Age-related Changes in the Microstructural Organization of the Femoral Neck Suggest Degradation in Bone Quality Independent of Cortical Thinning and Increased Porosity

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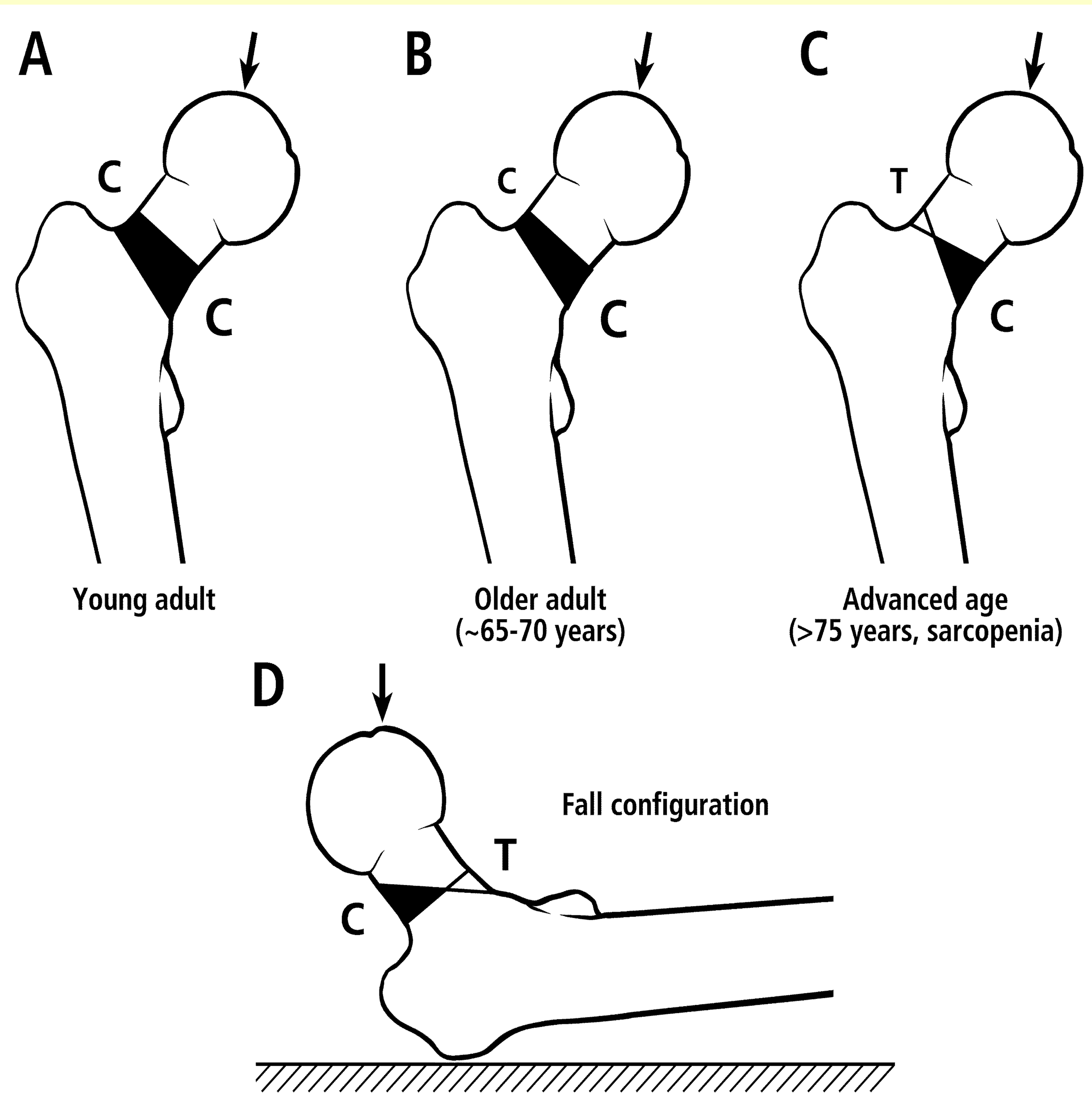
Introduction

Reduced elasticity of the femoral neck (FN) with age is due, in part, to increased porosity and to a lesser extent by a reduction in tissue density [1-4]. Elastic instability of the FN with aging might be more strongly influenced by regional changes in histomorphological characteristics that affect tissue toughness (e.g., regional changes in osteon heterogeneity, collagen cross-linking, and predominant collagen fiber orientation) [5]. If this is the case, then this could represent a therapeutic target for reducing age-related hip fragility that is likely different from the stimuli that naturally increase overall FN diameter with age (which is considered the primary means for curbing age-related increased elastic instability) [6,7]. The present study advances our previous work [8] that was aimed at determining if there are material changes in the FN cortex that might contribute to elastic instability with aging. We examined age-related changes in collagen fiber orientation (CFO), osteon population density (OPD), and osteon morphotype scores (MTS). Here we evaluate a more comprehensive set of microstructural characteristics, including many that are known to influence the toughness of bone. We hypothesized that with aging the superior FN cortex experiences reduced stress that might eventually become net tension in the elderly (Fig. 1). It is predicted that because tension is comparatively more deleterious than compression this change in load history would evoke strain-mode-related adaptation of the bone material in ways that might not be closely associated with age-related increased porosity or thinning of the cortex.

Figure 1



Methods

28 human FNs (3 M, 25 F; 18-95 yrs) were embedded in methacrylate and mid-transverse sections were mounted on glass and ultramilled (100µm). 50X circular polarized light images were obtained in octants. Predominant CFO was expressed as the mean gray-level of each image, and population densities of complete secondary osteons (OPD, no./mm2) and their morphotype scores (MTS) were also quantified [8,9]. Osteon morphotypes are based on collagen lamellar patterns that correlate with regional differences in habitual strain mode (compression vs. tension) [9]. We also quantified: fractional area of secondary bone (FASB, %), porosity (%), osteon area (On.Ar, µm2), osteon circularity (On.Cr) (1.0 = perfect circle), Haversian canal area (HC.Ar), Haversian canal circularity (HC.Cr), osteon formation/infilling (On.Ar - HC.Ar), and cortical thickness (CT, mm). The regions quantified were defined as the superior (Sup) cortex (posterior, posterior-superior, superior; combined data) and inferior (Inf) cortex (anterior, anterior-inferior, inferior; combined data). These groups are based on data showing the posterior-superior to anterior-inferior axis is where fracture resistance is most compromised in the elderly [1].

1. RESULTS OF CORRELATIONS (r values) & PAIRED COMPARISONS (p values)

	MTS	CFO	OPD	FASB	POROSITY
CORRELATIONS WITH (ALL BONES; SUP/INF RATIO	NS	NS	NS	NS	NS
CORRELATIONS WITH (YOUNGER BONES, <60 YEARS; SUP/INF RATIO)	NS	NS	0.60 (0.011)	NS	NS
CORRELATIONS WITH (OLDER BONES, ≥60 YEARS; SUP/INF RATIO)	NS	NS	NS (0.058)	0.76 (0.004)	NS
SUPERIOR vs. INFERIOR CORTEX [PAIRED COMPARISONS OF SUP vs. INF CORTICES]	Sup>Inf*	Sup>Inf*	Inf>Sup*	Inf>Sup*	Sup>Inf*
All Bones	Sup>Inf*	Sup>Inf*	Inf>Sup*	Inf>Sup*	Sup>Inf*
Younger Bones (<60 yrs.)	Sup>Inf*	Sup>Inf*	Inf>Sup*	Inf>Sup*	Sup>Inf*
Older Bones (≥60 yrs.)	NS (0.14)	NS (0.11)	Inf>Sup*	Inf>Sup*	NS (0.11)

Results

In younger bones (< 60 years) (see Tables), CFO, osteon MTS, OPD, FASB, and porosity showed a statistically significant Sup vs. Inf ("Sup/Inf") cortex difference. In the older bones (> 60 years), only the Sup/Inf differences in OPD and FASB remained (final Table shows p values for all Sup vs. Inf comparisons). Although the porosity difference (Sup > Inf) seen in younger bones was no longer significant in older bones, the porosity of these cortices each increased by ~67% (Sup cortex p=0.06; Inf cortex p=0.04). The Sup/Inf difference in CT thickness also persisted in the older bones, but unlike data reported in Mayhew et al. [1] the Inf. cortex did not thicken significantly with age. But the Sup cortex did thin significantly with age as expected.

Discussion

Only OPD and FASB showed a significant Sup/Inf difference in the ≥60 year-old group. The two characteristics that are most sensitive to strain mode (CFO and osteon MTS) showed significant Sup/Inf differences only in the younger bones. We previously [8] concluded that this is most consistent with reduced loading of the femoral neck with age as suggested by Mayhew et al. [1] (like Fig. 1B); this does not support the idea of an age-related change in strain-mode distribution (i.e., not like Fig. 1C). Absence of age-related differences in other potentially strain-mode-sensitive characteristics (e.g., On.Ar and On.Cr) is consistent with this interpretation. These results support the idea that the strain environments of the Sup and Inf cortices become more similar with age; perhaps underloading of the superior FN becomes prevalent with age [1]. Assuming that the Sup/Inf microstructural differences seen in the younger group provide increased FN strength and/or toughness, then retaining these differences with age would be beneficial. Material changes coupled with structural changes (e.g., enlargement of FN diameter [1]) leads to the proposal that enhancing only the subperiosteal bone apposition in the FN would not be sufficient to curb fracture risk.

2. INTER-PARAMETER CORRELATIONS (THESE ARE OCTANT COMPARISONS; ALL BONES)

OPD vs. MTS	r= -0.22	CT vs. CFO	r= -0.15
OPD vs. CFO	r= -0.14	CT vs. OPD	r= 0.31
OPD vs. POROSITY	r= -0.16	CT vs. FASB	r= 0.33
MTS vs. CFO	r= 0.52	CT vs. POROSITY	r= -0.28
CT vs. MTS	NS		

3	Young Means±SD			P	Old Means±SD			P
	Sup	Inf	Sup/Inf		Sup	Inf	Sup/Inf	
CFO	117.1±16.9	105.2±20.3	1.2±0.2	<0.01	106.4±15.5	98.8±11.8	1.1±0.1	NS (0.1)
MTS	3.0±0.4	2.8±0.3	1.1±0.2	0.03	2.8±0.4	2.7±0.3	1.0±0.1	NS (0.1)
OPD	7.1±2.5	9.1±2.2	0.8±0.2	<0.01	6.0±1.8	9.6±2.7	0.7±0.3	<0.01
FASB	25.7±11.6	34.1±17.8	0.9±0.6	0.04	21.6±11.2	31.7±12.9	0.8±0.5	0.05
On.Ar	37000±12000	35000±10000	1.1±0.4	NS	29000±11000	31000±17000	1.1±0.4	NS
On.Cr	0.86±0.07	0.87±0.07	1.0±0.15	NS	0.87±0.04	0.88±0.02	0.98±0.06	NS
On.Form	0.93±0.08	0.95±0.02	1.0±0.12	NS	0.86±0.14	0.92±0.03	0.93±0.14	NS
Porosity	5.1±3.2	3.2±1.6	2.2±1.7	0.03	8.7±6.7	5.4±3.9	1.8±1.2	NS (0.1)
CT	1.5±0.2	2.6±0.6	0.6±0.2	<0.01	1.1±0.3	2.5±0.6	0.5±0.1	<0.01

Significance

Identifying regional microstructural characteristics helps to advance understanding of the specific characteristics of normal bone matrix organization that degrade with age in the fracture-prone FN and how these material characteristics interact with structural characteristics.

References

[1] Mayhew et al. 2005 Lancet 366:129-; [2] Holzer et al. 2009 Bone 24:468-; [3] Bell et al. 1999 Bone 24:57-; [4] Loveridge et al. 2004 Bone 35:929-; [5] Reeve and Loveridge 2014 Bone 61:138-; [6] Kaptoge et al. 2003 Osteoporos Int 14:941-; [7] Power et al. 2005 Osteoporos Int 16:1049-; [8] Skedros et al. 2013 ORS 38:1419; [9] Skedros et al. 2009 Bone 44:392-.

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