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QUS measurements in dialysis patients

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ABSTRACT

Background: It was aimed to evaluate the bone measurements by quantitative heel ultrasound (QUS) in patients undergoing chronic haemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD), and healthy controls. It was also aimed to investigate the relationship between weight, body mass index (BMI), smoking and parathyroid hormone (PTH) with QUS parameters.

Method: Present study included 25 patients on chronic HD (Group 1), 16 patients treated by CAPD (Group 2) and 32 controls (Group 3). QUS (Hologic, Sahara bone sonometer) measured broadband ultrasound attenuation (BUA; dB/Mhz), quantitative ultrasound index (QUI; g/cm^2), speed of sound (SOS; m/s). The WHO (1997) classification of BMI was used for weight classification. The smoking criterion was defined as smoker and non-smoker.

Results: Mean age of cases was 40.2±15.5, 36.0±9.9 and 36.6±12.4 years, in groups 1, 2 and 3 (p>0.05), and mean dialysis duration time was 31.8±12.6 and 42.8±12.8 months, in groups 1 and 2 (p=0.015). Depending on the QUS parameters, both osteoporosis and osteop zenia were diagnosed in five (56%) of women and in 11 (69%) of men in HD vs in two (33%) of women and in four (40%) of men in CAPD, respectively (p=0.584). QUS measurements were not correlated with serum PTH and BMI in both HD and CAPD groups, respectively. In HD group, we found

SOS to be lower (1526±27 vs. 1548±19 *m/s*, p=0.016) in smokers compared to non-smokers. There were negative correlations between smoking and QUS parameters (r= -0.34; p= 0.044). Conclusion: Our findings suggest that there is an unfavorable influence of HD and smoking on bone mineralization compared to CAPD.

Key words: Quantitative heel ultrasound (QUS); osteoporosis; continuous ambulatory peritoneal dialysis (CAPD), haemodialysis (HD); parathyroid hormone (PTH).

INTRODUCTION

Reduced bone mineral density (BMD) is associated with renal osteodystrophy (ROD) and osteoporosis in end-stage renal disease (ESRD) patients. On the other hand, ROD is very heterogeneous, and is characterized by high as well as by low bone turnover disease [1,2]. The currently accepted definition of osteoporosis is "a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with consequent increase in bone fragility and susceptibility to fracture risk" [3].

The underweight state is associated with malnutrition and osteoporosis; other factors occurring in malnutrition, besides body composition changes, such as protein deficiency, could be involved in the association between underweight and osteoporosis. Persons who are underweight [Body Mass Index (BMI <18.5)] are at increased risk of osteoporosis and fracture risk. Reduction of body weight has been shown to reduce these risks [4]. In addition, some recent studies demonstrate corresponding positive associations between moderate overweight and bone mass and density in the elderly [5,6].

Dual-energy X-ray absorptiometry (DEXA) is the standard non-invasive method to assess BMD, but is not always widely available. Quantitative heel ultrasound (QUS) is a mobile, relatively inexpensive, easy to perform and radiation-free method, which can predict fractures to the same extent as DEXA [1]. Large prospective studies have demonstrated the strong exponential relationship between heel ultrasound and X-ray results and the risk of fracture [7-11]. According to 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada, it was accepted that "QUS may be considered for diagnosis of osteoporosis, but not for follow-up at this time" [12].

The aim of the study was to evaluate the bone measurements by QUS in chronic haemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) and healthy controls. Additionally, we also aimed to determine the effect of weight, classified by BMI, smoking and biochemical parameters such as PTH on QUS parameters.

SUBJECTS & METHODS

Subjects

In present descriptive study, 25 patients [16 Male (M), 9 Female (F)] on chronic HD and 16 patients (10 M, 6 F) treated by CAPD in Dialysis Centre of Dicle University, and 32 healthy controls (15 M, 17 F) were studied. Forty-one (26 M, 15 F) HD and CAPD patients for at least 6 months and with dialysis efficiency >1.0 measured by KT/V were included in the study. The investigation was conducted in accordance with the local ethics committee and the Declaration of Helsinki II and the Guidelines of Good Clinical Practice. None of the studied patients had

suffered fractures of long bones, and none of the patients had undergone partial parathyroidectomy for severe secondary hyperparathyroidism. Gastric acid suppression therapy (either H2 receptor antagonists or proton pump inhibitors) was being taken by three HD patients, and warfarin therapy was being taken by only one CAPD patient. None of the post-menopausal females were receiving hormone therapy (HT). All patients were receiving daily <500 mg dietary calcium and RhuEPO therapy (Epoetine alpha or beta, weekly mean dose as 2840±2400 IU Sc.) except two patients in CAPD and five patients in HD groups.

Haemodialysis: The patients received HD this for 5 hours, three times per week with a high-flux PS hollow fiber disposable dialyser (Fresenius Medical Care, Germany) and dialysers were never reused. HD was carried out using Braun-Dialog and Fresenius-4008S (Germany) dialysis machines and bicarbonate as dialysate. All patients were receiving heparin [low molecule weight heparin (LMWH)]. Machines were heat disinfected between treatments and chemically every month. There were no major changes in dialysis dose and efficiency during either study period.

Continuous ambulatory peritoneal dialysis: Most CAPD patients were prescribed four 2-liter exchanges daily. A minority were treated with four 1.5-liter exchanges daily if they couldn't tolerate 2 liters in the peritoneum. All patients received peritoneal dialysis via a Tenckhoff coil catheter. CAPD patients used a Baxter's Ultra Bag system (Baxter Healthcare Corp., USA) or Fresenius' Freedom Y-set system (Fresenius Medical Care, Germany).

Methods

<u>*Laboratory methods:*</u> Blood samples were collected after an overnight fast and before breakfast in CAPD patients and controls, and immediately before dialysis session in HD patients. Serum intact parathyroid hormone (1–84) (iPTH) (normal range: 10-55 pg/ml) was measured by RIA (Immulite 2000, DPC, Los Angeles, USA). Serum calcium (Ca^{+2}) (normal values range from 8.5 to 10.9 mg/dl), phosphate (P) (normal range: 2.4 to 4.1 mg/dl) and alkaline phosphatase (ALP) (normal range: 44 to 147 IU/L) were analysed standard laboratory methods. Standard medications such as calcium carbonate ($CaCO_3$), or calcium acetate (PhosEX®), were prescribed with meals and snacks to bind phosphorus in the bowel. 1,25 $(OH)_2D_3$ (calcitriol) or 1 alpha $(OH)D_3$ (alpha calcidol) was administered orally at a low dose (0.25 mcg/day), or at a higher dose (0.5 to 1.0 mcg/day) (n=15, HD Group and n=6, CAPD Group).

<u>*Definition of Osteoporosis:*</u> The WHO definition was not suitable for use with SOS measurements, therefore definition of osteoporosis was stated according to study of Knapp et al [13]. Revised T-score thresholds for the diagnosis of osteoporosis of -2.6 and for osteopenia of -1.4 were used.

<u>*Bone mineral density*</u>***:*** Quantitative ultrasound of the left heel examination was performed by measurement of broadband ultrasound attenuation (BUA, dB/MHz), speed of sound (SOS, m/s), and QUI [QUS index defined as (0.67 BUA) + (0.28 SOS)] using the Sahara Clinical Bone Sonometer (Hologic Inc, Bedford, MA, USA) by a single operator. There is no cutoff level for osteoporosis criterion specific for men and women.

The reported coefficients of variance (CV) for estimated BMD, QUI, SOS, and BUA are 3, 2.6, 0.22, and 3.7%, respectively [14]. One measurement of the left foot was obtained on all participants. A second measurement with repositioning of the foot was obtained if the first measurement was technically inadequate.

Some limitations of this study deserve comment. First, QUS measurements may lack precision especially if the room temperature varies. To avoid this, the sonometer was calibrated with a

standardized phantom daily and showed an in vitro precision error of 0.85% for BUA and 0.50% for SOS during the study period. We examined the subjects after at least 30 min rest in the test room, where the temperature was maintained at 25 ^{0}C.

System components: The key components of the sahara advanced clinical bone sonometer system include the ultrasound unit (including positioning aid), power supply, power cord, QC phantom, sahara ultrasound coupling gel, and an external desktop or laptop Windows-based PC.

Obesity: The WHO (1997) classification of BMI was used for weight classification, i.e. underweight (BMI <18.5), normal weight (BMI 18.5-24.99), and overweight as moderate overweight (BMI 25.0-29.99) and obese subjects (BMI 30+). Weight is measured before and after dialysis in all patients. The weight used in this study was the average of three post-dialysis weights recorded in the week prior to entry.

Smoking status: The smoking criterion was defined as non-smoker included "all time non-smoker", "stopped smoking", and "less than 10 Per day", and current smokers included "between 10 and 20 per day", and "a pack or greater per day" at least five years. Smokers were compared to non-smokers.

Statistical methods

Analyses were done by SPSS (Statistical Package for Social Sciences) 7.5 PC program. Results were expressed as mean±SD. The one-way ANOVA and post hoc Bonferroni tests were used to compare independent-unpaired parametric samples of different groups and the Pearson correlation test was used to determine the correlations. Differences between the means of multiple subgroups were assessed with a Kruskal–Wallis test and the Spearman correlation tests were used to determine the non-parametric correlations. Logistic regression analyses were performed with adjustment for clinical (dialysis type, PTH and smoking status), anthropometric (weight, age, gender and BMI) and QUS variables. A $p<0.05$ was considered statistically significant.

RESULTS

Socio-demographic, biochemical and QUS parameters of HD, CAPD and Control groups are given in Table 1. Twenty-five HD patients as group 1 (36.6% women), 16 CAPD patients as group 2 (37.5% women) and 32 healthy controls as group 3 (53.1% women) were studied. Mean age of cases was 40.2±15.5, 36.0±9.9 and 36.6±12.4 years, in groups 1, 2 and 3 ($p>0.05$), and mean dialysis duration time was 31.8±12.6 and 42.8±12.8 months, in groups 1 and 2 ($p=0.015$), respectively. Depending on the QUS parameters, both osteoporosis and osteopenia were diagnosed in five (56%) of women and in 11 (69%) of men in HD vs in two (33%) of women and in four (40%) of men in CAPD, respectively ($p=0.584$).

In HD patients (group 1) compared to other groups, the serum Ca^{+2} levels, BMI ($p=0.291$, $p=0.001$) and QUS parameters such as BUA (Figure 1) and QUI ($p=0.015$ and $p=0.208$) were lower. However, serum PTH (Figure 2) and ALP levels were higher ($p<0.0001$, $p=0.001$). Bone measurements were not correlated with serum PTH and BMI in HD group ($r=0.24$; $p=0.314$ and $r=0.18$; $p=0.395$) and CAPD group ($r=0.09$; $p=0.753$ and $r=-0.239$; $p=0.373$), respectively. We did not find any significant correlations between QUS parameters and PTH, dialysis duration, gender, age and menopause in both HD and CAPD groups. Additionally, there were not associations between BUA values and serum intact PTH values, duration time of HD, age and gender.

Depending on the WHO weight classification, underweight (BMI <18.5) vs. normal or overweight (BMI ≥18.5) condition was observed as 9/16, 6/10 and 0/32 in HD, CAPD and Control groups (p=0.001), respectively (Figure 3).

We divided also both CAPD and HD patients into two groups according to BMI: group A (BMI <18.5 kg/cm^2), and group B (BMI ≥18.5 kg/cm^2); [Group A (n=9) and group B (n=16) in CAPD and group A (n=6) and group B (n=10) HD patients]. Data related with BMI subgroups were showed in table 2. Mean BUA value was higher in CAPD groups A and B (p=0.003, Figure 4). We separated both CAPD and HD patients into two groups: group A (iPTH < 200 pg/mL), and group B (iPTH ≥200 pg/mL); [Group A (n=9) and group B (n=7) in CAPD and group A (n=9) and group B (n=16) HD patients]. However, we did not find any correlation between PTH levels and QUS parameters both in two sub-groups of CAPD and HD patients. Data related with PTH subgroups were showed in table 3. Mean BUA value was lower in HD group A (Figure 5).

In HD group, there were differences in QUI, BUA and T *score* of the calcaneus between smokers and non-smokers. However, there was significant difference in only SOS (1526±27 vs. 1548±19 *m/sn*, p=0.016) and Z *score* (-1.48±0.59 vs. -0.82±0.58, p=0.031). There was a slight positive correlation between smoking and T score (r=0.35; p=0.044). However, there were negative correlations between smoking and QUS parameters (r=-0.34; p=0.044). Bone mass as assessed by ultrasound of the left heel was lower for SOS (p=0.016) and QUI (p=0.056) in smokers than in non-smokers (Table 4). Increased OR was found only for smoking and dialysis type (HD). The adjusted OR and 95% confidence interval (CI) for osteoporosis were 4.96 (95% CI: 1.16-24.79) for smoking, and 2.81 (95% CI: 1.05-8.37) for dialysis type (HD) (p=0.008 and p=0.024). The weight was not quite significant (OR = 0.94, 95% CI 0.87-1.02).

DISCUSSION

Uremia and HD are associated with a high frequency of ROD, and osteodensitometry has shown decreased BMD and BMC in patients compared with controls [15]. Frequency of osteoporosis in patients on dialysis varies in different studies depending of method and measured region of BMD (16-22). In the study of Taal *et al*. [19], the prevalence of femoral neck BMD below the fracture threshold was 19.3%.

In our study, depending on the QUS parameters, both osteoporosis and osteopenia were diagnosed in five (56%) of women and in 11 (69%) of men in HD vs. in two (33%) of women and in four (40%) of men in CAPD, respectively (p=0.584). We have also found a moderate however significant reduction in mean BUA in present chronic HD patients compared to CAPD patients and healthy controls (p=0.015). The average Z-score of -1.12 for the QUS measurement of the calcaneus implies that these patients are only moderately worse off than CAPD patients and age-matched controls. This is similar to the results of other studies using different methods of BMD measurement [20,21].

In a recent study from Turkey, Arici and his colleagues [23] evaluated the diagnostic potential of QUS of calcaneum and to correlate it with DEXA in chronic HD patients. They reported that BUA and SOS values were markedly reduced in dialysis patients compared to controls (59.1±13.8 *vs*. 73.0±16.2 dB/MHz, p<0.001 and 1533±28 *vs*. 1560±29 m/s, p=0.014). Both BUA and SOS scores were inversely correlated with age (r=-0.69, p<0.001) and duration of menopause (r=-0.74). Additionally, BUA values showed a moderate negative association with serum intact PTH values (r=-0.38, p=0.018). They concluded that chronic HD patients have reduced calcaneal BUA and SOS values.

As with previous studies [23,24], our findings also showed that dialysis affects the bone status and HD patients have worse bone mineral metabolism compared to age and gender matched CAPD patients and healthy controls. In our study, mean BUA of HD patients (61±17 *dB/Mhz)* was significantly lower than those of CAPD patients (69±17 *dB/Mhz)* and controls (74±14 *dB/Mhz)*, respectively (p=0.015) (Figure 1). As it is expected, the mean ALP and PTH levels significantly higher in HD patients (p<0.0001 and p<0.0001) (Table 1, Figure 2). QUI and BUA were also lowest in HD patients compared to the other two groups (p=0.208 and p=0.015). We did not find any significant correlations between BUA and PTH, dialysis duration, gender and age in both HD and CAPD groups. Hormonal factors also affect bone density in HD patients. It was reported that female sex was negatively associated with total hip BMD in the group as a whole and in the subgroup of patients over 60 years [19]. However, we were unable to show any effect of menopause on QUS parameters in HD or CAPD patients in the present study.

Caloric imbalance (intake exceeding expenditure) can lead to overweight and obesity. It is well established that obesity is also a risk factor for a number of serious disorders. However, moderate overweight plays a protective role for osteoporosis [6]. Studies in HD patients have not assessed patient weight; some recent studies have reported a positive association between BMI and measures of BMD [19]. According to BMI, nine (36%) of 25 HD patients and six (37.5%) of 16 CAPD patients were underweight (BMI <18.5 kg/m^2). However, none of controls were underweight (Figure 3). We did not found any association between BMI and BUA in our three groups. We divided also both CAPD and HD patients into two groups according to BMI (Table 2). Mean BUA value was higher in CAPD groups A and B (p=0.003, Fig. 4).

Secondary hyperparathyroidism remains the most common type of renal bone disease found in HD patients. Several studies have reported a similar negative association between PTH levels using a variety of measurements of BMD [19,20,25-27]. In the present study, however, we did not find any significant correlations between BUA and iPTH, dialysis duration, gender, age and menopause in both HD and CAPD groups. Additionally, there were not associations between BUA values and serum intact PTH values, duration time of HD, age and gender. Similarly with our results, previously it was reported that bone measurements were not correlated with serum PTH in patients on maintenance HD. The regression lines of SOS, BUA, and stiffness to BMD were not significantly different from that of the controls [28]. According to study of Peretz and colleagues [28], when dividing the patients into two subgroups according to their median PTH (203 pg/mL), the slopes of the regression lines of BUA to BMD were significantly different between these two subgroups (p=0.052). Similar correlation also was reported by other researchers [29,30]. One of them, Pecovnik Balon and co-workers [29] suggested that there is a negative correlation between iPTH and BMDc in patients beginning HD treatment (r=-0.34, p<0.02). Pasadakis and coworkers [30] tried to evaluate any correlation between BMD and iPTH levels in CAPD patients that were separated into two groups: group A (iPTH <200 pg/mL), 13 patients, and group B (iPTH >200 pg/mL), 20 patients. Data analysis revealed a negative correlation between PTH levels and BMD values (r= -0.66, p=0.014) as PTH and serum calcium (r= -0.77, p=0.002) only in-group A. No other statistically significant changes were observed. They considered that these findings suggest there is a favorable influence of CAPD modality on bone mineralization, while no special DEXA findings are representative of the possible appearance of a dynamic bone disease [30].

In the present study, we also separated both CAPD and HD patients into two groups: group A (PTH ≤200 pg/mL) and group B (PTH >200 pg/mL). In contrast to the previous two studies, data analysis in the present study did not reveal any correlation between PTH levels and BMD values both in two sub-groups of CAPD and HD patients. Serum Ca^{+2} level was higher (p=0.034) in HD patients (group A). However, QUI and BUA (p=0.056 and p=0.012) were higher in CAPD patients (group A) compared to other three groups (Table 3, Figure 5).

In a recent study [31], effects of cigarette-smoking on bone mass were investigated in 75-year old women (n=1042) on a population basis [Osteoporosis Prospective Risk Assessment (OPRA)] study, by DEXA and ultrasound, and it was found that smoking has a negative influence on bone mass independent of differences in weight and physical activity. Bone mass as assessed by ultrasound of the calcaneus was lower for SOS ($p<0.01$), BUA ($p<0.0001$) and QUI (stiffness) ($p<0.0001$) in smokers than in never-smokers. In the HD group, we found BMD to be lower (0.42 ± 0.11 vs. 0.49 ± 0.09 g/cm^2, $p=0.056$) in smokers compared to non-smokers. There were also differences in QUI and BUA of the calcaneus between smokers and non-smokers. However, there were significant differences in only SOS (1526 ± 27 vs. 1548 ± 19 g/cm^2, $p=0.016$) and avarage Z *score* (-1.48 ± 0.59 vs. -0.82 ± 0.58, $p=0.031$). Bone mass as assessed by ultrasound was lower for SOS ($p=0.016$), BUA ($p=0.580$) and QUI ($p=0.056$) in smokers than in non-smokers (Table 4). In our study, increased OR was found only for smoking and dialysis type (HD). The adjusted OR and 95% confidence interval (95% CI) for osteoporosis was 4.96 (95% CI: 1.16-24.79) for smoking (independent of differences in weight), and 2.81 (95% CI: 1.05-8.37) for dialysis type (HD) ($p=0.008$ and $p=0.024$).

In conclusion, while we have failed to confirm PTH-related bone disease in affecting QUS parameters in dialysis patients, we have found that other factors, which are known to be risk factors for osteoporosis, are also important. Smoking has also a negative influence on QUS parameters especially QUI and SOS. Chronic HD patients have reduced calcaneal BUA. These findings suggest that there is an unfavorable effect of smoking and dialysis type (HD) on bone mineralization.

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Table 1. ***Demographic, biochemical and QUS parameters of HD, CAPD and Control groups.***

	Groups			p
	HD n=25	CAPD n=16	CONTROL n=32	
Patients (M/F)	16/9	10/6	15/17	=0.367
Age	40.2±15.5	36.0±9.9	37.7±13.1	=0.494
Dialysis Duration (*month*)	31.8±12.6	42.8±12.8	0	=0.011*
Height *(cm)*	163±8	168±8	165±7	=0.185
Weight *(kg)*	55±12	61±12	68±13	=0.001
BMI (kg/m^2)	20.7±4.7	21.8±4.3	24.9±4.1	=0.001
QUI *(g/cm^2)*	85±16	93±17	89±14	=0.208
BUA *(dB/Mhz)*	61±17	74±14	69±17	=0.015
SOS *(m/s)*	1537±25	1545±30	1540±19	=0.597
T – *score*	-2.72±0.96	-1.01±0.73	-1.04±0.72	=0.008
Z – *score*	-1.12±0.66	-0.87±0.67	-0.81±0.69	=0.189
PTH (*pg/mL*)	376±291	238±195	46±19	<0.000
ALP (*IU/L*)	170±114	131±53	79±24	=0.001
Ca^{+2} (*mg/Dl*)	8.5±1.6	9.4±1.7	9.0±1.0	=0.291
P (*mg/dL*)	5.7±1.5	6.2±1.7	4.5±0.6	=0.003
Smoker	12	5	9	=0.258
Menopausal Women	6	2	6	=0.262
Underweight/Overweight	9/3	6/4	0/15	=0.001
Ca^{+2} carbonate or acetate	25	16	0	>0.05*
Hydroxylated Vitamin D	15	6	0	>0.05*
RhuEPO	20	14	0	>0.05*

* HD and CAPD groups were compared.

Table 2. ***Demographic, biochemical and QUS parameters of HD and CAPD subgroups according to BMI levels.***

	HEMODIALYSIS		PERITONEAL DIALYSIS		
	Group A (BMI <18.5 *kg/cm²*) n=9	Group B (BMI ≥18.5 *kg/cm²*) n=16	Group A (BMI <18.5 *kg/cm²*) n=6	Group B (BMI ≥18.5 *kg/cm²*) n=10	p
Age	28.4±7.6	46.9±15.0	29.3±5.7	40.0±9.9	=0.002
Dialysis Duration (*mo*)	33.1±14.8	31.1±11.6	40.7±12.9	44.0±13.3	=0.004
QUI *(g/cm²)*	85±16	84±17	98±25	90±10	=0.046
BUA *(dB/Mhz)*	59±17	62±18	73±20	74±10	=0.003
SOS *(m/s)*	1541±25	1536±25	1558±43	1538±16	=0.171
T - *score*	-1.43±0.76	-1.51±1.08	-1.13±1.07	-0.97±0.49	=0.110
Z - *score*	-1.26±0.78	-1.06±0.61	-1.35±0.98	-0.68±0.42	=0.086
PTH (*pg/mL*)	405±359	362±268	221±111	250±248	=0.494
ALP (*IU/L*)	171±91	168±132	109±5	144±65	=0.676
Ca^{+2} (*mg/dL*)	7.9±1.5	9.0±1.6	8.9±1.7	9.6±2.2	=0.066
P (*mg/dL*)	6.0±1.2	5.6±1.7	6.3±2.1	6.0±1.1	=0.819

Table 3. ***Demographic, biochemical and QUS parameters of HD and CAPD subgroups according to PTH levels.***

	HEMODIALYSIS		PERITONEAL DIALYSIS		
	Group A (PTH <200 pg/mL) n=9	Group B (PTH ≥200 pg/mL) n=16	Group A (PTH <200 pg/mL) n=9	Group B (PTH ≥200 pg/mL) n=7	p
Age	Age	45.0±15.1	42.8±8.9	42.8±8.9	=0.092
Dialysis Duration (*mo*)	Dialysis Duration (*mo*)	32.0±13.7	36.0±15.7	36.0±15.7	=0.021
BMI (*kg/m²*)	BMI (*kg/m²*)	21.9±13.7	22.8±4.6	22.8±4.6	=0.371
QUI *(g/cm²)*	QUI *(g/cm²)*	90±18	98±10	98±10	=0.054
BUA *(dB/Mhz)*	BUA *(dB/Mhz)*	66±18	81±9	81±9	=0.012
SOS *(m/s)*	SOS *(m/s)*	1546±27	1550±18	1550±18	=0.169
T - *score*	T - *score*	-1.46±1.12	-0.65±0.44	-0.65±0.44	=0.037
Z - *score*	Z - *score*	-1.04±0.50	-0.45±0.16	-0.45±0.16	=0.008
ALP (*IU/L*)	ALP (*IU/L*)	162±109	109±21	109±21	=0.239
Ca^{+2} (*mg/dL*)	Ca^{+2} (*mg/dL*)	9.3±1.7	10.5±1.6	10.5±1.6	=0.034
P (*mg/dL*)	P (*mg/dL*)	5.5±1.7	7.0±1.8	7.0±1.8	=0.150

Table 4. ***Demographic, biochemical and QUS parameters of non-smokers and smokers in HD patients.***

	HEMODIALYSIS PATIENTS		p
	Non-smoker n=13	Smoker n=12	
Age	40.0±13.3	43.2±17.2	=0.644
Dialysis Duration (*month*)	33.6±14.8	31.5±11.1	=0.967
BMI (kg/m^2)	21.7±5.8	20.4±3.4	=0.853
QUI (g/cm^2)	90±14	79±18	=0.056
BUA *(dB/Mhz)*	63±18	59±18	=0.580
SOS *(m/s)*	1548±19	1526±27	=0.016
T – *score*	-1.29±1.12	-1.77±0.83	=0.064
Z – *score*	-0.82±0.58	-1.48±0.59	=0.031
PTH (*pg/mL*)	467±282	308±289	=0.137
ALP (*IU/L*)	178±104	145±130	=0.155
Ca^{+2} (*mg/dL*)	8.1±1.5	9.5±0.8	=0.020
P (*mg/dL*)	5.7±1.5	5.5±1.4	=0.819

FIGURE 1

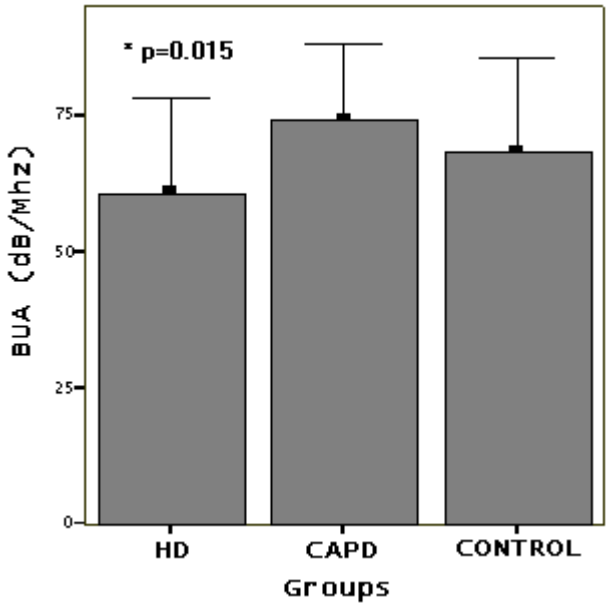

FIGURE 2

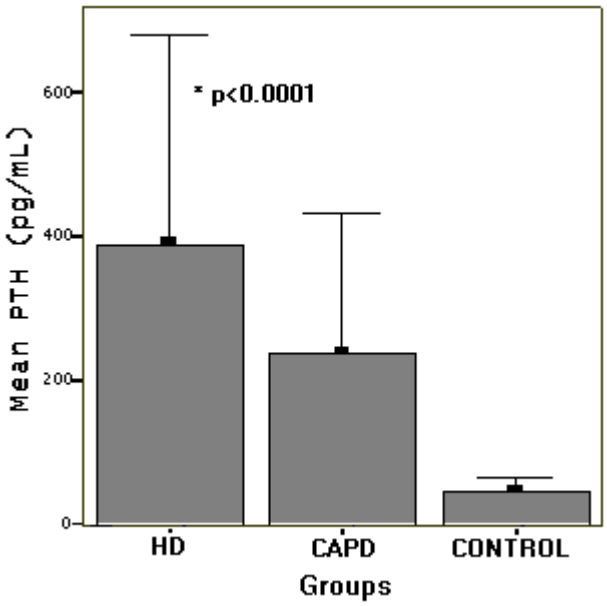

FIGURE 3

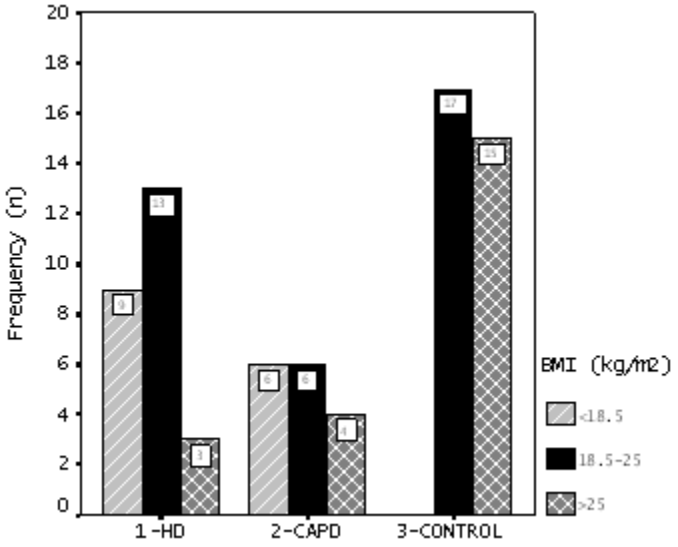

FIGURE 4

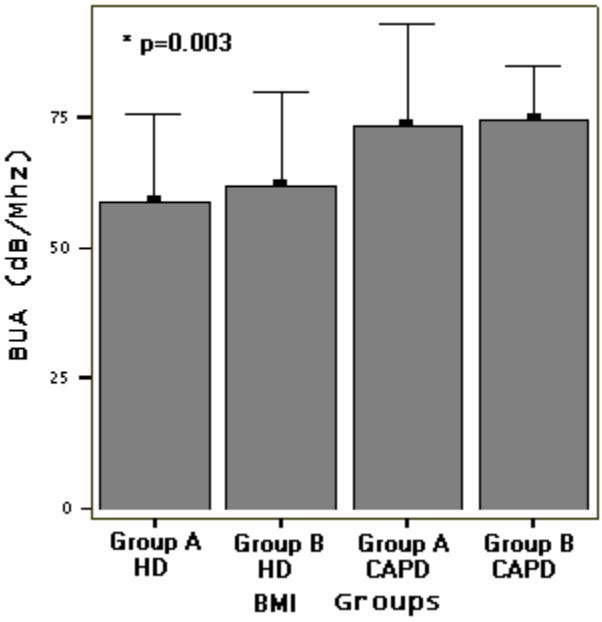

FIGURE 5