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ACTA ORTHOPAEDICA ET TRAUMATOLOGICA HELLENICA

HELLENIC ASSOCIATION
OF ORTHOPAEDIC SURGERY
AND TRAUMATOLOGY

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Omirou 29, Peta Saronikou, Attica, Greece, 190 01,
tel.: +30 22994 40962, fax: +30 22990 66029,
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INSTRUCTIONS TO AUTHORS

1. Scope

"Acta Orthopaedica Et Traumatologica" is the official journal of the Hellenic Association of Orthopaedic Surgery and Traumatology, first published in 1948. This revived edition of Acta Orthopaedica Et Traumatologica, published in English, aspires to promote scientific knowledge in Orthopaedics and Traumatology worldwide. It is a peer-reviewed Journal, aiming at raising the profile of current evidence-based Orthopaedic practice and at improving the scientific multidisciplinary dialogue. Acta Orthopaedic Et Traumatologica Hellenica presents clinically pertinent, original research and timely review articles. It is open to International authors and readers and offers a compact forum of communication to Orthopaedic Surgeons and related science specialists.

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If there is no conflict of interest, this should be stated in the manuscript before the Reference sec-

tion as follows: "The authors declared no conflicts of interest".

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- **Case Reports:** Reports on new or very rare clinical cases on Orthopaedics, Orthopaedic Pathologyand Trauma, new diagnostic criteria, new therapeutic methods with proven result. Maximum 1,500 words, 10 references and 6 figures. Abstract up to 100 words.
- **Letters to the editor:** Communication to the editor is welcomed and will be published if they offer pertinent and/ or constructive comment on articles published in the Acta Orthopaedica Et Traumatologica Hellenica. Letters are published at the discretion of the Editorial team and should be received within three months after on-line publication of an article. Following acceptance, letters will be sent to authors for response. Letter communications should include text of no more than 500 words, up to 2 figures and 10 references, without any abstract or keywords and a maximum of 3 authors.

9. Manuscript organization

A manuscript must contain the following parts for submission:

- *Cover letter:* Each manuscript needs to be accompanied by a cover letter signed by the corresponding author on behalf of the rest of the authors stating that the article is not under consideration in another journal. In case of article resubmission a point-by-point answer to the reviewer's comments needs to be submitted with the cover letter.
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- *Measurement Units:* All measurements should be mentioned in international units (SI). The full stop should be used as a decimal (i.e. 3.5 cm). Spaces should be added around the plus/minus symbol (i.e. 13.6 ± 1.2). There should not be any spaces around range indicators (i.e. 15-20) or equality/inequality symbols (i.e. r=0.37, p<0.005).

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All figures and tables need to be cited in text consecutively in the order in which they appear in text into brackets and in Arabic numbers: i.e. (Fig. 1) and (Table 1). Figure parts need to be identified with lower case letters, i.e (Fig. 1a).

Figures need to be of high quality. Vector graphics, scanned line drawings and line drawings need to be in bitmap format and should have a minimum resolution of 1,200 dpi. Halftones (photographs, drawings or paintings) need to be in TIFF or JPEG format, up to 174 mm wide and up to 234 mm high and in minimum resolution of 300 dpi.

Patient anonymity should be ensured. All identifying data (name, identification numbers, initials) must be removed from text, images and tables. If it is mandatory for a patient's face to be included in the manuscript, the eyes should be sufficiently masked. If there is a possibility that a patient may be identified from a photograph or relevant legend and text, the patient's written consent should be submitted.

A figure caption and a table caption need to be added in the figure and table section respectively for each figure and table.

Tables should appear at the end of the main document, numbered in Arabic numerals, each on a different page. Each table should have a title describing its content. Abbreviations appearing in the table need to be explained in a footnote. All table columns must have a subhead that describes the type of data included in the column.

11. References

The accuracy of references is the responsibility of the authors.

References need to be cited in the text in the order in which they appear. The numbering needs to be in Arabic numbers and placed in the respective areas of text into square brackets i.e [1].

References that have not been published at the point of submission need to cited with the respective DOI (digital object identifier) number given for online first articles.

All authors (surnames and initials of first name) should be listed when they are three or fewer. If authors are more than three, the first three authors should be listed, then 'et al.' needs to follow the name of the third author.

When a book chapter is cited, the authors and title of the chapter, editors, book title, edition, city and country, publisher, year and specific chapter pages should be mentioned.

For Online Document, the following should be mentioned: authors (if any), title of page, name of institution or owner of Web site; URL; dates of publication, update, and access.

Reference examples:

■ Journal article:

Trianafyllopoulos IK, Lampropoulou-Adamidou K, Schizas NP, et al. Surgical treatment of acute type V acromioclavicular joint dislocations in professional athletes: An anatomic ligament reconstruction with synthetic implant augmentation. *J Shoulder Elbow Surg* 2017; doi: 10.1016/j.jse.2017.05.032 Epub 2017 Jul 21.

or

Papaioannou NA, Triantafyllopoulos IK, Khaldi L, et al. Effect of calcitonin in early and late stages of experimentally induced osteoarthritis. A histomorphometric study. *Osteoarthritis Cartilage* 2007; 15(4): 386-95.

■ Book chapters:

Triantafyllopoulos IK, Papaioannou NA. The Effect of Pharmacological Agents on the Bone-Implant Interface. In: Karachalios Th. (ed). Bone-Implant Interface in Orthopaedic Surgery. Springer – Verlag, London 2014, pp 221-237.

■ Online document:

National Institute for Health and Care Excellence. Fractures (Complex): Assessment and Management. Available via www.nice.org.uk/guidance/ng37. Published Feb 2016. Updated Sept 2017. Accessed January 2014.

12. Review of manuscripts

Acceptance of manuscripts for publication is decided by the Editor, based on the results of peer review. Authors need to make proof corrections within 72 hours upon pdf supplied, check the integrity of the text, accept any grammar or spelling changes and check if all the Tables and Figures are included and properly numbered. Once the publication is online, no further changes can be made. Further changes can only be published in form of Erratum.

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LETTER TO THE EDITOR

John K. Dimitriou
18 Dimokritou Street
Athens 10673
Email: johndimitriou@hotmail.gr

5th February 2018

To: The Editor Acta Orthopaedica et Traumatologica Hellenica

Dear Editor,

In the paper entitled "Spine Surgery at the Penteli Children's Hospital from its foundation until nowadays" by K. Markatos et al., in the Greek version of the manuscript, the authors state that the first spinal fusion using the Harrington rod in Greece took place at their institution in 1973 [1].

I would like to comment on this statement and clarify that the first ever Harrington procedure in Greece was performed in July 1972 at the "Aghia Sophia Children's Hospital" in Athens by myself and my team as published in 1976 in the official journal of the Hellenic Association of Orthopaedic Surgery and Traumatology [2].

I appreciate that this official letter to the Editor is far beyond the three-month period after the on-line publication of the article but the delay is due to the delayed circulation of the printed version of the paper at the time as well as our email correspondence since January 2017.

Thank you
Sincerely,

John K. Dimitriou
Paediatric Orthopaedic Surgeon – Spine Surgeon
Former Clinical Director of the Paediatric Orthopaedic Department
Aghia Sophia Children's Hospital, Athens, Greece

REFERENCES

1. Markatos K, Petra M, Korres D et al. Spine Surgery at the Penteli Children's Hospital from its foundation until nowadays. Acta Orthopaedica et Traumatologica Hellenica 2016; 67(1):4-6.
2. Dimitriou J, Cavadias A. Results of Surgical Treatment in 17 cases of scoliosis. Acta Orthopaedica et Traumatologica Hellenica 1976; 27(1):2-11.

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BASIC SCIENCE

The role of muscle tissue in the homeostasis and development of a joint

Alexandros M. Vasilakis, Ioannis K. Triantafyllopoulos

Laboratory for the Research of Musculoskeletal System
Medical School, National & Kapodistrian University of Athens, Greece

ABSTRACT

The articular joint as an "organ" is interlinked with other tissues via metabolic and endocrine pathways and interacts via vascularization with muscle, adipose, nervous tissue and the circulatory system. In this review article, the mechanical action of muscles on the joint is analysed as well as the biological and endocrine effect of muscle tissue on joints metabolism and homeostasis. Pathological conditions such as degenerative osteoarthritis and inflammatory arthritides are also explained through pathways related to sarcopenia and obesity.

Mechanical load is an important factor in cartilage homeostasis. Muscle tissue has the ability to distribute mechanical stress in a joint. When mechanical stress is applied onto the cartilage, physical, electrochemical and biological phenomena occur through hydraulic pressure changes, fluid flow, osmotic pressure, diffusion and changes in the concentration of extracellular molecules, ions and pH. Furthermore, chondrocytes have mechanical stress receptors such as integrin receptors, connexins and Ca^{2+} ion channels, which induce the production and function of collagenases and aggrecans in the cartilage. It has also been found that low-intensity circular loading in joint prevents the production of inflammatory factors that induce articular cartilage catabolism. The role of proprioception through the muscular spindle regulate the function of the muscles around the joint providing articular stability through protective contraction.

Skeletal muscle, in addition to its basic function in motion, stance and stability of the body and joints, has a second role as an endocrine organ. Myokines belong to the family of cytokines. They are small peptides produced in muscle tissue either during normal conditions or in exercise and induce autocrine, paracrine and endocrine activity. The study of the role of myokines in the joint is recent and mainly focus on their action in the bone and subchondral bone. Some myokines have a negative effect on subchondral bone metabolism, such as IL-6, myostatin, activin and ciliary neurotrophic factor (CNTF). Other myokines have anabolic activity on bone metabolism such as IL-15, IGF-I, FGF-2, follistatin, and irisin. Finally, muscle contraction in fetal life, both biochemically and morphologically, determines joint growth, in terms of structure of articular surfaces, proliferation and differentiation of chondrocytes, expression of extracellular matrix components.

KEY WORDS: Muscle tissue; Myokines; Joint; Homeostasis; Osteoarthritis

CORRESPONDING AUTHOR, GUARANTOR

Ioannis K. Triantafyllopoulos, MD,MSci,PhD
Ass. Professor of Orthopaedics, Laboratory for the Research of Musculoskeletal System, Medical School, National & Kapodistrian University of Athens, Greece
ioantria@med.uoa.gr

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Introduction

A skeletal muscle during contraction transmits mechanical loading onto the articular cartilage, inducing dimensional, hydraulic changes and finally structural changes in the extracellular matrix participating in the cartilage homeostasis. Muscular system is involved in normal homeostasis of the joints, their formation in fetal life, their metabolism, as well as in inducing pathological conditions such as degenerative osteoarthritis and inflammatory arthritis. This effect of the muscular system on articular cartilage, subchondral bone and synovial tissue occurs in two ways: through the biomechanical changes and mechanical loading and through its biological and endocrine action.

The role of muscle tissue in joint development

The interaction of muscle, bone and synovial tissue commence during fetal development during osteogenesis and myogenesis. Mesenchymal stem cells (MSCs) are multipotent stromal cells that differentiate, with appropriate stimuli, in analogous cell lines to produce osteogenesis, chondrogenesis or myogenesis. Muscle tissue through mechanical forces affects the growth of long bones by acting in the physeal growth plate. Regarding the morphology of the peripheral bones, it appears that during the final embryonic development of the skeleton, muscles exert loads by either traction or compression and affect the ossification centres. These loads play role to the development of the final architecture of the joints, shape, cavities, articular cartilage and apophyses (tubercles).

Two different stages, one creating an intermediate zone (interzone) and the other forming a cavitation perform the development of the joint. It appears that mechanical irritation through muscle contraction affects both stages of joint development. In 1966, studies on chicken embryos [1] found an association between the muscular system and the formation, shape and size of the cavities of the joints. In other studies [2,3] in mutant mice without muscles, the absence of hip, elbow and carpal joints was observed. Similar research was also performed in chick embryos where pancuronium bromide and decamethonium bromide were injected as muscle paralytics and absence of joint development, reduction of hyaluronic acid, reduction of expression of collagen XII and FGF2 in cartilage was observed [4].

Similarly, fetal chicken knees treated with decamethonium bromide were studied histologically, analysed by the expression of specific molecules and genes and finally compared with 3D digital imaging of the knee joint. Paralysed embryos found to have reduced height and width of the femoral condyles, narrower femoral notch, more flat and shallow articular surfaces and morphological simpler joints. Cellular proliferation and differentiation were affected histologically with changes in the articular structure. [5,6]

In another experimental research, the effect of muscle contraction on the development and maturation of the hip joint was studied. [7] Botulinum toxin A was inserted intramuscularly to newborn rats by paralysing gluteus and quadriceps muscles and hip joint was studied retrospectively by micro-tomography scanning (μCT scan). The results were evident in rats with insufficient contraction in hip flexors and hip extensors, which act as stabilizers, showing dysplastic hip, hypoplastic triradiate cartilage of acetabulum and hypoplastic femoral head.

It appears that mechanically irritated cells induce the expression of certain genes and molecules involving in joint development. These genes are called mechanosensitive or mechanoresponsive and have been studied in cell cultures, however, in vivo studies are still limited [5]. (**Table 1**)

Although the regulation of joint development by the muscular system appears to be experimentally proven, there are still some unclear fields. One such unclear field is the theory that mechanical stimuli regulate the size of the progenitor cell pool necessary for joint formation. The Wnt / β-catenin signalling pathway is the key mechanism of early joint development, chondrocyte differentiation and inhibition of chondrogenesis. Experimentally it appears that muscle contraction induces activation of β catenin. However, it does not explain clearly the mechanism, as in mice models with absence of muscle tissue, some joints remained intact (knees, fingers), while others like the elbow were absent in the embryos. These findings suggest that other mechanisms may also be involved in fetal development of the joints. [2-5].

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TABLE 1 *Mechanosensitive genes (modified by Rody et al. [5])*

Genes	Function	Evidence
BMPs	Chondrocyte maturation and proliferation	In vivo
CD44	Formation of joint cavity	In culture
INTEGRIN β1	Formation of interzone	In scaffolding
PTHLP	Chondrocyte proliferation	In culture
FGF2	Joint cavity formation, chondrocyte maturation	In vivo
FGFR2	Proliferation of osteoprogenitor cells	In culture
COL2A1	Matrix component, chondrocyte proliferation index	In vivo
TNC	Cartilage matrix component	In vivo

The mechanical effect of muscle tissue in joint

Mechanical stress and joint homeostasis

The articular cartilage is biphasic; it has a solid phase that depends on the structure of the matrix and a liquid phase that depends on the movement of the water inside it. During loading and movement of the joint, water is transported to and from the synovial fluid through the diffusion of macromolecules, thus affecting their metabolism and concentration. A three-phase theory has also been proposed, in which a third parameter is introduced, that of ionic diffusion and flow and their electrokinetic effects [8]. Thus, the interaction of these three phases (solid, liquid and ionic) through mechanical load, shear and compressive forces, stress and strain deformation of cartilage, osmotic and hydrostatic fluid pressure, cartilage viscoelasticity, flow and diffusion of molecules and ions synthesize the theory of the three-phase model of articular cartilage. [9]

Chondrocytes also have mechanoreceptors that detect mechanical stress. Such mechanosensitive receptors are integrin receptors, connexins and Ca^{2+} ion channels which, on the stress stimulation, induce the production of collagenases and aggrecans. Mechanical joint stimulation increases the concentration of aggrecan and reduces the expression of MMP-3 (matrix-metalloproteinase-3) in chondrocytes. The activity of MMPs and ADAMTS is also controlled by chondrocytes with tissue inhibitors of metalloproteinases (TIMPs). Aggrecan is an extracellular proteolytic enzyme belonging to the family of metalloproteinases ADAMTS (A Disintegrin And Metalloprotease with Thrombospondin Motifs) and its role is to break down the aggrecans of proteoglycans (PGs).

The role of Integrins

Significant mechanoreceptors for the transmission of mechanical signals to chondrocytes are the integrins [10, 11]. They carry mechanical signals between matrix and chondrocytes. Various types of integrins are connected with collagen II, fibronectin, osteopontin, vitronectin and other matrix proteins. The activation of many signaling pathways, such as the MAPK pathway, p38, SAPK, and ion channel function, is mediated by initial stimulation of the integrins [12]. Their action is related to the cellular connectivity of the chondrocytes, their survival, their differentiation and development as well as the production of the matrix. The linkage between chondrocytes and matrix proteins via integrins appears to be regulated by IGF-1 and TGF and the opposite.

The role of Ion channels, TRPs and osmotic pressure

Chondrocytes respond to changes in osmolarity when moving the fluids through their membrane and changing their volume. The membrane contains protein water channels (Aquaporins - AQP) that al-

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low the water to move based on osmotic gradient. The regulation of Ca^{+2} and Na^{+} ions is done through ion channels such as: VGSC (voltage-gated sodium channels), VGCC (voltage-gated calcium channels), ENaC (epithelial Na channels) and Na^{+}/Ca^{+2} pumps. These ion channels are mechanical signals for chondrocytes by regulating cell volume, intracellular calcium concentration and membrane polarity, thereby determining gene expression [11]. TRPs (transient receptor potential) are Ca^{+2} channels in the chondrocyte membrane. They are a link between mechanical, osmotic, hydrostatic stimuli and cellular metabolism and differentiation in homeostasis of both normal and osteoarthritic cartilage.

The role of extracellular hydrostatic pressure

During walking, hydrostatic pressure varies cyclically between 0.2 MPa and 5 MPa. This change appears to affect chondrocytes in the matrix composition. The possible involving mechanism is the deformation of the morphology and volume of cartilage exerted via the cytoskeleton and their Golgi system. In addition, hydrostatic pressure indirectly affects membrane permeability, transmembrane ion channels and osmolality, and therefore also determines the intracellular concentration of molecules and pH [10, 11].

Signalling pathways involved in homeostasis through stress stimulation

Mitogen-Activated Protein Kinase (MAPK) pathway is a mechano-inducive pathway that acts on chondrocytes through loading as described above [12]. The Hedgehog (Hh) / Smoothened (Smo) pathway contains molecules expressed in chondrocytes in response to mechanical stimuli and activate the expression of RUNX2, the aggrecanase ADAMTS 5 and Parathyroid Hormone related Protein (PTHrP). Expression of PTHrP in mature articular cartilage induces the differentiation and maturation of chondrocytes [12]. Nuclear Factor-Kappa B (NF-κB) pathway mainly regulates inflammatory and immune responses as regards differentiation and survival of chondrocytes by mediating factors such as TNF, COX-2, NO, IL, various cytokines, metalloproteinases and catabolic enzymes [12]. Wnt / β-catenin pathway participates not only in homeostasis and in development of cartilage but also in its lesions and mechanisms of osteoarthritis pathophysiology. Wnt are glycoproteins that bind to Frizzled (FZD0 receptors in the cell membrane and activate the β-catenin nuclear factors that translate specific target genes [12,13]

The role of Fibrin Growth Factors (FGFs)

FGFs (fibroblast growth factors) are a family of growth factors that have mixed activity. Two factors have been studied mainly in cartilage homeostasis, the FGF-2 (or bFGF) and FGF-18 [14]. FGF-2 is a mechanosensitive factor and is released from chondrocytes in cartilage injuries and lesions as well as in normal mechanical stimulation. It appears to act as a transducer of protective mechanical signals to the cartilage matrix by inhibiting the expression of collagenases and aggrecans (MMPs, ADAMTS). Its action is controversial though. Studies [14] report its anabolic activity and role in repairing cartilage through its effect on chondrocyte differentiation and proliferation. Conflicting studies have shown that FGF-2 exerts mainly catabolic activity on cartilage, promotes chondrocyte degeneration and fibrous cartilage synthesis, increases MMP3 and ADAMTS 4,5 and cytokines such as IL1 and TNF. In addition, it has been reported the antagonistic activity of FGF-2 by the positive effect on BMP7 and IGF-I in articular cartilage. Therefore, the effect of FGF-2 may be dependent on the force or the mode of mechanical loading (circular, static) or on the type of its receptor, so FGF-2 has sometimes protective and sometimes catabolic role in the joint.

Joint Homeostasis and Motion

The role of low intensity cyclic loading

Although the mechanisms are not yet fully clear, in vivo and in vitro studies seem to indicate the beneficial effects of motion and stress on the joint and the cartilage. Specifically, in vitro low intensity cyclic loading of the joint was found to prevent the production of inflammatory factors including the pro-inflammatory IL-1 cytokine, the TNF-a (tumour necrosis factor), NO (nitric oxide), prostaglandin PG-

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TABLE 2 *The role of muscle tissue on the onset and progression of osteoarthritis (modified by Bennel K, 2013 [21])*

OA Onset	OA Progression
Quadriceps muscle weakness may increase the risk of knee osteoarthritis (mainly women)	Controversial results, increased muscle strength may be associated with slow progression in women and patellofemoral joint
Hamstrings weakness does not seem to be associated with the onset of OA	Quadriceps, hamstrings, hip abductors weakness is associated with functional joint decline
Knee proprioception does not seem to be associated with the onset of radiological and symptomatic OA	Poor proprioception is associated with functional joint decline

E2 and cyclooxygenase COX-2. Activation of chondrocyte mechanoreceptors through a p38 kinase pathway (MAPK) inhibits IL-1 formation and prevents transcription of NF-κB. In contrast, in other animal model studies, joint immobilization results loss of proteoglycans concentration in articular cartilage by increasing MMP-3 and ADAMTS-5 as described above. [15]

The role of of static loading on articular cartilage

MAPK (mitogen activated protein kinase) signalling pathways are mechanical pathways that act on chondrocytes through compression and load. In static loading, they are activated by phosphorylation through EPK1 / EPK2, p38 kinase pathways and the stress activated protein kinase (SAPK) pathway. The effect of these processes is through WNT signaling, increasing expression of metalloproteinases MMP3, MMP13, ADAMTS-4, ADAMTS-5 and reducing aggrecan content and collagen II in the matrix of cartilage. Therefore, the raise of degradation proteins and the reduction of proteoglycan synthesis potentially leads to destruction of articular cartilage in some studies. [15]

The absorption of mechanical stress by the muscle tissue

Muscle tissue has the ability to redistribute voluntarily or involuntarily the mechanical stress and the energy that is exerted both in space and in time by discharging the joint. During the impingement phase, muscle initially plays the role of a spring, providing a non-linear deceleration and then the role of a suspension, through viscosity properties, for absorbing energy of the loading. Although many studies have focused on muscle elasticity, their viscosity has been underestimated and some studies have shown that viscous resistance to active muscle is comparable to the force of isometric contraction.

Muscle strength and arthropathy

Numerous studies have shown that there is a correlation between muscle weakness and joint cartilage damage. The problem in most studies was the accurate measurement and comparison of muscle strength among individuals as it is determined by various factors such as the length of the limb being studied (different torque), the BMI of the individuals, whether they are athletes, etc. There is a small number of studies seem to be able to have comparable results by meeting the measurement criteria and the somatometric characteristics of the individuals. Ikeda et al, [17] demonstrated that patients with knee osteoarthritis had 20-40% less quadriceps strength than healthy control groups. Also, it was found a loss of 12% cross-section of quadriceps in women with radiographic knee osteoarthritis and higher rates in advanced OA stages. On the other hand, it is not clear whether reduced muscle strength existed before the OA or possibly caused after OA due to pain, inflammation and oedema of the area. In another clinical study [18] in 280 volunteers with a 31-month average follow-up, showed that absolute quadriceps power was 18% lower in those who developed radiological signs of OA than those who did not develop such signs. Similar results, were found in a large study group of 3081 people; those with increased quadriceps strength, had a 55% reduced risk of developing osteoarthritis [19]. In experimental level, rabbits were injected with botulinum toxin A in their one-leg quadriceps to induce muscle weakness [20]. The results showed that car-

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tilage degeneration developed in the weak leg and concluded that muscle weakness may be a risk factor for osteoarthritis. A recent review of the literature [21] comparing the results of long-term studies on the role of muscle tissue in the development and progression of osteoarthritis. (**Table 2**)

Proprioception and arthropathy

During movement, stretched ligaments - through their mechanoreceptors - activate γ-motor neurons in the spinal cord and increase the tone of the fibres of the muscular spindle, making it more sensitive to the stimuli. Therefore, muscular reflexes result to muscle contraction protection against disproportionate and harmful articular loads, coordination in movement and joint stabilization in the static position.

The role of proprioception in the pathophysiology of osteoarthritis has been established by clinical and experimental studies. Eleven studies [22] of 387 osteoarthritic knees showed a significant reduction in proprioception and position sensation, by studying proprioception with different protocols. Two other studies [23] linked the severity of radiological osteoarthritis with reduced proprioception. In a clinical study of Hassan et al. [24], 77 subjects with symptomatic and radiographic knee osteoarthritis compared to normal, were found to have a reduced proprioception response, lower strength and rate of quadriceps activation in voluntary contraction. These results did not clearly answer to the question of whether the lack of proprioception is the cause of osteoarthritis or osteoarthritis causes this deficit. Significant conclusions, however, appear to be extracted from other studies [25-27] where proprioception was analysed in unilateral knee osteoarthritis. In the normal knee, a deficit in proprioception seems to be measured with the decrease in sense of movement and position. These results may lead to the conclusion that abnormal proprioception may be a risk factor for the progression and pathogenesis of osteoarthritis, but further investigation is certainly needed.

The biological effect of muscle tissue on joint homeostasis

For many years, despite the fact that interaction of muscle tissue with distant targets was assumed, the pathways were unknown. Recently, it has been found that muscle cells and satellite muscle cells, interacted with neighbouring cells by secreting molecules and their concentration depended on muscle contraction. These molecules are called myokines. They are cytokines; thus, peptides produced in the muscle tissue and exert autocrine, paracrine and endocrine activity [28-31]. Some myokines have a common origin and secretion from the adipose tissue and are called adipomyokines. The first myokine that was discovered 20 years ago was IL-6 followed by myostatin. (**Table 3**)

TABLE 3 *The most important myokines belonging to different families with different actions and targets.*

• Myostatin (MSTN)
• Decorin, (DCN)
• Activins και Inhibins
• Follistatin
• Irisin
• Interleukins IL-6, IL-7, IL-8, IL-15
• CNTF (ciliary neutrophic factor),
• BDNF (brain-derived neurotrophic factor)
• VEGF (vascular endothelial growth factor)
• FGF-21 (fibroblast growth factor)
• IGF-I (insulin-like growth factor)
• Myonectin (CTRPs)
• Osteonectin
• Follistatin-like protein-1 (Fstl1)
• Chitinase-3-like protein-1 (CHI3L1)
• Angiopoietin-like 4 (ANGPTL4)
• Secreted protein acidic and rich in cysteine (SPARC)

During or after exercise, the concentration of some cytokines and proteins in muscles appeared to be increased, by introducing the name exercise-regulated human myokines. These are IL-1,6,8,10,15, CCL, Angiopoietin-like 4 (ANGPTL4), SPARC, BDNF, Irisin, Decorin, IGF1 and many others.

The muscles are connected to bones and joints via

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ligaments, tendons, cartilage and connective tissue. Periosteum constitutes a natural filter between the two structures and contributes to the functional exchange of molecules and fluids. Experimentally, using fluorescent-labeled myokines, the periosteum has been found to be permeable for molecules of approximately 40 kDa. Myokines that fulfil this criterion such as IGF-1, interleukins and FGF are likely to diffuse through the periosteum from muscles to bone [32]. Other myokines can reach the bone and joint through vascular circulation. Factors that affect the transfer of these molecules to their target are quantity of secretion, polarity, muscle activity, age or co-existed disease.

The role of Myostatin

Myostatin (MSTN), the most common myokine, is a member of the superfamily of TGF-β proteins and is mainly expressed in muscle tissue. Myostatin is a negative regulator of muscle growth and lack of myostatin promotes muscle hypertrophy. In conditions of long-term immobility, chronic inflammation and decreased gravity, myostatin has been found to lead to loss of muscle mass. In exercise, myostatin concentration appears to be decreased. Myostatin is distributed at the cell surface receptors and common kinases with other members of the TGF-β family. In bone tissue, it appears that myostatin affects negatively the differentiation of osteoblasts. It has been found experimentally in myostatin-deficient mice that myostatin increases the differentiation of mesenchymal stem cells in osteoblasts and in vitro calcification [33]. In addition, myostatin enhances expression and activity of RANKL by regulating Smad2 of the activated T cell nuclear factor (NFATc1) leading to a raise of osteoclastic differentiation [33, 34]. Thus, in addition to the negative regulation of muscle mass, myostatin also regulates negatively bone formation and positively bone resorption, resulting to reduced bone mass.

Increased secretion of myostatin by synovial cells has been reported during rheumatoid arthritis. In an experimental study of Dankbar et al. [34] in Rheumatoid Arthritis mice, deficiency of myostatin and its inactivation with an antibody lead to an improvement in clinical arthritis and a reduction in joint destruction. Another in vitro study on synovial fluid samples from rheumatoid arthritis patients showed that the expression of myostatin and IL1-β, a major proinflammatory cytokine for the pathogenesis of rheumatoid arthritis (RA), was increased [35]. Myostatin has been shown to increase dose-dependent expression of IL1-β through signal pathways of ERK, JNK and AP-1 [35]. It therefore appears that myostatin is involved in the formation and differentiation of osteoclasts, in bone resorption and arthritic lesions of rheumatoid arthritis and it is an interesting field for future research into the treatment of clinical effects of RA on joints by targeting its inhibition.

The role of Activin and Follistatin

Activin is expressed in various tissues, among them in the muscle and bone tissue. It is a ligand of the myostatin ACVR2B receptor. Activin has been found to affect negatively osteoblastic differentiation through the BMP pathway and increase the number of osteoclasts [36]. Follistatin enhances bone metabolism and induces osteoblastic activity by signalling myostatin and activin. It substantially antagonizes myostatin or activin-induced phosphorylation of Smad2 / 3 and the ACVR receptor.

The role of Interleukins

During exercise, interleukin 6 (IL-6) levels are increased in the circulation and been expressed in type II muscle cells in response to muscle contraction. IL-6 is generally characterized as a proinflammatory cytokine and at high chronic levels is associated with the pathophysiology of rheumatoid arthritis [37]. On the other hand, the transient increase of IL-6, associated with exercise, (except that it exerts endocrine action on fat tissue by promoting fat oxidation), has anti-inflammatory activity and offers beneficial activity on bone metabolism. The anti-inflammatory activity of IL-6 may possibly be due to inhibition of TNF-α factor by IL-6 and IL-10 [37,38]. On one hand, IL-6 enhances osteoclastogenesis by stimulating RANKL secretion from osteoblasts resulting to bone resorption and it is correlated to postmenopausal osteoporosis [38]. On the other hand, IL-6 appears to raise

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the differentiation of osteoblasts in the early stages and possibly exerts osteoanabolic action.

In an experimental study [39], secreted cytokines-myokines were counted in autoimmune arthritis (SKG/Jcl) mice following continuous stimulation as exercise at the onset of the disease. Exercise increased the levels of IL-6,10,15 and reduced the secretion of TNF-α in systematic circulation. Exercise-stimulated mice had histologically reduced arthritic joint lesions, thicker articular cartilage and more chondrocyte accumulations compared to the control group. They also had a delay in the onset of the disease and a slower progression. These results show the potential anti-inflammatory activity of IL-6 and IL-10 in exercise by inhibiting the inflammatory activity of TNF-α.

IL-15 has been detected and secreted in many tissues but mainly in muscle tissue. In population of volunteers, IL-15 was elevated in muscle tissue after intensive exercise for twelve weeks [40]. IL-15 is a myokine that affects the metabolism of glucose, fat and bone tissue. The raise of IL-15 levels in both muscles and circulation seems to lead to increased bone mass and muscle hypertrophy. It is likely involved in the induction of osteoblasts depositing an organic foundation. Similar to the findings for IL-6, IL-15 has an anti-inflammatory effect through exercise in the onset and progression of rheumatoid arthritis. [39]

IL-7 secreted by muscle cells affects bone metabolism in both osteoblasts and osteoclasts. Overexpression of human IL-7 in female mice was found to increase bone mass. [41] Additionally, in bone marrow cultures, IL-7 was found to be an inhibitor of osteoclastogenesis.

The role of CNTF

CNTF or ciliary neurotrophic factor is part of the IL-6 cytokine family. It has recently been identified as a myokine along with the sCNTFR receptor and it is probably a bone formation inhibitor [42]. Specifically, in female mice, in vitro overexpression of CNTF has led to inhibition of osteoblast differentiation. Female mice deficient in CNTF showed increased bone density. Because the results were not correlated with male mice, it is likely that the mechanism would also involve sex hormones. Therefore, CNTF may be associated with osteoporosis in people who have increased sedentary life and reduced muscle activity. On the other hand, secretion from inactive muscle fibres may protect the muscles and joints from ectopic ossification.

The role of decorin

Decorin is a leucine-rich proteoglycan. It is released from the muscles after acute and chronic muscular exercise. Its secretion is associated with raised gene expression of the follistatin and MyoD. Decorin competes with myostatin activity directly binded with it. Studies show that decorin binds to type I collagen and induces collagen mineralization by osteoblasts [43]. Additionally, decorin appears to bind to TGF-β factor and enhance its activity when bound to osteoblast receptors.

The role of irisin

Irisin is a newly found myokine produced by the muscles during exercise and mechanical stress. Generally, it appears to exert a protective effect on insulin resistance, metabolic syndrome, cardiovascular disease and reduces fat tissue increasing brown adipose tissue. In the subchondral bone of the joint, irisin enhances osteoblastic activity and differentiation through the known mechanisms of Wnt / β-catenin, p38 MAPK and ERK [44]. In addition, Qiao et al, [44] has shown in vitro that irisin increases transcription factor-2, Ostrix / sp7, ALP, col1-a1, osteocalcin, osteopontin and calcium deposition in cell cultures. Irisin, besides inducing bone production, also reduces bone resorption by inhibiting the RANKL / NFATc1 pathway. An in vivo mice study found that insertion of irisin increased cortical bone [45]. Finally, in humans, it was found a correlation of level of irisin with the incidence of osteoporotic fractures in osteopenic postmenopausal women [46].

The role of IGF-I

IGF-I (insulin-like growth factor) is secreted by the muscles during mechanical loading. It is expressed to a large level by the muscles, but also by the bone, liver and systemic circulation. It has a direct effect

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on bone and muscle growth and is implicated in the pathogenesis of sarcopenia. IGF-I acts on bone remodelling by enhancing osteoblastic activity and osteoclastic absorption and is associated with achieving bone density [47]. Associated proteins with IGF (IGFBP2, IGFBP-5), inhibitors and regulatory proteins of IGF-I, are produced in the muscle tissue and potentially exert a negative effect on bone osteoblastic activity. However, because IGF-I is not specifically expressed in the muscle tissue, the role of muscle IGF-I is not clearly defined.

The role of FGF

FGF-2 or bFGF (fibroblast growth factor-betta) is produced from various tissues, chondrocytes, bone and muscle cells. In muscles, it is expressed in heavy exercise and muscular injuries. It is a growth factor involved in osteoblastic anabolic activity, cartilage and bone regeneration, chondrogenesis and fracture callus [48]. In the cartilage, it is stored in the matrix and after an injury it is released inducing cell proliferation and increases the expression of catabolic enzymes such as metalloproteinases (MMPs) and aggrecanases. Probably its paracrine effect as myokine enhances the action of FGF-2 derived from other tissues.

In an in-vitro study [49], FGF-2 was administered to cultured human mesenchymal cells. It was found that this population developed enhanced chondrogenesis. Increased levels of Sox9 protein, a transcriptional factor that activates chondrocyte genes for chondrogenesis, were found.

The role of CHI3L1

CHI3L1 or Chitinase-3-like protein 1 (YKL-40) is secreted by many tissues such as chondrocytes, fibroblasts, macrophages, hepatic, endothelial, epithelial cells, adipose tissue and others [50]. Recently, the expression and secretion of CHI3L1 by muscle cells was discovered. Muscle cell differentiation decreases its levels. Mechanical load, exercise and inflammatory cytokines increase its levels. In vitro studies in cultures of guinea pig and rabbit cells have shown that normal concentrations raise chondrocyte and synovial cell proliferation and synthesis of proteoglycans. It acts as inhibitor of cellular apoptosis, induces myoblastogenesis and participates in glucose metabolism and insulin resistance. On one hand, some studies show its anti-inflammatory activity, on the other hand, it correlates with chronic inflammatory arthritis by activating the PAR-2 receptor. Other studies report the increased concentration of CHI3L1 in osteoarthritic cartilage and characterize it as a potential marker of osteoarthritis progression. An in-vitro research [51], however, reveals the protective anti-inflammatory effect of CHI3L1 as it inhibits TNFα and IL1β and reduces the metalloproteinases MMP1, MMP3. CHI3L1 needs further research as a promising molecule.

The role of sarcopenia in the joint

The most important myokine involved in the pathophysiology of sarcopenia is the IGF1 associated with muscle growth and most probably the GH / IGF axis. Myostatin is also increased as an anti-anabolic factor of muscle tissue, IL-1,6, TNF and NfκB.

Sarcopenia associated with osteoarthritis is not only related to the neighbouring muscles of the affected joint but to the whole muscular system. [52] Sarcopenic obesity is more common than non-sarcopenic obesity in osteoarthritis. There is an interrelated association, a vicious circle, between the muscular tissue and the joint, osteoarthritis causes sarcopenia and sarcopenia is also a causal factor in the onset and progression of osteoarthritis.

On one hand, the role of adipokines and other paracrine molecules such as leptin, adiponectin and resistin, contribute to the state of chronic low-grade inflammation resulting to sarcopenia [53]. Furthermore, indirect biomechanical factors such as decreased joint range of motion, pain, decreased physical activity and obesity contribute to the pathogenesis of OA-related sarcopenia. On the other hand, pathologically reduced muscle mass appears to be associated with increased damage to the cartilage. Sarcopenia, due to muscle weakness, causes increased joint loads, reduced stability, and possibly decreased neuromuscular response to movement, gait and stasis. Clinical studies in populations [54-59] correlate the weakness of the quadriceps as a risk factor for the progression of osteoarthritis, pain and knee dysfunction.

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Inflammatory muscle markers were studied after biopsy from vastus lateralis of quadriceps in osteoarthritic patients during total arthroplasty surgery. [60] Muscle inflammatory factors were isolated such as IL-6, MCP1 (monocyte chemotactic protein 1), NF-κB and STAT3 and correlated to reduced muscle activity, slower gait and increased joint dysfunction, according to WOMAC grading and patient walking analysis. Although MCP1 is normally secreted by muscle cells and macrophages during muscle inflammation and injury, it appears to be elevated also in osteoarthritis. In addition, the systemic raise of IL-6 has been clearly associated with loss of articular cartilage and radiographic osteoarthritis [61]. Therefore, questions are raised about the role of inflammatory processes in the correlation of muscle weakness and osteoarthritis progression.

Conclusions

Muscle tissue plays an important role in joint homeostasis, metabolism, repair, protection, fetal joint development and probably in the pathogenesis of articular cartilage. This role is achieved by mechanical and biological interactions.

Muscle derived mechanical loading of the joint, propagates biomechanical changes to cartilage, involving physical, electrochemical and metabolic phenomena through fluid flow, hydrostatic pressure, cartilage deformation, osmotic pressure, diffusion and changes in concentrations of molecules, ions and pH. Chondrocytes have mechanical stress receptors such as integrin receptors, connexins and Ca^{2+} ion channels which induce the function of collagenases and aggrecans in the cartilage matrix. At the same time, muscle tissue protects and offers stability to the joint either intentionally or inadvertently by proprioception.

The biological interactions are still not very well known. Myokines secretion by muscle tissue during exercise or even in the absence of it, affects bone metabolism and the joint as a whole organ. Some myokines have a negative effect on subchondral bone metabolism, such as IL-6, myostatin, activin and CNTF. Other myokines have anabolic activity on bone metabolism such as IGF-I, FGF-2, IL-15, follistatin, and Irisin. It seems to be at an early stage about understanding how muscle tissue affects the metabolism of both articular cartilage and bone. Questions arise on how myokines affect osteoblastic and osteoclastic activity and how they interact with adipocytes and overall body metabolism. It is still a question on how muscle function in terms of, concentric or eccentric loading, prolonged or repeated loading, affect joint structural integrity. Although growth factors and cytokines secreted by muscle tissue have already been detected, it seems that new myokines are emerging from research. On the other hand, existing myokines need further investigation about the effect of their molecular and cellular signal pathways on bone and joint. This research is likely to be helpful for understanding the pathophysiology of arthropathies, and planning new therapeutic strategies.

Conflict of interest:

The authors declared no conflicts of interest.

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ORIGINAL PAPER VOLUME 70 | ISSUE 1 | JANUARY - MARCH 2019

Arthroscopic repair of massive rotator cuff tears an effective and safe treatment option.

Avramidis G, Trellopoulos A, Brilakis E, Antonogiannakis E

3rd Orthopaedic Department, Hygeia Hospital

ABSTRACT

Purpose: The aim of the study is to evaluate the functional outcomes and the safety of arthroscopic repair in patients with rotator cuff massive tear at mid-term follow-up.
Materials and Methods: During a period of 4 years, 74 patients with average age of 65.5 years were treated with arthroscopic rotator cuff repair by the same surgeon in our department for massive rotator cuff tears. The mean time of follow up was 42 months. Functional outcomes were evaluated preoperatively and postoperatively with the Visual Analog Scale (VAS) for Pain, the active range of motion, the American Shoulder and Elbow Surgeons (ASES) Score and the Constant Score.
Results: The mean range of motion and the mean VAS for pain improved significantly from preoperatively to postoperatively. The mean ASES score improved from 50,4 preoperatively to 95 postoperatively and the mean Constant score improved from 40,7 to 77,4.
Conclusions: Patients with massive rotator cuff tears improved significantly the functional outcomes after arthroscopic repair as evaluated with ASES and Constant score, VAS and the mean Range of Motion. The majority of patients state that they are very satisfied with this treatment option. The arthroscopic repair is an effective and safe procedure to manage massive rotator cuff tears.

Keywords: Rotator cuff; massive rotator cuff tear; shoulder arthroscopy

Introduction

The treatment of massive rotator cuff tear poses a significant challenge for all orthopedic shoulder surgeons, because they are often complicated by structural failure and poor outcomes. The failure rate varies from 20 to 94% and usually occurs at the tendon-bone interface [1].

According to DeOrio and Cofield, the definition of massive rotator cuff tear is tear that is >5 cm in size in either the anterior-posterior or medial-lateral dimension. Definitions by other authors suggest that the tear must involve two tendons in order to be classified as massive [2, 3]. More recently Davidson and Burkhart proposed a system that connects rotator cuff tear patterns to treatment and prognosis [4]. Many surgical procedures have been described for treating these lesions and they have been classified in open, mini open and all arthroscopic operations. The arthroscopic re-

CORRESPONDING AUTHOR, GUARANTOR

Emmanuel Brilakis,
MD, PhD, Consultant Orthopaedic Surgeon
3rd Orthopaedic Dpt, Hygeia Hospital
emmanuel.brilakis@gmail.com

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pair includes complete repair, partial repair, medialized repair, muscle tendon transfer, superior capsule reconstruction, patch augmentation, in-space balloon implantation and finally with a reverse shoulder arthroplasty [5-9].

The chronicity of tear plays a significant role to the options of the treatment and the outcome of the rotator cuff tears. In fact, the acute tears have a good quality of rotator cuff tissue, there is no fatty infiltration or atrophy and are minimally retracted and mobile. The patients tend to be younger than those with chronic atraumatic massive tears and they have been combined with better surgical outcomes [10].

Patients with acute on chronic tears compose two groups, the first group consists of those that have a pre-existing symptomatic rotor cuff tearing which has an acute extension after an injury and the second group does not have any history of a significant shoulder symptom but a massive tearing of the rotator cuff [11].

Large chronic atraumatic tears are often present with no history of a significant injury and are frequently associated with pain, weakness because of the muscle atrophy and fatty infiltration. Usually they are older and less active people. Because of the chronicity, the poor tissue quality or the severe retraction of the tendon are height technically demanding, even with advance arthroscopic techniques and these can differentiate the surgical treatment [11].

The purpose of this study was to perform a retrospective review evaluating patients with a symptomatic massive rotator cuff tear treated arthroscopically. Furthermore, this study intends to assess the arthroscopic repair as an effective and safe treatment option to manage these types of tears.

Materials and Methods

This was a retrospective review of patients treated from January 2009 through December 2014. The patients of this study had a symptomatic massive rotator cuff tear and had no signs of glenohumeral degenerative changes to preoperative x-rays and during the diagnostic arthroscopy at the time of surgery. The primary preoperative goal was to attempt a complete rotator cuff repair if possible or a low-tension medialized repair and if that was not attainable a partial rotator cuff repair. All patients were placed in a shoulder immobilizer postoperative and physical therapy focusing on scapular strengthening exercises, pendulum exercises and active elbow, wrist and hand motion for the first six weeks. The patients started active assisted motion at weeks 6 to 10, active motion at weeks 10-16 and then continued with rotator cuff and deltoid strengthening exercises.

Seventy-four patients with massive rotator cuff tears were subjected to an arthroscopic repair by the same senior surgeon in our department and were available for follow up. The subjects of the study were 48 men and 26 women and the average age was 65,5 years (range 45-82). The average follow-up was 42 months (range 22-78). According to the type of tear, the patients were classified to acute traumatic tears 20 out of 74 (27%) patients, acute on chronic tears 35 patients (47,3%) and chronic tears 19 patients (25,7%). According to repair type, complete repair was achieved to 43 out of 74 patients (58,1%), 16 out of 74 (21,6%) patients were treated with medialized repair and 15 out of 74 (20,3%) patients with partial repair.

All patients had preoperative evaluation through clinical examination radiography and magnetic resonance imaging. All patients were assessed with the Visual Analog Scale (VAS) for pain, the active range of motion, the American Shoulder and Elbow Surgeons (ASES) score and the Constant score. This data was recorded at the preoperative examination and at 1, 3, 6,9,12 months postoperatively and then every 6 months at subsequent follow up visits.

Continuous variables are presented as means (SD) or medians (95% confidence intervals, interquartile ranges) when normality, as assessed by the Kolmogorov-Smirnov criterion, holds or not respectively. Categorical variables are expressed as absolute and relative frequencies (%). Differences between pre-operative and post-operative continuous variables were compared by paired sample t tests and Wilcoxon paired rank test (for normally distributed differences between pre-postoperative, respectively). All reported p values were based on two-sided tests and compared to a significance level of 5%. Data analysis was performed with SPSS software (Version 15.0, SPSS Inc., Chicago, Illinois).

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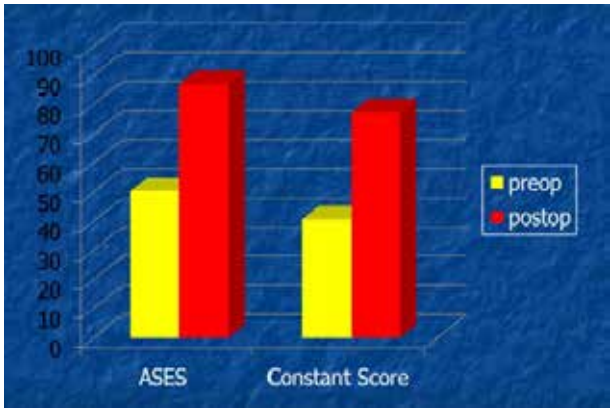

Fig. 1: *The ASES & Constant scores preoperatively (yellow) compared to postoperatively (red)*

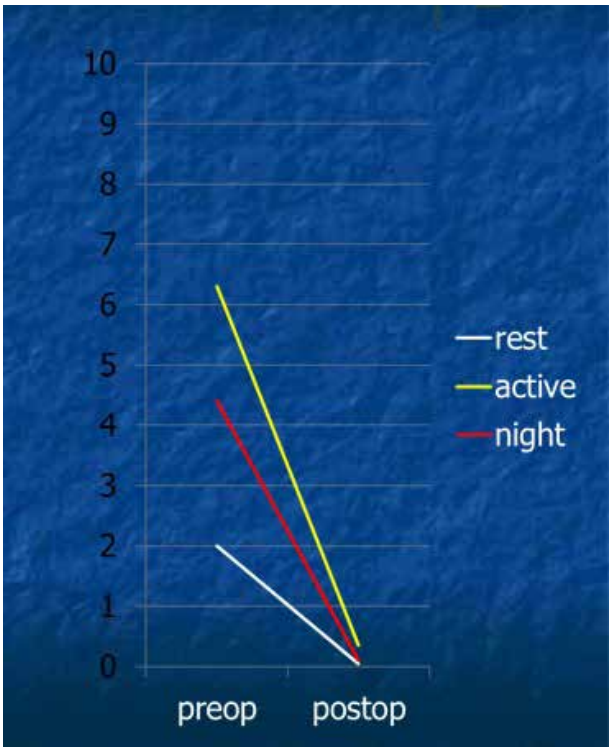

Fig. 2: *The reduction in VAS pain score at rest, at night and during activity.*

Results

The patients' evaluation was recorded preoperatively and at final follow up with the American Shoulder and Elbow Surgeons (ASES) score and the Constant score and are included in **Figure 1**. At final follow-up, patients maintained statistically significant improvement in their average preoperative to postoperative ASES scores from 50.4 to 95 [P < .001] and significant improvement in their Constant scores from 40.7 to 77.4 [P < .001].

They also demonstrated and maintained a decrease in average VAS pain scores at rest from 2.0 to 0.05 [P < .001], in average VAS pain score in activity from 6.3 to 0.35 [P < .001] and in average VAS pain score at night from 4.4 to 0.1 [P < .001]. The patients' outcomes, according to VAS scores, are depicted in **Figure 2**.

The patients had statistically significant change in their average preoperative to postoperative active range of motion during the study period as depicted in **Figure 3** and **Table 1**. Specifically, the mean increase of active forward flexion was 55.4° from 105.9° to 157.7° [P < .001], the mean increase of active abduction was 60.3° from 100.9° to 158.2° [P < .001]. The mean increase of active external rotation with upper limp at side was 30.8° from 35° to 63.5° [P < .001], the mean increase of active external rotation with upper limp at 90 abduction was 35.4° from 37.8° to 71.2° [P < .001]. Active internal rotation was evaluated as excellent (T6-T9) to 6.8% of patients preoperatively and 21.9% postoperatively, was satisfied (T10-L3) to 65.8% of patients preoperatively and 69.9% postoperatively and poor (L4- I5) to 27.4% of patients preoperatively and 8.2% postoperatively. 32 patients had positive external rotation lag test preoperatively and converted to negative to 20 out of 32 patients.

All patients except 6 (68 of 74 patients) were available to complete questionnaires to determine the level of satisfaction, the residual pain and the strength of the affected shoulder. The remaining 6 (8,1%) patients had progression to rotator cuff arthropathy and evaluated as dissatisfied, painful and with poor strength and elected for revision to reverse shoulder arthroplasty. Subjectively, 49 out of 74 (66.2%) patients were completely satisfied with their surgical result, 3 out of 74 (4,1%) were just satisfied and 16 of 64 (21.6%) were less satisfied. Patient reported pain was recorded during the questionnaire and 62 of 68 patients (83.8%) of patients had no pain, 6 of 68 patients (8.8%) feel pain sometimes or during certain activities. Finally, concerning the strength to the effected shoulder, 25 out

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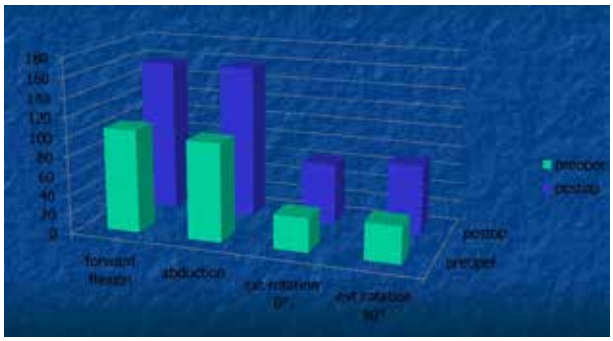

Fig. 3: *The mean degrees of Range of Motion preoperatively (green) vs postoperatively (blue).*

INTERNAL ROTATION	PREOP		POSTOP	
EXCELLENT (T6-T9)	5	(6,8%)	16	(21,9%)
VERY GOOD (T10-L3)	48	(65,8%)	51	(79,9%)
POOR (L4-GLUT)	20	(27,4%)	6	(8,2%)

Table 1: *The men degrees Internal Rotation preoperatively and at last follow up.*

of 68 patients (33.8%) report that there is no strength reduction, 16 out of 68 (21.6%) patients reported that their shoulder is weaker compared to healthy side and 27 of 68 (36.5%) report great weakness to the effected shoulder .

Discussion

The most important finding of this study is that the ASES score, Constant score and VAS score significantly improved after arthroscopic repair of massive rotator cuff tears. In addition to this, the arthroscopic repair of massive tears resulted in the great majority of our patients (70.3%) that they were subjectively completely satisfied or simply satisfied with their surgical procedure in more than 3 years postoperatively. 83.2% of patients reports no pain at final follow up. On the other hand, 36.5% report great weakness to the repaired shoulder compared to healthy side. Finally, 6 out of 74 patients (8.1%) have been considered as failures due to progression to rotator cuff arthropathy and revised to RSA.

The arthroscopic treatment of rotator cuff massive tears is a real challenge for a shoulder surgeon. An anatomical, water-tight complete repair is the main goal of an arthroscopic rotator cuff repair. However, a complete anatomic repair is often not possible when the cuff tear is massive and chronic, the tissues are severe retracted and have poor quality. In that case, a medialized repair or a partial repair has been reported as a treatment option with satisfactory results [12,13].

Our goal with this treatment option is to offer a minimal invasive procedure as arthroscopic repair, with low morbidity and low complication rate attempting to repair as much rotator cuff as possible in order to reduce pain and increase the shoulder function. Our total complication rate considered low, including 2 patients with post-op infection (both diabetic type I) treated successfully with arthroscopic debridement and antibiotics. Additionally, 3 patients underwent revision surgery and finally one of them develops rotator's cuff arthropathy two years postoperatively. A patient who presented Axillary nerve paresis postoperatively, restored spontaneously at 3 months. Finally, 6 rotators' cuff arthropathies in total were treated with reverse shoulder arthroplasty.

There are several limitations to this study. Firstly, it was a retrospective review with the inherent limitations. In addition, in this study there were not follow up imaging studies to assess the rate of healing to our patients.

Clinical relevance of this study is to demonstrate the outcomes of arthroscopic repair of massive rotator cuff tears in order to advise beforehand an orthopedic surgeon about the expectations of this treatment option.

Conclusion

Patients with massive rotator cuff tears improved significantly the functional outcome after arthroscopic repair as evaluated with ASES and Constant score, VAS and the mean Range of Motion. The majority of the patients stated that they were very satisfied with this treatment option. The arthroscopic repair is an effective and safe procedure to manage massive rotator cuff tears.

Conflict of interest:

The authors declared no conflicts of interest.

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VOLUME 70 | ISSUE 1 | JANUARY - MARCH 2019 REVIEW

What was Quasimodo suffering from?

Nikolaos G. Markeas[1], Athanasios Verdis[2]

[1]2nd Department of Orthopaedics, General Children's Hospital "P. & A. Kyriakou"
[2]Department of Philosophy-Pedagogy-Psychology, University of Athens

ABSTRACT

One of the fictional characters in Victor Hugo's novel "Notre-Dame de Paris" is without doubt Quasimodo: the hunchbacked bell-ringer of the Cathedral. From a medical perspective, the affliction of Quasimodo has remained a mystery for two centuries. Recent research however has linked his condition to a particular pathogenicity. Specifically, some passages in Hugo's novel suggest that a form of mucopolysaccharidosis, a deformity associated with many congenital and hereditary changes affecting the skeletal system, could explain Quasimodo's somatometric characteristics. In the present study we support the above claim and we discuss a number of related issues in the point between medicine and literature.

KEY WORDS: Notre-Dame de Paris; Quasimodo; literature; mucopolysaccharidosis; neurofibromatosis

Introduction

Deformities and monstrous characters have always been an important element in art [1]. Books and films have for a long time depicted outcasts, like Captain Hook in "Peter Pan", Erik in the "Phantom of the Opera", and the "creature" in "Frankenstein". In this paper we focus on Quasimodo, the emblematic fictional character in Victor Hugo's novel "Notre-Dame de Paris". The aim of our investigation is firstly to examine Quasimodo's condition from a medical point of view but also to discuss the symbolic gravity of this character both in relation to Victor Hugo and the times in which this famous French novelist has lived.

A question arises at this point. Why do we start a discussion on Quasimodo? And in general, what attracts people in ugliness? A possible psychological explanation is that the aesthetic capacity towards ugliness has been attributed to our early experience of the feminine-maternal [2]. According to a number of psychologists, beauty is experienced at a certain stage of our development as both awesome and awful. From a philosophical perspective Immanuel Kant [3] has given the explanation that a person can be attracted on an ugly object simply because of the expectation that a certain order and harmony will eventually be found in it. Umberto Eco, in his book "On Ugliness" [4], unfurls a taxonomy of stark visual images of violence, deformity, immorality and cruelty, as well as quotations from sources ranging from Plato to radical feminists.

Quasimodo probably was suffering by a muco-

CORRESPONDING AUTHOR, GUARANTOR

Nikolaos G. Markeas MD, PhD
Director of 2nd Department of Orthopaedics, General Children's Hospital "P. & A. Kyriakou", Athens 42 Sikelianou street, Egaleo, tel.: 6975856940, 122 43 Athens,
E-mail: markeasn@otenet.gr

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polysaccharidosis, although the literature is still suggesting that neurofibromatosis is the most possible cause of his deafness and skeletal deformities [5, 6].

Who was Quasimodo?

Quasimodo draws the attention of the reader from the first moment in Hugo's novel, with his awful appearance, distorted body and strange behavior (**Fig. 1**). Hugo's descriptions in the chapter "Quasimodo" of the first book are presented below [7]:

We shall not try to give the reader an idea of that tetrahedral nose, that horseshoe mouth; that little left eye obstructed with a red, bushy, bristling eyebrow, while the right eye disappeared entirely beneath an enormous wart; of those teeth in disarray, broken here and there, like the embattled parapet of a fortress; of that callous lip, upon which one of these teeth encroached, like the tusk of an elephant; of that forked chin; and above all, of the expression spread over the whole; of that mixture of malice, amazement, and sadness. Let the reader dream of this whole, if he can.

A few lines later, Hugo shares more information about his hero:

A huge head, bristling with red hair; between his shoulders an enormous hump, a counterpart perceptible in front; a system of thighs and legs so strangely astray that they could touch each other only at the knees, and, viewed from the front, resembled the crescents of two scythes joined by the handles; large feet, monstrous hands; and, with all this deformity, an indescribable and redoubtable air of vigor, agility, and courage, – strange exception to the eternal rule which wills that force as well as beauty shall be the result of harmony. … One would have pronounced him a giant who had been broken and badly put together again.

Among other things Quasimodo is deaf. In the following dialogue we read:

"What a devil of a man!" said Robin Poussepain still all bruised with his fall. "He shows himself; he's a hunchback. He walks; he's bandy-legged. He looks at you; he's one-eyed. You speak to him; he's deaf. And what does this Polyphemus do with his tongue?"

"He speaks when he chooses," said the old woman; "he became deaf through ringing the bells. He is not dumb."

Fig. 1: *Lon Chaney as Quasimodo and Patsy Ruth Miller as Esmeralda in the 1923 film, The Hunchback of Notre Dame.*

Hugo uses Quasimodo's character to promote specific views: the unstable female nature as in the case of Esmeralda, who is moved by the charms of young Phoebus while staying indifferent to the feelings of ugly Quasimodo; the hypocrisy of a society that accepts the rejection of the outcast by soothing its conscience with ploys and all this with the help of the clergy, as it is the case of the informal adoption of Quasimodo by the archdeacon Claude Frollo; the inability to overcome one's sexual urge because of the religious prejudices that he serves, as is the case of the archdeacon, whose silent passion leads him to crime and his tragic end.

With regards to the name that Hugo chooses for his character, it turns out that this is not at all unplanned. The name Quasimodo obeys to an unwritten law of the literature according to which names often serve the logic and foreshadow of the plot [8].

The day that Frollo discovered the newborn in a sack, was the Sunday after Easter, the one called in the Eastern Church tradition as "Thomas Sunday" and in the Western Roman Catholic Church

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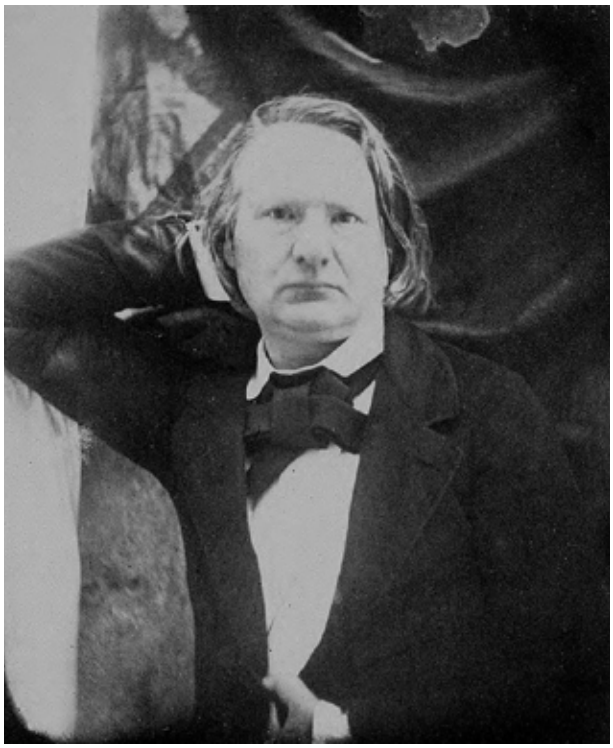

Fig. 2: *Daguerreotype of Victor Hugo in 1853.*

as "Divine Mercy Sunday" or "Octave of Easter" or "Quasimodo day". The latter comes from the words of the introit in Latin: "Quasi modo geniti infantes, rationabile, sine dolo lac concupiscite", which is translated as "as newborn babies, desire the rational milk without guile" [9]. We read in chapter "Claude Frollo" from the fourth book of the Hugo's novel [7]:

He baptized his adopted child, and gave him the name of Quasimodo, either because he desired thereby to mark the day, when he had found him, or because he wished to designate by that name to what a degree the poor little creature was incomplete, and hardly sketched out. In fact, Quasimodo, blind, hunchbacked, knock-kneed, was only an "almost."

In a footnote, Hugo gives another explanation for the choice: *The Latin word Quasimodo also means "almost" or "nearly".*

Victor Hugo and his era

"Romanticism" is the intellectual movement in literacy and music that appeared in Europe in the early 19th century, expressing an idealistic approach of the world as opposed to the rationalism of the Enlightenment. Victor Hugo (**Fig. 2**) was at the forefront of this movement. In his theatrical plays, novels and poems he described the struggles in the social life and the suffering of the lower classes. But Hugo's biggest contribution to Romanticism is his firm interest for universal values. With the range and power of his pen Hugo criticized the injustices that were produced by the ruling classes at a time when it was difficult for anyone to understand injustices let only to fight against them [10]. Rightfully so, Hugo is considered today as a classic representative of liberalism in literature.

Hugo decides to write "Notre-Dame de Paris" while still studying at the Paris School of Philosophy [11]. The novel comes out in 1831, when Hugo was 29 years old and is a success and translated in other languages. On the pretext of a love affair between Esmeralda and Phoebus de Châteaupers, the unfulfilled libido of archdeacon Frollo that results in his deadly jealousy, but also the emblematic figure of Quasimodo slipping among the other characters in the drama, the author grasps the opportunity to beat the drum of the need to protect the medieval cathedrals that are about to collapse, something that in fact was the subject of doctorate thesis at that times. In Notre Dame, Hugo finds the perfect example in order to pass his positions to a society that turns a deaf ear to his words of warning about the decay of these buildings. It is in one such building that his hero has grew up and it is there where he has been deaf supposedly by the sound of the bells.

For the unsuspecting traveler who decides to visit Paris, Notre Dame is not only an unparalleled attraction, but summarizes in its niches and pediments the local history from the Middle Ages to the present day (**Fig. 3**). This metropolitan temple stands majestically on the isle of the River Seine, the famous Ile de la Cité. Its construction began officially in 1163 at the initiative of the Paris bishop Maurice de Sully, but its basic form was only completed in the 13th century [12]. During

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Fig. 3: *Notre Dame of Paris. Towers on west facade.*

the 17th century, but mainly during the difficult years of the French Revolution, it suffered serious damage that led to frequent repairs and repeated reconstructions. In the mid-19th century, Eugène Viollet-le-Duc underwent a radical restoration. It is quite remarkable that the restoration work took place in the quarter century 1845-1870, immediately after the publication of Hugo's novel, practically giving affirmative response to his calls to rescue to Gothic's medieval cathedrals that were progressively collapsing [13-15]. In the third book of the novel [7], in the chapter titled "Notre-Dame", we read:

Thus, to sum up the points which we have just indicated, three sorts of ravages to-day disfigure Gothic architecture. Wrinkles and warts on the epidermis; this is the work of time. Deeds of violence, brutalities, contusions, fractures; this is the work of the revolutions from Luther to Mirabeau. Mutilations, amputations, dislocation of the joints, "restorations"; this is the Greek, Roman, and barbarian work of professors according to Vitruvius and Vignole.

From the turbulent history of the cathedral, it is worth mentioning the coronation of King Henry VI of England on December 16, 1431, during the Hundred Years' War, as well as the brilliant Te Deum in the Choir of the cathedral on the reign of Louis XIV in 1669. At Notre Dame was also celebrated the Cult of Reason at the time of the reestablishment in 1793. And there was the coronation of Napoleon I on December 2, 1804. On August 26, 1944, with the withdrawal of occupying German troops from the city, a Mass is being attended to celebrate the liberation of Paris [16].

Notre Dame in Hugo's work is the point of reference for the episodes that evolve on many different levels: the geographical common place where the heroes' fates meet, the canvas where the plot of the drama unfolds. It is there where the adopted Quasimodo grows up, and it is there where he is supposedly deafened by the toll of the bell. Esmeralda escapes in the crypt of the church. Notre Dame is surrounded by beggars from the Court of Miracles with Clopin Trouillefou as their King (the King of Thunes) seeking to release the beautiful gypsy from the hands of archdeacon Claude Frollo. Notre Dame is also besieged by King Louis' troops to capture Esmeralda and hang her.

Mucopolysaccharidosis or neurofibromatosis?

The classic description of neurofibromatosis has been published by von Recklinghausen in 1882, while he was professor of pathology in Strasbourg, 51 years after the work of Victor Hugo [17]. Nevertheless, the disease had been partially described in 1783 by Tilesius [18]. According to Cox [5], the affliction that Hugo imposes on his character (extensive soft tissue and skeletal deformity with the preservation of motor skills and normal higher mental function) may be seen in severely affected cases of neurofibromatosis. The wart over Quasimodo's right eye could well have been a cutaneous neurofibroma affecting the eyelid. His spinal scoliosis, distorted thighs and legs, large hands and feet, club foot, huge head, and

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irregular teeth are also seen in neurofibromatosis when central lesions of bone result from expansive growth of neurofibromas within the medullary cavity.

About forty years after the publication of von Recklinghausen, Gertrud Hurler, a German pediatrician, described a strange syndrome that is characterized by corneal clouding, skeletal abnormalities, and mental retardation [19]. Two years ago, during World War I, Charles Hunter had described a similar disease [20]. Hurler did not mentioned Hunter's paper because of interrupted communications caused by the war. Nowadays, due to the evolution of molecular biology, we know the pathogenesis of both diseases. They belong to the great family of "mucopolysaccharidoses".

Mucopolysaccharidoses are hereditary, progressive diseases caused by mutations of genes coding for lysosomal enzymes needed to degrade glycosaminoglycans. The major glycosaminoglycans are chondroitin-4-sulfate, chondroitin-6-sulfate, heparin sulfate, dermatan sulfate, keratin sulfate, and hyaluronan. These substances are synthesized and linked to proteins to form proteoglycans, major constituents of the ground substance of connective tissue, of nuclear and cell membranes [21]. The hyaluronan is an exception in this mechanism.

Failure of degradation because of absent or grossly reduced activity of mutated lysosomal enzymes results in the intralysosomal accumulation of glycosaminoglycan fragments. The characteristic pattern of clinical, radiologic, and biochemical abnormalities are due to cell dysfunction caused by the accumulation of distended lysosomes in the cells [22].

Mucopolysaccharidosis I (MPS-I), or Hurler syndrome, is caused by mutations of the *IDUA* gene on chromosome 4p16.3 encoding α-L-iduronidase. Deficiency of α-L-iduronidase results in a wide range of clinical involvement, which are ends of a broad clinical spectrum. Hurler disease is a severe, progressive disorder with multiple organ and tissue involvement. Its

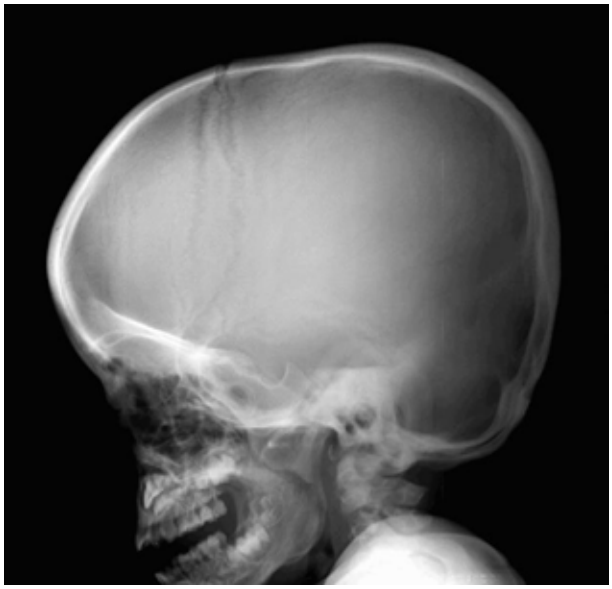

Fig. 4: *In Hurler syndrome, the head can be large with prominent frontal bones and the skull can be elongated.*

transmission is autosomal recessive. Diagnosis is usually made between 6 and 24 months with evidence of hepatosplenomegaly, coarse facial features, corneal clouding, large tongue, prominent forehead, joint stiffness, short stature, and skeletal dysplasia [23]. Facial deformities are usually pathognomonic (**Fig. 4**): frontal bossing, prominent eyes with hypertelorism and depressed nasal bridge, gapped teeth, gingival hypertrophy and (as it has already been described) a thickened tongue.

Facial features resemble the gargoyles, the carved or formed grotesque with a spout designed to convey water from a roof and away from the side of a building, thereby preventing rainwater from running down masonry walls and eroding the mortar between. [24]. Architects often used multiple gargoyles on a building to divide the flow of rainwater off the roof to minimize the potential damage from a rainstorm, like Eugène Viollet-le Duc in Notre-Dame. Hunter used the term "gargoylism" in order to describe his own cases (**Fig. 5**), but nowadays the term is used for Hurler's disease.

Most patients have recurrent upper respirato-

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Fig. 5: *A gargoyle on the tower of Notre Dame of Paris.*

ry tract and ear infections, noisy breathing, and persistent copious nasal discharge. Most children with Hurler syndrome acquire only limited language skills because of developmental delay, combined conductive and neurosensory hearing loss, and enlarged tongue. Progressive ventricular enlargement with increased intracranial pressure caused by communicating hydrocephalus also occurs. Corneal clouding, glaucoma, and retinal degeneration are common. Radiographs show a characteristic skeletal dysplasia (**Fig. 6a**). The earliest radiographic signs are thick ribs and ovoid vertebral bodies. The long bones have enlarged, coarsely trabeculated diaphysis with irregular metaphyses and epiphyses. With progression of the disease macrocephaly develops with thickened calvarium, premature closure of lambdoid and sagittal sutures, shallow orbits, enlarged J-shaped sella, and abnormal spacing of teeth with dentigerous cyst.

The body's height remains short with kyphoscoliosis at thoracolumbar spine. Mental retardation also exits. In a broad pelvis there are dysplastic acetabuli. The femoral necks are in valgus position. The appearance of ossific nucleus of the femoral heads retards. A subluxation or true dislocation of both hips is also exists (**Fig. 6b**). These patients die early in life because of cardiac insufficiency or respiratory infections.

Hunter disease, or mucopolysaccharidosis II (MPS-II), is a linked disorder caused by the deficiency of iduronate 2-sulfatase. As an X-linked recessive disorder, Hunter disease manifests almost exclusively in males. Marked molecular heterogeneity explains the wide clinical spectrum of the disease. Patients with severe MPS-II have features similar to those of Hurler disease except for the lack of corneal clouding and slower progression of somatic and central nervous system deterioration. Coarse facial features, short stature, dysostosis multiplex, joint stiffness, and intellectual disability manifest between 2 and 4 years of age. Extensive, slowly progressive neurologic involvement precedes death, which usually occurs between 10 and 15 years of age [20].

Patients with the mild form can have a near-normal or normal life span, minimal central nervous system involvement and slow progression of somatic deterioration with preservation of cognitive function in adult life. Survival to ages 65 and

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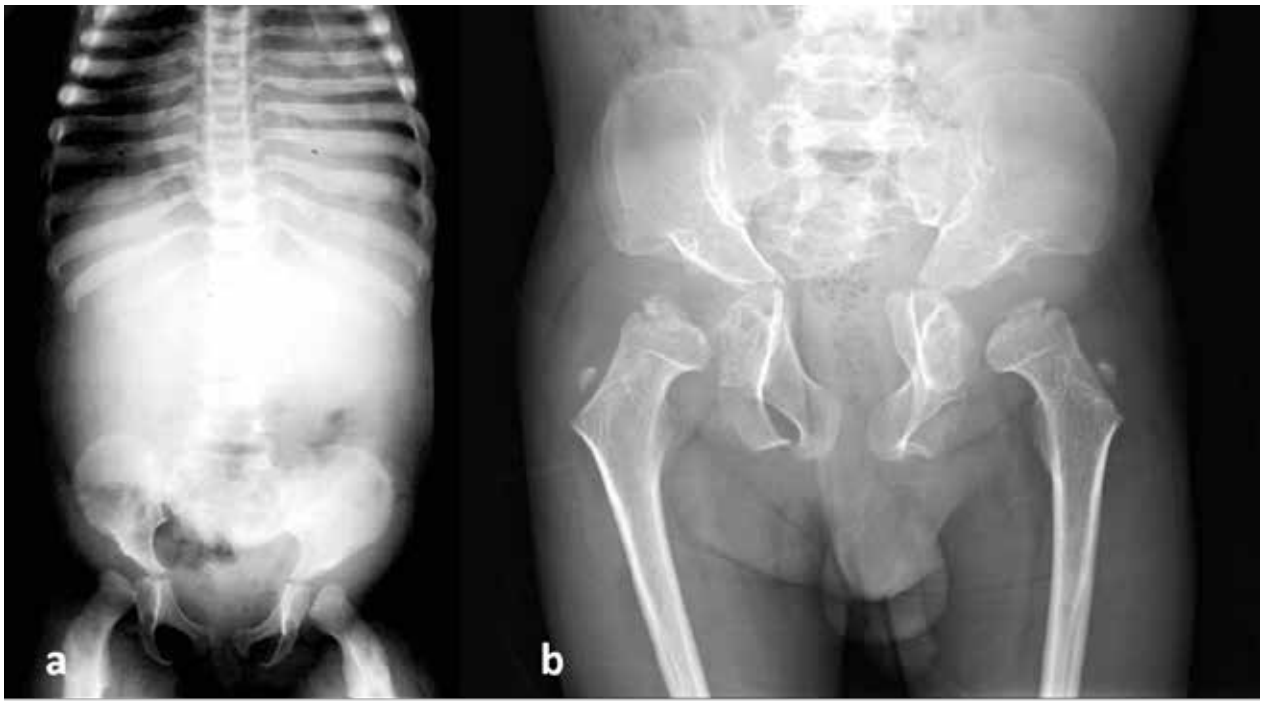

Fig. 6: *Kyphoscoliosis of thoracolumbar spine (a), and subluxation of both hips (b) in a patient suffering by Hurler syndrome.*

87 years has been reported. Somatic features are Hurler-like but milder with a greatly reduced rate of progression. Adult height may exceed 150 cm. Airway involvement, valvular cardiac disease, hearing impairment, carpal tunnel syndrome, and joint stiffness are common and can result in significant loss of function in both the mild and severe forms.

Discussion based upon a hypothesis

Hugo's work gives a believable description of the Quasimodo's looks and this could well fit in to Hurler's description. However, the absence of an obvious mental disability in Hugo's hero makes it difficult to come to reliable conclusions with regards the above statement and we surely accept that it is Hugo's privilege to form a character according to his imagination, perceptions, and foreshadowing. Under these circumstances and beyond his somatometric measurements, Quasimodo, as a fictional character, ought to have the ability to understand the events in his surroundings; the will to think and act with efficiency; the sensibility to feel and to love.

It is a common secret that parthenogenesis does not exist, both in nature and the creative mind of an author. From this point of view, it would be utopian to suggest the opposite and, as in the case of Notre Dame, it is very likely that Hugo's perception of a known person with similar characteristics stirred him to design his own hero [26]. Based on this assumption, the center of gravity of our discussion should be shifted from Quasimodo himself to the man who apparently inspired his creator. Hugo in a particularly revealing apostrophe writes in the chapter "Three human hearts differently constructed" of the eight book of the novel [7]:

No one had yet seen in the gallery of the statues of the kings, carved directly over the arches of the portal, and strangled the spectator, who had, up to that time, observed everything with such impassiveness, with a neck so strained and visage so hideous that, in his motley accoutrement of red and violet, he might have

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been taken for one of those stone monsters through whose mouths the long gutters of the cathedral have discharged their waters for six hundred years.

Quasimodo's resemblance to gargoyles, the grotesque demonic figures that project from buildings, is obvious. Gargoyles supposedly removed the satanic forces. From a practical point of view however, they just conveyed water from a roof of a building away from its sides. Gargoyles were in fact artful gutters and were proposed by Eugène Viollet-le-Duc himself [24].

In August 2010, Adrian Glew published an article about the "true life of Quasimodo," a lithographer working in Notre Dame in 1820. The story taken down by Glew can be found in the memoirs of Henry Sibson, a sculptor from England who worked at Notre Dame at the same time that Hugo wrote his novel [27]. Sibson describes the sculptor as hunchback and deformed giant, although his name misses him. As Victor Hugo supervised the restoration work of the cathedral, it is quite possible that he aware of the existence of this man who went by the name "Le Bossu" ("the hunchback" in French). His real name was Monsieur Trajin, and Adrian Glew reveals that Hugo and Le Bossu lived in the same town of Saint Germain-des-Pres in 1833. Apparently Hugo used this man's name, transforming it from Jean Trajin to Jean Valjean to create the central hero in his masterpiece "Les Misérables".

Epilogue

Regardless of whether the real Quasimodo existed and irrespectively of what his real affliction was, our fictional hero is a universal symbol of resistance with his "indescribable and redoubtable air of vigor, agility, and courage", according to Eco [4].

Quasimodo is a "strange exception to the eternal rule which wills that force as well as beauty shall be the result of harmony" [7]. It is common place that there has been discrimination against the disabled people and the people with unusual bodies in a number of fields, like employment, voting, marriage and parental rights, the right to travel, the right to be free from institutionalization, and the right to have access to the courts of law.

In our opinion, Quasimodo symbolizes our fellow man; our fellow "other" who overcomes social and ideological obstacles. Quasimodo hopes, loves and fights.

Conflict of interest:

The authors declared no conflicts of interest

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CASE REPORT
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Crystall deposition arthritis of the knee complicated by a lipoma arborescens. A case report

A.P. Fortis[1], Z.Milis[1], A.Tsatsaragkou[2], A.Varatsos[2], M. Katsigianni[1]

[1]*Orthopaedic Dept. Panarkadiko Hospital, Greece*
[2]*Pathology Dept. Panarkadiko Hospital, Greece*

ABSTRACT

A case of a knee lipoma arborescens in a 60 yrs. old male is presented. The patient complained for persistent knee pain and denied any history of trauma. He has had an MRI where a medial meniscal tear was found and after a knee arthroscopy the diagnosis of crystal deposition arthritis was established. The symptoms did not subside and then he had another arthroscopy, where a large fatty mass in the suprapatellar area was found and excised. Pathology report established the diagnosis of a lipoma arborescens.

KEYWORDS: Lipoma arborescencs; knee; arthroscopy

Case report

A 60 yrs-old male patient presented in outpatients clinic complaining of left knee pain. He referred that the pain was occasionally bothering him during sleep and that he had also experienced locking of the knee in some occasions. He denied any significant history of injury. Initially, he visited an Orthopaedic surgeon who advocated a knee MRI, where a medial meniscal tear and a synovial inflammation were found.

The patient underwent a knee arthroscopy and according to the operating report a large crystalline deposit underneath the lateral meniscus was found which was then washed out. A month after the operation the patient had no improvement of the symptoms. On examination the knee was stable, having a 10o degrees lag of extension and 20o of flexion, no pain on palpation, but there was some swelling around the suprapatellar area. Ultrasound revealed a well-defined soft tissue in the suprapatellar pouch (**fig. 1**). FBC and ESR were within the normal limits, but CRP was slightly elevated (value of 3 with the normal range 0-0.7)

A second arthroscopy was scheduled. During the arthroscopy, several areas of crystallin deposition were found all around the knee (**fig.2**). In the suprapatellar pouch a large mass of fat tissue was found with a tree-like folds within it (**fig.3**). Biopsy of that tissue was sent for histology and then the whole area was shaved using a 4.5 mm arthroscopic shav-

CORRESPONDING AUTHOR, GUARANTOR

A.B.Fortis
Consultant Orthopaedic Surgeon
Panarkadiko General Hospital, Tripoli, Greece

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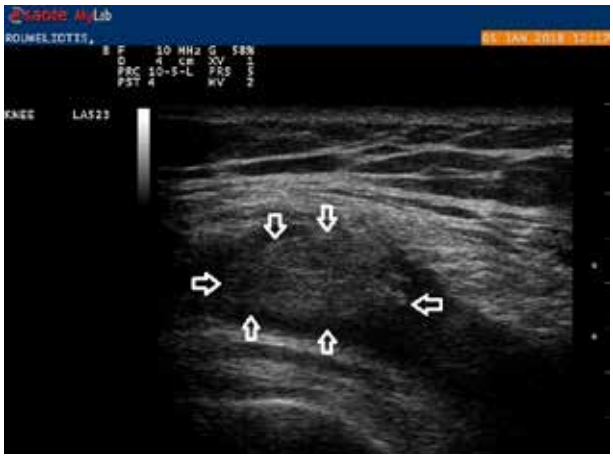

Fig. 1: *Longitudinal view of the suprapatellar pouch (linear probe 12 MHz) where a soft tissue mass has been labeled by arrows.*

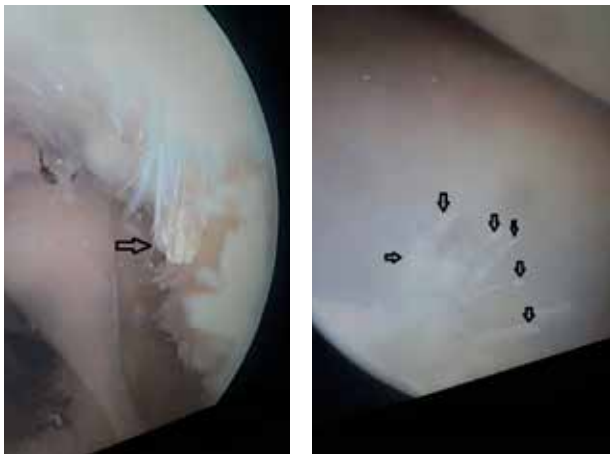

Fig. 2: *Crystal deposition on the medial meniscus (2a) and in the synovium (2b)*

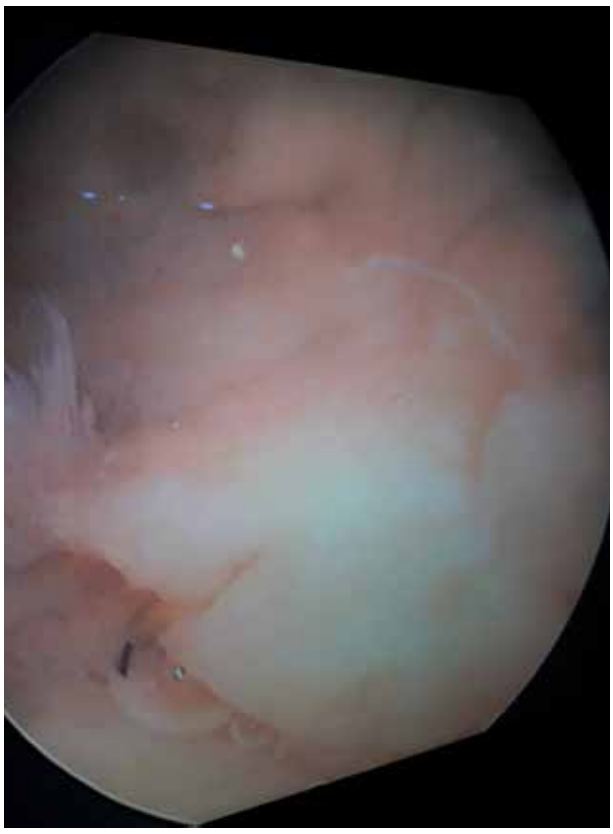

Fig. 3: *The lipomatous mass found in the suprapatellar area*

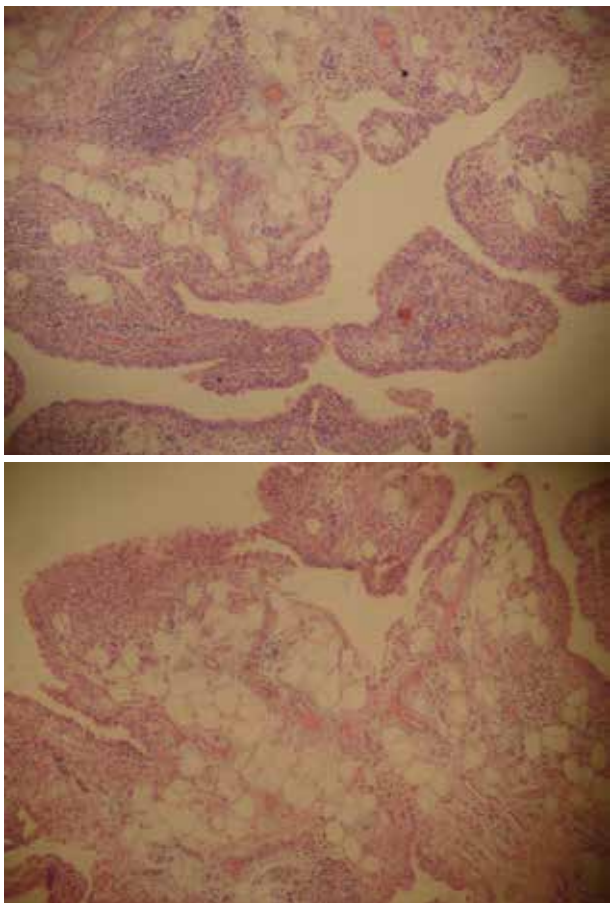

Fig. 4: *H - E x20.* ***4(a)*** *Synovial lipoma. Focal lymphocytic aggregation among mature adipocytes.* ***4(b)*** *Synovial lipoma. Hypertrophied villi structures lined by synovial epithelium. The core of the villi and the subepithelial area is diffusely infiltrated by mature adipocytes.*

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er. A thorough irrigation of the joint was then performed at the end of the procedure. The patient was mobilized the next postoperative day with partial to full weight bearing as tolerated and discharged from the hospital.

Histological report referred to a macroscopically yellowish synovium thickened with villous proliferation. Microscopically there were hypertrophied villi structures lined by synovial epithelium. The core of most villi and the subepithelial area were diffusely infiltrated by mature adipocytes (**fig. 4a**). Among the adipocytes there were lymphoid aggregates (**fig. 4b**).

At one month follow up, the patient reported remarkable improvement regarding the knee pain and discomfort and he gained nearly all ROM, whereas FBC, ESR and CRP were within the normal limits.

Discussion

Lipoma arborescens is named after the term lipoma because of lipomatous proliferation of the synovium and arborescens from the Latin word "arbor" meaning the tree because of the tree like shape of the synovial proliferation. Hallel et al. introduced the term lipomatous proliferation of the synovial membrane as a medically appropriate term in order to distinguish it from the true lipoma which is basically a tumor [1].

Lipoma arborescens mainly affects the knee joint and suprapatellar pouch, but it can also be found in several joints or rarely outside the joints like in subacromial subdeltoid bursa and around the peroneal tendons. [2-4] Normally it is a non-symptomatic condition but occasionally it can give recurrent symptoms of joint pain, discomfort and limited range of motion mainly due to effusion. It can rarely cause joint locking. These symptoms can slowly progress in terms of frequency and intensity. [2]

The mononuclear cell infiltration found microscopically led several authors to the hypothesis that the cause of the disease was a reaction to a chronic inflammation. In fact, it could be complicated with early osteoarthritis, but according to the present literature it cannot be the cause of osteoarthritis. It can be found in rheumatoid arthritis, psoriasis or psoriatic arthritis, uveitis, and juvenile spondyloarthropathy.

In the present case the crystal deposition arthritis was probably the cause of joint inflammation. Though it is difficult to distinguish whether the patient's symptoms were due to either the crystal deposition arthritis or the presence of lipoma arborescens, the remarkable improvement of the patient's symptoms after the second arthroscopy is a clear indication of their cause.

In symptomatic non-responding to conservative treatment cases, surgical excision is the treatment of choice.

In conclusion, even if lipoma arborescens is a benign and non-symptomatic condition, we should always keep it in the back of our head as the cause of non-explainable symptomatic swollen joint or tendon.

Conflict of interest:

The authors declared no conflicts of interest.

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