VI CONGRESSO NAZIONALE DELLA SOCIETÀ ITALIANA
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PALAZZO ZACCO

IMPATTO DELLA COMPOSIZIONE CORPOREA SULLE FRATTURE VERTEBRALI IN PAZIENTI OPERATE PER CARCINOMA MAMMARIO ED IN TRATTAMENTO ADIUVANTE CON INIBITORI DELL'AROMATASI.

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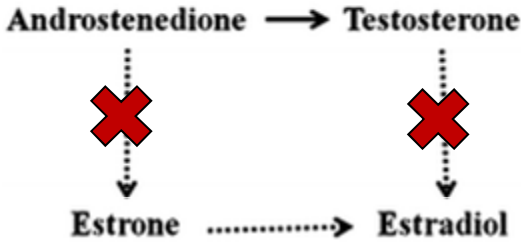
AROMATASE INHIBITOR-ASSOCIATED BONE LOSS

Aromatase inhibitors (AIs) are the most frequently used endocrine therapy in postmenopausal women with early stage Breast Cancer (5-10 Yrs)



Effects

reduction in circulating and intratumoral estrogen levels

Side effects

Arthralgia

Menopausal symptoms, Hot flashes and night sweats

Increased cholesterol, CV risk

decrease in BMD, increase in bone turnover markers, bone fractures

AROMATASE INHIBITOR-ASSOCIATED BONE LOSS

Fractures in the major randomized aromatase inhibitor trials

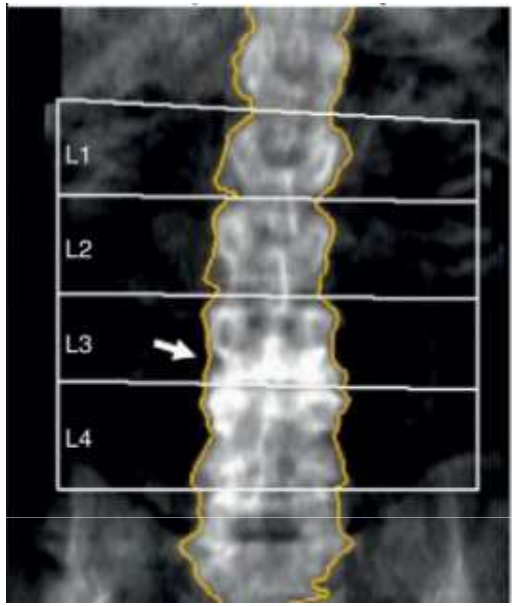
Trial	Treatment	Clinical fractures rate, percent
AI vs TAM		
ATAC	ANA vs TAM	11.0 vs 7.7 [p<0.001]
BIG 1-98	LET vs TAM	8.6 vs 5.8 [p<0.01]
AI after 2-3 years of TAM		
IES	EXE vs TAM	7.0 vs 5.0 [p = 0.003]
ABCSG8/ARNO	ANA vs TAM	2.0 vs 1.0 [p = 0.015]
AI after 5 years of TAM		
MA-17	LET vs Placebo	5.3 vs 4.6 [p = 0.25]

ANA: anastrozole; TAM: tamoxifen; EXE: exemestane; LET: letrozole

risk of underestimate

adapted from Pant, S, et al Drugs 2008

AROMATASE INHIBITORS and VERTEBRAL FRACTURES



about **2/3** VFs are **asymptomatic**

VFs were associated with
↑ risk of future fractures, independent of BMD status
↓ quality of life, ↓ survival

AROMATASE INHIBITORS and VERTEBRAL FRACTURES

Full Length Article

Bone 97 (2017) 147–152

Morphometric vertebral fractures in breast cancer patients treated with adjuvant aromatase inhibitor therapy: A cross-sectional study

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263 postmenopausal women hormone receptor-positive early BC

AI-naive **(169 pts)**

AI-treated **(94 pts)**

Each woman underwent

- a dual-energy X-ray absorptiometry (DXA) to evaluate bone mineral density (BMD) and identify VFs by a quantitative morphometric approach.

- Blood samples were collected to measure serum hormone and calcium levels.

AROMATASE INHIBITORS and VERTEBRAL FRACTURES

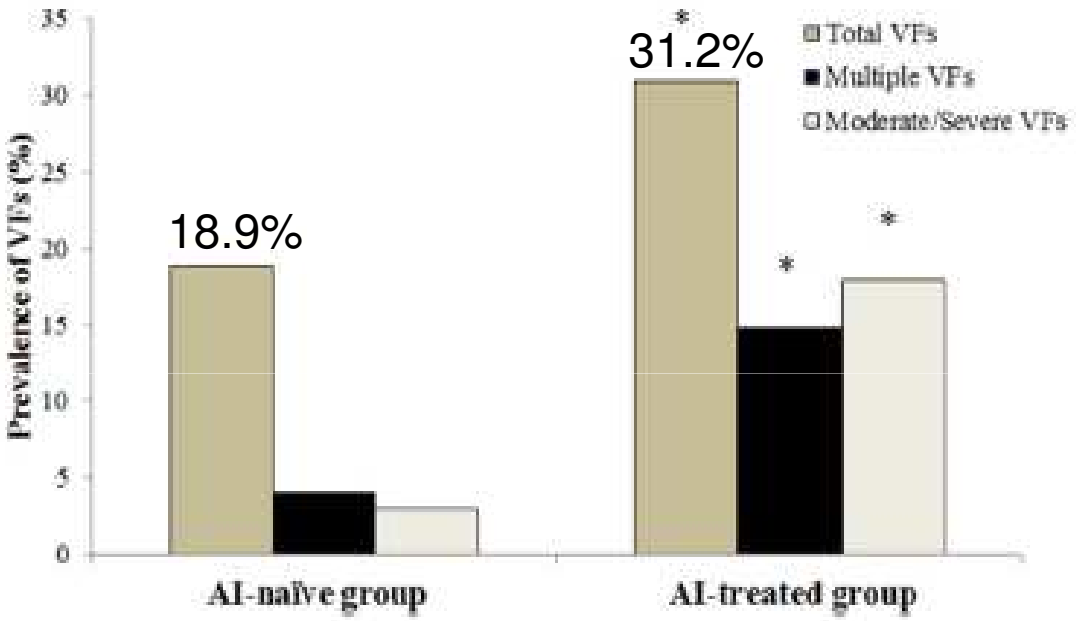


Fig. 1. Prevalence, number and severity of vertebral fractures (VFs) in aromatase inhibitor (AI)-treated patients as compared to AI-naïve patients. * $p < 0.05$, AI-treated vs. AI-naïve group.

+ 12,3% VFs
in AI-treated

odds ratio 1.90, 95% CI 1.1–3.5, p = 0.03

AROMATASE INHIBITORS and VERTEBRAL FRACTURES

Table 2
Univariate analysis of determinants of vertebral fractures (VFs) in aromatase inhibitor (AI)-naïve and AI-treated patients. Data were presented as median (range) and percentages, and the comparisons were performed by non-parametric tests. * $p < 0.05$, AI-treated vs. AI-naïve group.

	Groups	Patients without VFs	Patients with VFs	p-values
Age (years)	AI-naïve	64 (41–81)	68 (52–83)	**0.002**
	AI-treated	65 (51–85)*	66 (57–77)	0.52
BMI (kg/m^2)	AI-naïve	26 (18–39)	24 (18–34)	0.10
	AI-treated	25 (16–37)	27 (18–34)*	0.08
Prior chemotherapy (N, %)	AI-naïve	38 (27.7%)	8 (25.0%)	0.75
	AI-treated	19 (29.2%)	12 (41.4%)	0.25
Lumbar spine BMD (g/cm^2)	AI-naïve	0.874 (0.630–1.370)	0.858 (0.610–1.170)	0.37
	AI-treated	0.852 (0.571–1.070)*	0.824 (0.670–1.101)	0.75
Femoral neck BMD (g/cm^2)	AI-naïve	0.700 (0.540–1.072)	0.643 (0.470–1.020)	**0.04**
	AI-treated	0.679 (0.361–0.943)	0.707 (0.510–0.870)	0.19
Total hip BMD (g/cm^2)	AI-naïve	1.000 (0.580–1.930)	0.927 (0.772–1.194)	**0.007**
	AI-treated	0.949 (0.770–1.812)	0.955 (0.671–1.600)	0.82
Serum progesterone (ng/ml)	AI-naïve	0.10 (0.1–0.3)	0.32 (0.1–0.4)	0.18
	AI-treated	0.10 (0.1–0.4)	0.10 (0.1–0.5)	0.98
Serum testosterone (ng/ml)	AI-naïve	0.29 (0.15–2.2)	0.32 (0.17–0.75)	0.48
	AI-treated	0.35 (0.02–0.67)*	0.36 (0.17–0.72)	0.35
Serum FSH (UI/ml)	AI-naïve	56 (22–125)	67 (43–85)	0.67
	AI-treated	56 (29–111)	54 (15–176)	0.31
Serum 25(OH)-vitamin D (ng/ml)	AI-naïve	22 (5–63)	18 (6–53)	0.71
	AI-treated	31.5 (9–62)*	32.5 (14–63)*	0.58
Serum calcium (mg/dl)	AI-naïve	9.3 (8.4–10.0)	9.2 (8.2–10.1)	0.44
	AI-treated	9.4 (8.5–10.6)	9.4 (8.4–10.2)	0.81
Serum PTH (pg/ml)	AI-naïve	33 (11–167)	33 (9–102)	0.83
	AI-treated	38 (13–132)	46 (20–114)*	0.06

VFs occurred without association with any parameter analyzed in AI-treated patients.

Prevalence of VFs in AI treated pts
36.7% with osteoporosis vs 20.0% with normal BMD; p=0.31

AIM of the STUDY

explore determinants of Vertebral Fractures

correlation between VFs prevalence and body composition in a larger case series

315 postmenopausal women hormone receptor-positive early BC

AI-naive **(N 187)**

AI-exposed **(N 128)**

•no bone metastases

•no bone metabolic disease (e.g. osteoporosis, Paget's disease, primary hyperparathyroidism, kidney stones, or chronic hypercortisolism)

•no renal failure (baseline serum creatinine less than 1.5 mg./dl.)

•treatment with bisphosphonates or drugs that affect bone metabolism (e.g., steroids or calcitonin)

METHODS

- DXA to evaluate BMD and identify VFs by a quantitative morphometric approach

- Body composition: total body mass, fat body mass (FBM) and lean body mass (LBM) was measured using body composition software on a Hologic QDR-4500A bone densitometer (Hologic Inc., Bedford, MA).

RESULTS

Study population characteristics

	AI naïve patients	AI treated patients	P value
N	187	128	
Age (yrs)	64 (47-83)	65 (50-84)	0,022 *
Prevalence of VFs	41 (21,9%)	40 (31,2%)	0,067
BMI (Kg/mq)	25,22 (17,58-39,04)	26,00 (15,94-39,04)	0,194
Lumbar spine BMD	0,869 (0,539-1,374)	0,850 (0,571-1,260)	0,444
Femoral neck BMD	0,689 (0,447-1,072)	0,685 (0,357-1,009)	0,786
Total Hip BMD	0,808 (0,579-1,114)	0,809 (0,565-1,089)	0,779
Lean Body Mass	38433,0 (22481,1-56431,9)	38533,1 (29663,3-56053,1)	0,833
Fat Body Mass	24620,1 (10709,1-48659,4)	24729,6 (8458,0-49878,2)	0,231

RESULTS

Univariate analysis of VFs determinants

	Groups	No VFs	VFs	P value
N	AI naive	146 (78,1)	41 (21,9)	
	AI exposed	88 (68,8)	40 (31,2)	0,067
Age (yrs)	AI naive	62 (48-83)	68 (53-82)	0,000 *
	AI exposed	64 (50-84)	68 (55-82)	0,112
Lumbar spine BMD	AI naive	0,871 (0,539-1,374)	0,847 (0,605-1,172)	0,220
	AI exposed	0,858 (0,571-1,127)	0,851 (0,672-1,260)	0,839
Femoral neck BMD	AI naive	0,698 (0,447-1,072)	0,656 (0,473-0,874)	0,020 *
	AI exposed	0,679 (0,358-0,938)	0,699 (0,507-1,009)	0,294
Total Hip BMD	AI naive	0,814 (0,579-1,114)	0,782 (0,579-0,984)	0,065
	AI exposed	0,807 (0,631-1,089)	0,827 (0,565-1,062)	0,335

RESULTS

Univariate analysis of VFs determinants

	Groups	No VFs	VFs	P value
Lean Body mass	AI naive	38754,7 (22481,1-49234,9)	38266,0 (30920,3-56431,9)	0,322
	AI exposed	38353,2 (29663,3-56053,1)	38883,6 (34058,8-50347,4)	0,235
Fat Body Mass	AI naive	25083,0 (10709,1-48659,4)	23341,4 (12445,9-42882,3)	0,347
	AI exposed	23605,6 (8458,0-49878,2)	29296,6 (12903,7-47642,4)	0,022 *
BMI	AI naive	25,39 (17,58-39,03)	25,21 (17,71-34,53)	0,901
	AI exposed	24,97 (15,94-37,47)	27,26 (18,82-39,04)	0,046 *

During AIs positive correlation between VFs and FBM

DISCUSSION

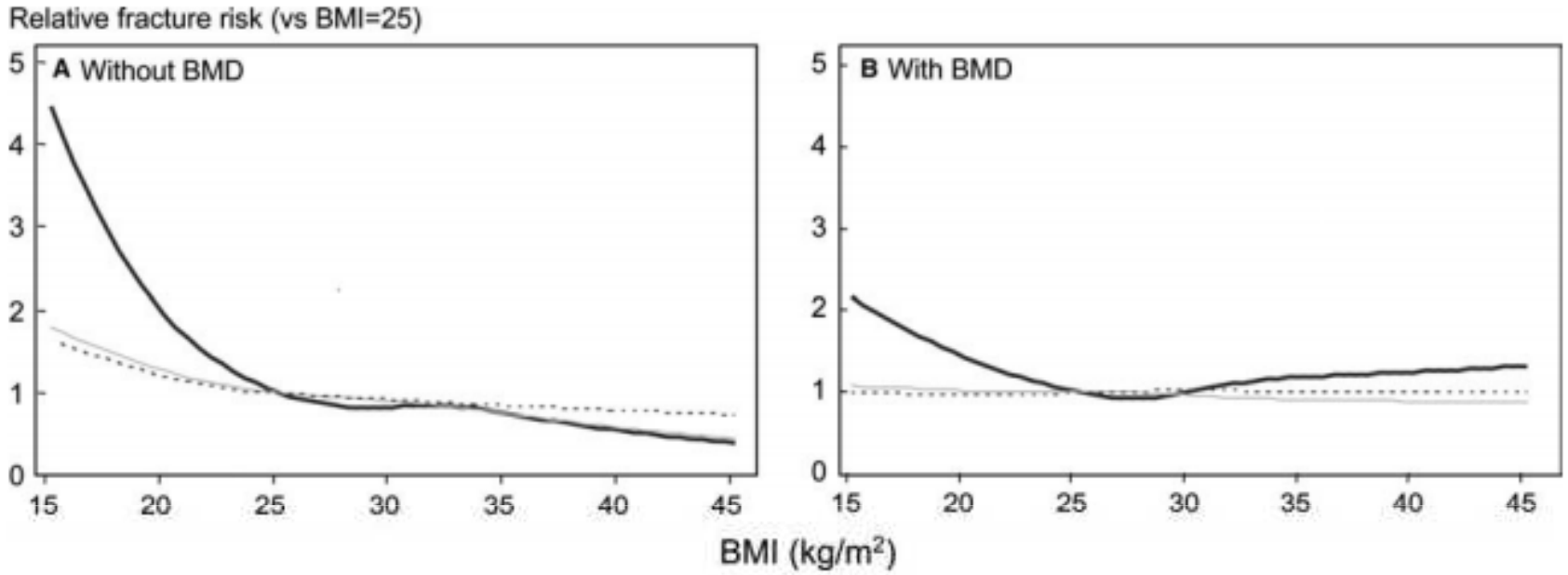


Fig. 3 Relative fracture risk at various levels of BMI (kg/m^2) for men and women combined. The reference is a BMI = 25, **(A)** adjusted for current age and time since start of follow-up, and **(B)** additionally adjusted for BMD. The *bold solid line* describes hip fracture, the *solid line* any osteoporotic fracture, and the *dotted line* any fracture (*BMI* body mass index, *BMD* bone mineral density) [04Ca003]

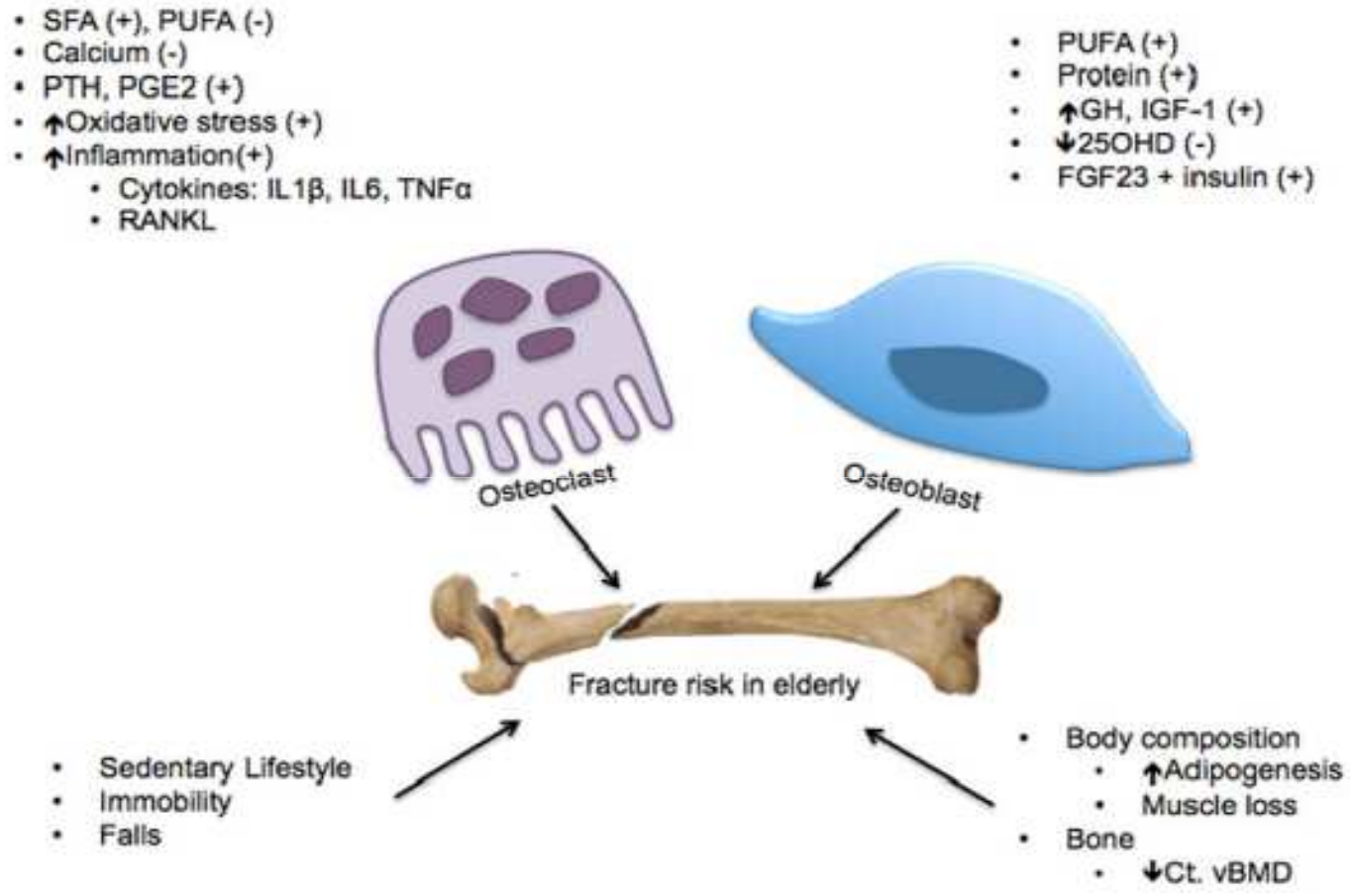
De Laet et al Osteoporosis Int, 2005

overweight and obesity → in the past positively correlated with increased BMD and reduced risk of fragility fractures.

greater mechanical loading on the bone
adipose tissue source of estrogen production (postmenopausal women)

DISCUSSION

Obesity may also influence bone fragility



Shapses et al Nut Res, 2017

Trabecular Bone Score (TBS) negatively correlated to BMI and weight.
An increase in BMI increases bone density, but with an adverse effect on bone structure.

Young-Seong Kim et al Osteoporosis and Sarcopenia, 2017

CONCLUSIONS

As expected, in women with early BC on AIs we observed

high prevalence of radiological VFs

VF were associated with higher FBM

performing **body composition assessment**,

together with **morphometric evaluation of VFs**

in women undergoing treatment with Ais

predict fracture risk

plan pharmacological or behavioral interventions

in high-risk patients

Grazie per l'attenzione