Hormone replacement therapy has favorable effects on bone microarchitecture, bone mineral density and body fat mass, without affecting lean mass: the OsteoLaus Cohort

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OBJECTIVES

Aim N°1: To assess for the first time the effect of hormonal replacement therapy (HRT) on bone microarchitecture, as assessed by trabecular bone score (TBS)

○ Hypothesis 1.1: In addition to higher BMD values, HRT will be associated with higher TBS values, thus suggesting an effect on enhancing bone quality as well as bone quantity

Aim N°2: To explore if a residual benefit on BMD and TBS persists after HRT discontinuation

○ Hypothesis 2.1: A protective bone effect of HRT is present after its withdrawal and can be mediated by the preservation of BMD and/or the maintenance of bone microarchitecture, as assessed by TBS

○ Hypothesis 2.2: The protective effect will be positively correlated with HRT duration and inversely correlated with time since HRT withdrawal

Aim N°3: To evaluate the effect of HRT on body composition parameters and possible associations with its bone effects

○ Hypothesis 3.1: HRT will increase lean body mass (LBM), which may contribute to the higher BMD by increased mechanical load

○ Hypothesis 3.2: HRT reduces fat mass (FM), which may participate in the increase of BMD by various mechanisms: reduction of pro-inflammatory cytokines , increase of adipokines (leptin), promotion of osteoblastogenesis instead adipogenesis

METHODS

• **OsteoLaus population-based study: 1445 ♀ aged 50-80yrs**

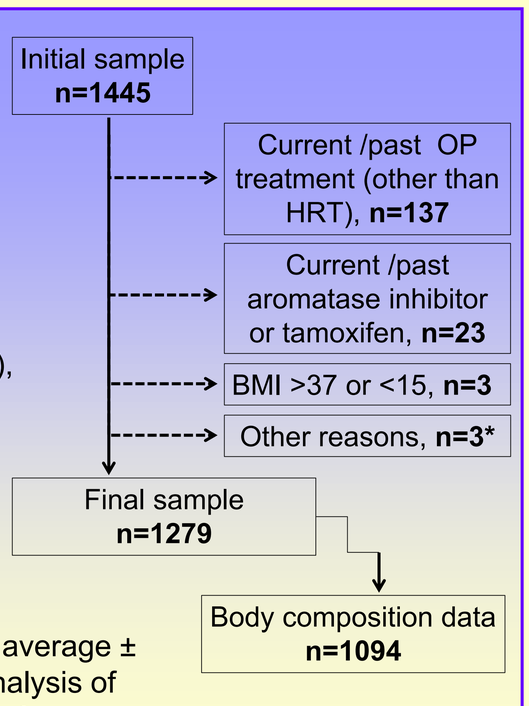
➢ Questionnaire: conditions with possible effect on bone (including HRT status). FRAX® score: risk for OP fractures in 10 yrs.

➢ BMD at lumbar spine, femoral neck and total hip + body composition by dual X-ray absorptiometry (DXA, Hologic, USA)

➢ Blind processing of TBS (TBS iNsight v2.1, medimaps, France)

➢ Vertebral fracture assessment (semi quant approach of HK. Genant)

➢ CoLaus cohort: available data on physical exercise (total energy expenditure, TEE), nutrition (alternative healthy eating index, AHEI), dietary calcium intake, vitamin D levels and depression prevalence



• **Groups: Current (CU, n=282), Past (PU, n=380) or Never (NU, n=617) HRT users**

• **Outcomes: BMD at lumbar spine (LS), femoral neck (FN), total hip (TH), spine TBS. Fat mass index (FMI), lean mass index (LMI), appendicular lean mass index (ALMI)**

Statistical analysis: Descriptive results (number of participants or average ± SD). Bivariate analyses (chi-square for categorical variables and analysis of variance for quantitative variables). Multivariate analyses (analysis of (co)variance; results expressed either as adjusted average ± standard error or as slope and 95% confidence intervals). Statistical significance, p-value <0.05

RESULTS

TABLE 1: BASELINE CHARACTERISTICS OF SAMPLE

	NU (n=617)	PU(n=380)	CU (n=282)	p-value
Age (years)	62.1 ± 8.0	67.4 ± 6.2	64.0 ± 6.8	<0.001
BMI (kg/m²)	25.9 ± 4.5	26.0 ± 4.2	25.3 ± 4.0	0.084
Vertebral # (%)	32 (5.2)	30 (7.9)	6 (2.1)	0.005
Atraumatic # (%)	94 (15.2)	89 (23.4)	39 (13.8)	0.001
Major # (%)	69 (11.2)	58 (15.3)	17 (6.0)	0.001
Calcium, diet (mg)	954 ± 524	982 ± 506	1038 ± 571	0.102
Supplements (%)	215 (34.9)	212 (55.8)	105 (37.2)	<0.001
Vitamin D (nmol/L)	51.1 ± 22.5	55.7 ± 23.1	56.6 ± 24.7	0.002
FRAX (%)	11.2 ± 7.1	13.4 ± 7.5	10.5 ± 5.6	<0.001
TEE (kcal/day)	2320 ± 347	2265 ± 349	2253 ± 293	0.021
AHEI	32.3 ± 10.4	33.6 ± 9.7	34.3 ± 9.5	0.019
Depression (%)	58 (11.1)	36 (11.3)	28 (11.0)	0.995

TABLE 2: BONE AND BODY COMPOSITION OUTCOMES

AGE & BMI-ADJUSTED VALUES				P-value	
	NU (n=617)	PU (n=380)	CU (n=282)	CU vs. NU	PU vs. NU
BMD LS	0.91 ± 0.01	0.94 ± 0.01	0.98 ± 0.01	<0.001	0.017
TBS	1.27 ± 0.01	1.29 ± 0.01	1.31 ± 0.01	<0.001	0.066
BMD FN	0.72 ± 0.01	0.73 ± 0.01	0.76 ± 0.01	<0.001	0.219
BMD TH	0.84 ± 0.01	0.86 ± 0.01	0.89 ± 0.01	<0.001	0.026
AGE-ADJUSTED VALUES					
	NU (n=504)	PU (n=262)	CU (n=205)	CU vs. NU	PU vs. NU
FMI	9.4 ± 0.1	9.4 ± 0.2	8.9 ± 0.2	0.098	0.993
LMI	16.9 ± 0.1	16.7 ± 0.1	16.7 ± 0.1	0.213	0.395
ALMI	7.1 ± 0.1	6.9 ± 0.1	7.0 ± 0.1	0.307	0.188

TABLE 3: SUBGROUPS OF PAST USERS

	BMD LS	TBS	BMD FN	BMD TH
HRT duration (years)				
(0-2)	0.92 ± 0.02	1.27 ± 0.01	0.73 ± 0.01	0.85 ± 0.01
(2-5)	0.95 ± 0.02	1.28 ± 0.01	0.73 ± 0.01	0.87 ± 0.01
(>5)	0.94 ± 0.01	1.28 ± 0.01	0.72 ± 0.01	0.85 ± 0.01
P-value	0.485	0.640	0.672	0.326
Time since HRT discontinuation (years)				
(0-2)	1.02 ± 0.03	1.33 ± 0.02	0.77 ± 0.02	0.90 ± 0.02
(2-5)	0.93 ± 0.02	1.28 ± 0.01	0.71 ± 0.01	0.85 ± 0.01
(>5)	0.93 ± 0.01	1.27 ± 0.01	0.72 ± 0.01	0.85 ± 0.01
P-value	0.007	0.002	0.007	0.009

FIGURE 1: ASSOCIATION OF DIFFERENT OUTCOMES WITH AGE ACCORDING TO HRT STATUS (A: BMD LS, B: BMD FN, C: BMD TH, D: TBS, E: FMI, F: LMI)

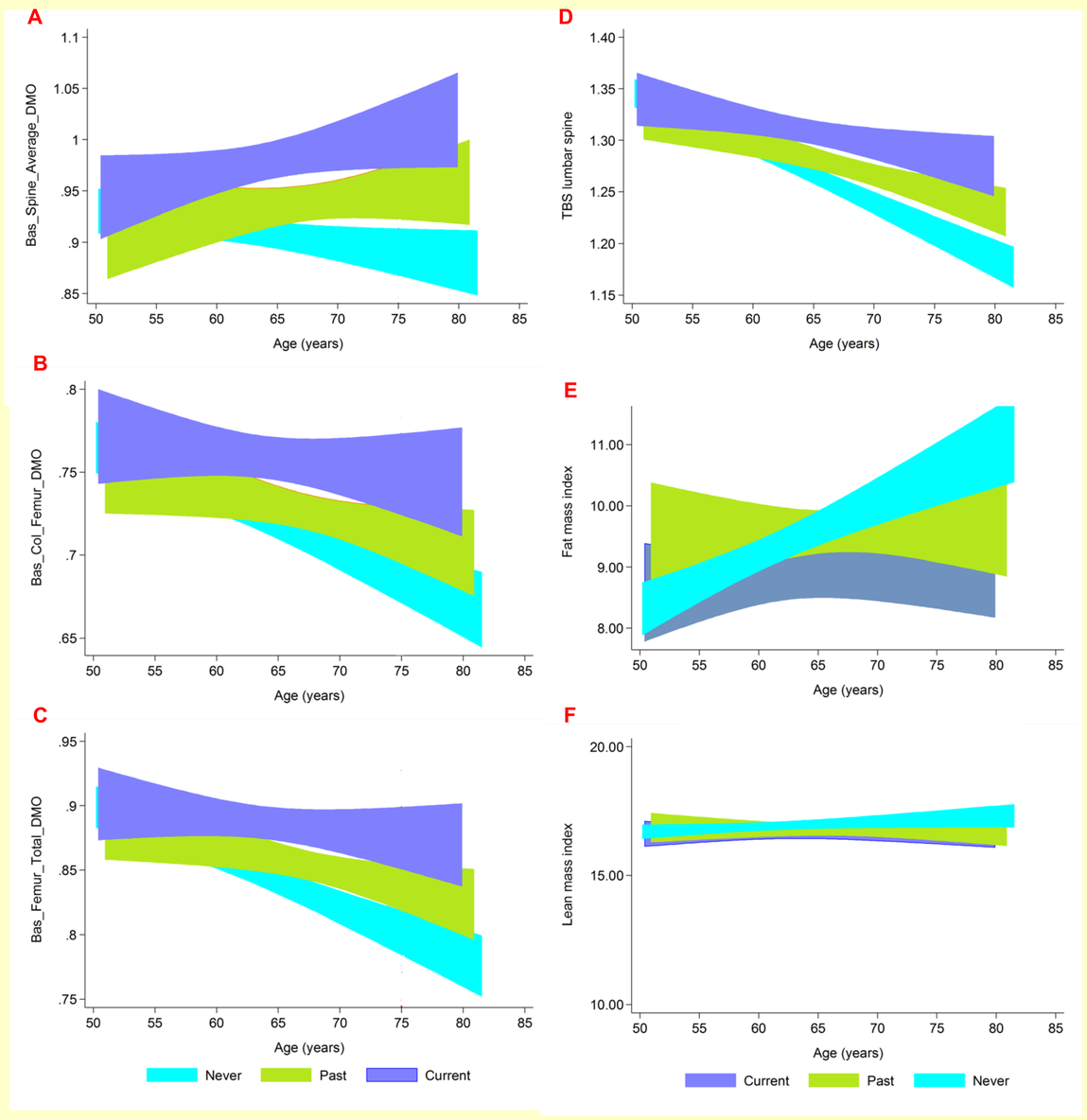


TABLE 4: ASSOCIATION OF BONE AND BODY COMPOSITION OUTCOMES WITH AGE, ACCORDING TO HRT GROUP

	NU (n=617)	PU (n=380)	CU (n=282)	CU vs. NU	PU vs. NU
BMD LS	-0.026 (-0.040; -0.011)	0.014 (-0.013; 0.041)	0.025 (-0.001; 0.050)	0.001	0.008
TBS	-0.051 (-0.060; -0.041)	-0.032 (-0.048; -0.017)	-0.022 (-0.038; -0.005)	0.003	0.048
BMD FN	-0.038 (-0.048; -0.028)	-0.019 (-0.035; -0.002)	-0.010 (-0.027; 0.008)	0.006	0.055
BMD TH	-0.048 (-0.059; -0.038)	-0.023 (-0.04; -0.006)	-0.011 (-0.028; 0.007)	<0.001	0.012
	NU (n=504)	PU (n=262)	CU (n=205)	CU vs. NU	PU vs. NU
FMI	0.887 (0.566 ; 1.208)	0.084 (-0.463 ; 0.631)	0.225 (-0.350 ; 0.800)	0.049	0.013
LMI	0.198 (-0.001 ; 0.398)	-0.061 (-0.392 ; 0.270)	0.044 (-0.308 ; 0.396)	0.455	0.195
ALMI	0.026 (-0.071 ; 0.122)	-0.135 (-0.292 ; 0.021)	-0.079 (-0.245 ; 0.087)	0.291	0.091

Results are expressed as BMI-adjusted slope (95% confidence interval) for a ten-year increment

CONCLUSIONS

1. **Our results show for the first time that, in addition to higher BMD values, current HRT use is associated with better preservation of bone microarchitecture as assessed by TBS**
2. **The benefits of HRT seem to persist for past users regarding BMD at lumbar spine and total hip, as well as TBS. This protective effect is independent of the duration of HRT treatment, however it is less prominent in late discontinuers (time since HRT withdrawal > 2 years)**
3. **The increase of BMD produced by HRT does not seem to be mediated by a rise in muscular mass. No difference in lean body mass was detected between the different groups of HRT status**
4. **We demonstrate, however, that the age-associated increase of fat mass is lessened in HRT users. The bone implications of this finding need to be clarified. Further analysis is ongoing to determine if the reduction of fat mass concerns the subcutaneous or intravisceral fat**

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