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ORIGINAL ARTICLE

The Relationship Between Hemoglobin Levels and Femoral Cartilage Thickness

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ABSTRACT

Objective: To explore the relationship between hemoglobin (Hb) levels and ultrasonographic (US) femoral cartilage thickness in healthy subjects.
Methods: Thirty-eight women who were admitted to our outpatient clinic for musculoskeletal complaints other than knee joint problems were recruited. Nineteen women (mean age: 34.6 ±7.3 years (22-43) and mean body mass index (BMI): 26.0 ±5.0 kg/m^2) with Hb levels ≤12 g/dL and nineteen healthy women with Hb levels >12 g/dL were included in the study. Distal femoral cartilage thickness was measured from the mid-points of the right medial condyle (RMC), right lateral condyle (RLC), right intercondylar area (RIA), left medial condyle (LMC), left lateral condyle (LLC) and left intercondylar area (LIA) using US.
Results: Subjects with low Hb levels (<12 g/dL) had thinner femoral cartilage thickness values at RMC (p = 0.001), at LMC (p = 0.008) and LIA (p = 0.017) when compared to those subjects with higher Hb levels (>12 g/dL).
Conclusion: Lower Hb levels seem to have negative impact on the femoral cartilage thickness. Additional studies are necessary to provide a better insight into understanding the clinical relevance of our finding and whether anemia treatment can reverse this process.

Key words: Hemoglobin, knee, femoral cartilage, thickness, ultrasound

INTRODUCTION

Anemia is a worldwide health problem affecting an estimated 25% of the world's population [1]. Iron deficiency is the leading cause about 50% of cases [2]. Anemia is associated with adverse outcomes including increased risk of fractures, renal injury, heart failure, cardiovascular events, re-admissions, worse functional outcome and lower quality of life [1,3-7].

Articular cartilage gains most of its nutrition and oxygen supply via diffusion from synovial fluid. There are several factors that control the cartilage integrity such as anabolic or catabolic growth factors and enzymes [8]. In a recent study, an association between low levels of serum vitamin D and femoral cartilage thinning was found [9]. Hypoxia is also accepted as one of the permanent stresses that impact the adult articular cartilage [8]. However, to the best of our knowledge, the association between low hemoglobin (Hb) levels and ultrosonographic knee cartilage thickness has not been investigated in the literature. Accordingly, the aim of the study is to explore whether Hb levels are associated with femoral cartilage thickness among healthy women.

PATIENTS AND METHODS

This study included 38 women (aged 20-43 years) who were admitted to our outpatient clinic for musculoskeletal complaints other than knee joint problems were recorded. The study protocol was approved by the Local Ethical Committee. Participants were informed about the study procedure and consented to participate.

Demographic and clinical characteristics (age, weight, height, body mass index (BMI), exercise and smoking status) and laboratory data (complete blood count, kidney/liver/thyroid function tests, 25-OH Vitamin D, parathyroid hormone [PTH]) of the participants were recorded. If they performed physical activity of moderate to heavy-intensity for at least 30 min/day and at least 3 times/week, patients assumed to be exercising.

Patients with history of knee trauma, any systemic and/or chronic disease, includingdiabetes mellitus,

thyroid abnormalities, rheumatoid arthritis, megaloblastic anemia, any treatment for anemia within the last six months and those with any abnormal laboratory results regarding renal/liver/thyroid/parathyroid function tests were excluded. Ultrasonographic measurements were performed bilaterally by the same physiatrist (F.U.M.) using a 7-12 MHz linear probe (Logiq P5, GE Medical Systems, Wisconsin, USA). The performer was blinded to patients` data. Distal femoral cartilage thickness measurements were done while the patient lied in supine position with knees in maximum flexion. The probe was positioned axially on the patellar outer edge [10,11]. The cartilage thickness was interpreted as the distance between the thin hyperechoic line at the synovial space/cartilage interface and the sharp hyperechoic line at the cartilage-bone interface [12]. Central points of right medial condyle (RMC), right lateral condyle (RLC), right intercondylar area (RIA), left medial condyle (LMC), left lateral condyle (LLC) and left intercondylar area (LIA) were measured (Fig. 1).

Hemoglobin levels of the cohort were grouped as ≤12 g/dL (patient group) and >12 g/dL (control group) according to previous literature [13].

Statistical Analysis

Data are expressed as mean ±standard deviation or percentage. Normal distribution has been assessed with Kolmogrov-Smirnov test. Comparisons of the mean values were done using independent samples-t test or Chi-square test where appropriate. Statistical analysis was performed by using SPSS 16.0 and statistical significance was set at $p < 0.05$.

RESULTS

Demographic and clinical characteristics of the cohort were provided in Table 1. The groups were similar regarding age, height, weight, BMI, smoking and exercise characteristics and also vitamin D and parathyroid hormone levels. ($p > 0.05$). Subjects with Hb levels ≤12 g/dL had thinner femoral cartilage thickness values at RMC ($p = 0.001$), at LMC ($p = 0.008$) and LIA ($p = 0.017$) when compared to those of subjects with Hb levels >12 g/dL.

DISCUSSION

Our results have revealed a negative effect of low levels of Hb on the distal femoral cartilage thickness. To the best of our knowledge, this is the first study exibiting thinning of the distal femoral cartilage in correlation with lower Hb levels.

Anemia related risks of mortality and morbidity are well-known and mostly related to anemia induced tissue hypoxia resulting in organ failure and even death in severe cases [14]. Hypoxia and mechanical loading are two permanent stresses for articular cartilage. Although loading and compression are widely agreed to be potent regulators of chondrocyte physiology [15-18], the effect of hypoxia on chondrocyte function is less well-established.

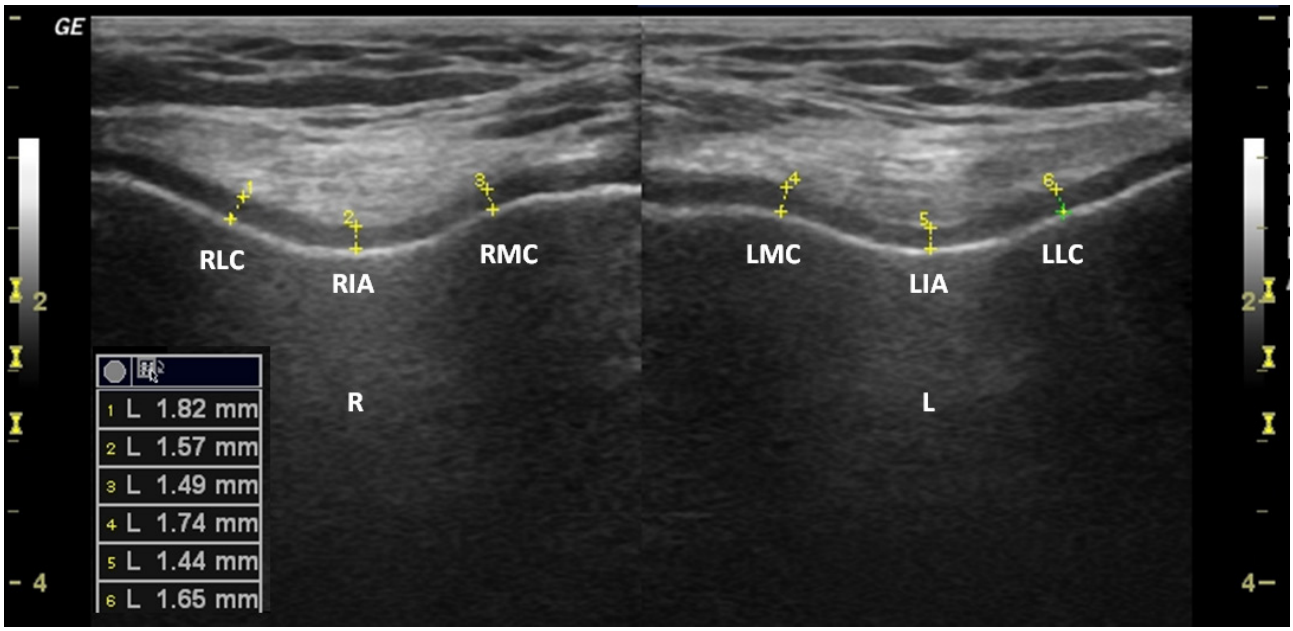

Figure 1. Suprapatellar axial view showing bilateral femoral distal cartilage measurements with ultrasonography. (RLC; right lateral condyle, RIA; right intercondylar area, RMC; right medial condyle, LMC; left medial condyle, LIA; left intercondylar area, LLC; left lateral condyle)

Table 1. Some of the clinical and laboratory data of the cohort.

	Hb ≤12 mg/dL (n = 19)	Hb >12mg/dL (n = 19)	p
Age (year)	34.6 ±7.3 (22-43)	34.3 ±6.9 (22-43)	0.910
Height (cm)	159.9 ±7.2	162.1 ±7.3	0.343
Weight (kg)	66.3 ±12.3	66.1 ±10.6	0.966
BMI (kg/m^2)	26.0 ±5.0	25.3 ±4.6	0.642
Hb (g/dl)	11.1 ±1.0	13.3 ±0.5	<0.001
25 OH vit D (ng/ml)	13.2 ±6.9	15.8 ±7.2	0.136
PTH (pg/ml)	67.9 ±19.4	64.2 ±17.5	0.575
Smoking (%)	21	16	0.983
Exercise (%)	16	32	0.438
RLC	1.82 ±0.24	1.86 ±0.32	0.643
RIA	1.74 ±0.30	1.97 ±0.49	0.093
RMC	1.62 ±0.23	1.98 ±0.37	0.001
LMC	1.77 ±0.33	2.09 ±0.38	0.008
LIA	1.64 ±0.20	1.90 ±0.41	0.017
LLC	1.65 ±0.23	1.65 ±0.24	0.946

Hb; Hemoglobin, RLC; right lateral condyle, RIA; right intercondylar area, RMC; right medial condyle
LMC; left medial condyle, LIA; left intercondylar area, LLC; left lateral condyle
Values are given in mean ±SD or %.

Chondrocyte response to hypoxia may be different from most tissues, because cartilage develops in a hypoxic environment throughout life [19-22]. Cartilage cells assumed to have developed specific and adapted mechanisms to promote its function in response to chronic hypoxia (i.e. inducing increased expression of cartilage matrix components [23-25] and inhibition of angiogenesis [26]. On the other hand, in different pathologies which affect cartilage such as rheumatoid arthritis and osteoarthritis, oxygen measurement in synovial fluid showed many differences [20,27] suggesting that oxygen level is essential for normal healing and repair in the joint [8].

Hemoglobin delivers oxygen to tissues and retrieves carbon dioxide. Hb also has the capacity to bind nitric oxide (NO) with its high affinity through its iron moiety [28]. Although, NO can be regulatory and even protective [29] at high concentrations this unstable radical gas and its metabolites can exert profound toxic effects [30]. Hemoglobin has the capacity to behave as a scavenger to reduce the NO. In a study Mc Cartney-Francis et al. [28] designed arthritic rats model. They used the natural affinity of NO to Hb and prevented joint swelling and erosive bone loss. This data may indicate that lower Hb levels may have a negative effect on protecting the joint integrity.

This study has some limitations. First of all, although we have a control group, we believe that higher patient numbers might sharpen the differences between groups. Secondly, our patients comprised only females, thus the results can not be extrapolated to males. Thirdly, we do not consider the anemia period of the patients which may be effective on the cartilage integrity. However, as our patients were young-aged women without any systemic or chronic diseases and we excluded patients whose femoral cartilage would have been affected by several other factors, therefore, the relationship between femoral cartilage thickness and Hb levels of the subjects seems to be noteworthy.

Overall, in light of our findings lower Hb levels seem to have negative impact on the femoral cartilage thickness. Additional studies are necessary to provide a better insight into understanding the clinical relevance of our finding and whether anemia treatment can reverse this process.

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