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REVIEW ARTICLE

BONE GRAFT SUBSTITUTES IN ORTHOPEDICS: A REVIEW

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Clinical and experimental research are trying to find the optimal bone substitute to improve bone healing. Various materials and elements could be classified according to three functional properties: osteoconductive, osteogenic and osteoinductive. Osteoconduction is a property of a natural or artificial matrix (scaffold) that supports the attachment of bone forming cells for subsequent bone formation. Osteogenic property is the intrinsic capacity of cells to form bone. Osteoinduction is a property of materials or growth factors that can stimulate cells to produce bone. Although all these processes contribute in different ways to bone healing in nature, in the past a specific substance or material was singularly investigated. In later years orthopedic research has begun to evaluate combinations of various biomaterials and substances with different properties to simulate, in the best way possible, bone repair. This review analyses present knowledge and offers some new perspectives on bone substitutes. Narrative Review.

Bone healing is a specialized form of wound-healing where bone is rapidly regenerated. Despite the biologically optimized nature of the repair process, patients still require substantial time before a fracture achieves complete return to mechanical stability. Consequently, there is currently an increasing interest in treatments that could enhance the speed of repair, providing a more rapid return to an active lifestyle and work.

Bone graft substitutes are currently used to obtain healing in delayed bone unions or nonunions, to achieve spinal fusion, to fill bone defects in revision prosthetic surgery and in the treatment of tumour lesions (1). Delayed union and nonunion are associated with approximately 5%-10% of fractures. Impaired fracture healing is associated with a number of risk factors including poor blood supply, associated soft tissue injuries, extensive bone loss, instability, infection, poor general conditions and smoking. Surgical interventions often involve bone graft procedures to accelerate the bone healing process (2).

Spinal fusion is one of the most commonly performed procedures in spinal surgery. Fusion may be obtained through a surgical procedure that is characterized by cartilage and soft tissue removal in articular joints, decortication of bone surfaces to be involved in the fusion mass, and placement of graft material to induce bone formation. Nonunion rate in spinal fusion has been reported to range 5-35 % and many variables are believed to affect the outcome of fusion (3).

Revision total hip arthroplasty is a common surgical procedure that is frequently complicated by acetabular and/or femoral bone loss, requiring impaction bone grafting.

To date autogenous cancellous bone, usually from the iliac crest, is considered the most efficient

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material in stimulating an osteogenic response and represents the gold standard to which all graft alternatives are compared (2). However, autologous bone grafting is associated with morbidity (13-30%), including pain, surgical scars, blood loss, increased use of blood products, higher risk of infections and higher operative time. Furthermore, autograft harvesting may provide insufficient material to place onto a wide fusion area that needs a large quantity of bone graft, or in patients with previous graft harvests (4).

Bone Graft Substitutes

A bone graft substitute is any implanted material that, alone or in combination with other materials, promotes a bone healing response by providing osteoconductive, osteogenic or osteoinductive activity to a local site (5). Osteoconductive activity is the physical property of a graft material that allows the ingrowth of neovasculature and infiltration of osteogenic precursor cells during the process known as creeping substitution. An osteoconductive graft material promotes migration and attachment of cells that contribute to bone tissue apposition to its own surface, functioning as a nonviable scaffold to facilitate enhanced bone formation (5).

Osteogenic activity is the ability to synthesize new bone tissue by the living bone cells contained in the graft and/or in the graft site. These cells are represented by osteoblastic lineage cells (determined osteogenic precursor cells-DOPC's) and mesenchymal stem cells (inducible osteogenic precursor cells-IOPC's), that may differentiate in osteoblast-like cells if stimulated by growth factors like TGF-β, BMP-2, BMP-4, BMP-7, PDGF, IGF-I, IGF-II and by cytokines such as IL-1 (6).

Osteoinductive activity is the ability to stimulate bone formation using biological stimuli that induce local or transplanted cells to differentiate leading to mature osteoblasts. In the osteoinduction process, diffusible or matrix-bound peptide growth factors and cytokines promote mesenchymal stem cells and osteoblastic progenitors to migrate, proliferate and differentiate into osteoblast-like cells (5).

The ideal bone graft substitute should be osteogenic, osteoconductive, osteoinductive, biocompatible, bioresorbable, and easy to use, it should have a limited cost and provide structural support. Several substances have been proposed as a bone graft substitute. This review will focus on osteoconductive, osteogenic and osteoinductive substances and elements.

OSTEOCONDUCTIVE MATERIALS

Mineralized bone matrices

Synthetic or biologic mineralized bone matrices provide a scaffold for new bone formation through osteoconductive activity, but lack osteoinductive and osteogenic properties. They offer immediate structural support and may contribute to the creation of a microenvironment that promotes osteogenesis. However, their mechanical strength and fatigue properties are inferior to those of cortical bone (7). Mineralized bone matrices used in orthopedic surgery include allograft and ceramic matrices.

Allograft

The allograft represents the most common alternative grafting material to autogenous bone in orthopedics and offers an unlimited quantity of graft material. Allograft is osteoconductive with weak osteoinductive capacity and no osteogenic potential because graft cells do not survive on processing and transplantation (7). The use of allografts may involve complications such as the transmission of infectious diseases and an immunological response which may cause complete resorption without concomitant bone deposition (8). However, donor screening, tissue testing and processing make the procedure safer and reduces the risk of viral transmission to less than one event per million grafts. The allograft is harvested from healthy donors or cadavers that are carefully selected to avoid the complications previously described, in accordance with the American Association of Tissue Banks guidelines for all accredited centres (9) or with the European Parliament's directive 2004/23/EC concerning setting standards for the quality and safety of donations, storage and distribution of human tissues and cells (10). Allografts may be harvested by two different methods, sterile and clean or non-sterile (8). The sterile and clean method is performed with a sterile surgical technique within 12 hours after cardiopulmonary death. The time can be increased to 24 hours if the cadaver is stored

at 4°C. The non-sterile is performed less than 24 hours after cardiopulmonary death and is followed by a sterilization procedure with either ethylene oxide or with high-dose gamma irradiation (1.5-2.5 megarads). Although effective, sterilization procedures induce a decrease of osteoinductive activity and mechanical integrity in the grafts. Allografts are then processed and preserved using different methods which significantly affect bone graft strength, immunogenicity, capacity of incorporation and potential for disease transmission (8). Tissue processing techniques include high pressure lavage to clear out marrow elements and donor cells, and chemical treatments to eliminate virus and reduce graft immunogenicity. Depending on the processing techniques used, allograft can be classified as follows: 1) fresh bone graft; 2) fresh-frozen bone graft; 3) fresh-dried bone graft (lyophilized); 4) demineralized bone matrix (DBM).

Fresh bone is not subjected to any additional processing and its mechanical properties are completely preserved; on the other hand, it is associated to the highest risk of disease transmission and is the most immunogenic type of allograft, hence it is not currently used. Fresh-frozen bone is washed in antibiotic solution and then processed by deep-freezing at -70 °C or in liquid nitrogen at -196 °C. This technique does not affect the mechanical properties of fresh-frozen bone and the bone morphogenetic proteins of extracellular matrix are preserved. Nevertheless, fresh-frozen grafts, although less than fresh allografts, act as an antigenic substrate and HIV may be transmitted to a recipient. However, to date, the only cases of disease transmission have involved frozen, unprocessed grafts.

Freeze-dried bone (lyophilization) is washed in an antibiotic solution, cooled to -70 °C and its water content is reduced to less than 5%. This type of allograft is the least immunogenic and no case of HIV or viral disease transmission has been reported yet. However, bone morphogenetic proteins are destroyed by the processing technique and mechanical resistance is decreased to less than 50% (8).

Demineralized bone matrix (DBM) is prepared by decalcification of cortical bone and it is characterized by high osteoinductive activity due to bone morphogenetic proteins. The major pathway of osteoneogenesis induced by DBM is by direct induction of resident mesenchymal stem cells to osteoblasts. An et al. compared the osteogenic activity of DBM and allograft with that of autograft in patients who underwent cervical spinal fusions (11). The authors described higher rates of graft collapses and nonunions when DBM and allograft were used, suggesting that demineralized preparations did not offer sufficient osteoinductive property to induce reliable arthrodesis. Cook et al. did not observe a valid arthrodesis with the use of DBM alone or in combination with the allograft (12). DBM offered no structural or mechanical stability independently of its carrier and currently does not seem to be a reliable substitute for autogenous bone graft. It may be used as a graft extender or as a supplement in bone defects, delayed unions or nonunions and in cases of decreased bone forming capacity (7).

Ceramic matrices

Ceramic matrices are natural or synthetic inorganic composites that mimic the mineral phase of bone, that is mainly constituted of hydroxyapatite (98% of bone dry weight). Ceramic matrices commonly used in orthopedic surgery include hydroxyapatite (HA), tricalcium phosphate (TCP) and biphasic calcium phosphates (BCP) which have the advantage of incorporating at a slower rate than calcium sulfate materials.

Ceramic matrices are available in solid or porous phases and can be obtained in block, granular, powder, or putty form. They do not provide a high level of structural support because they are brittle and have little tensile strength, but they increase bone formation by providing an osteoconductive matrix for host osteogenic cells to create bone under the influence of host osteoinductive factors (13). These materials have variable rates of osteointegration based on their crystalline size and stoichiometry. In fact, osteoid formation requires a minimum pore size of 100 μm, while pore sizes of 300 to 500 μm have been reported ideal for osseous ingrowth.

Calcium sulfate is thought to act as an osteoconductive matrix for the ingrowth of blood vessels and associated fibrogenic and osteogenic cells. Over a period of 5–7 weeks the calcium sulfate is reabsorbed by a process of dissolution (14). Its rapid reabsorption may be used to advantage in the context

of osteomyelitis where an antibiotic-impregnated form could be used in place of gentamicin beads, thus alleviating the need for a second operation. Synthetic hydroxyapatite is a crystalline calcium phosphate osteoconductive bone substitute that is also manufactured as a ceramic through a sintering process. Animal studies have suggested that hydroxyapatite may have some osteoinductive properties in addition to its osteoconductive ones (15). However, because of slow *in vivo* resorption and its extreme brittleness, hydroxyapatite is not commonly used alone as an osteoconductive bone substitute. Tricalcium phosphate is less brittle and has a faster resorption rate than hydroxyapatite (16).

Tricalcium phosphate and hydroxyapatite have been combined into a biphasic calcium phosphate composite that has a faster resorption rate than pure hydroxyapatite. Calcium phosphate can also be manufactured as a cement, by adding an aqueous solution to dissolve the calcium, which is followed by a precipitation reaction in which the calcium phosphate crystals grow and the cement hardens. The primary advantage of cements over blocks, granules, or powders is their ability to custom-fill defects and their increased compressive strength (Tab.I).

The more recent availability of calcium phosphate as a cement has increased the applications of this osteoconductive material because of its increased compression strength and improved custom-filling of bone defects. For these reasons calcium phosphate cement products are used for the augmentation of the repair of fractures of the distal radial metaphysis, tibial plateau, calcaneus, hip and spine. Several studies have shown that patients treated with cement augmentation and fixation had a faster regain of grip strength and range of motion than those treated with fixation alone (17).

The lack of osteoprogenitor cells and osteoinductive potential of calcium-based bone substitutes has led to the development of composite grafts in an attempt to accelerate bone formation. A composite graft is created by adding an osteoinductive factor to an osteoconductive calcium phosphate matrix to theoretically increase bone formation. Chapman et al. conducted a prospective, randomized clinical trial to compare autogenous bone graft with a composite material made of purified bovine collagen, a biphasic calcium-phosphate ceramic, and autogenous marrow for the treatment of 249 fractures of long bones. They observed no significant differences between the two treatment groups with respect to rates of union, complications or functional measures (use of analgesics, pain or impairment while performing daily tasks), and they concluded that, for traumatic defects of long bones that need grafting, the use of composite graft material appears to be justified (18).

OSTEOGENIC CELLS

Mesenchymal stem cells

Human mesenchymal stem cells (hMSC) represent an attractive cell source for tissue engineering purposes (19). The regeneration potential of autogenous hMSC has been demonstrated in various studies. Several studies on the regeneration of bone have shown that hMSC cultured on different bioabsorbable implants are able to induce ectopic bone formation *in vivo* and lead to improved healing of critical-size defects (20).

In addition to their regeneration potential, hMSC present another very attractive property which makes them suitable for tissue engineering purposes: several immunological surface antigens important for B-cell and T-cell recognition are not expressed on the surface of hMSC, including MHC-II, CD-40, CD40L, CD80 and CD-86 (21). In a previous study it has further been demonstrated that, in co-culture with allogenic lymphocytes *in vitro*, the addition of hMSC does not lead to significant immunological stimulation, and that the addition of hMSC to previously activated allogenic lymphocytes even suppresses their proliferation rate (22). Therefore, it seems well-accepted that undifferentiated hMSC are immunoprivileged and might even contain immunosuppressive properties (21). Niemeyer et al. tested the ability of hMSC to build new bone after xenogenic transplantation on a calcium-deficient hydroxyapatite (CDHA) scaffold. The evaluation was performed using conventional radiography, micro-computed tomography (μ-CT), conventional histology and biomechanical testing. While autogenous MSC seeded on CDHA led to increased healing of critical-size bone defects from radiological and histological perspectives compared with unloaded CDHA, it was not possible to demonstrate

Table I. *Calcium phosphate properties*

	Hydroxyapatite	Tricalcium phosphate	Cementable calcium phosphate
Form	Granules, blocks, powder	Granules, blocks, powder	Paste
Reabsorption	1-2% per year	6-18 months	Years
Incorporation of antibiotics	Not possible	Not possible	Yes
Mechanical properties	Good compressive strength, brittle	Porous form similar to cancellous bone, brittle	Good compressive strength, weak in distraction
Uses	Bone graft expander, void filler, prosthetic coatings	Bone graft expander, void filler	Metaphyseal defects, void filler

Table II. *Level of evidence of bone graft substitutes.*

	BONE GRAFT SUBSTITUTE	Level of evidence
Osteoconductive	Allograft	IV-V
	Ceramic matrices (Calcium phosphate)	I-II
	Ceramic matrices (Calcium sulfate)	II-III
Osteogenic	Mesenchymal stem cells	II-III
Osteoinductive	BMPs	I
	PRP	IV-V
	Other growth factors	IV-V

analogous effects for the xenogenic transplantation of hMSC. The xenogenic treatment group displayed inferior results in all parameters compared with the autogenous MSC treatment group. Nevertheless, no local or systemic inflammatory response resulting from xenogenic transplantation was observed (23). Beside the tolerance and inflammatory aspects of the MSC, clinical trials have been performed to assess the osteogenic properties of the hMSC.

Jeger et al. studied the clinical outcomes of ten patients with volumetric bone deficiencies treated with mesenchymal stem cells and bone marrow aspirate. Results were evaluated with radiographs. In addition to the *in vivo* data, they also presented *in vitro*

data of Bone Marrow Concentrate (BMC) cultivated onto a porous collagen I scaffold and the technique of bone marrow aspiration via a commercially available system (BMAC™, Harvest Technologies GmbH). Results demonstrated that there was the rationale for a clinical application of BMC in the treatment of osseous defects. The intraoperative harvest procedure appeared to be a safe method and did not significantly prolong the time of surgery. In addition, MSC isolated from the aspirate was able to adhere and proliferate in significant numbers on a collagen scaffold after a 15 min incubation period. These cells then enabled osteogenic differentiation *in vitro* without any osteogenic stimuli. The authors concluded that the local application of BMC in the treatment of bone deficiencies could be a promising alternative to autogenous bone grafting and help in reducing donor site morbidity (24).

Neen et al. in a prospective case controlled study compared the clinical and radiographic performance of Healos™ (a Type 1 collagen/hydroxyapatite matrix) soaked, for at least 20 minutes, in bone marrow aspirate (BMA) versus iliac crest autograft when used in lumbar spinal fusion. Healos and BMA had similar results to autologous iliac crest bone as a graft material in posterolateral lumbar spine fusions but were radiographically ineffective in lumbar interbody fusions (25).

OSTEOINDUCTIVE MATERIALS AND SUBSTANCES

Growth factors

The recent advances in basic science research and in orthopedic technology have led to the clinical application of human growth factors to enhance bone tissue repair. In fact, it is well known that several growth factors are expressed during the different phases of experimental fracture healing and that based on these findings, growth factors may act as potential therapeutic agents.

Nevertheless, many problems related to their clinical application must be solved, such as the choice of the growth factor, the right dose, the moment of administration during the bone healing process and the administration method. Regarding the administration of growth factor, two different possibilities are currently available: the release of growth factors from autologous platelet-rich plasma (PRP) or the direct application of extractive or recombinant proteins alone or bonded to carriers.

PRP represents a natural source of growth factors and has been shown to stimulate bone healing and to reduce significantly the time needed for graft consolidation and maturation, with increased bone density compared to autogenous bone graft alone (26). The emergent interest in the growth factors contained in human platelets is related to their activity in the bone healing process. Platelet growth factors are released in the fracture healing callus and stimulate anabolic activity of osteoblast-like cells, providing a chemotactic effect on mesenchymal stem cells and angiogenic activity on capillary endothelial cells (27). Platelet growth factors are stored in the α-granules and are released as a consequence of cell activation by thrombin or calcium. PRP may be obtained from whole blood using a technique which provides an enhanced growth factor concentration (26).

The use of platelet-rich plasma (PRP) in bone reconstruction therapy was introduced in the late 1990's. Since then, many scientists and clinicians have employed it in orthopedic and oral surgery but controversial results have been obtained in experimental studies using PRP as a bone substitute alone or in association with other bone grafts (28-29).

Bone morphogenetic proteins (BMPs) are members of TGF-β superfamily: they were discovered by Urist in 1965 and more than twenty molecules have been identified so far. BMP-2, 4 and 7 have been shown to play a critical role in bone healing by means of their ability to stimulate differentiation of mesenchymal cells to osteoblast-like cells and chondroblastic cells (6).

Numerous preclinical studies have assessed the efficacy of recombinant human bone morphogenetic proteins (rhBMP) in the healing of critical bone defects and the acceleration of fracture healing (30-32). Although experimental studies have provided promising results, they highlight the need of high doses of rhBMP to obtain adequate bone formation, but to date the minimal effective dose has not been established. Furthermore, different carriers were tested, but none of them was identified as the most appropriate for delivering rhBMPs to the

site of fracture or bone defect (33). rhBMP-7 was used to treat tibial nonunions and no significant difference was shown, with respect to either clinical or radiographic outcome, between patients treated with rhBMP-7 and those who were treated with autologous bone graft (34). The authors of this paper demonstrated that patients affected by nonunion had poor bone healing when treated with rhBMP-7 alone. By contrast, a wider and quicker bone formation was observed after implantation of rhBMP-7 with autologous cancellous bone, suggesting the need of a large availability of target cells for the growth factor at the nonunion site (35). In another study, they compared the *in vitro* capability of two recombinant human bone morphogenetic proteins (rhBMP-2 and rhBMP-7) and activated platelet-rich plasma (PRG) to stimulate proliferation and/or differentiation of cells derived from nonunion patients. Treatment with rhBMP-7 or rhBMP-2 showed an enhancement in the expression of osteoblastic marker (osteonectin and osteocalcin) in cells derived from human nonunion sites and in MSCs, while no significant changes were observed in osteoblast cultures. The PRG treatment produced a considerable increase in cells proliferation without affecting cell differentiation in all analysed samples (36).

In a recent Cochrane review, Garrison et al. highlighted a paucity of data on the use of BMP in fracture healing and they concluded that the limited available economic evidence indicates that BMP treatment for acute open tibial fractures may be more favourable economically when used in patients with the most severe fractures (37).

Two insulin-like growth factors (IGF) were identified: IGF-I and IGF-II. IGF-II is the most highly concentrated growth factor, while IGF-I is 10-20 times inferior. IGF-I, however, is 4-7 times more powerful than IGF-II (38). IGF production in bone tissue is promoted by PTH and GH. Both IGF-I and IGF-II increase the osteoblast proliferation, and the collagen's synthesis and degradation (39).

PTH is a major systemic regulator of the concentrations of calcium, phosphate, and active vitamin-D metabolites in blood and cellular activity in bone. In 1999, Andreassen et al. reported the results of the first study on the influence of intermittent PTH administration on callus formation and mechanical strength in tibial fractures in healthy and sexually mature adult rats after twenty and forty days of healing (40). Further studies by Andreassen et al. in 2004, Nakajima et al. in 2002, Alkhiary et al. in 2005, and Komatsubara et al. in 2005 all resulted in similar outcomes (41-44).

Recently, a biomimetic bone matrix that simulates the cellular environment of hard tissue, identified as P-15, was introduced to the orthopedic community. P-15 is a synthetic, 15-amino-acid residue found in the chain of type I collagen. Bhatnagar et al. have demonstrated that P-15, containing the potent cell-binding domain of collagen, could be adsorbed onto a calcium phosphate substrate and could enhance cell attachment and extracellular matrix and factor production, resulting in the formation of bone (45). P-15 bone graft substitute (P15-BGS) is a combination of mineral component of bone and a peptide representing the cell-binding domain of type I collagen and it has been found to be statistically and clinically superior to both demineralised bone matrix (DBM) and synthetic calcium phosphate bone graft substitutes in the oral cavity (46). Gomar et al. published a report of the use of P15-BGS in human orthopedic indications. They treated a total of 22 patients for malunion or delayed union fractures with P15-bone graft substitute (P15-BGS) at the fracture site and mostly with internal fixation. They achieved a full consolidation in 90% (20 out of 22) of the patients treated with P15-BGS and the average time for full consolidation was 4.2 months. Their results compare favourably with those in published literature as an alternative to autograft (47).

LIM Mineralization Protein (LMP-1) was identified in RNA from osteoblasts stimulated by glucocorticoid and isolated from an osteosarcoma complementary DNA (cDNA) library. Based on its association with bone development *in vivo* and on the results of suppression and overexpression experiments *in vitro* and *in vivo*, it was demonstrated that LMP is an essential intracellular positive regulator of the osteoblast differentiation program. Furthermore, its temporal and spatial association with bone morphogenetic protein-6 (BMP-6) suggests that it may be involved in the signalling pathway of BMPs (48). Strohbach et al. evaluated the potential of LMP-1-based retroviral gene therapy in stimulating osteoblast differentiation *in vitro* and enhancing fracture repair *in vivo*. They demonstrated

that LMP-1 could be a better potential candidate for gene therapy for fracture repair than BMP-4. These findings indicate that LMP-1-based gene therapy may be potentially a simple and effective means to enhance fracture repair that warrants further investigation (49).

Vitamins also became protagonists of studies which try to understand their potential as valid bone substitutes or bone healing supports. Currently, vitamin D and K are considered as the most important in the bone healing process. Vitamin D is a promoter of bone remodeling and new bone apposition, by interaction with osteoblasts, osteoclasts and PTH. Different studies show that vitamin D with its metabolite 24, $25(OH)_2D$ plays an important role in fracture reparation due to the elevated concentration in plasma following a fracture (50).

The great importance of vitamin K's role in bone metabolism has been known for a long time thanks to the studies on osteoporosis (51). Vitamin K is involved in the carboxylation of certain glutamate residues in proteins to form gamma-carboxy-glutamate residues (abbreviated Gla-residues). The Gla-residues are essential for the biological activity of osteocalcin, a protein associated with the incorporation of calcium in hydroxyapatite crystals that form bone matrix. An *in vitro* study demonstrates that vitamin K combined with vitamin D is able to modulate the differentiation towards osteoblastic phenotype of hMSCs derived from fracture sites, thus offering clinicians a promising and low-cost strategy for reparative osteogenesis (52).

CONCLUSIONS

Several new materials, cells and methods may be used as bone substitutes and they represent a challenge for orthopedic researchers and a therapeutic option in the near future. Even though autologous bone is the only bone substitute that provides osteoconductive, osteoinductive and osteogenic properties, its use as an augmentation of bone-healing is currently supported by very little direct clinical evidence. Indeed, there are no studies in literature where the effectiveness of autograft has been compared with that of no graft. Additionally, complications such as donor site morbidity or wide fusion areas limit its use. A possible solution to determining the ideal bone graft substitute would be performing multicenter prospective randomized studies, however these would be extremely difficult to design and perform as they are extremely expensive. For these reasons, currently, evidence-based medicine uses a rating system to provide a level-of-evidence to help surgeons attempt solving clinical dilemmas. For example, a randomized controlled trial or well-done review article, Level I, provides excellent information, while Level V is essentially based on an expert's personal opinion offering only a little help (53). The osteoinductive effects of rhBMP-2 and 7 are well documented, and Level-I evidence supports their clinical use. However, there is less documentation for many of the osteoconductive bone substitutes: only some calcium phosphate and hydroxyapatite grafts are supported by Level-I evidence; data regarding the use of autologous bone marrow are nowadays inconsistent (1) (Tab.II).

One of the emerging surgical options may be the use of a ''composite graft'' that contains osteogenic cells and/or osteoinductive growth factors along with a synthetic osteoconductive matrix. Composite materials tested in preclinical and clinical trials show function comparable to autograft and allograft (Level II-III evidence) (54).

Despite all the information in literature, the surgeon's choice of the right graft must also be based on what is required from the graft (either a structural or bone-forming function, or both), the availability of the graft and its cost. The surgeon must also remember that stable fixation is necessary for the use of any of these materials.

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REVIEW ARTICLE

DIFFERENT TREATMENT OPTIONS IN GIANT CELL TUMOR OF THE WRIST: A REVIEW OF THE LITERATURE

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The authors review the different management options for giant cell tumor of the distal radius. The goal of treatment of this lesion is the complete removal of the tumor. Curettage alone of giant cell tumor is associated with local recurrence independently of tumor grading. Adjuvant treatment of the bone bed with liquid nitrogen or phenol after removal of the tumor has been suggested to decrease the risk of local recurrence. The advantages of using cement include low cost, easy to use, lack of donor-site morbidity, no risk of disease transmission related to allograft use, immediate structural stability and it enhances an earlier detection of local recurrence. The authors recommend the treatment with curettage for grade I and II giant cell tumors as it offers a very good (90%) rate of cure. A high rate of local recurrence and complications is to be expected with curettage alone in grade III tumors. The patient should be counseled about other options including resection and reconstruction. Narrative Review.

Giant cell tumor is classified as a locally aggressive bone neoplasm. Ten percent of these lesions appear in the distal radius (Fig.1-2). This is the 3rd most common site for this tumor after proximal tibia and distal femur (1-2).

Giant cell tumors are classified as locally aggressive tumors that can metastasize to the lung (3).

Giant cell tumor of the bone may present with pain in the joint, effusion and swelling. In about 10-15 % of the patients it will present with a pathological fracture. This tumor is locally aggressive and has a high incidence of recurrence (1-2, 4-8).

The medical imaging for tumor screening includes standard radiography of the wrist, magnetic resonance of the wrist, chest and total body bone scan.

When the tumor grows larger, the endosteal surface of the cortex is destroyed and a thin shell of reactive bone is formed. This neocortex appears thin and expanded on X-rays; in some cases it may be difficult to see.

Magnetic resonance shows an alteration of the signal of intensity of the bone with the possible involvement of soft tissue. Angiography may be useful in all cases even if it is not routinely performed.

The diagnosis is confirmed by histological examination of the biopsy. According to Campanacci giant cell tumors should be classified in three grades. Grade I tumors have a well-defined border with a thin rim of mature bone and intact bony cortex. Grade II lesions have relatively well-defined margins but there is no radio-opaque cortical rim. Grade III is designated to the lesions with fuzzy borders,

Key words: giant cell tumor, bone tumor, distal radius

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suggesting a rapid, and possibly a permeative growth pattern of the tumor (9-10).

This grading system differs from Enneking's, which is based on clinical and radiographic features, isotope scan, angiography, computerized tomography as well as the macroscopic and microscopic appearance of the tumor (11).

The goal of treatment is complete removal of the tumor from the distal radius. Giant cell tumor of the bone in the distal radius affects young adults so the reconstruction of the bone defect is necessary to preserve the maximum function of the wrist joint.

Treatment consists of either extended curettage followed by packing of the cavity with bone graft or methyl methacrylate, or resection of the lesion followed by reconstruction with autograft or allograft.

Treatment options are: curettage alone or with bone grafting; curettage of the tumor and packing of the cavity with methyl methacrylate; or resection of the lesion followed by reconstruction. Local radiotherapy is also used in some institutions.

TREATMENT OPTIONS

Curettage alone

Curettage of the tumor and bone grafting

Curettage of the tumor and packing of the cavity with methyl methacrylate

Resection of the lesion followed by reconstruction

The aim of this article is to review the different surgical procedures for giant cell tumor located in distal radius.

Curettage alone or with bone grafting

The lesion is approached through a dorsal incision or volar incision. In the dorsal incision the extensor tendons are identified and protected throughout the procedure.

In the volar incision the carpal radial flexor tendon, the radial vessels and nerve, and the median nerve are identified and protected. In this approach it is necessary to cross the pronator quadratus. The tumor is accessed via a cortical window. All the neoplastic tissue must be removed using curved curettes under the overhanging bone margins. Chemical detergents may be used to sterilize the cavity (phenol or cryotherapy with liquid nitrogen) (1,4,10,12-13).

Curettage alone or with bone grafting has been associated with a high incidence of local recurrence in giant-cell tumors. High rates of recurrence (23–80%) have been reported in some studies after curettage of the tumor. While packing the cavity created after removal of tumor provides structural support, it has been criticized for obscuring possible local recurrences of the neoplasm (13).

Packing with methyl methacrylate

Acrylic bone cement (methyl methacrylate) has been suggested as the alternative filler for bone cavities. It has been thought that the use of cement would extend the area of curettage, due to the toxic effect of the monomer and the exothermic reaction of the polymer. The free radicals and the thermal effects of the polymerization reaction can cause as much as 2 or 3 mms of necrosis in the cancellous bone. Additional advantages of the use of cement include low cost, easy to use, lack of donor-site morbidity, no risk of disease transmission related to the use of allograft bone, immediate structural stability and maybe enabling an earlier detection of local recurrences (1,6,8,10,12-13). The use of cement may lead to the premature onset of degenerative changes of the adjacent wrist joint due to heat damage. The bone cement inserted under pressure may also force the residual tumor into the local soft tissue (13).

Resection of lesion

After resection of the lesion, a complex reconstruction procedure (arthroplasty) or arthrodesis of the wrist is required. These procedures have a lower rate of local recurrence. Arthroplasty has an associated risk of deep infection and dislocation of the carpus. Wrist arthrodesis on the other hand has a risk of delayed or non-union at the arthrodesis site and may lead to a significant limitation of joint articulation (4,12,14,16).

Other procedures that may be used to reconstruct the defect include vascularized or non-vascularized bone graft from tibia or proximal fibula, osteoarticular allograft, or transposition of the carpus.

Free vascularized fibula transfer is an established method for reconstruction of the wrist following tumor resection. In cases of resection of the radial

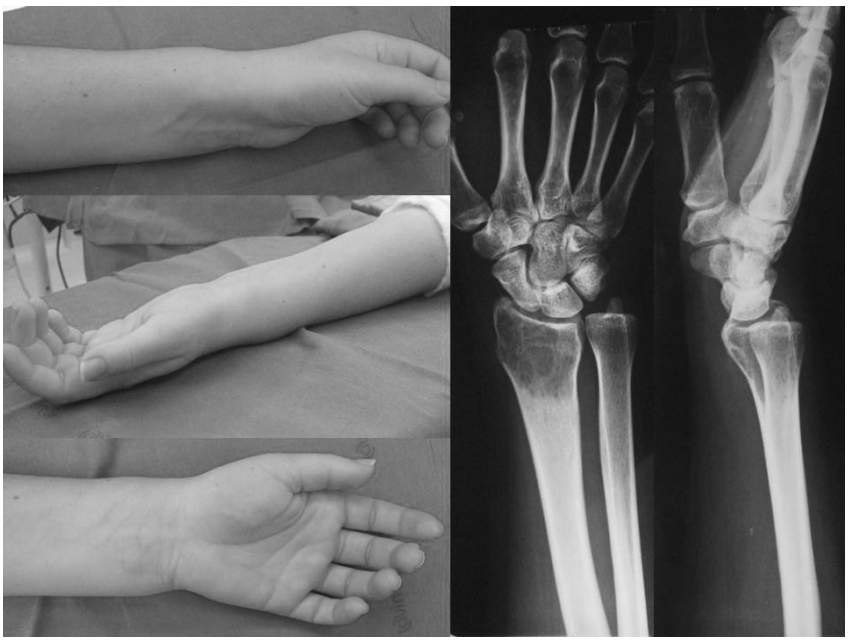

Fig.1. *Clinical and radiological views of the giant cell tumor in the distal radius.*

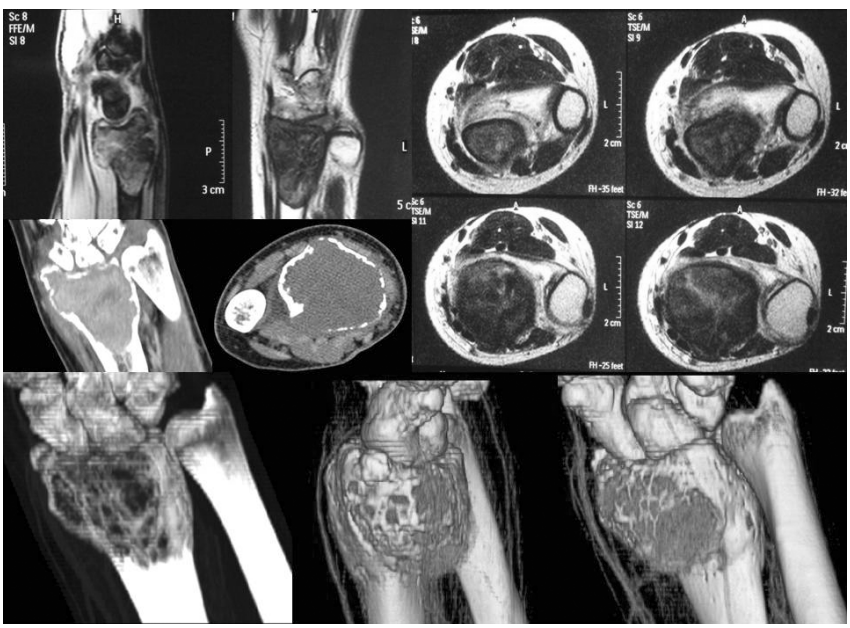

Fig.2. *MRI and TC pictures of the giant cell tumor in the distal radius.*

articular surface, three reconstructive options are possible: fibular head transfer along with the shaft to replace the radial joint surface, fixation of the fibula to the scaphoid and lunate, or a complete wrist fusion. (4,7,15-19).

All these procedures have morbidities and complications associated with them; nevertheless, resection and reconstruction may be the only option in the case of aggressive tumors which have eroded the cortex.

RECONSTRUCTION OPTIONS

Arthroplasty
Arthrodesis
Vascularized bone graft proximal fibula
Non-vascularized bone graft from tibia osteoarticular allograft
Transposition of the carpus

DISCUSSION

In the case of a giant cell tumor localized in the wrist, treatment options should ensure either complete tumor resection or maintain the function of the upper limb.

Simple curettage of giant cell tumor guarantees wrist function but is associated with local recurrence independently of the tumor grading (1,6-10,12,15-19).

It is difficult to comment the causes of local recurrence. It has been suggested that curettage alone may not have completely removed the tumor, and a local recurrence may well be the residual tumor. Enneking thought that the high rate of local recurrence was due to the indiscriminate use of curettage for all lesions including the highly aggressive tumors, and so local relapse is related more to the grade of tumor than to the technique used (11).

Curettage alone or combined with adjuvant (phenol or nitrogen liquid), followed by bone grafting or filling the resultant cavity with bone cement has never been gauged against the type of tumor. We agree that curettage alone may not be the best treatment option for grade III giant cell tumors, but associated with adjuvant it gives the lowest rates of recurrence in most of the grade I and II and some grade III patients. Several authors believe there is no proof that phenolisation of the cavity is required after curettage. O'Donnell et al. have shown that, over a 9-year period, the highest incidence of recurrence was observed in Campanacci grade III tumors of the distal radius. The chances of recurrence were increased if curettage was performed without using a high speed burr(6).

Adjuvant treatment of the bone bed with liquid nitrogen or phenol after removal of the tumor has been advocated to decrease the risk of local recurrence.

Liquid nitrogen results in effective osteonecrosis to a depth of 1 to 2 centimeters. Osteonecrosis induced by liquid nitrogen is difficult to control, thus it may induce bone weakness and lead to fracture. Phenol has been proposed as a safer agent than liquid nitrogen for adjuvant therapy, but phenol causes protein coagulation, damages DNA, causes necrosis, and is toxic to the nervous system, heart, kidney and liver.

Autogenous bone grafting is associated with donor site morbidity, risk of disease transmission, as well as the risk of resorption of the grafted bone. The cavities that have been filled with bone graft often show areas of radiolucency. This may be due to incomplete packing, inflammatory changes, bone graft resorption or even a low-grade infection. These changes may be difficult to distinguish from a tumor recurrence (1,6-10,12).

Bianchi et al reported the results of a technique for the osteoarticular allograft reconstruction of bone defects in 12 patients retrospectively with a minimum follow-up of 2 years. Three patients had a malignant tumor and nine had a giant cell tumor. Non-union of the osteotomy line was diagnosed 6 months after surgery in one case and needed bone grafting. Distal radioulnar joint instability was observed in eight cases. Subchondral bone modifications and joint narrowing were present in all cases but were painful in only one patient. The mean range of motion was 51 degrees of flexion and 37 degrees of extension (16).

Muramatsu et al reported their experience with both radio-carpal hemiarthroplasty and fibulo-scapho-lunate fusion which similarly provided successful for both wrist stability and functional range of motion. Even when the wrist was totally fused with the fibula, its function was still acceptable (17).

Kumta et al reported the clinical results of vascularized bone grafts in 39 patients with giant cell tumor affecting the extremities. In 18 cases the sites also involved the distal radius. Osteoarticular replacement was performed in patients with giant cell tumor involving the radius; in 15 of these a suitably tailored vascularized iliac crest graft was used, and in the remaining three, the fibula was used. The eighteen patients with distal radius involvement

were followed-up for periods ranging from 2 to 12 years. Non-union was seen in one, carpal subluxation in five, and spontaneous radiocarpal fusion in one patient. A pain-free functional wrist was attained in 17 of these 18 patients. Three local recurrences were observed (2.5 percent). The vascularized bone graft provided a good biological and mechanical support to the subchondral bone and overlying articular cartilage. Satisfactory reconstruction was thus possible following wide resection, without sacrificing joint function and with good oncologic results. The use of a suitably tailored block of vascularized iliac crest is an acceptable method to preserve wrist and radioulnar joint motion, following excision of the distal radius affected by a giant cell neoplasm (18).

The advantages of using cement include low cost, easy use, lack of donor-site morbidity, no risk of disease transmission associated with the use of allograft bone, immediate structural stability and it may enhance the earlier detection of local recurrences.

Some authors have reported evidence of premature degenerative changes of adjacent wrist joint due to heat damage.

The bone cement inserted under pressure may also force the residual tumor into the local soft tissues. Furthermore the acrylic cement leads to the development of radiolucent lines in the cyst cavity which makes the diagnosis of recurrence difficult.

Khan et al reported a total of 287 patients with giant-cell tumor (1972–2000). Of these, 24 were found to have lesions in the distal radius. One patient underwent endoprosthetic replacement of the distal radius for an aggressive tumor unsuitable for curettage. The remaining 23 patients underwent curettage of the primary neoplasm and they were followed up carefully at regular intervals for any evidence of local recurrence or systemic metastasis (13).

Khan et al observed eradication of the tumor in 19 (78.2%) patients with one curettage and 21 (91.4%) patients were treated with further curettage. Recurrence was seen mainly in the aggressive grade III tumors with one exception. Complications requiring further surgical intervention were seen only in patients with grade III tumors. Of the 21 patients without any previous treatment, curettage was successful in 17 (80%) (13).

While single extended curettage performed carefully by an experienced orthopedic oncologist offers a good chance of eliminating the disease, the results are not as predictable in aggressive grade III tumors.

Resection of the tumor followed by arthroplasty or arthrodesis is the alternative option in aggressive tumors. Arthroplasty has an associated risk of deep infection and carpal dislocation. Wrist arthrodesis on the other hand has a risk of delayed or non-union at the arthrodesis site as well as morbidity from the operation.

Puri et al reported 14 patients with a Campanacci grade III giant cell tumor of the distal radius who were treated by en bloc resection and reconstruction by ulnar translocation with arthrodesis of the wrist. All the patients were followed until bone union and all except one patient had an excellent range of pronation and supination. The remaining patient developed a radio-ulnar synostosis. Ulnar translocation provided a local vascularized bone graft to reconstruct the defect left after excision of the distal radius for giant cell tumor. It also avoided the need for a microvascular procedure while it maintained rotation of the forearm and a good function of the hand (15).

Bhan reported translocation of the ipsilateral ulna in six cases after radical resection of a giant cell tumor of the distal radius. All the patients had very good forearm rotation and an acceptable appearance. There were no significant complications.

The patients had to attend follow-up in the orthopedic oncology clinic for a minimum of 5 years. Repeat X-rays of the wrist and chest must be performed at each visit as well as the clinical assessment (19).

Wrist X-rays and magnetic resonance imaging were to assess for evidence of local tumor recurrence and distal radio-ulnar impingement

Any change in the ulnar variance after the curettage which could be attributed to radial collapse was recorded.

Neither the patient's age nor the tumor size seemed to influence the risk of recurrence in any grade of tumor. There was not much difference in the volumetric size of the two groups.

We recommend the treatment with curettage for grade I and II giant cell tumors as it offers a very

good chance of cure. A high rate of local recurrence and complications is to be expected when curettage alone is used for grade III tumors. The patient should be told about other options including curettage and cementation or resection and reconstruction.

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SURGICAL TECHNIQUE

ARTHROSCOPICALLY ASSISTED LATARJET – LAFOSSE PROCEDURE: HOW TO MAKE IT EASIER IN LATERAL DECUBITUS POSITION THROUGH 3 STANDARD PORTALS

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Anteroinferior instability appears to be a significant problem nowadays. There is a variety of techniques, both open and arthroscopic used to deal with it. The Bankart procedure remains the most popular. Although when there are massive defects of the glenoid cavity and the humeral head, bony block procedures (1) are recommended. The Latarjet procedure (2) is considered to be an effective and reproducible method and has good long-term results (3). Arthroscopic modifications of the Latarjet procedure are becoming increasingly popular, but are rather difficult to perform and have a steep learning curve. We describe a new safe and reliable arthroscopically-assisted technique. It combines the advantages of the Lafosse (4) and the Boileau (5) arthroscopic methods and offers the possibility of treating anteroinferior instability with the patient in the lateral decubitus position through 3 standard portals and a 2.5-3 cm graft harvest incision. Our procedure was created to simplify the arthroscopic Latarjet method and to make it reproducible among those surgeons who prefer the patient in the lateral decubitus position.

Anteroinferior instability (6) including the massive deficit of the glenoid cavity and the humeral head is a significant problem nowadays. One of the principal methods of treatment for this combined pathology is the arthroscopic Bristow-Latarjet procedure. Geoffrey Noirissat (7) describes a cadaver study, where he shows it is possible to performa a mini-open arthroscopically-assisted Bristow procedure with 1 cannulated screw in a standing position through 15mm and 20mm incisions with a skin bridge of approximately 10mm. The Laurent Lafosse technique (4) provides a stable fixation of the coracoid process to the anterior border of the glenoid by 2 cannulated screws with Top Hats, but it requires removal of all rotator interval tissue, joint labrum and glenohumeral ligaments. The Pascal Boileau`s procedure (5) attempts to save the joint capsule, to reconstruct glenohumeral ligaments, to perform Bankart repair and to fix the coracoid`s graft in the standing position with one interference screw.

These 3 arthroscopic techniques are performed by the surgeons in the beach-chair position (8). We tried to combine these 3 surgical approaches and create a technique which allows us to perform the arthroscopic Latarjet-Bankart procedure with the patient in the lateral decubitus position (8), which is widely used by a significant number of surgeons.

Surgical technique

The arthroscopically assisted Latarjet - Lafosse technique in the lateral decubitus position can be performed on a standard operating table with the

Key words: shoulder, anterior instability, arthroscopy, Latarjet, Bankart, lateral decubitus position; bony defect; Bristow

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shoulder to be operated lifted vertically by the traction device. Approximately 5 kg of weight is be loaded on the traction device, and the angle of abduction and forward flexion of the shoulder depends on the surgeon`s preference. The operating table is tilted back to 20 to 30 degrees to make the glenoid parallel to the floor (Fig.1).

Our surgical technique consists of 5 surgical steps (arthroscopy and mini-opening) performed through 3 standard portals. The location of the portals is marked on the skin at the preoperative stage.

First step: Diagnostic arthroscopy

At this stage the final decision must be made whether to perform the Latarjet – Lafosse procedure (9) .The indications are: anteroinferior glenoid bone loss < 25% (Fig.2), Hill- Sachs lesion (10) (Fig.3), capsular deficiency, ligamentous insufficiency, HAGL lesion and previously failed Bankart repair. Diagnostic arthroscopy is made through the standard posterior portal A.

Second step: Coracoid graft harvesting and preparation of the holes in the coracoid

In the second step the traction is removed, the arm is adducted. The 2.5-3 cm incision is made in the projection of the coracoid process. The space between the deltoid and pectoralis major is identified, these muscles are divided bluntly and the base of the coracoid is exposed. The coracoacromial ligament is detached from the lateral side of the coracoid and the pectoralis minor is detached from its medial side as described in the open procedure by Burkhard (11-13) and Garcia (14). The brachial plexus, which lies just behind the pectoralis minor and pectoralis minor itself is inspected bluntly by finger. By using the curved osteotome the coracoid process is osteotomized at approximately 15 mm from the coracoid`s tip.

The coracoid process together with the conjoined tendon are then pulled out from the incision as previously described by Nourissat (7). To provide good healing the inferior side of the coracoid is abraded with the burr to the trabecular bone (Fig.4A). Using the Coracoid Drill Guide (DePuy Mitek, Wokingham, UK), two Kirschner (K)-wires are introduced in the two holes. The holes should be placed at 1/3 and 2/3 of the coracoid process and strictly perpendicular to its superior surface. The Coracoid Drill Guide is removed, leaving both K-

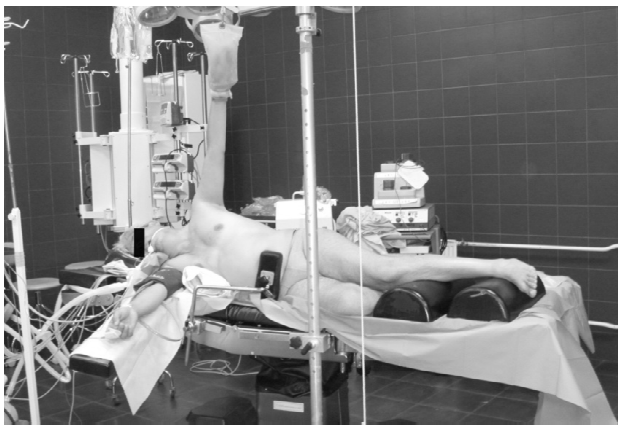

Fig.1. *The lateral decubitus position of the patient.*

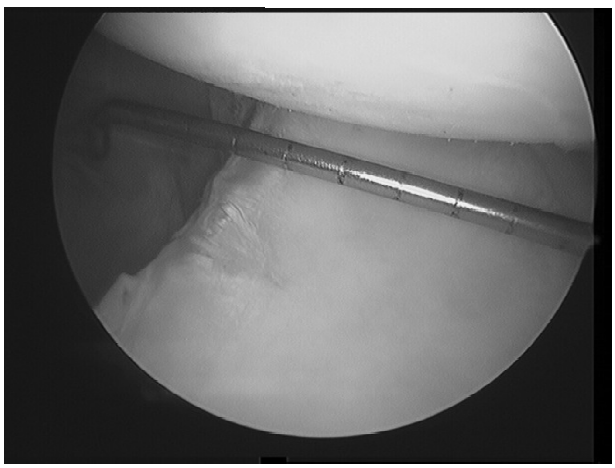

Fig. 2. *The glenoid bone loss.*

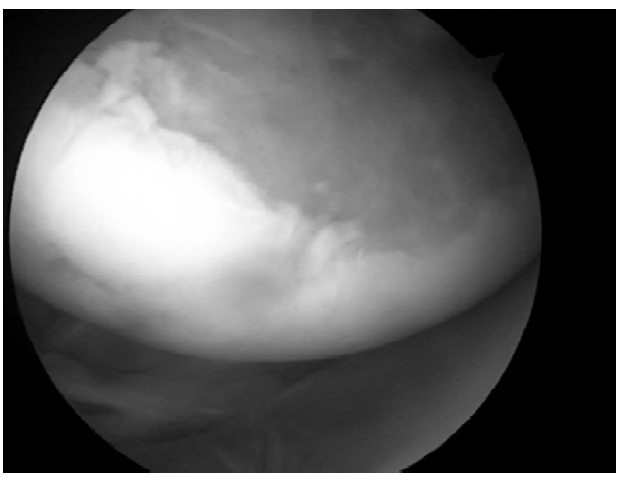

Fig. 3. Hill-Sachs lesion.

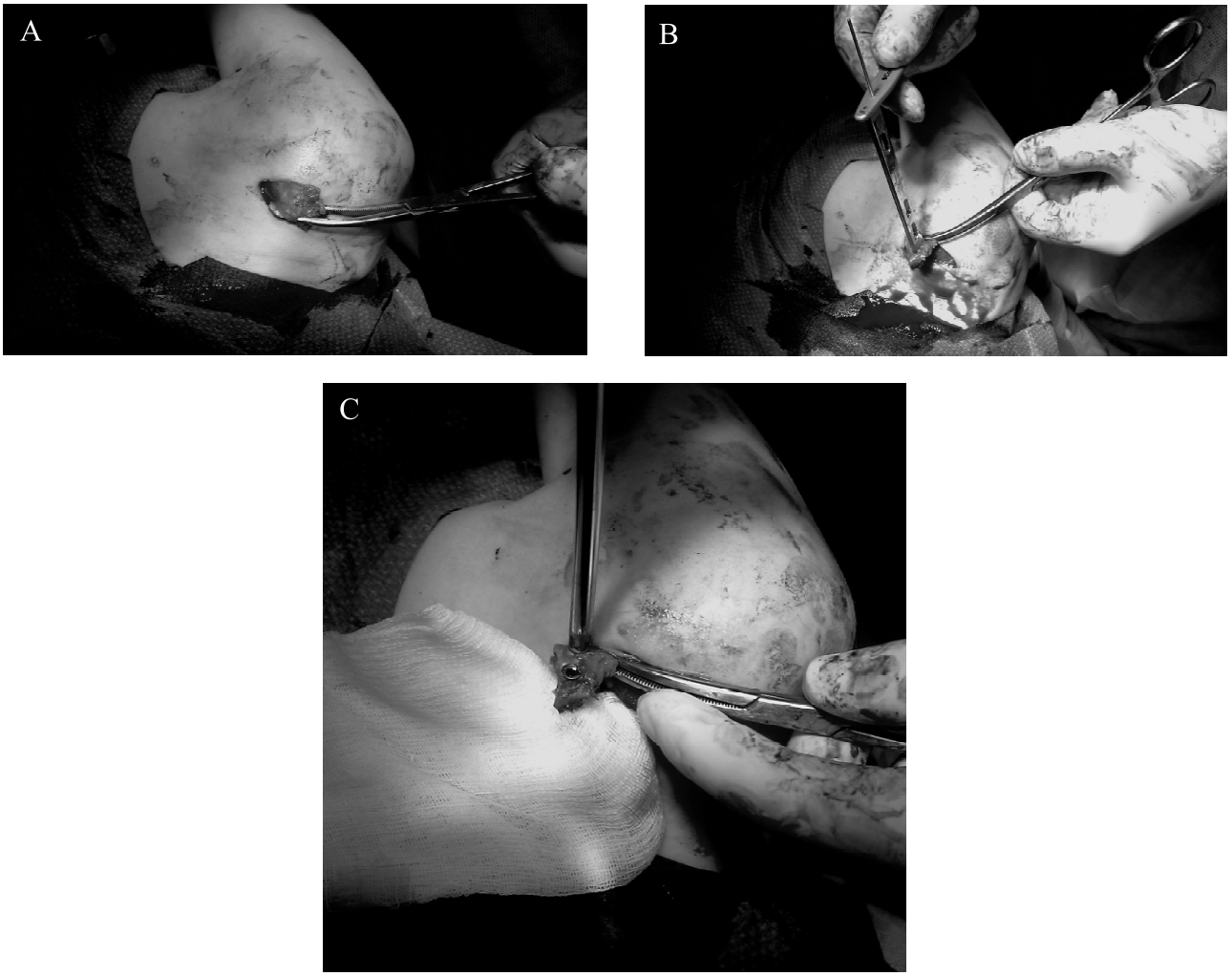

Fig. 4 A) B) C) *Pulling the coracoid graft out of the incision*

Wires in the holes. Using the cannulated Coracoid Step Drill (DePuy Mitek, Wokingham, UK) the coracoid is drilled completely through the holes (9). Using Coracoid Step Taps the tunnel is threaded as in the original Lafosse technique and Top Hats are screwed into the holes (9). Through the holes in the coracoids, the flexible wire (CHIA) (DePuy Mitek, Wokingham, UK) PDS suture is passed and the coracoid process is put back into the incision (Fig4 B-C).

Third Step: Preparation of glenoid neck

The arm is abducted and the patient is positioned on the lateral side with the abduction at 45 degrees, the body is tilted back 20 degrees. The standard anterior-superior portal is made by the spinal needle and the scope is inserted. The 6.5 mm cannula is put in. Through the incision of the graft harvest the rotator interval is penetrated and the third anterior portal C is inserted. (Fig. 5). During joint evaluation we can deal with the concomitant pathologies, such as SLAP, so at this stage these lesions should be repaired.

The labrum and glenohumeral ligaments that were left are sutured by the shuttle at the middle glenohumeral ligament`s attachment to the labrum. The labrum is completely separated from the antero-inferior glenoid rim. The glenoid is abraded with the burr to make it flat and is prepared for the coracoid`s

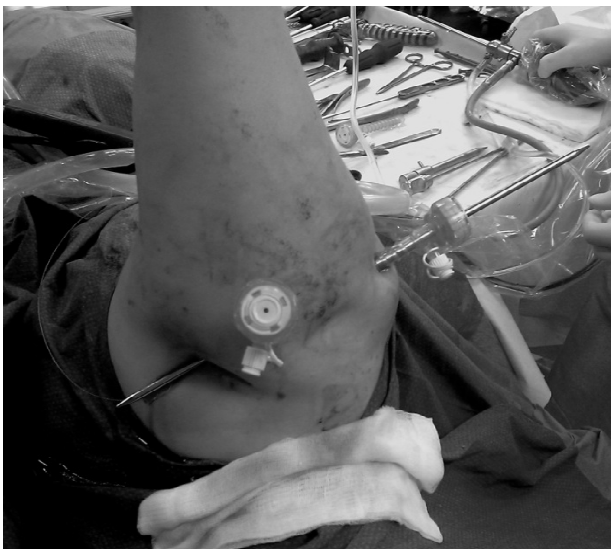

Fig. 5. *The placement of the three standard portals. The third (anterior) portal C was made through the graft harvest incision.*

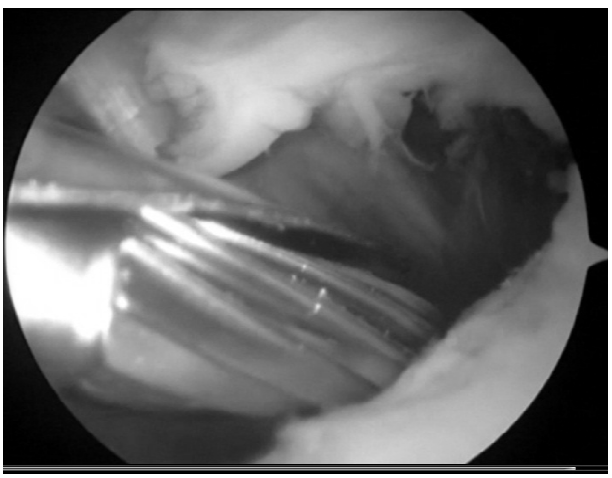

Fig. 6. *The site for the coracoid graft on the glenoid is abraded by the burr.*

insertion (Fig. 6-7).

Fourth Step: Coracoid graft transfer

The anterior surface of m. supscapularis is inspected by palpation and by the scope, inserted through the coracoid graft harvest incision (Fig.8). A Wissinger rod is installed through the posterior portal, m. subscapularis is penetrated by it from the inside out in a 5 o`clock glenoid position point (Fig.9). Brachial plexus medially and n. axillaris distally are identified by palpation. The tip of the switching

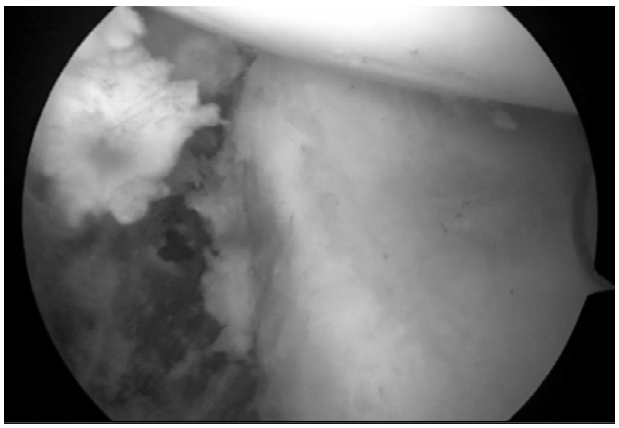

Fig. 7. *Glenoid is prepared for the coracoid graft placement.*

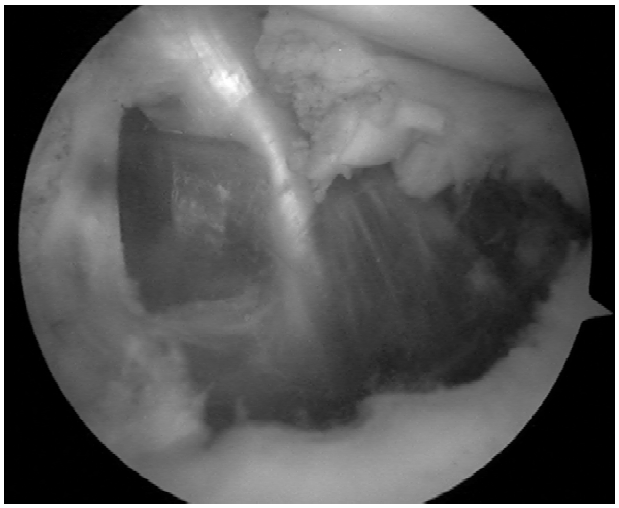

Fig. 8. *Preparing the place for the m. subscapularis split*

stick is determined by palpation and by visualization through the graft incision. After the identification of the position, the finger of the surgeon divides m. subscapularis in the lateral-medial direction at 2/3 superior and 1/3 inferior outside in, grabbing the tip of the Wissinger rod and elevating the upper part of m. subscapularis and pulling the switching stick out. Performing this stage correctly there is no risk of damaging the brachial plexus and n. axillaris. The Positioning Double Cannula is put on the anterior surface of the coracoid graft, the 3.5mm cannulated coracoid guiding screws are threaded into the Top Hats in the holes (Fig.10). The coracoid is put back in the incision. The coracoid graft is passed through the subscapularis muscle intraarticularly with the

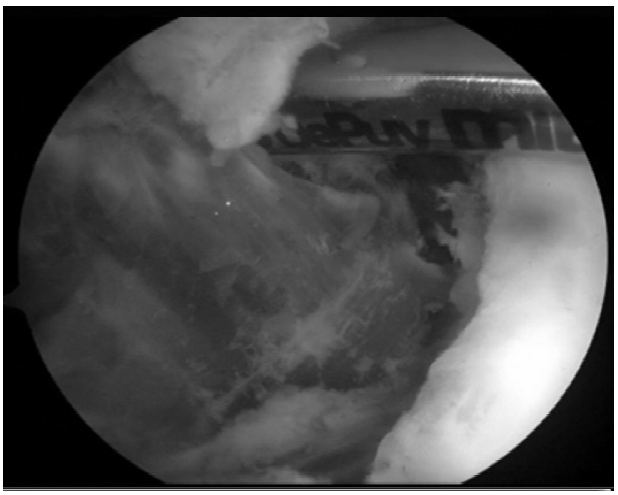

Fig. 9. *Splitting bluntly m. subscapularis with the help of the switching stick*

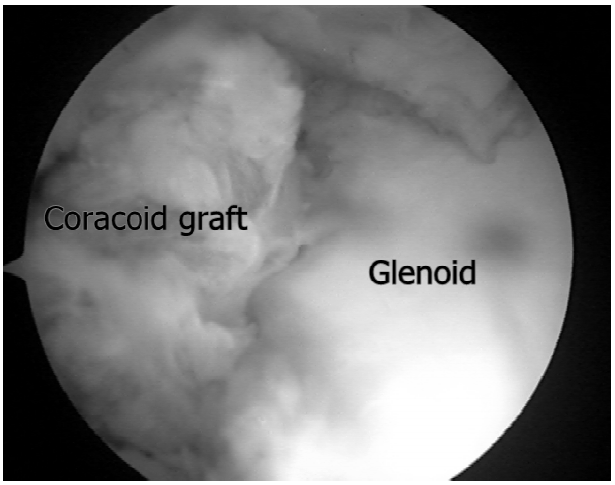

Fig. 11. *The coracoid graft is placed in the previously prepared site on the glenoid.*

Fig.10. *The Positioning Double Cannula is put on the anterior surface of coracoid graft, the 3.5mm cannulated coracoid guiding screws are threaded into the Top Hats through the holes.*

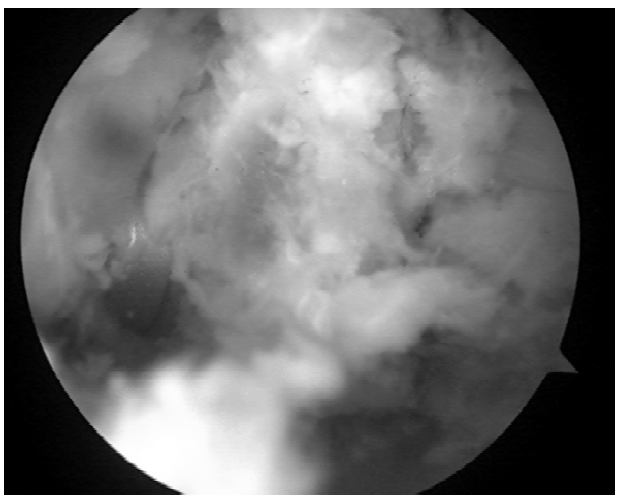

Fig .12. *The coracoid graft is fixed to the glenoid rim.*

help of the blunt switching stick. The coracoid graft is placed in the desired position on the anterior glenoid rim in the site previously prepared (Fig.11).

Fifth step: Coracoid–glenoid fixation

The glenoid K-wires are drilled through the 3.5 coracoid screws. The 3.5 mm coracoid cannulated screw is removed from the first hole and then this hole is drilled using the glenoid 3.2mm drill over the K-wire. The first Latarjet cortical screw is threaded over the glenoid K-wire into the hole. The same procedure is performed with the second hole. The glenoid K-wires are then removed and the screws are tightened with the solid screw driver from the C portal at rotator interval (Fig.12). Using suture anchors we reattach the remaining labrum and glenohumeral ligaments to the anterior rim of the glenoid (Fig.13).

Indications

In our practice we use the Instability Severity Index Score (ISIS), invented by P.Boileau (15) superior to 4 points. The main criteria for the Latarjet procedure are significant glenoid bone loss (16), pure capsule, engaged Hill-Sachs, revision cases after failed Bankart (17) and for patients, who practice high-risk sports (e.g. air-gymnastics, acrobatics, mountain climbing) and sports with collision and/or

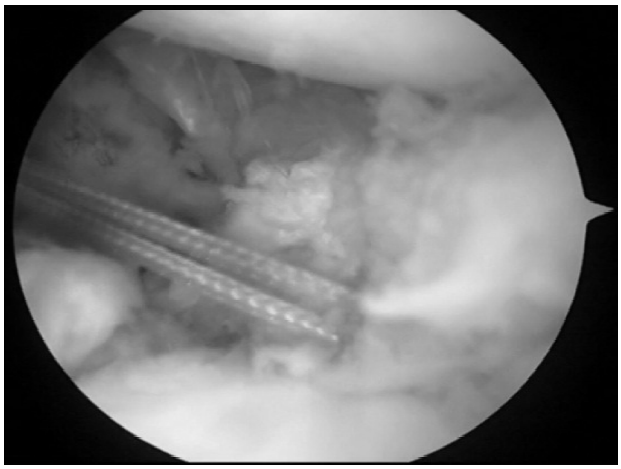

Fig. 13. *Reattaching the middle glenohumeral ligament to the glenoid.*

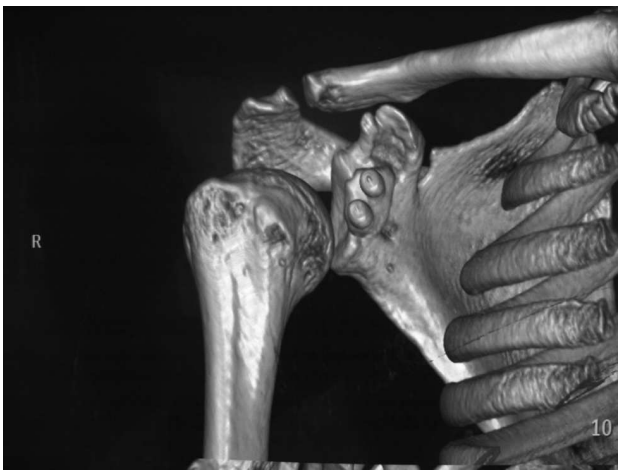

Fig.15. *Three-dimensional reconstruction showing graft and screw position.*

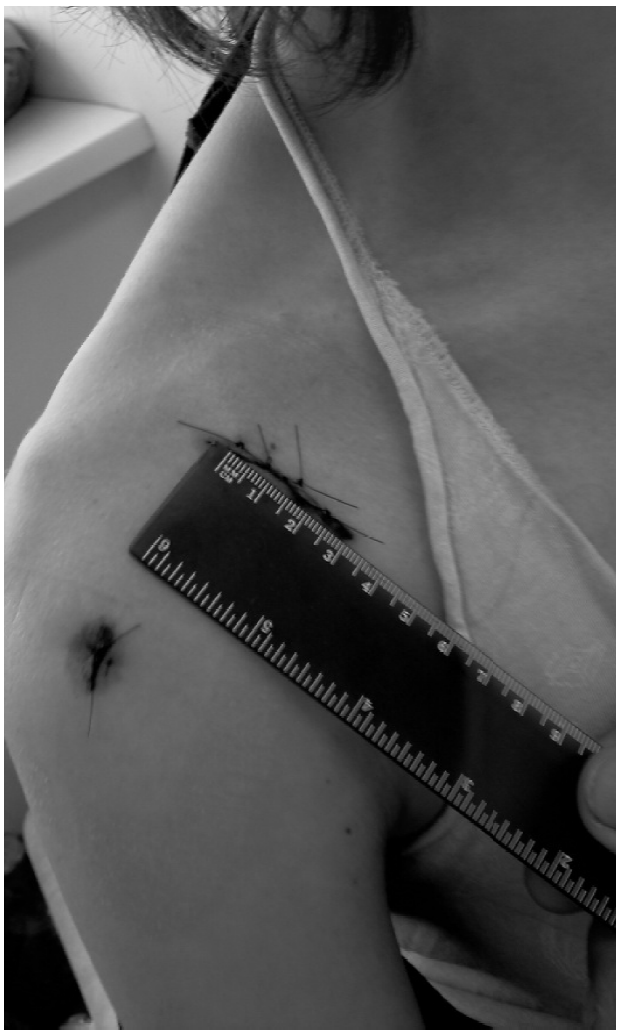

Fig.14. *Cosmetic appearance of a shoulder after the arthroscopically assisted Latarjet – Lafosse procedure.*

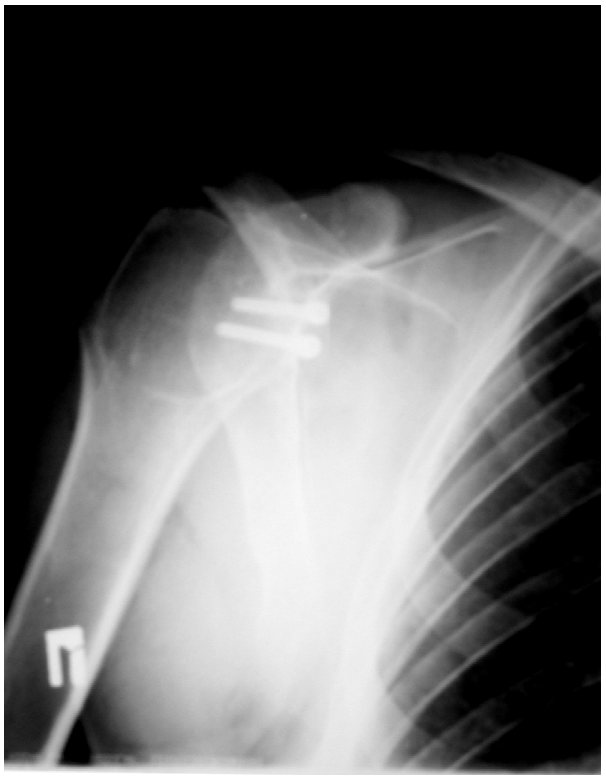

Fig. 16. *Final X-ray showing the screws placement after the arthroscopically assisted Latarjet – Lafosse procedure.*

throwing (e.g. handball, basketball, or judo).

DISCUSSION

In most techniques the arthroscopic Latarjet

procedure is performed with the patient in the "beach-chair position" (8). At the same time most surgeons still prefer to operate cases of instability in the lateral decubitus position because it provides easier access to the inferior and posterior-inferior parts of the shoulder and allows the tension of the ligaments via plication to be more correctly balanced (8). Changing the patient`s position has a steep learning curve and requires the surgeon to change his surgical skills. Hence with our technique surgeons do not need to change their style of operating (8).

Our technique has some elements in common with the Nourissat technique (7) tested on cadavers. However we use only one incision and the lateral decubitus position of patient so the upper part of m. subscapularis moves up and the second incision becomes unnecessary. Nourissat fixed the coracoid in a standing position and inserted it in a hole made in the glenoid by an ACL offset device. He did not reattach the joint capsule and glenohumeral ligaments.

Boileau (5) like Nourissat fixes the coracoid with one screw in a standing position, which in our opinion may cause non-union. The joint capsule and glenohumeral ligaments are reattached but the rotator interval is removed. The Latarjet technique proposed by Laurent Lafosse (4,9) is quite difficult to perform and requires advanced skills in extraarticular dissection of the tissues. One of the key points of Lafosse`s technique is dissection and drilling for the screws in the coracoid which must be performed arthroscopically. After this stage a 2 cm incision for positioning the coracoid cannula is made. To simplify this step we suggest pulling the coracoid process with the conjoined tendon through the incision following dissection. We also recommend to reattach glenohumeral the ligaments and joint capsule.

ADVANTAGES

1. The main advantage of the arthroscopic technique is the correct positioning of the coracoid flat to the glenoid surface via the scope.

2. Our technique saves rotator interval tissue, allows us to perform a dissection of m. supscapularis via arthroscopic and palpation evaluation and to palpate the brachial plexus and m. axillaris through the 2.5 cm incision.

3. By saving rotator interval tissue we can improve inferior stability and shoulder proprioreception.

4. Our technique saves the middle and inferior glenohumeral ligaments and their refixation, we extra-articulate the coracoid graft and protect the cartilage surface of the humeral head from the direct contact with the bone graft. This is believed to provide the additional stability in the downward direction. Our technique is an attempt to perform surgery in a more anatomic way.

5. Graft isolation from synovial fluid may decrease the risk of non-union.

6. Better cosmetic outcome (2.5-3 cm incision using our technique versus 5-7 cm with the open technique) (Fig.14).

RESULTS

All procedures were performed by a single surgeon (O.M.). Patients were clinically evaluated at a mean follow-up of 12-months (range 9-13). 12 patients (4 men and 8 women) with anterior instability were treated with this procedure, 1 was converted to open, because of a coracoid fracture. 10 patients had full range of motion and 1was satisfactory. The postoperative results were evaluated clinically, by X-ray and three-dimensional reconstructions. The early results are comparable with the results after the open technique.

COMPLICATIONS

Performing surgery in the lateral decubitus position may cause edema of the soft tissues which may spread to the neck.

However we did not observe this type of complication because we harvested the graft immediately after diagnostic arthroscopy without opening the rotator interval thus making the passage of fluid easier through the incision of graft harvest site; the latter is cone shaped with the base upwards. Furthermore many surgeons have performed prolonged surgeries for massive rotator cuff reconstruction without observe this kind of complication. Among inter-operative complications we had one case of coracoid fracture because the screw had been tightened too hard so we were forced to switch to open surgery. Lafosse recommends to scroll the screw using two fingers to prevent the coracoid fracture (Annecy Live Surgery International

Shoulder Advanced Course 2011).

CONCLUSIONS

Our surgical technique was created to simplify the arthroscopic Latarjet-Lafosse procedure. Our aim was achieved by using 3 standard portals and a 3 cm incision for graft harvest. We put our patient in a lateral decubitus position which is widely used among surgeons all over the world. This makes these surgeons feel comfortable about performing the Latarjet–Lafosse procedure. This method may also reduce damage to the m. subscapularis and the neurovascular structures by using a palpatory and blunt method as well as the arthroscopic view of the subscapularis split through the graft harvest incision. After 12 months of follow-up no cases of recurrent dislocation were identified.

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BASIC SCIENCE AND RESEARCH

BACKWARD WALKING ALTERS THE STRIDE-TO-STRIDE VARIABILITY FOR HIP, KNEE AND ANKLE JOINTS

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This study aimed to examine stride-to-stride variability in healthy individuals during backward walking (BW). We aimed to determine the temporal structure of stride-to-stride variability and not the amount measured by linear statistical tools (i.e. standard deviation). The variation of how motor behavior emerges in time is best captured by tools derived from nonlinear dynamics, for which the temporal sequence in a series of values is the facet of interest. Nine healthy volunteers walked on a motorized treadmill forwards and backwards at their self-selected pace while hip, knee, and ankle kinematic data were collected (50Hz) continuously for two minutes with an eight-camera optoelectronic system. The nonlinear measure of the Lyapunov Exponent (LyE) was estimated from the joint flexion-extension time series to assess stride-to-stride variability. Our results revealed that BW displayed significantly ($p<0.001$) increased LyE group values for the three joints. In conclusion, hip, knee and ankle joints of healthy individuals during backward walking exhibit significantly larger Lyapunov Exponent values compared to corresponding values during forward walking revealed a noisier and more unstable walking pattern. Compared to FW, BW leads to an altered variability, which could imply a decreased functional responsiveness to environmental demands for lower limb joints which may make them more susceptible to injury. Therefore, BW should be used with caution in rehabilitation programs after lower limb injuries and in the exercise regimens of several sports where it has been included for injury prevention and to improve the BW pattern and the ability of the athletes since this movement is often required during competition.

The investigation of backward locomotion has recently received particular attention from researchers. It has been used to provide insight into the neural control mechanisms that are used in gait (1-5). From an orthopedic and physical therapist perspective, backward walking (BW) on a treadmill is a common tool for injury prevention and for lower extremity rehabilitation in the clinical setting (6-7) since it has been demonstrated that BW is associated with less biomechanical strain on the knee joint than forward walking (FW) (3,8). Finally, athletic trainers and sports medicine practitioners have paid special attention to backward locomotion tasks because of their training effects. Since some authors have

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observed that BW increases energy expenditure to levels high enough to maintain cardiorespiratory fitness (9-10), it has been considered an interesting alternative exercise for aerobic training. Other authors have reported that BW appears to create "more muscle activity in proportion to effort" than FW (11). Finally, various sports such as soccer, football, tennis and basketball require the use of backward locomotion in a variety of situations, and for this reason trainers use backward locomotion as a regular exercise regimen.

Previous studies have examined the differences between BW and FW in terms of several locomotion parameters (2, 4-5, 12-14). Several studies have shown that kinematics of BW are mirror images of FW (2-4). On the contrary, Vilensky et al (13) and Kramer and Reid (14) concluded that BW is different from FW. BW is accomplished by a faster cadence but smaller stride length when compared to FW. The pattern of muscular activity between the two walking conditions is poorly correlated, and at any given speed, the mean electromyographic (EMG) activity over the gait cycle is generally higher during BW (4).

However, while backward walking training is currently being used by therapists, certain aspects of BW are not yet clearly understood. There are no studies that have focused on the examination of the variability during BW. Variability is an important characteristic of healthy human gait. Human movement variability can be described as the normal variations that occur in motor performance across multiple repetitions of a task. Similarly, fluctuations in the gait pattern from one stride to the next represent the stride-to-stride variability (15-16). However, no investigations have considered if any alterations in the stride-to-stride variability occur during BW In his benchmark study Winter et al studied the mechanics of BW, the authors reported coefficient of variation (CV) values of joint moments and mentioned that joint moments were more variable during BW than in forward walking (2). However, traditional linear measures such as CV can only estimate the magnitude of variability, while the temporal evolution of movement patterns is ignored. In addition, parameters such as joint moments are extensively "treated" algorithmically (i.e. smoothing, differentiation, normalization) to provide a "mean" picture of the subject's movement pattern. It is obvious that during these procedures the temporal structure of variability is distorted (17). On the contrary, measures from nonlinear dynamics estimate how motor behavior changes over time and provides information about the structure or organization of the movement over time (17). One such measurement is the largest Lyapunov Exponent (Fig. 1-2).

We investigated if any alterations are present in the structure of stride-to-stride variability after reversal of gait direction in humans. We used a nonlinear measure, the largest Lyapunov Exponent (LyE), to accomplish this goal. We hypothesized that BW would result in alterations in the structure of the variability profiles.

METHODS

Nine subjects (males; Age=29.6±3.4years; Weight=86.2±6.8kg; Height=1.85±0.04m) participated in this study. All subjects were in good health and free from any neuromusculoskeletal injuries and related disorders. None of the subjects had any previous experience at walking backward on a treadmill or was involved in activities that required walking or running backward on a regular basis. All subjects signed an informed consent according to the University Institutional Review Board requirements.

Each participant performed FW and BW on the treadmill (SportsArt 6005; SportsArt America, Woodinville, WA, USA), following the exact same procedures. Prior to any data collection, all subjects were given enough time to warm up and familiarize with treadmill walking. For this purpose all subjects were instructed to walk at their preferred normal speed. By using a self-selected pace, any variability changes detected were due to the reversal of walking direction and not to probable discomfort that may be associated with using a pre-determined speed for all subjects (18-19). The familiarization period was six minutes which is considered sufficient for obtaining reliable measurements (20). After the familiarization period, kinematic data were collected continuously for two minutes at 50Hz (at least 100 continuous walking strides). Participants were allowed ample rest between trials. An eight-camera system (Peak

Performance Technologies, Inc., Englewood, CO, USA) was used to capture (50Hz) the coordinates of 15 reflective markers placed on selected bony landmarks of the lower limbs and the pelvis according to Davis et al (21). Using the algorithms described by Davis et al (21), we calculated the three-dimensional angular displacement for hip, knee and ankle joints. We only examined the sagittal angular displacement because data from the other planes collected via skin markers are associated with increased error (22). An increased amount of measurement error in the data can mask the true structure of stride-to-stride variability and can lead to incorrect conclusions (23). We also collected three-dimensional data instead of two-dimensional to increase accuracy by minimizing perspective error.

Stride-to-stride variability was estimated with the largest Lyapunov Exponent (LyE) for the joint angle time series (both lower extremities were examined for each participant) (Fig. 1-2, 17, 24). Joint angle variability was examined because it has been shown that variability of stride characteristics (i.e. stride time) offers a less sensitive measure of differences between groups than does variability of the joint kinematics (25). Each time series consisted of 6000 data-points which is considered sufficient for the computation of the LyE (17). The data were analyzed unfiltered so as to get a more accurate representation of the variations within the system (26). It was assumed, because the same instrumentation was used for all subjects, that the level of measurement noise would be consistent for all subjects and thus differences could be attributed to changes within the system itself (17).

The LyE is a measure of the structure or organization of the variability present in a time series and is calculated as the divergence of the data trajectories in phase space, where the phase space is an n-dimensional space with n being large enough to unfold the attractor state. The LyE describing purely sinusoidal data with no divergence in the data trajectories is zero because the trajectories overlap rather than diverging in phase space (Fig. 2). This shows minimum variability over time in the data. The LyE for random noise, which has a lot of divergence in the data trajectories, is relatively large (Fig. 2). This shows maximum variability over time in the data (17,24). The LyE has been previously used in gait to characterize the underlying structure of variability during movement (27-29). A detailed description of the exact procedures used for the calculation of the LyE by our group is reported elsewhere (17, 27-29). Briefly, the LyE for each joint time series and for each subject-condition was calculated using the Tools for Dynamics (Applied Chaos LLC, Randle Inc., San Diego, CA, USA) and the Chaos Data Analyzer (Professional Version, Physics Academic Software, Raleigh, NC, USA).

Paired t-tests were used for the comparison of the LyE group mean values of FW and BW for each of the three joints in the lower limb. A paired t-test was also used for comparing the corresponding speeds of FW and BW. A Bonferroni correction was applied to account for the number of comparisons. Thus, the level of significance was set at 0.0125 (0.05 divided by 4).

RESULTS

Our results revealed that during BW all three examined joints exhibited significantly greater LyE values when compared to the corresponding LyE values for FW ($p<0.001$; Fig. 3, Table I). Significant differences were also found for the speeds of forward and BW (mean FW speed 0.86m/s; mean BW speed 0.49m/s; $p<0.000$). Fig. 4 illustrates the differences in the variability of the two walking modes: time series from a representative subject are plotted versus time with the corresponding phase plane plot for each walking direction. It is apparent

Table I. *Lyapunov Exponent (LyE) group mean values (SD) during FW and BW for the three examined joints*

	Forward walking (FW)	Backward walking (BW)
Hip joint	0.122 (0.02)	0.198 (0.021)*
Knee joint	0.121 (0.03)	0.185 (0.025)*
Ankle joint	0.162 (0.047)	0.251 (0.049)*

**Asterisks denote statistical significant differences as compared to FW. SD: Standard Deviation*

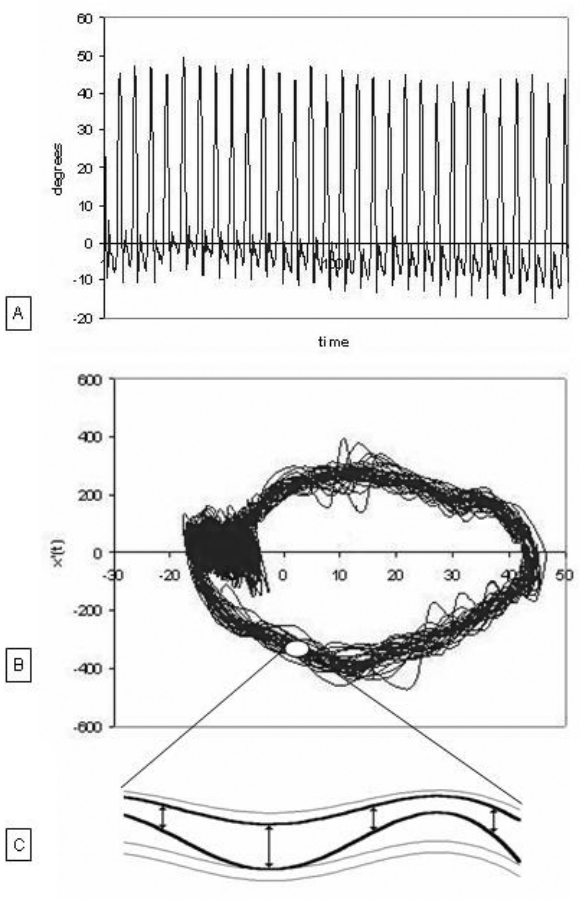

Fig. 1. *A graphical representation of the state of space and the calculation of the LyE.* ***A)*** *An original knee angle data set for several strides from FW.* ***B)*** *A two-dimensional phase space is generated from the entire data set using every single point.* ***C)*** *A section of the phase space where the divergence of neighboring trajectories is outlined. The LyE is calculated as the slope of the average logarithmic divergence of the neighboring trajectories for the entire time series. It should be noted though that before calculating the LyE, we estimated the number of embedded dimensions needed using the global false nearest neighbor (GFNN) analysis (20). The GFNN calculation revealed that five dimensions is required to reconstruct the phase space from a given time series. The estimation of the embedded dimensions value allowed us to calculate the LyE, which is a measure of the divergence of the data trajectories in phase space, where the phase space is an n-dimensional space with n being large enough to unfold the attractor state (13).*

that the phase plane plot for BW is more complicated than the corresponding one for FW indicating a reorganization of the movement patterns during backward locomotion.

DISCUSSION

The purpose of our study was to investigate the stride-to-stride variability during backward walking (BW) as compared to forward walking (FW) in healthy individuals using the nonlinear measure of LyE. We hypothesized that BW would result in alterations in the structure of the variability profiles. Our results confirmed our hypothesis since it was demonstrated that all three examined joints (i.e hip, knee, ankle) exhibit significantly larger LyE values during BW as compared to the corresponding values during FW.

The significance of our results can be approached using the concept of the variability of human movement. Human movement variability can be described as the normal variations that occur in motor performance across multiple repetitions of a task. Variability is an important characteristic of healthy human gait. Fluctuations in the gait pattern from one stride to the next represent the stride-to-stride variability (15-16). Healthy human gait is directly associated with an optimal state of structure variability (30). Decrease or loss of this state of variability makes the system more rigid while increases over this level make the system noisier and more unstable. Both situations render the system less adaptable to perturbations and environmental demands. According to our results, BW is associated with greater values of LyE in gait variability as compared to FW. The altered variability structure observed during BW means that all three examined joints exhibit greater divergence in the movement trajectory, which could imply inability to respond to environmental demands (30). Therefore, it could be speculated that BW should be used with caution by physical therapists and athletic trainers because the altered structure of variability that is noted for hip, knee and ankle joints compared to FW (a noisier and irregular pattern) making the joints less adaptable to environmental demands and more susceptible to injury.

The altered variability could be the result of the modifications that take place at the level of the spinal cord neuron function ("Central Pattern Generators" produce specific rhythmic movements and are to be

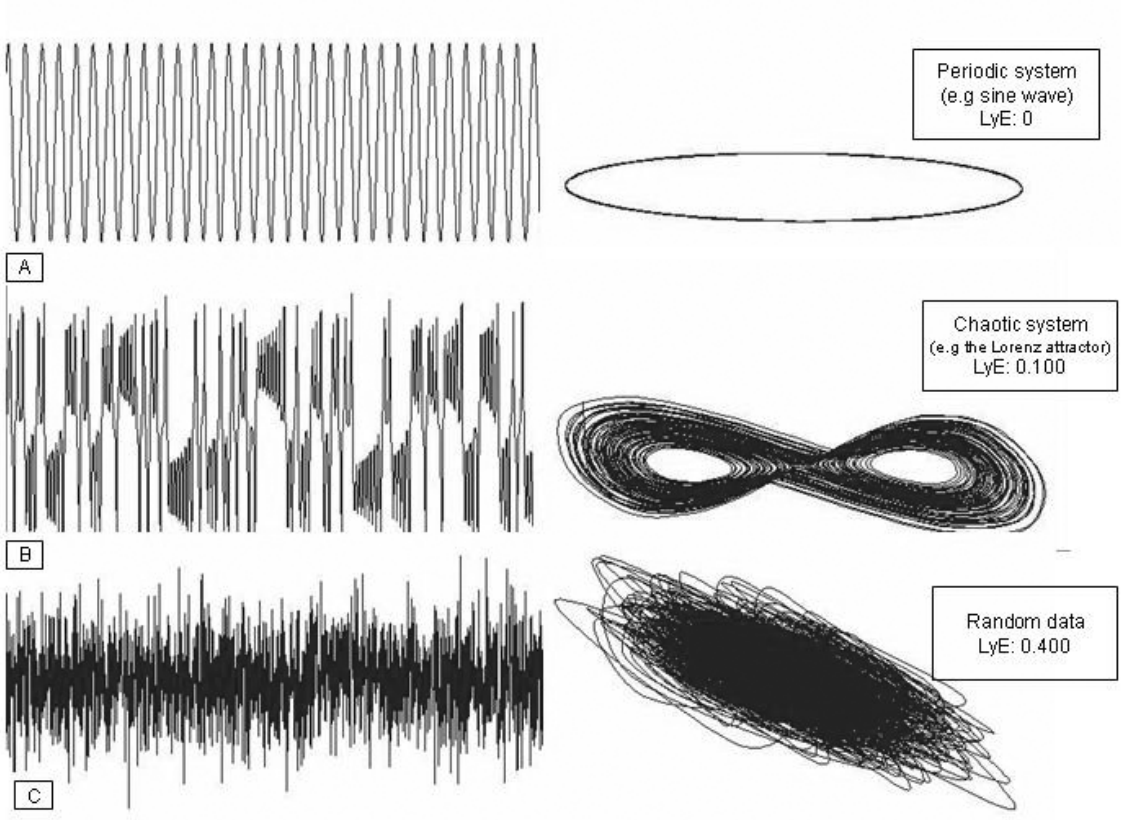

Fig. 2. ***A)*** *shows on the left a graph of a time series from a periodic system (i.e. a sine wave) and on the right the corresponding phase which is practically the amplitude (i.e. position) of the time series versus its first derivative.* ***B)*** *shows on the left a graph of the time series from a chaotic system, the Lorenz attractor, and the corresponding phase plane plot on the right.* ***C)*** *shows on the left a graph of the time series of completely random data (white noise), and on the right the corresponding phase plane plot. All the above time series consisted of 6000 data points.*

found largely in the spinal cord (spinal CPGs) (31). Thorstensson et al. demonstrated that BW EMG patterns were considerably different than those seen in FW, and thus, concluded that drastic changes in the normal locomotor program are required to produce BW (3). Other studies proposed that during BW the same motor program (neural mechanism) is used as during FW, but possibly running in reverse (4, 32). Also the interplay between central and sensory influences is also critical in the production of adaptive behavior. During BW the neuromuscular system does not receive the same information as in FW. The most obvious of such differences is the elimination of visual cues (exteroceptor activity), while the proprioceptors also provide a different feedback from the joint receptors including joint position and displacement, angular velocity and intra-articular pressure (Ruffini endings), tension in ligaments, especially at the extremes of the range of motion (Golgi endings), or mechanical stress (Pacinian corpuscles, free nerve endings). These alterations are plausable since BW has been correlated with alterations in tibiofemoral (compressive and shear) and patellofemoral joint forces (4). Muscle spindles and tendon organs, the other two types of proprioceptors, also provide modified information during BW since this task leads to modified muscle activity (concentric contraction of quadriceps muscle instead of the eccentric during FW, increased electromyographic activity of quadriceps and hamstring muscles). It should be noted that these neural mechanisms which may interfere with the variability alterations during BW, may well be related to the fact that we have had a lot more practice walking forward than backward

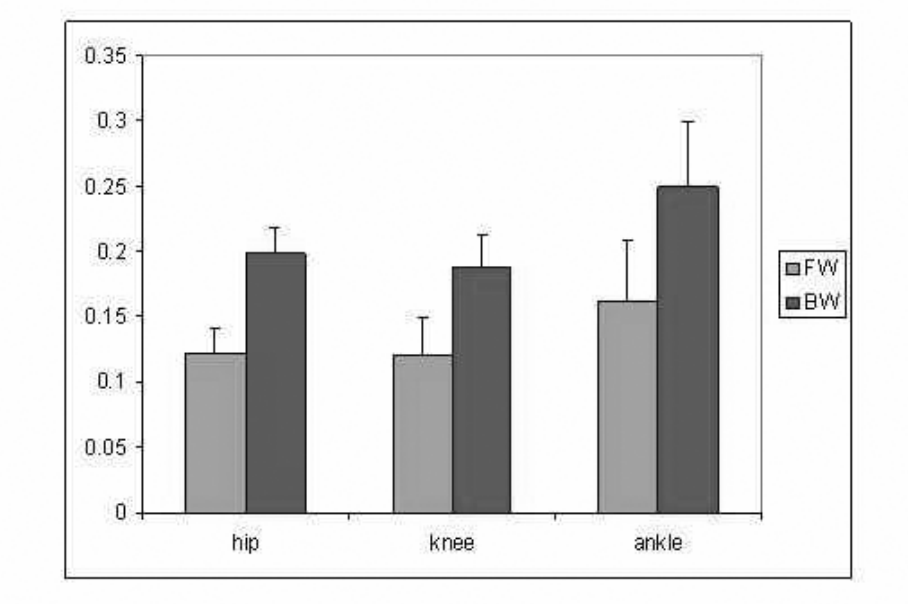

Fig. 3. *A bar graph that indicates the group mean Lyapunov exponent (LyE) values for the sagittal angular displacement time series of hip, knee and ankle, after forward walking (FW) and backward walking (BW). BW generates significantly higher LyE values than FW ($p<0.001$) for all joints.*

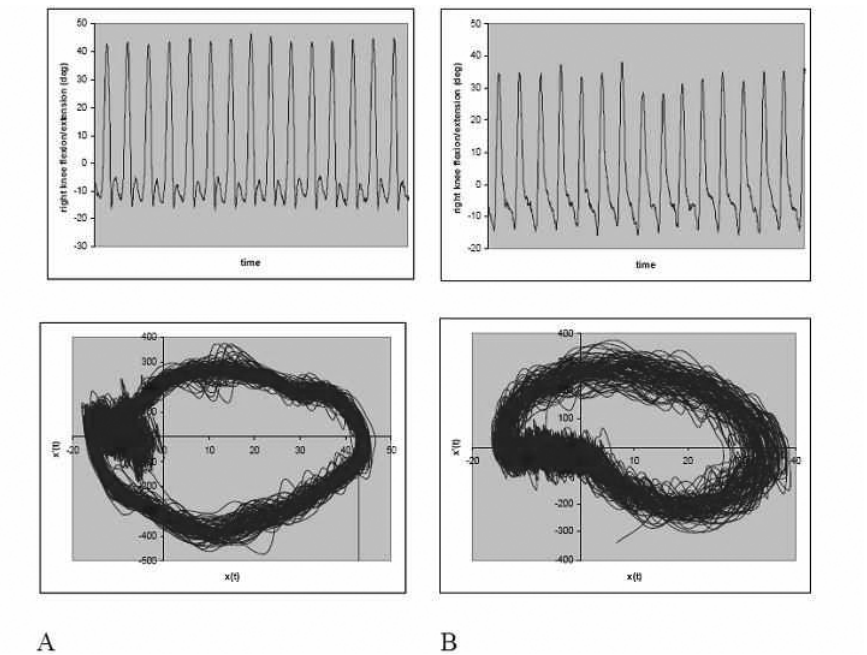

Fig. 4. ***A)*** *shows on the top a graph of the time series of knee flexion-extension from a FW trial and on the bottom the corresponding phase plane plot which is practically the amplitude (i.e. flexion-extension degrees) of the time series versus its first derivative (i.e the angular velocity). The LyE value for knee flexion-extension for this particular participant during FW is 0.141.* ***B)*** *shows on the top a graph of the time series of knee flexion-extension during the BW trial of the same participant, and the corresponding phase plane plot on the bottom. The LyE value for knee flexion-extension for the same participant during BW is 0.166. It is apparent that the phase plane plot of BW is more complicated than the corresponding from FW resulting in more divergence in the movement trajectories that were demonstrated with the calculation of the bigger value for the LyE.*

and that further research is needed to demonstrate which mechanism primarily governs the variability alterations during BW.

Our results also indicate that the LyE measure could prove to be an important tool for evaluating various conditions or special circumstances which are related to the human neuromusculoskeletal system. This is consistent with previous studies in which the nonlinear measures such as LyE have been successfully used to evaluate conditions such as anterior cruciate ligament (ACL) deficiency (28) or ACL reconstruction (33-34) or even when these patients walk backwards (35).

Our results should be viewed considering the following limitations. Our subjects walked on a treadmill instead of overground. However, Matsas et al. has demonstrated that knee joint kinematics during familiarized treadmill walking are comparable to walking on the overground (20). Furthermore, in order to collect enough continuous data necessary for the calculation of stride-to-stride variability as well as the need to ensure that walking speed remains constant, the measurements must be made while walking on the treadmill. Walking overground is not typically associated with a constant speed for long periods of time (i.e. in the case of multiple footfalls) due to intermittency (36-37). Furthermore, the group mean LyE values identified for FW from our study are similar to the values reported by other investigators (0.107 for the knee angle in healthy young individuals in the Buzzi et al. study (27) versus 0.120 for the same joint in our study).

CONCLUSION

Hip, knee and ankle joints of healthy individuals during backward walking exhibit significantly larger Lyapunov Exponent values as compared to corresponding values during forward walking revealing a noisier and more unstable walking pattern. Compared to FW, BW leads to altered variability, which could imply decreased functional responsiveness to environmental demands for lower limb joints which may make them more susceptible to injury. Therefore, BW should be used with caution in rehabilitation programs after lower limb injuries where it is used as therapy as well as in the exercise regimens of several sports where it has been included for injury prevention and to improve the BW pattern and ability of athletes where this is required during competitions.

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CASE REPORT

UNUSUAL PRESENTATION OF CLAW HAND FOLLOWING ULNAR NERVE PALSY

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The common cause for ulnar nerve palsy is injury to the ulnar nerve by forearm fractures, laceration to the fascicules of the medial cord and leprosy (1). Other causes include poliomyelitis, syringomyelia or Charot Marie-Tooth Disease and neglected cubitus valgus deformity that progresses to tardy ulnar nerve injury (2). Inflammatory diseases like rheumatoid arthritis and osteoarthritis have also been reported as the cause of the ulnar nerve palsy (3-4). The anatomic causes could be anomalous accessory muscles, fibrous bands or ligaments in the cubital or Guyan channel (5-7). Depending on the location of the injury the ulnar nerve presents with predictable motor and sensory deficits (8-9). In proximal nerve palsy all the extrinsic and the intrinsic muscles are affected. The sensory loss is on the palmar and dorsal side of the little finger and the ulnar half of the ring finger. In distal ulnar nerve palsy the extrinsic muscles are spared and the intrinsic muscles are affected with sensory loss on the palmar side of the medial third of the palm, the entire palmar side of the little finger, the ulnar half of the ring finger and the dorsal side of both the little and ring finger distal to the proximal interphalangeal joint (PIP). The difference in sensory loss compared to proximal lesions is the sparing of the dorsal cutaneous branch of the ulnar nerve. When the deep branch of the ulnar nerve is involved only the intrinsic muscles are affected, the hypothenar muscles are spared with no sensory loss. The patient with ulnar nerve injury usually presents with the claw or benediction hand; a flattened palm, wasting of hypothenar muscles as well as shallow mid-palmar receptacle distal to thenar and hypothenar eminences. The dorsum of the hand shows wasting with the shallow concavities in the intermetacarpal spaces more prominent in the thumb web. The mechanism of the paralytic claw hand was studied by Landsmeer (10); the metacarpal phalangeal joint and interphalangeal joint (IP) are normally independent whereas in the case of the paralytic claw hand he observed the IP joint movements to be limited or somewhat coordinated. He considered this to be a biarticular system comprising the MP joint and PIP joint with proximal phalanx forming the intercalated bone. This biarticular system remains stable when the flexors and the extensors of the opposing tendon are equally balanced when the intrinsic system are functioning. If the intrinsic system is not functioning the long extensors function is blocked at the MP joint by diversion of this tension to the sagital band providing hyperextension at the MP joint which effectively blocks the extensor's ability to extend the PIP joint (11-13). The aim of this case report is to report an unusual presentation of claw hand following ulnar nerve palsy.

A 55 year old professional driver fractured both bones in his right forearm following a road accident in May 2010. He had no history of any previous injury/disease. His fracture was surgically fixed with

Key words: ulnar nerve palsy, claw hand

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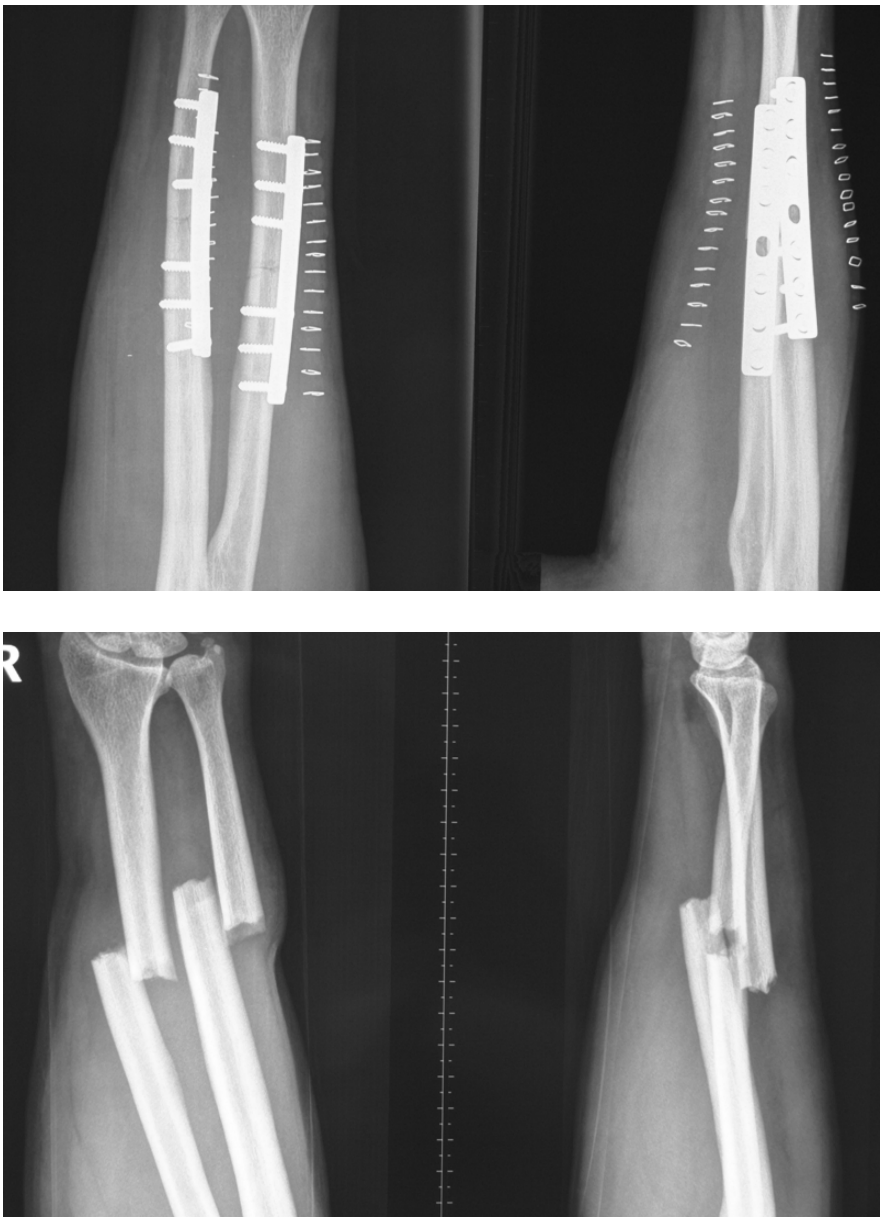

Fig. 1-2. *An unusual presentation of claw hand, the patient has hyperextension at the MP joint and flexion of the PIP joint while the little finger is in extension at the MP, PIP and DIP joint.*

open reduction internal fixation and was referred to Occupational Therapy after 6-8 weeks post-op due to right ulnar nerve palsy (Fig. 1-2). The nerve Conduction Velocity (CV) study performed in June suggested right distal to elbow ulnar neuropathy with mild prolonged distal latency, low amplitude and normal CV along with absent F – Wave latency. (The right ulnar sensory nerve showed normal onset latency, low amplitude and normal conduction velocity). On examination the patient had wasting of the first dorsal interossei. The patient could flex the MP joint of the right little finger but could not flex the MP joint of the ring finger. The patient had grade 4-5 (MRC Scale) muscle power of his hypothenar muscles and he presented with right claw hand. The presentation of claw hand was

MOTOR NERVES:	Lat [ms]	SD	Amp [mV]	SD	CV [m/s]	SD	Amp% [%]	SD	F-M [ms]	SD
Right Median									22.4	
Pos. 1 - Rec pos	3.2		13.3							
Pos. 2 - Pos. 1	6.9		12.1		59.5		-9			
Right Ulnar									---	
Pos. 1 - Rec pos	3.1		3.5							
Pos. 2 - Pos. 1	6.8		3.6		51.4		4			
Pos. 3 - Pos. 2	8.4		3.6		56.3		-2			
Pos. 4 - Pos. 3	10.4		2.9		65.0		-18			
Left Ulnar									24.3	
Pos. 1 - Rec pos	2.8		14.2							
Pos. 2 - Pos. 1	6.1		13.3		57.6		-7			
Pos. 3 - Pos. 2	7.5		13.4		64.3		1			

SENSORY NERVES:	Lat [ms]	SD	Amp [uV]	SD	CV [m/s]	SD	Amp% [%]	SD
Right Median								
Stim 1 - Rec 1	2.6		27		57.7			
Right Ulnar								
Stim 1 - Rec 1	2.0		21		65.0			
Stim 2 - Rec 2	2.0		18		65.0			
Left Ulnar								
Stim 1 - Rec 1	2.4		39		54.2			

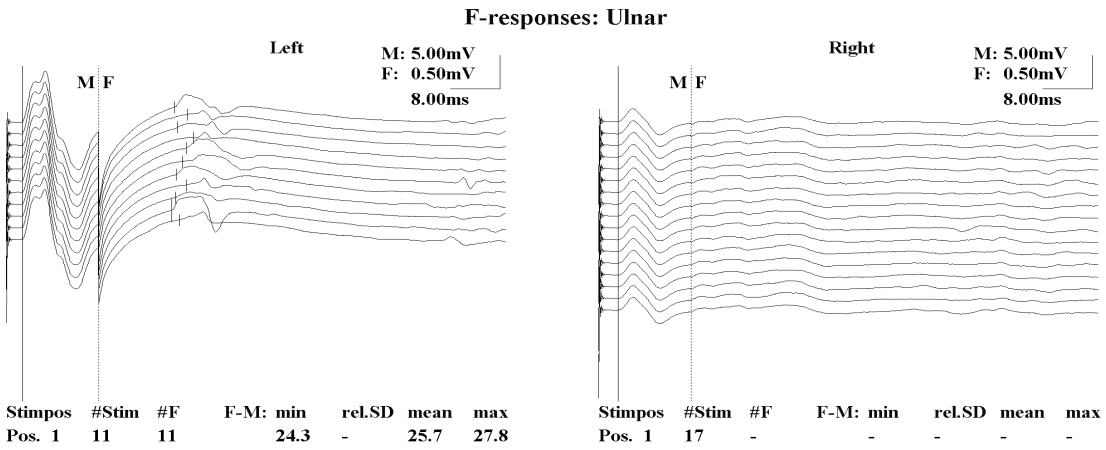

Fig 3. *EMG and NVC findings.*

unusual with hyperextension at the MP joint of ring finger and flexion at PIP joint, while the little finger was in extension at the MP and PIP joints (Fig. 3-5). The sensory testing using the Semmes–Weinstein Monofilament was normal along the ulnar nerve distribution. Upon examination the patient had a positive Froment's sign and a Waternberg's sign on his right little finger.

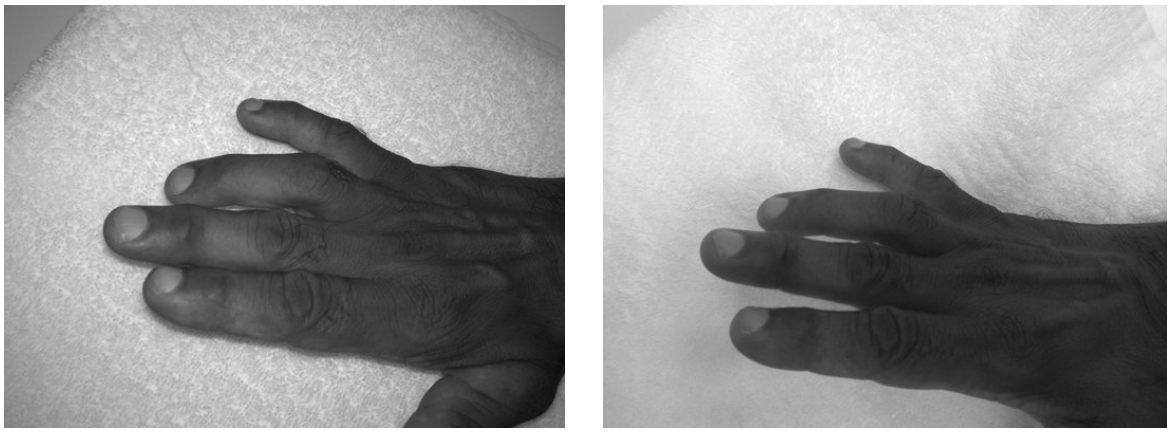

Fig 4-5. *Unusual presentation of claw hand following ulnar nerve injury.*

DISCUSSION

Anomalous innervation patterns of muscle controlling the hand unit are not common. The motor neural interconnection between median and ulnar nerve in the forearm is called Martin (1963) - Gruber (1870) anomalous connections (8) which in the hand motor branch of the ulnar nerve interconnect with the recurrent branch of the median nerve called Riche (1989) - Cannieu (1987) anomalous connections (8). These anomalous interconnections gain attention when the patient with zone V ulnar nerve injury presents with no detectable intrinsic deformity and complete sensory loss in autonomous zone. On the other hand the median nerve innervated muscle may function despite severance of the median nerve (14). It has been reported that the 3rd lumbrical has dual innervation in 50% of the cases and in such a hand a complete ulnar nerve palsy would result in clawing only in the little finger (8). In our case we believe that anomalous innervation of the median nerve to abductor digiti minimi unopposed by 4th palmar interosseous, resulted in the Waternberg's sign being in little finger which may also explain why our patient had clawing only of the ring finger.

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