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Applied Study on Changes of Bone Metabolic Markers and Lipid Metabolites after Non-Joint Replacement Treatment for Avascular Necrosis of the Femoral Head

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Abstract: Currently, the combination of radiographic images and patient signs remains the cornerstone in the diagnosis of femoral head necrosis. However, the high cost of these techniques, the exposure of patients to toxic and radioactive compounds, and poor monitoring of treatment responses, have driven the exploration of alternative screening methods and the development of predictive tools for evaluating the progression of femoral head avascular necrosis. Current studies have shown that although bone turnover in patients with avascular necrosis of the femoral head will change after non-joint replacement treatment, for the evaluation of the evolution of femoral head avascular necrosis, we cannot simply look at the rise and fall of bone resorption or bone formation markers. We should evaluate the changes in bone turnover markers as a whole. At the same time, abnormalities in hyperlipidemic conditions manifest themselves, rather conspicuously, as a contributory element to the advancement of non-traumatic femoral head necrosis. This phenomenon emerges discernibly across a spectrum of variously-laden exposure determinants. It has been proved by searching relevant literature that the combined application of bone biochemical indicators and lipid metabolites can predict the risk of avascular necrosis of the femoral head. Because they can reflect the status of bone metabolism in a short period of time, they also have certain clinical value in evaluating treatment effects.

Keywords: Avascular Necrosis of the Femoral Head; Bone Resorption; Bone Formation; Bone Metabolism Markers; Lipid Metabolites.

1. Introduction

Osteonecrosis of the femoral head is a condition characterized by localized death of bone cells and bone marrow elements, resulting from venous stasis in the femoral head or compromised or disrupted arterial blood flow. This leads to progressive degradation and eventual collapse of the femoral head, resulting in hip joint pain and impaired function. Based on the underlying causes, femoral head necrosis can be classified into two types: traumatic osteonecrosis of the femoral head, which occurs following injury, and non-traumatic osteonecrosis of the femoral head, which develops without direct physical trauma. The etiology of traumatic femoral head necrosis is relatively clear, while the main causes of non-traumatic femoral head necrosis include long-term use of corticosteroids, heavy alcohol consumption, autoimmune diseases and idiopathic factors. However, the specific pathogenesis of NONFH has not yet been fully established [1]. Bone has metabolic activity, and bone absorption and bone formation are the two main manifestations. Osteoclasts are responsible for resorbing aged bone tissue, while osteoblasts play a key role in the formation of new bone. These two processes are inseparable and together constitute bone reconstruction or bone transformation. The rate of bone turnover is called bone turnover rate. During bone turnover, some metabolites are produced, which can be used as biochemical indicators of bone metabolism and reflect the condition of the bone [2]. Therefore, bone metabolism in the blood of patients after avascular necrosis of the femoral head will be abnormal, and bone metabolism markers in the body may undergo corresponding changes [3]. However, some studies have found that there is also a certain correlation between lipid metabolism in patients with non-traumatic femoral head necrosis. Therefore, whether the progression of femoral head necrosis and its recovery after non-joint replacement treatment can be evaluated based on this [4].

2. Overview of Bone Metabolism and Lipid Metabolism

Bone is an organ that changes dynamically. As one of the few organs that can regenerate in adulthood, the bone itself has a strong regenerative ability. However, the complex mechanism of bone metabolism, the long research cycle and difficulty have seriously restricted the progress of bone regeneration and repair research. Its metabolic process is marked by two contrasting mechanisms: osteoblasts forming new bone and osteoclasts degrading (absorbing) old bone, which under normal circumstances are closely coupled in time and space [5]. In recent years, biochemical markers of bone remodeling have been introduced, which serve as specific indicators of either bone formation or bone resorption processes. To date, few studies have covered changes in bone conversion after femoral head necrosis and corresponding postoperative success or failure. Bone metabolic markers are typically categorized based on the specific process they represent: either bone formation or bone resorption[6]. However, some compounds in bone matrix can also reflect bone formation and bone resorption to some extent [7]. Although biochemical bone markers can be used to study

changes in bone turnover in metabolic bone disease, they are not disease-specific but rather reflect metabolic disorders independent of the underlying cause [8]. However, some biochemical bone markers are also present in other tissues and are affected to some extent by non-skeletal diseases. Therefore, abnormal or normal bone metabolism markers do not necessarily mean changes in bone [9]. In recent years, the mechanisms related to lipid metabolism in non-traumatic necrosis of the femoral head have also been summarized, providing reference for studying the pathogenesis and treatment direction of non-traumatic necrosis of the femoral head [10].

3. Bone Metabolism-Related Markers

3.1. Markers Indicative of Osseous Genesis Encompass Alkaline Phosphatase (ALP), Osteotropic Alkaline Phosphatase Isoenzyme (B-ALP), Osteocalcin (OC), Alongside type I Procollagen Carboxyl-Terminal Propeptide (PICP) and Type I procollagen amino-terminal propeptide (PINP), among sundry others. By Active Osteoblastic Action Produced, These Biomarkers Become Discernible Within Serum or Plasma Matrices Observable in Manifold Instances of Bone Formation Analysis.

ALP are a group of enzymes derived from various tissues. Alkaline phosphatases are the most abundant in bone and liver subtypes. They are coded by way of solely one gene and fluctuate solely in post-translational carbohydrate adjustments [11]. Hydrolysis of phosphate and pyrophosphate during osteogenesis is the main physiological function of bone-type alkaline phosphatase (B-ALP). It is secreted by osteoblasts and is conducive to the osteogenesis process [12]. In a retrospective find out about involving 401 sufferers with avascular necrosis of the femoral head and eighty one healthful subjects, serum alkaline phosphatase tiers in sufferers with ONFH had been greater than in wholesome individuals. This enlarge is idea to take place all through restore after femoral head necrosis[13]. However, new research results have established no causal relationship between ALP levels and ONFH [14].

Studies have shown that when alendronate is used to treat avascular necrosis of the femoral head, a relatively small decrease in osteoblast activity (bone alkaline phosphatase) compared to a strong decrease in osteoclast activity may inhibit the repair response around the necrotic lesion and maintain mechanical integrity, while the hip joint did not continue to collapse on x-ray after 12 months of follow-up [15]. However, it has been recently found that a decrease in bone-specific alkaline phosphatase means an increase in apoptosis of osteoblasts around the joint. Long-term exposure to this inflammatory environment will seriously affect hip joint angiogenesis and bone repair and regeneration. Combined with previous relevant research results, this indicates that with the growth of NONFH, the destruction of neighborhood bone tissue in sufferers and the non-stop erosion of inflammatory elements [16].

After human increase stops, osteocalcin is synthesized solely by way of osteoblasts and odontoblasts. Therefore, nearly all circulating osteocalcin originates from osteoblasts. Osteocalcin is a particular marker of its metabolic activity, and its serum stage is positively correlated with the histomorphology of bone formation[17]. In the blood, osteocalcin undergoes rapid catabolic metabolism, forming smaller fragments. Current studies have shown that negative feedback mechanisms may play a role in bone reconstruction [18]. Arguably, in a new study, osteocalcin did not regulate bone mass in mice with osteocalcin deficiency [19]. In steroid-induced avascular necrosis of the femoral head, we can prevent the development of non-invasive avascular necrosis of the femoral head with other treatments to stimulate bone formation and blood vessel formation and delay lipogenesis, among which we found a significant increase in serum osteocalcin compared to the control group [20].

Biomarkers of bone formation are synthesized by means of kind I collagen from osteoblasts. Initially, kind I collagen is synthesized into procollagen with the aid of osteoblasts. Subsequently, procollagen assembles into a triple helical shape inside the endoplasmic reticulum, which is additionally known as procollagen. Procollagen incorporates two propeptides, PINP and PICP[21].Type I procollagen N-propeptide (PINP) is one of the markers of bone turnover. It is produced by osteoblasts and can reflect the formation of collagen and the activation status of osteoblasts. It is really worth noting that PINP is no longer affected by using exogenous elements such as hormones, so it is regarded to be a extra precise and touchy indicator for measuring the balance of bone formation[22].In a disorder severity learn about of non-traumatic avascular necrosis of the femoral head, we discovered that serum PINP in non-traumatic avascular necrosis of the femoral head diminished in contrast with healthful controls, and with the improvement of sickness severity, serum PINP additionally lowered extra [23].Unlike PINP, PICP is extensively affected through bone metabolic illnesses such as Paget's disease, with ranges in affected sufferers growing by means of 2-6 instances in contrast to healthful individuals. Due to these limitations, PICP is no longer viewed a reference marker of bone formation [21].

3.2. Commonly Used Bone Resorption Markers Consist of Hydroxyproline, Pyridinoline, tartate-resistant Acid Phosphatase-5b(TRACP-5b), Deoxypyridine, the Carboxy-terminal cross-linked Telopeptide of kind 1 collagen (CTX-1) and the Amino-terminal Cross-linked Telopeptide of Kind 1 Collagen (NTX-1), etc. [24].

Osteoclasts are multinucleated bone-resorbing cells derived from the monocyte/macrophage line, and their erosive exercise is primarily based on the secretion of H+ ions and lytic enzymes such as proteases and TRACP-5b[25]. TRACP-5b is mainly suitable for assessing osteoclast activity because compared with CTX and NTX, its serum levels are not affected by circadian changes, food intake or renal dysfunction, and it is more promising to find new clinical applications [26]. Icariin can promote the increase of bone biochemical markers (TRACP-5b, BAP, NTX-I, CTX-I and OC) in serum of ONFH rats. These facts endorse that icariin promotes osteogenic differentiation of Rat Bone Marrow Mesenchymal Stem Cells and stimulates bone formation,

thereby enhancing ONFH[27]. Gujiansan can speed up the formation of new bone, promote the absorption of broken bone, and inhibit inflammatory reactions. Studies have found that it increases the levels of specific markers of bone formation and bone absorption (osteocalcin (OC), BAP, TRACP-5b, NTX-1 and CTX-1, and reduces the level of pro-inflammatory cytokines (Tumor necrosis factor-α, interleukin-6 and C-reactive protein) [28].

Hydroxyproline is a regular marker of bone resorption, but it is neither specific nor sensitive. Compared with hydroxyproline, hydroxylysine glycosides, mainly Gal-Hyl, are higher markers of bone resorption. They are extra particular to bone, are now not metabolized, and are now not affected by using dietary ingredients. However, due to the fact there are few research associated to non-invasive avascular necrosis of the femoral head and lack corresponding specificity, it is now not considered as a events marker of bone resorption[29, 30, 21].

Pyridinoline and deoxypyridinoline cross-linked merchandise are bridge molecules shaped at some point of the extracellular maturation of collagen fibers to stabilize the bone extracellular matrix. Pyridinoline and to a lesser extent deoxypyridinoline are primarily derived from kind I collagen of the bone matrix [29]. Due to the specific location of pyridinoline and deoxypyridinoline crosslinks in bone and kidney excretion, measuring their levels in urine provides insight into bone metabolism and helps us better understand the pathological changes of bone and cartilage. Urinary pyridinoline and urinary deoxypyridinoline crosslinks levels in patients with Kashin-Beck disease were also higher than healthy controls ($P<0.001$). This suggests that collagen breakdown of articular cartilage occurs in patients with Kashin-Beck disease, which is consistent with previous studies[31].In sufferers with mucopolysaccharide kind I, we determined that their plasma osteocalcin, pyridinoline, and deoxypyridinoline had been greater than in healthful patients, however the sketch of Therapeutic scientific trials was once confined by means of the lack of manage information on the natural records of bone ailment development and the lack of facts on early biomarkers that predict disorder development[32].

Although comparable effects had been bought by means of two immunoassays in human urine samples, CTX and NTX, the consequences confirmed that a giant phase of CTX existing in organic fluids corresponds to β-CTX, instead than the NTX-I[21].A joint working crew between the International Osteoporosis Foundation (IOF) and the International Union of Clinical Chemistry and Laboratory Medicine (IFCC) specified serum kind I collagen beta-isomerized carboxy-terminal telopeptide (s-β-CTX; hereinafter referred to as "CTX") as a trendy marker of bone resorption, and serum procogen kind I N-terminal propeptide (s-PINP) as a preferred marker of bone formation, recommending its use in all future medical research[33].In patients with non-traumatic NONFH, we found that serum levels of β-CTx and N-MID were significantly higher than those in healthy controls[34].In investigating the use of bone turnover markers to predict the progression of femoral head osteonecrosis in elderly men, we found that levels of t-P1NP (N-terminal collagen type 1 extender peptide), OC, and β-CTx were significantly increased in patients with non-traumatic ONFH compared to healthy controls. Bone metabolism disorders, high levels of bone formation and absorption, are things we can directly observe [35].

4. Lipid Metabolites

Osteonecrosis of the femoral head (ONFH) is a common clinical disease with complex etiology, and insufficient blood supply to the femoral head is a key pathogenic factor in its development [36]. At present, the important motives of NONFH encompass coagulation disorders, unusual lipid metabolism, oxidative stress, fats embolism, vascular endothelial disease, thrombosis, diabetes and genetic mutations. The fundamental threat elements and their estimated frequency include: SONFH, which has an incidence of 35%-40%, normally precipitated by way of long-term use of steroid hormones; AONFH, which has an incidence of about 20%-40%; and IONFH, which additionally has an incidence of between 20%-40%[4, 37]. In research inspecting the relationship between lipid metabolism, coagulation function, bone metabolism and the contributing elements and ranges of non-traumatic femoral head necrosis, peculiar hypercoagulability and odd hyperlipidemia are hazard elements for the development of non-traumatic femoral head necrosis beneath a range of publicity factors, such as non-high-density lipoprotein cholesterol, apolipoprotein B, etc.[4]. Interestingly, in poultry studies, it was found that when broilers suffered from spontaneous necrosis of the femoral head (FHN), their serum high-density lipoprotein content was significantly reduced, and triglyceride levels were significantly increased, consistent with previous studies [38]. In a comprehensive lipidomic analysis of the two main types of ONFH, TONFH and NONFH, the up-regulation and down-regulation of these lipids in patients with ONFH indicate widespread disruption of lipid metabolic pathways[39].In a retrospective experimental study, we found that compared with healthy groups, the degrees of lipophilic metabolic coagulation markers such as high-density lipoprotein, low-density lipoprotein A1, lipoprotein B1, complete protein, albumin, and globulin had been statistically significant, which ability that femoral head necrosis is associated to a sequence of variables, which include lipid metabolism[40].Recent studies have also shown that the serum total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) levels, low density/high density lipoprotein (LDL/HDL) ratio, and apolipoprotein B (Apo-B) levels in patients with ONFH are significantly higher than those in the control group.In contrast, serum HDL and apolipoprotein A (Apo-AI) levels in patients with ONFH were significantly lower than those in the control group [41].

5. Conclusions and Future Directions

Measuring bone metabolism and lipid metabolism indicators has the advantages of non-invasive, cheap, convenient and repeatable. The combined application of bone biochemical indicators and lipid metabolism can predict the risk of avascular necrosis of the femoral head. Because they can reflect the status of bone metabolism in a short period of time, they also have certain clinical value in evaluating treatment effects. However, the disadvantage is that different locations, different degrees of damage, patients 'own metabolism, and eating habits will change the concentration of bone metabolites or lipid metabolites in their serum and urine [4].Although the main mechanism of bone metabolism is the result of breaking the balance between bone formation and bone resorption to achieve bone healing or bone destruction, and the mechanism has been studied thoroughly, over the years, there are still few research results on

abnormalities in bone metabolism markers and lipid metabolism caused by related bone diseases in specific locations. Therefore, the selected references have certain limitations [21, 32].Through years of lookup on bone metabolites, we have special serum kind I collagen β isomerized carboxy-terminal telopeptide as a trendy bone resorption marker, and serum kind I collagen N-terminal propeptide as a widespread bone formation marker, which is encouraged to be used in all future scientific research[33].We are mainly committed to accurately, promptly, conveniently, economically, rigorously and non-invasively predicting the progress and efficacy of avascular necrosis of the femoral head for patients. Current research have proven that bone turnover in sufferers with avascular necrosis of the femoral head has modified after non-joint substitute treatment. For predicting the development of avascular necrosis of the femoral head, we can't truly seem to be at the upward thrust and fall of bone resorption or bone formation markers. The modifications in bone turnover markers ought to be evaluated ordinary[28, 34, 35]. In recent years, we have found that enhanced intramedullary fat cell deposition in the femoral head can lead to impaired blood circulation in the femoral head. Therefore, lipid metabolism in vivo has also given a new direction for evaluating the progress of avascular necrosis of the femoral head [20].Through research, we found that abnormal hyperlipidemia status is a risk factor for the progression of non-traumatic femoral head necrosis under various exposure factors [38, 40].In general, we cannot judge the progress of avascular necrosis of the femoral head by single indicators of bone metabolism or lipid metabolism, but should combine and apply how they correlate with clinical outcomes. Best integrating these new predictive methods in clinical practice to reduce further avascular necrosis of the femoral head allows us to further improve the accuracy of our assessment of the progression of femoral head necrosis.

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