48% the average load, required for the synthesis de bricolage. Meanwhile applying of calcar screws enhances the construction stability by 31%. Later on the usage of auto – and allografts was more and more promoted as well the filling of the metaphyseal defect with bone cement. It was proven

In accordance with order Nr. RD-26-52/04.01.2019 by the director of UMHATEM Pirogov Dr. Hristov has been appointed an individual PhD candidate on individual plan in specialty Orthopaedics and Traumatology. The dissertation topic has been discussed, voted and referred for defending by Primary scientific unit in Orthopedics and Traumatology at UMHATEM Pirogov. After discussing the topic, members of the Scientific Council of the hospital decided that the topic is dissertation worthy, meets the necessary contribution criteria and can be defended in front of a competent jury.

Dr. Hristov has been holding membership of following scientific societies: Bulgarian doctor's union, Bulgarian Orthopedics and Traumatology Association, AO Trauma Bulgaria, SICOT, EFFORT, EPOS, ESTES. Dr. Hristov speaks English, German and Russian.

Dr. Hristov has been occupying the position of Head of Department for orthopedics and Traumatology since 06.07.2017 after winning the competition at UMBAL Burgas.

Dr. Hristov has personally contributed for the good practice development in the area of orthopaedics and traumatology in Burgas city. After starting his work as specialist at MBAL Burgas he successfully implemented the ultrasound screening of hip joints within newborns (2005), the Ponseti method for treatment of clubfoot in children and elastic intramedullary nailing in cases of diaphyseal fractures in children. Dr. Hristov consistently applies the AO principles in osteosynthesis being actually the first specialist with such training in the region. Since end of 2019 he has been implementing reversed shoulder arthroplasty as a treatment method in the region.

specialized courses by AO Trauma: Madrid (AO Recon Masters Course with Anatomical Specimen – Periprosthetic Fractures), Graz/ Austria (AO Trauma Course – Acetabular and Pelvic Fracture Management), Barcelona (AOFAS Principles of Reconstruction Foot& Ankle) , Istanbul (Recon Endoprosthetic Course)

that fibular allograft usage doesn't completely obviate the bone defect which affects the osteosynthesis' stability.

PMMA usage for augmentation of proximal humeral fractures fills well and completely the metaphyseal bone defect and helps for the load forces' evenly distribution on the screw fixation. With this method stability is optimal and allows safer and earlier rehabilitation with lower risk for secondary dislocation and osteosynthesis failure. Present thesis represents the potential of this PMMA augmentation method in fixation with LP in patients with poor bone quality and severe fracture morphology.

The dissertation of Dr. Hristov is in volume of 132 standard pages, illustrated with 53 pictures and 41 charts. It's structured in a dissertation- typical way, adhering to the normal chapter ratio.

Bibliography includes 251 titles, only two of Bulgarian authors, working in the area of shoulder surgery.

Five scientific papers, published in Bulgarian scientific journals have been presented in connection with the dissertation paper:

1. Hristov St. "Necessary augmentation in proximal humeral fractures- when and how? ", Emergency medicine, 2020/23/1: 15-20
2. Hristov St. "PMMA augmentation technique in proximal humeral fracture fixation with PHILoS" Emergency medicine, 2020/23/1:21-26
3. Hristov St. "Improved functional outcomes in surgical treatment of proximal humeral fractures via angle stable locking plate and PMMA augmentation" Orthopedics and Traumatology, 57, 4-2020
4. Hristov St., Baltov A., Sotirov S. "Predicting of functional outcomes in operated proximal humeral fractures through artificial neural nets " BioInfoMed Conference 3rd October 2020
5. Hristov St., Baltov A., Sotirova E., Bozov Hr. "Intuition based researches for analyses of operated proximal humeral fractures " BioInfoMed Conference 3rd October 2020

The dissertation paper goal is formulated clear and accurate – to analyze the PMMA augmentation potential in operative treatment of proximal humeral fractures with locking plate. The four assigned paper tasks have been fulfilled which allows the author to evidently accomplish the dissertation goal:

1. Review and analysis of proximal humeral treatment methods.
2. Applying of the tree methods of LP fixation with and without augmentation in sufficient patient cases with comparable factors - age, fracture morphology and bone quality.
3. Comparative analysis of obtained results, complications and required secondary interventions within the tree patient groups, treated via LP, with and without augmentation.
4. Establishing of an action algorithm in patient cases with proximal humeral fracture.

First of all I would like to point out that the dissertation paper is written extremely competent by someone, who has an in depth knowledge of the raised problem.

Chapter I: Literature review includes 44 pages. The author describes in details surgical anatomy, blood supply and biomechanics of proximal humerus and shoulder joint. Causes of such injuries /MOI, imaging diagnostic technique used and PFFx classifications known in literature are explained in details as well. Indications for operative and non-operative treatment and quoted two multi-centric studies prove how discussion worthy is the decision making behavior of the orthopedic surgeon. Both most applied in praxis approaches such as deltoid-pectoral and antero-lateral, have been described and diverse fixation techniques-marked. The focus lies on LP and required augmentation.

Chapter II: Patients and methods include 17 pages. Criteria for monitored units, selection of types of fractures and excluding criteria are met. 112 patients with 114 fractures are subject of monitoring. The research includes patients with 3- and 4 – fragment fractures, treated by LP, 103 of them- women, 11- men, average age- 67 years. 13 patients are with poly-trauma and 16 of them with accompanying fracture. Pre-operative planning includes complex assessment of patient's general status and her/ his expectations regarding chosen method of treatment, mineral bone density and fracture characteristic in accordance with performed X- rays and CT and prognosis of humeral head vitality. CT is considered necessary for a properly assessment of fracture morphology and bone quality/osteoporosis/ - factors defining the treatment plan and necessity of augmentation and choosing its type as well. Deltoid-pectoral approach is more frequently used – in 77 patient cases. Post- operative behavior is individual shaped, considering patient's age and bone quality. No early active rehabilitation necessary except to some extend patient with intact rotator cuff and PMMA augmentation.

The complex clinical research is explained in details and takes sufficient place in the paper. It is performed according Constant-Murley score system. This method of functional assessment is based on diagnostic of a certain number of individual subjective and objective parameters- pain, every day activity (ADL), ROM and muscle strength. Another assessment tool, used for clinical follow up of operated patient is DASH/ Disabilities of Arm, Shoulder and Hand/ Score. The goal is to achieve easy self-assessment of symptoms and functional status focusing on function – something, that could be of benefit for specialists in every day praxis. The questionnaire design is focused on self-assessment of function and symptoms in patients with significant muscle- skeleton problems of upper limbs and consists of 30 questions.

Statistic methods used are up to date and correlate to achieved functional results. For statistic analyses purposes the author uses following grades and methods: Variation analysis; Frequency analysis of quantitative variables/ nominal and rank/, which includes absolute frequencies, relative frequencies / in percentage/, cumulative relative frequencies/ in percentage/; Graphics, charts, diagrams; Methods for hypothesis checking; Correlation analysis and Regression analysis.

Chapter III: Results are presented in 24 pages. Operative records include – approach, reposition, augmentation, timeframe up to operative intervention, duration of operation, average intraoperative blood loss, duration of hospitalization, fixation types and

Seven pages of the dissertation paper present a detailed description of observed complications, definition of technical and tactical mistakes, causing disturbance or impairing bone healing and functional recovery, as well conditions, requiring initially unplanned operative interventions. 63 complications within 41 patients (36%) have been recorded and in 21 patient cases complications are more than one. In patent group without augmentation 19 cases have been recorded, within group with PMMA and BA respectively 8 and 14 patients with one or more complications. Complications are of intraoperative and postoperative origin. One of the often observed complications is the loss of primary reposition with following secondary varus. Such complication is observed in 9 cases (8%), 7 of the cases- without augmentation, and two- with bone augmentation. The significance of above stated complication is defined by the fact, that it could be complicated by screw penetration and sub-acromial impingement, problems frequently requiring revision procedures.

Comparing the DASH score results insignificant advantage in patient with augmentation is established, however the difference is of no statistical significance. The results are excellent displayed by charts and photo-documentation.

A complex functional assessment of all tree group of patient has been performed. The conclusion is as follows: within patient group with augmentation there is certain advantage in regard of absolute and relative CMS where the difference is statistical significant only at the beginning –3 months after operation and in regard of relative CMS ($p < 0.05$).

The author points out the greater number of preserved reposition after twelve months in cases with bone cement augmentation and the significant changes in patient cases without augmentation. Following the same protocol of mobilization and rehabilitation we can safely assume the non- augmentation fixation as a reason for the insufficient construction stability.

I personally would be interested in obtaining information about time to X-ray exposition. For proving of bone healing are used anatomic and X-ray data. The quality of achieved reposition is assessed in all tree patients' groups, namely without augmentation, with bone autograft (BA) and with bone cement. Restoring of proximal humerus normal anatomy is registered by X-ray imaging. The aim to achieve anatomic reposition is understandable considering its importance for the final outcome. The A-P view X-ray demonstrates achieved NSA/neck – shaft angle/, GT/great tuberositas/ - reposition, more precise the distance between GT - tip and HH/humeral head/ - tip. The author believes that there is change in primary reposition when the difference in measured NSA exceeds 10 degrees. The L-view X-ray allows observing the sagittal inclination of HH and considering the HH sphericity some deviations are assumed as acceptable, since they don't affect significantly the function.

Chapter IV: Discussion chapter consists of 25 pages. In literature you can find a number of researches aiming to identify the risk factors, related to complication probability – age, sex, accompanying diseases. In this line of thinking many specialists suppose complications' increase is related to intervention postponing. **Hertel R et al** clearly states, that bone healing is related to fracture morphology, the medial hinge rupture and depends on HH perfusion. Since the delay of surgical treatment can impair vital bone structures and affect negatively the healing process, **Siebenbueger et al.** study the hypothesis about early intervention (up to 48 hours after the injury) being in advantage in osteosynthesis cases. They have observed 497 patients with proximal humeral fracture, operated by LP and without augmentation. The main results of this research states that early surgical intervention (<48h) is not correlated with reduced level of complications (loss of fixation, screw penetration and AVN). Patients with intervention between 48h and 5 days after the injury do not demonstrate a tendency in developing a complication (OR=0.8) compared to the group of patients with early intervention (<48h, OR=0.9). In contrast the longer delay of operative treatment (> 5 days) is associated with higher level of fixation loss and AVN (OR=1.6). Both augmentation techniques, topic of the present dissertation paper, are methods for enhancing the stability of the osteosynthesis construction by filling of the metaphyseal void, resulting from the proximal humeral fracture in elderly patients. The poor quality of the bone with reduced mineral density causes the condition described as "egg's shell" with deficit of the bone tissue density, required for screw fixation. All quoted researches except **Egol et al.** study report good clinical results. The advantage of BA is due to its properties for osteoinductivity and osteoconductivity, the capability to relatively swiftly to incorporate into the recipient site and revascularize. That's the reason for its higher success rate compared to allograft. We should not underestimate the fact, that it does not carry risks of transmission diseases and holds tissue compatibility. **Kim SH et al.** prove, that creeping substitution, which in its nature constitutes an increasing penetration of osteogenic tissue through the fracture site, followed by bone formation, would be much faster when using processed morcelized autograft than structured bone allograft. The author points out that as a reason for the use of cortical spongy bone chips for faster bone healing and minimizing the risk of AVN and collapse.

The BA disadvantage lies in the lack of medial support and in generally its incapability to achieve mechanic stability of the structured allograft or the dense filling around the screws. Additional disadvantage is the requirement of an additional intervention with related risks and prolongation of operative time.

Present research work states that average operative time in augmentation cases with BA is 130 min compared to the group with PMMA augmentation (68 min), which presents statistically significant difference ($p=0.0001$). The risks of persisting hematoma condition in the harvest site and eventual secondary infection should not be underestimated. Extended pain in harvest site and damage of N. cutaneous femoris lateralis of different grade add to above stated disadvantages.

The question whether to use autograft instead of bone allograft is due a discussion as well. Present research paper states primary the fact that the allograft is expensive and not always existent. In addition the benefits are related to its biological properties and the fact, that the autograft is osteoinductive, easily revascularize and incorporates into the recipient site and considered low risky regarding transmissible diseases. As absolute opposite to above PMMA is bioinert as material, since it doesn't hold osteoinductive properties and does not integrate and reabsorb by the bone. It requires less time for applying, but the exothermic reaction caused by its use is considered by **Aroca M. et al.** as a possible reason for necrosis of bone and cartilage above with possible fixation failure. The author pays attention to **Blazejak et al.** research, according which possible temperature could reach approx. 38.3° - 43.5° degrees.

In chart 34 the author compares the results from his target group with PMMA augmentation to results from other target groups. In above stated target groups PMMA is used for augmentation of screw tips aiming for better anchorage in osteoporotic bone and reducing the micro-movements in the contact screw-bone interface. Based on recorded results the author believes that patients with PMMA augmentation have more stable osteosynthesis construction and the started early mobilization of operated limb allows better ROM in early periods to be achieved. Comparing the recorded number of complications in the target group for the follow up period we establish, that 32% of them are observed in patients with BA and 14% in patients with PMMA. In addition 34% of patients with complications belong to subgroup with BA (n=14) compared to 20% from the subgroup with PMMA (n=8).

In two cases a secondary varus has been observed (8% for the BA subgroup) and in another two cases (8%) with bone augmentation – secondary screw perforation. No such complications have been observed in cases with cement augmentation. Regarding AVN complications two cases (8%) are recorded in PMMA group and 3 (12%) in BA group. Currently two secondary operative interventions of two cases from BA group have been performed and not a single case from PMMA augmentation group. Complication, typical for BA subgroup is extended pain in harvest site, something than can not be observed in PMMA group for understandable reasons. Above stated complications could be related again to more stable osteosynthesis in PMMA subgroup and following reposition preservation and particularly of NSA (statistically significant difference between indexes, measured 12 months postoperatively, $p=0.011$) – unavoidable factor for final functional outcome and complication frequency.

Chapter V: Chapter Conclusion focuses on the fracture morphology specifics in tree- and four- fragments fractures. Difficulties in anatomic restoration arise from additional comminution in high-energy fractures or poor bone quality in elderly patients with low-energy fractures and manifested osteoporosis. These circumstances increase the requirements regarding the osteosynthesis stability and focus our attention on augmentation potentials. Keeping in mind comparable techniques, recovery, functional result and complications in the tree subgroup of patients with proximal humeral fractures the author

1. The indications for augmentation in PHFx treatment and clinical and biomechanical aspects of augmentation by bone cement have been analyzed through detailed literature review.
2. For the first time in Bulgaria cases of PHFx, treated by LP and augmentation with PMMA in the area of metaphyseal void have been purposefully subject of observation and research.
3. The potential PMMA augmentation to be applied in bone-preserving operations of PHFx has been justified based on middle-term results.

I agree in full with **accomplished contributions**, related to present dissertation paper:

1. Construction stability by PMMA augmentation is better and reduces the risks of penetration and varus secondary fracture dislocation.
2. Patients with augmentation achieve faster and better functional result.
3. Our results support the argumentation, that PMMA augmentation could replace BA as treatment method based on brief operating time ($p < 0.01$) and reduced percentage of complications. We recorded better CMS & DASH score compared to results achieved by BA augmentation and the difference is of statistical significance 3 and 6 months after operation ($p < 0.05$)
4. Through analysis of complications and achieved function we proved the importance of age and dynamic of NSA as prognostic factors and managed to find out correlation dependency and positive correlation coefficient between measurements of postoperative NSA and functional outcome, expressed by CMS, $p = 0.0292$, $a < 0.005$.
5. During the research period and based on recorded results we developed an action algorithm for PHFx treatment. We aim to optimize and facilitate the approach to patients in order to minimize complications in treatment and thus accomplish better functional outcome.

I agree in full with conclusions drawn:

The research has established that PMMA augmentation in proximal humeral fractures with bone deficit ensures better treatment results than treatment by LP only and comparable or better results that treatment by LP and augmentation with bone autograft. The author concludes that keeping in mind the dynamic implementation of primary arthroplasty in proximal humeral fractures in elderly patients with advanced osteoporosis, the treatment by LP with augmentation is reasonable choice of treatment algorithm after a careful selection of patients and precise assessment of fracture morphology and risk factors regarding expected complications.

This statement is confirmed by achieved functional outcomes and analysis of postoperative complications distribution. Based on achieved results the author proves age validity as prognostic factor in regard of complications and functional recovery. Another factor of statistical significance is the quality of NSA restoration as prognosis tool for functional recovery.

believes, that augmentation in certain extend neutralizes the main disadvantage of the LP, namely longer working lever. In his opinion stress reduction on proximal humerus medial wall enhances primary stability of the fixation while augmentation additionally compensates for poor bone quality and distributes the load over the entire screw length.

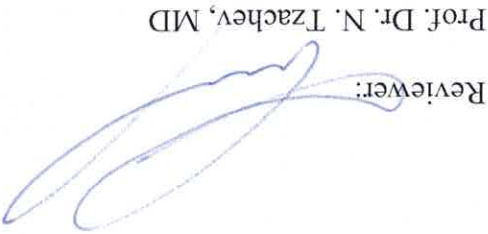
4. Results, recorded during PPHx treatment without and with both methods of augmentation of the osteosynthesis by LP, have been compared and analyzed.
5. Using recorded data we demonstrate the better functional and X-ray results in PPHx cases, operated by LP and augmentation.

CONCLUSION: In my opinion the dissertation paper of Dr. Stoyan Zhelyazkov Hristov on the topic **“Operative treatment of PPHx by locking plate, with and without augmentation-comparative analysis”** in its relevance, research volume and contribution significance fully meets the requirements of the Law on Development of the academic staff in Republic of Bulgaria and Regulation of Medical University of Sofia for its application.

Based on above stated I give my positive assessment and suggest the honorable members of the Scientific Jury to award Dr. Stoyan Zhelyazkov Hristov the **educational and scientific Ph. D. degree.**

11.04.2022

Reviewer:



Prof. Dr. N. Tzachev, MD