The role of IL-17A in postmenopausal inflammatory events, such as in osteoporosis

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IL-17 cytokine

IL-17 (called as IL-17A) is characterized by:

- T-cell-derived cytokine
- secreted from Th17 cells, which are distributed from other effector CD4+ T helper cells, such as Th1, Th2 and regulatory T (Treg) cells.

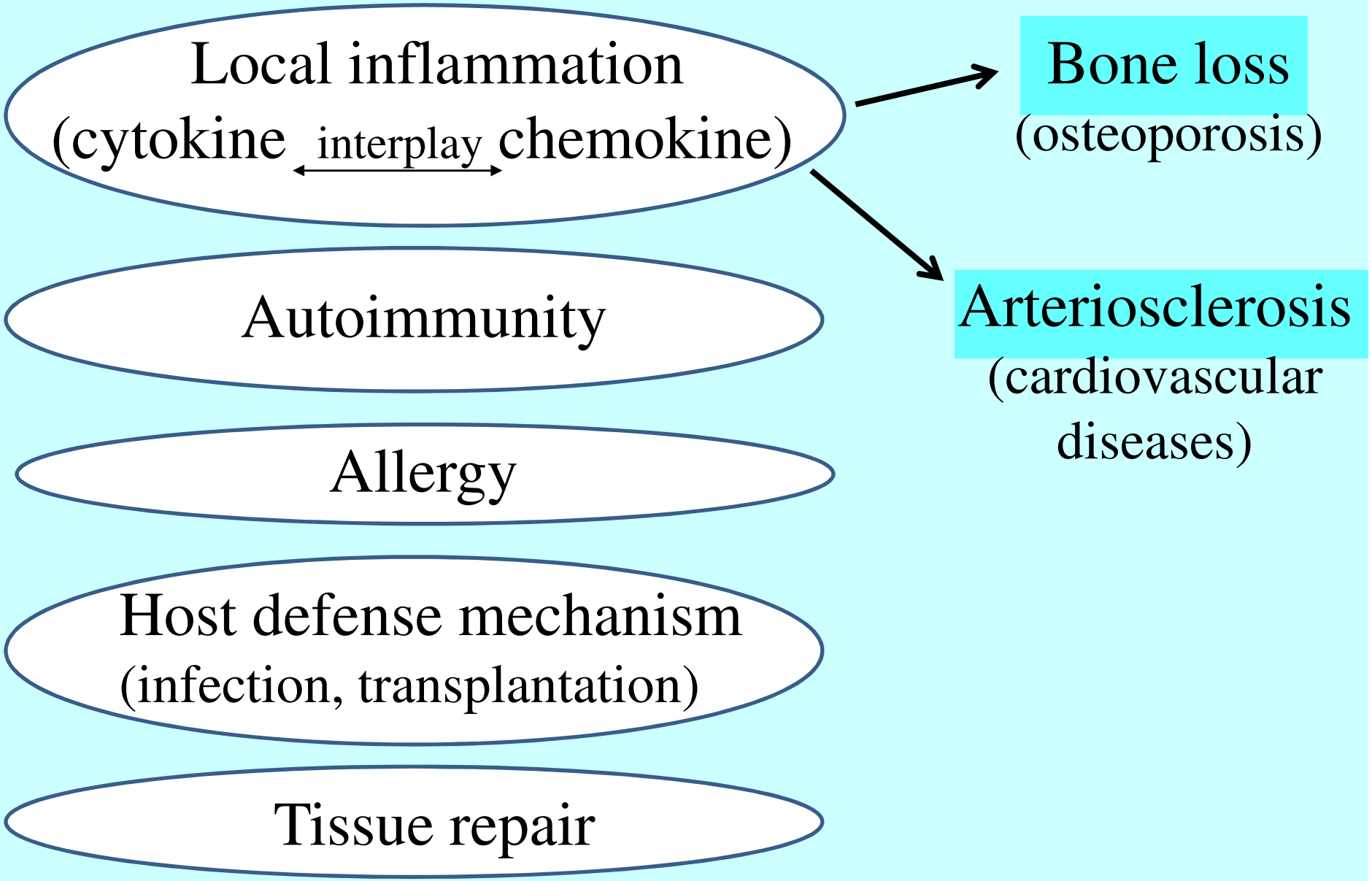
Sources of IL-17:

- Cells of innate and adaptive immunity (T and B cells, NK, NKT, γδ T cells, neutrophils, basophils, mast cells, monocyte-macrophages, dendritic cells).
- Epithelial, endothelial, vascular and stromal cells.

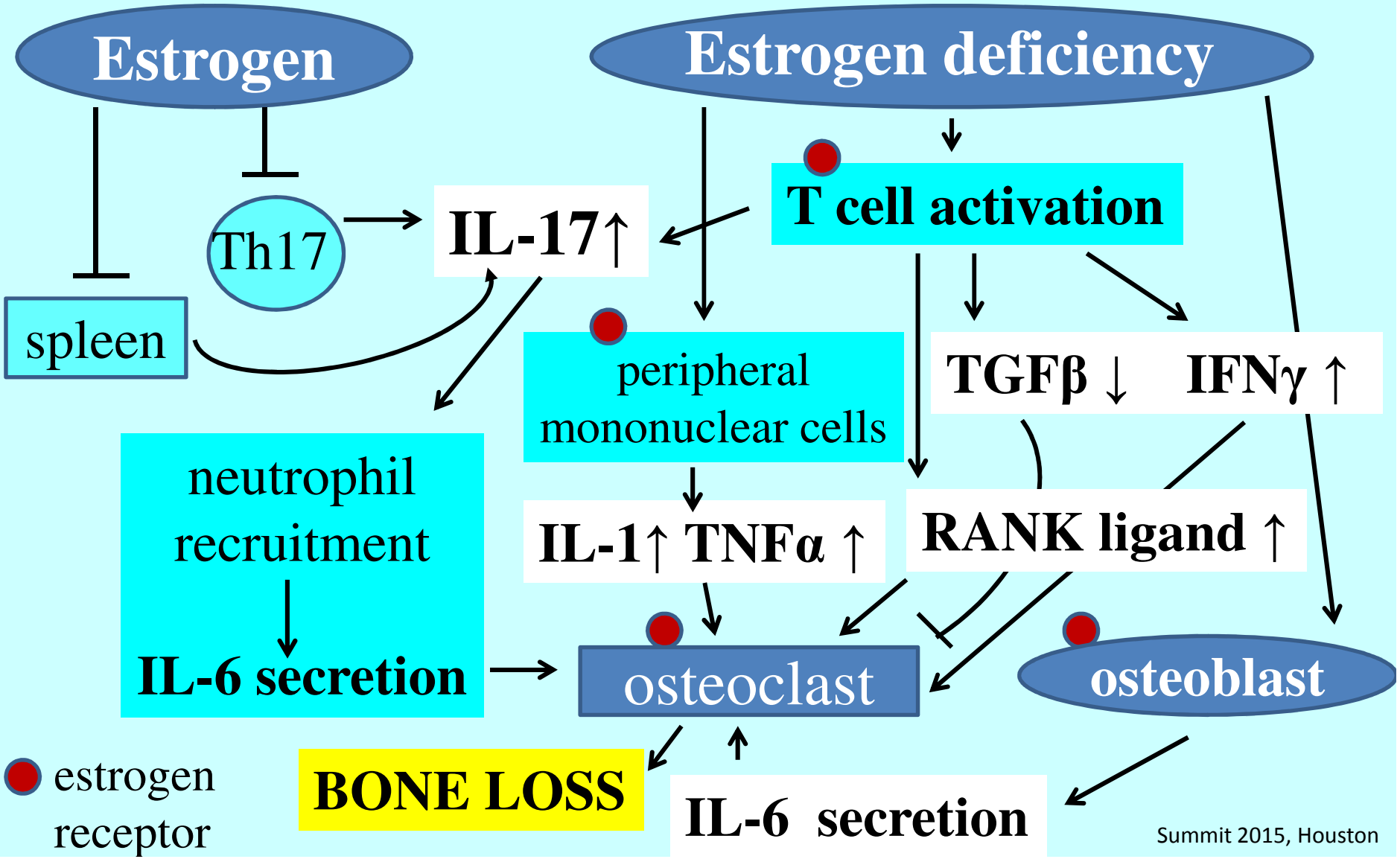
IL-17 initiated cytokine/chemokine productions:

IL-6, TNFα, IL-1β, IL-8, CXC1, CXC2, CXC8, CCL2, MCP-1

Increased IL-17 production-related diseases



Immune dysfunction associated with estrogen deficiency



Patients and methods

❖Pre- (n=22, mean age 41 yr) and postmenopausal (n=72, mean age 65 yr) women were studied.

❖Serum levels of IL-17A, IL-6, MCP-1 (macrophage-chemoattractant protein-1), sRANK (soluble receptor activator of NF-κB) ligand and OPG (osteoprotegerin) were measured by enzyme-linked immunosassay (ELISA).

❖Serum levels of estradiol were measured by chemi-luminescence assay in fully automatized manner.

❖Bone mineral density was detected by dual-energy X-ray absorptiometry (DXA) using Hologic Discovery equipment.

We studied in **pre- and postmenopausal women**:

- The relationship among serum IL-17A levels, estrogen deficiency and postmenopausal period.
- The relationships among serum IL-17A, sRANK ligand, OPG levels and bone mineral densities.
- The relationship between vitamin D_3 deficiency and serum IL-17A levels.
- The relationship between serum IL-17A and IL-6 or MCP-1 levels.

Synergism between bone loss and arteriosclerosis via IL-17 cytokine.

The relationship among serum IL-17A levels, estrogen deficiency and postmenopausal period.

Serum IL-17A levels were significantly higher in women with estrogen deficiency.

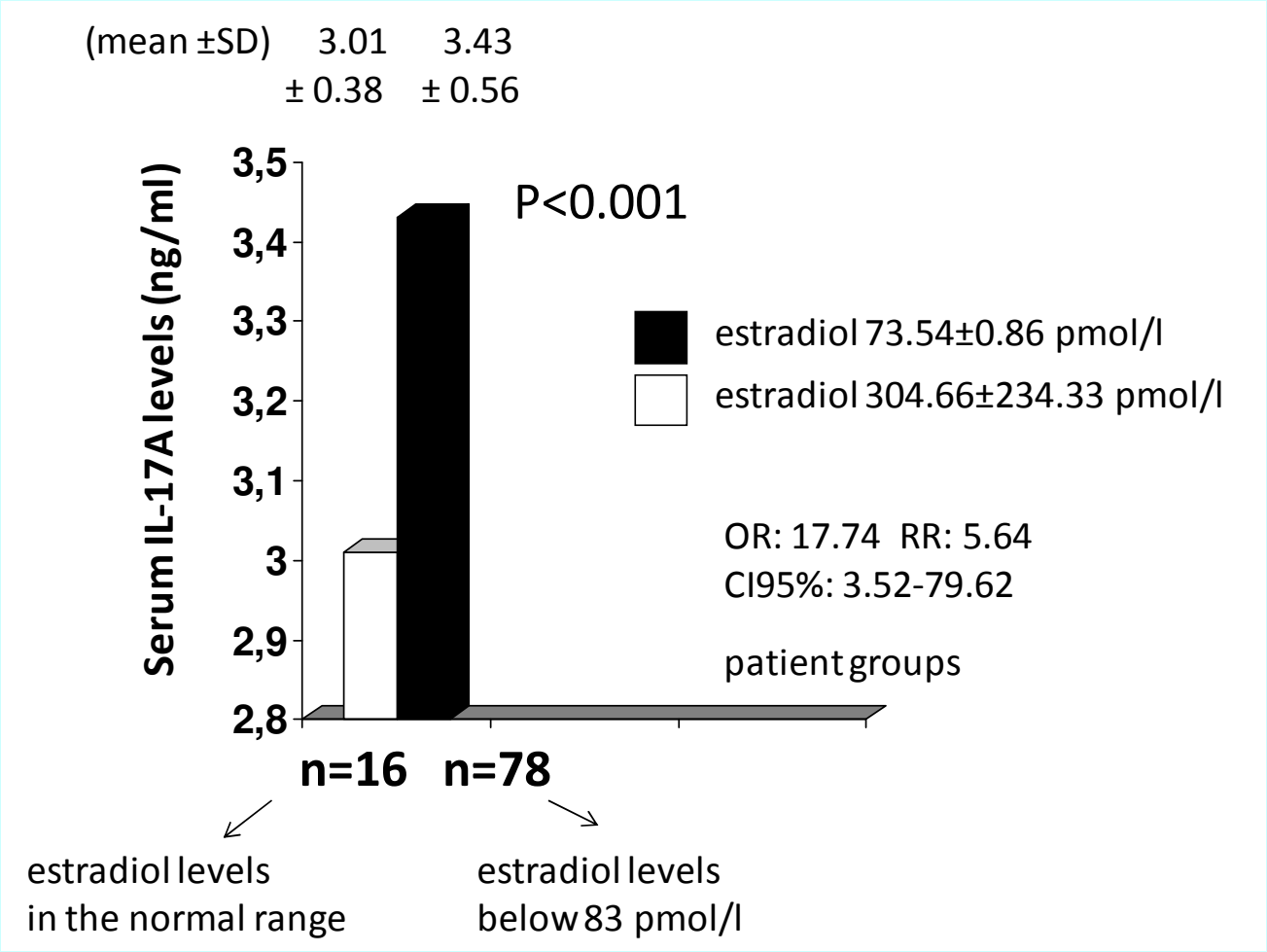


Figure 7

Inreased serum IL-17A levels showed an age-related dependency in postmenopause.

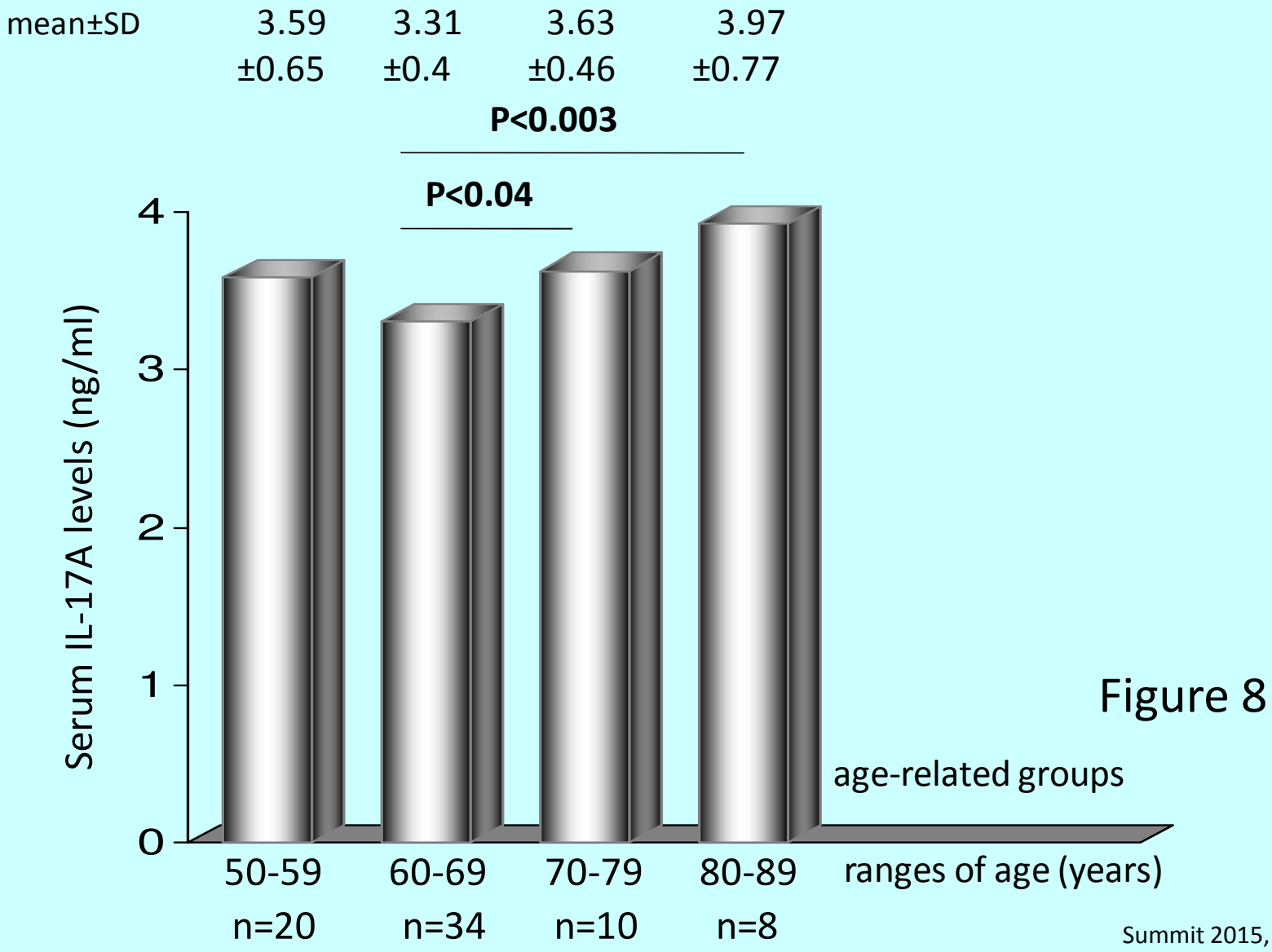


Figure 8

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Correlation between serum IL-17A levels and the post-menopausal period of women aged 60 to 89 years.

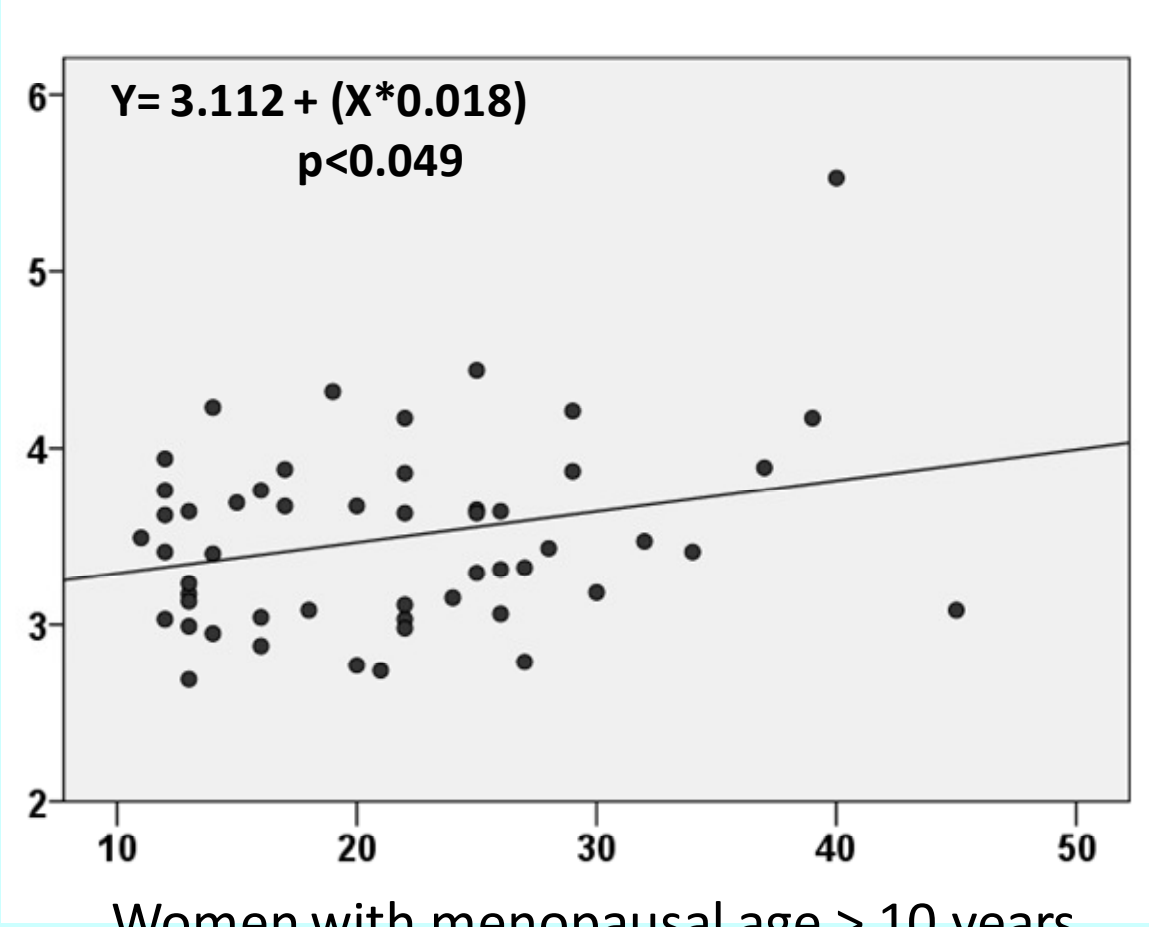

Figure 9

Inreased serum IL-17A levels showed a dependency on the history of hysterectomy in postmenopause.

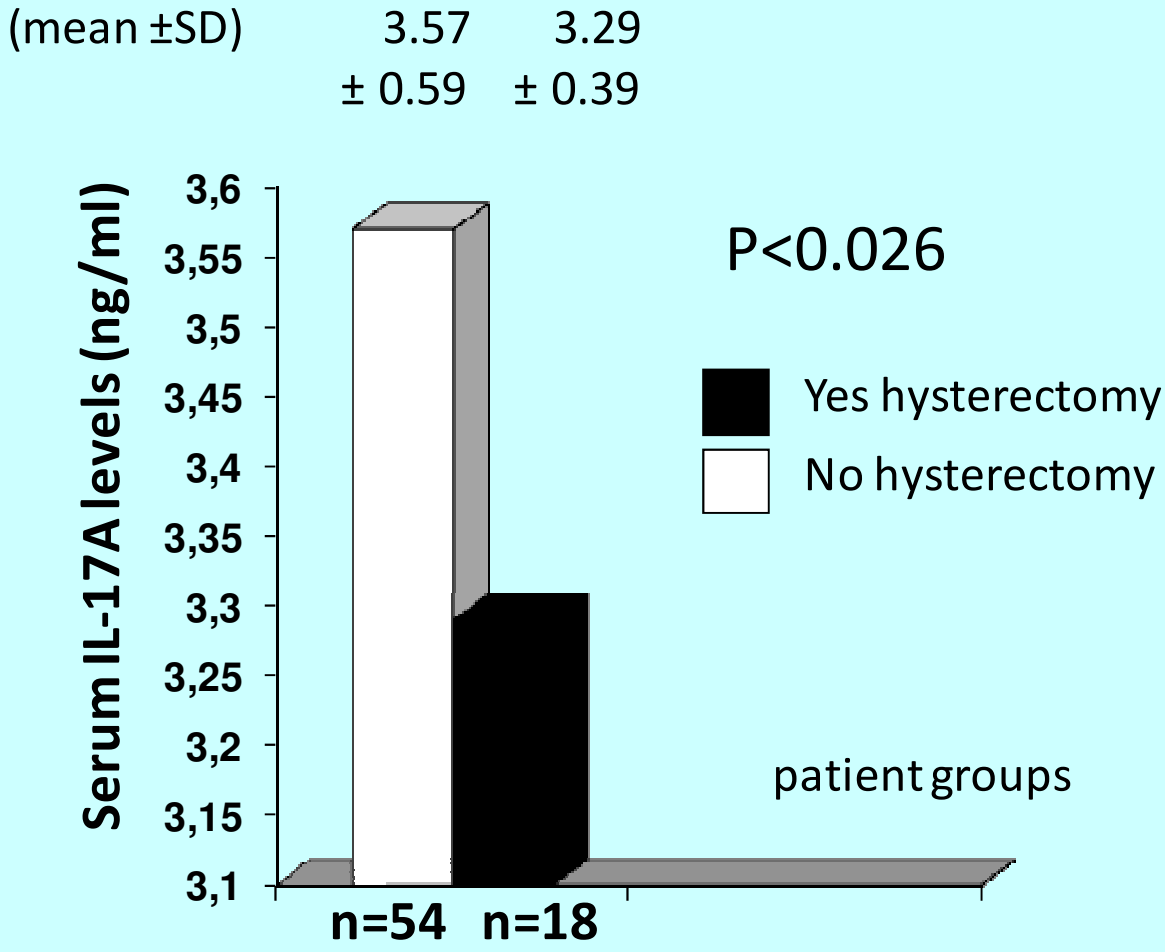

Figure 10

Inreased serum IL-17A levels showed a postmenopausal age-related dependency on the history of hysterectomy.

mean±SD	3.54 ±0.68	3.49 ±0.6	3.46 ±0.47	3.25 ±0.26	3.62 ±0.46	3.13 ±0.28	4.3 ±1.09	3.55 ±0.56

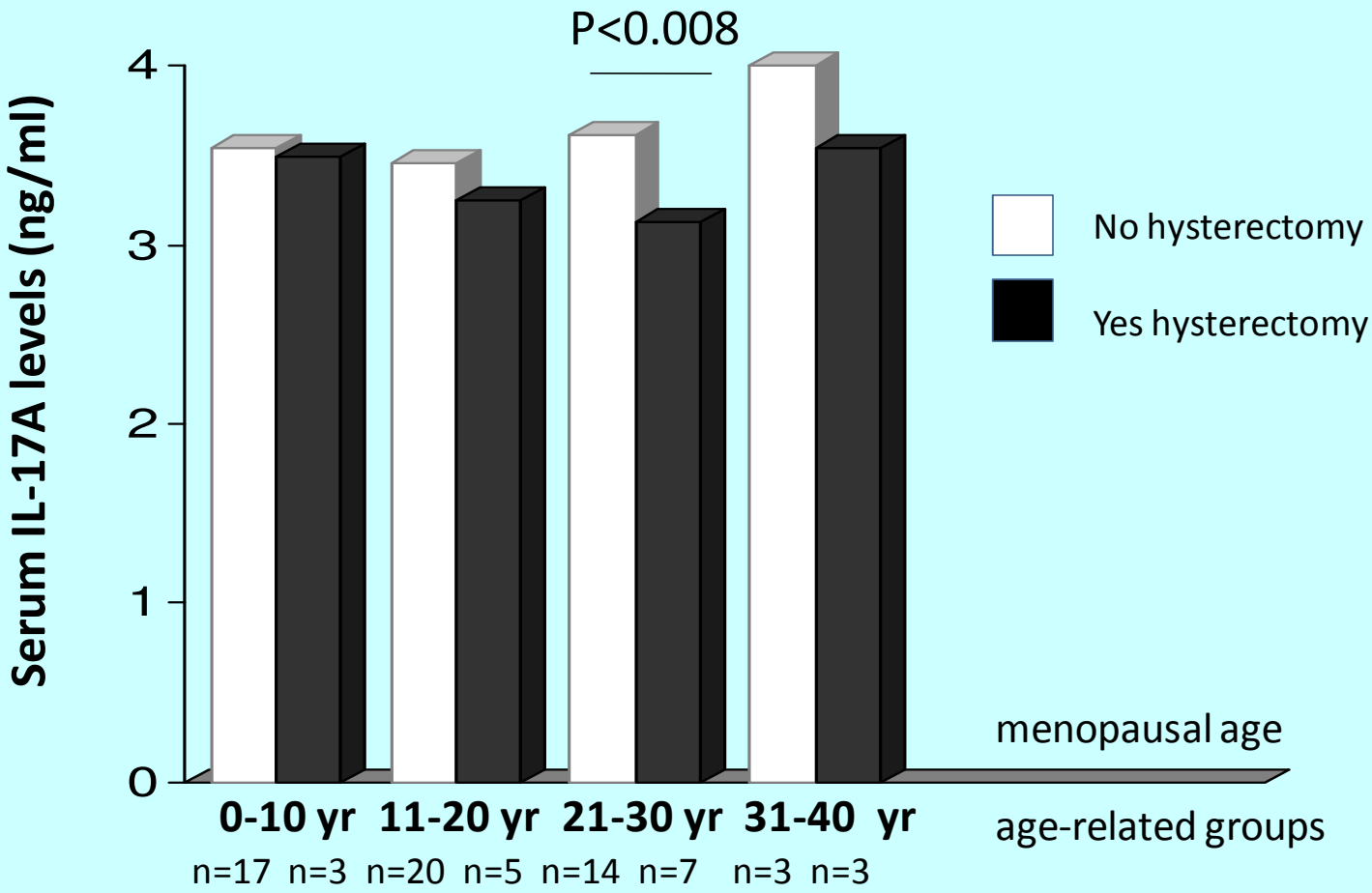

Figure 11

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Relationship between serum IL-17A levels and bone mineral densities (BMDs).

Increased serum IL-17A levels were associated with relevant bone loss in postmenopause compared to those in premenopause.

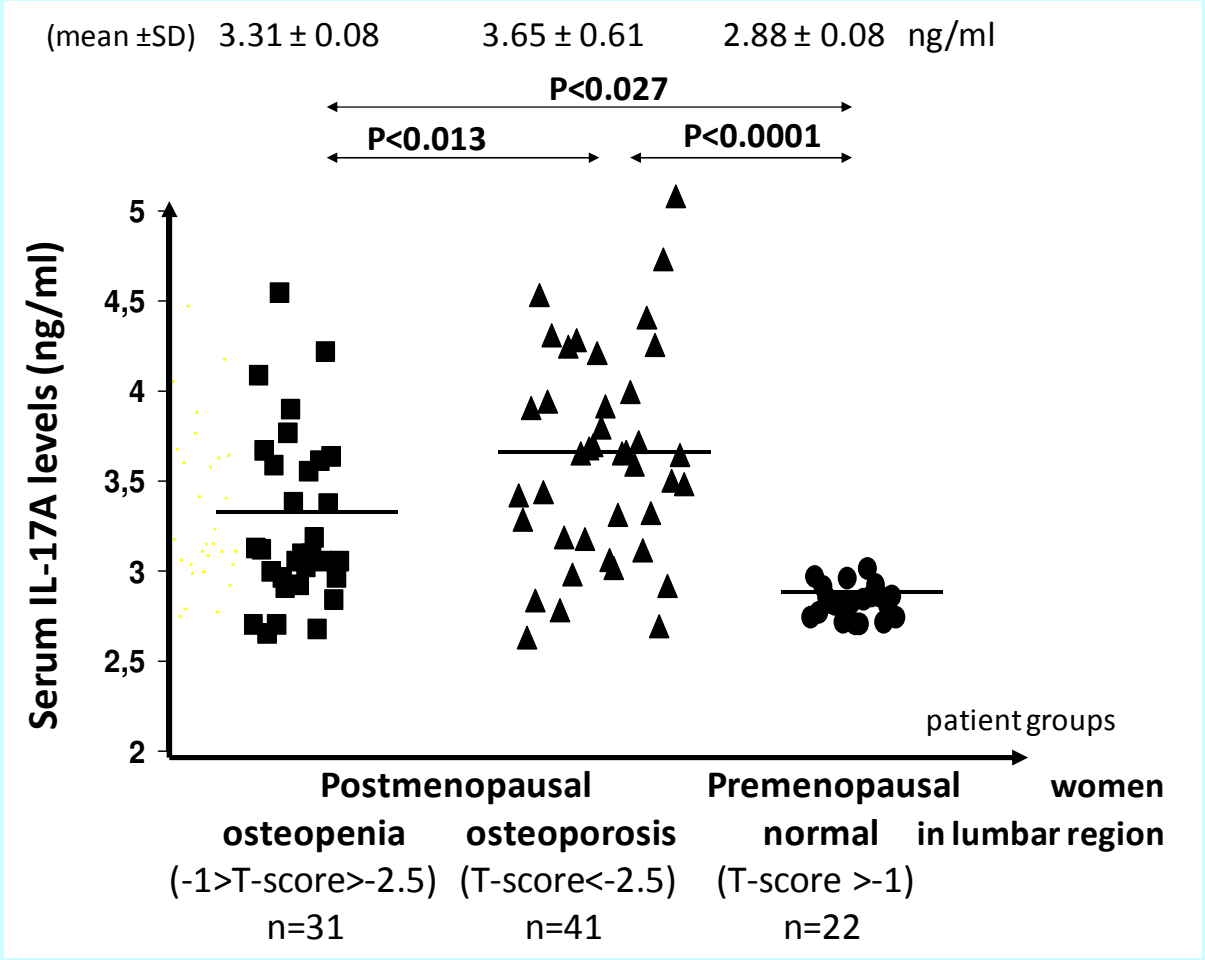


Figure 13

Serum IL-17A levels were significantly higher in post-menopausal osteoporotic women in the lumbar and femoral total regions.

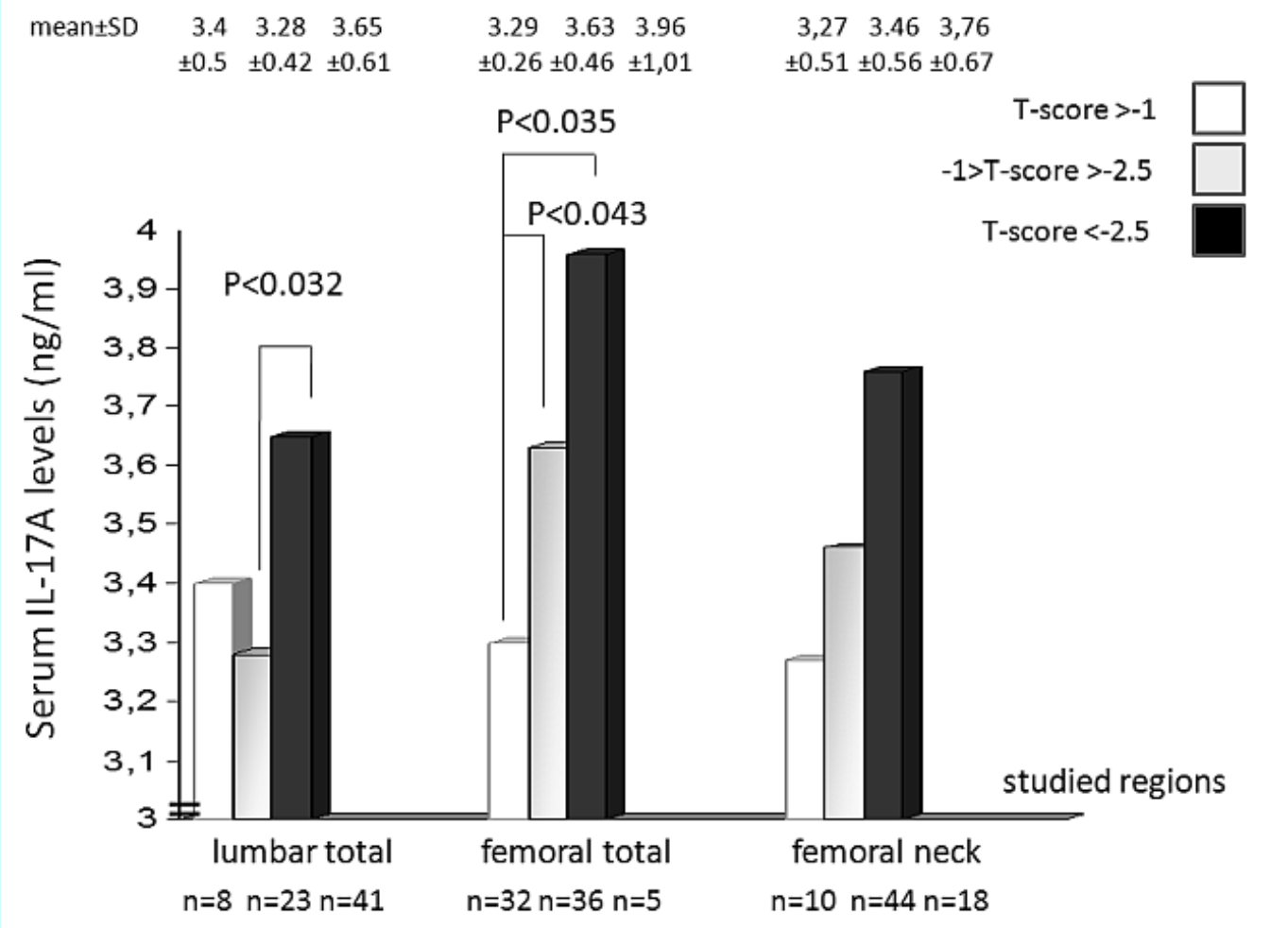
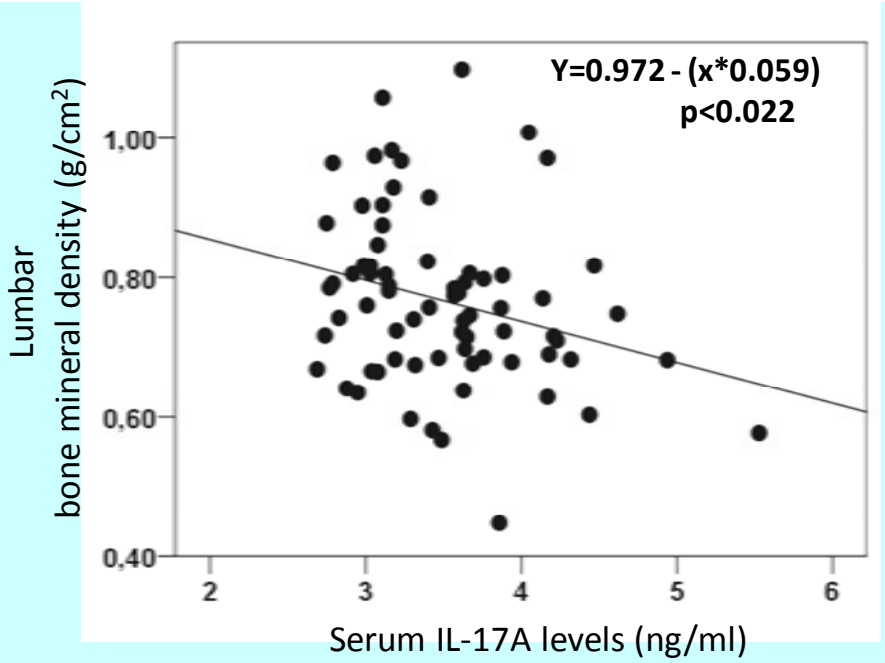
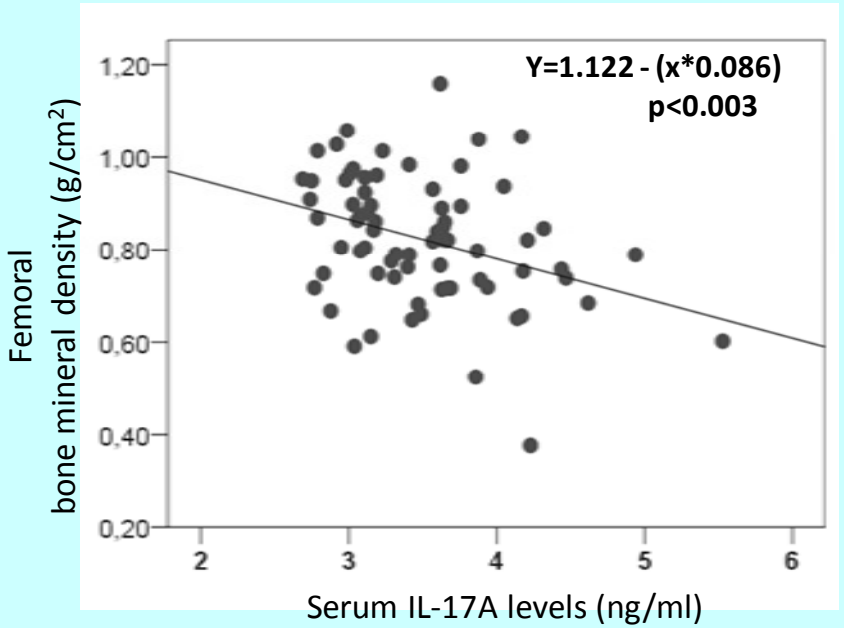


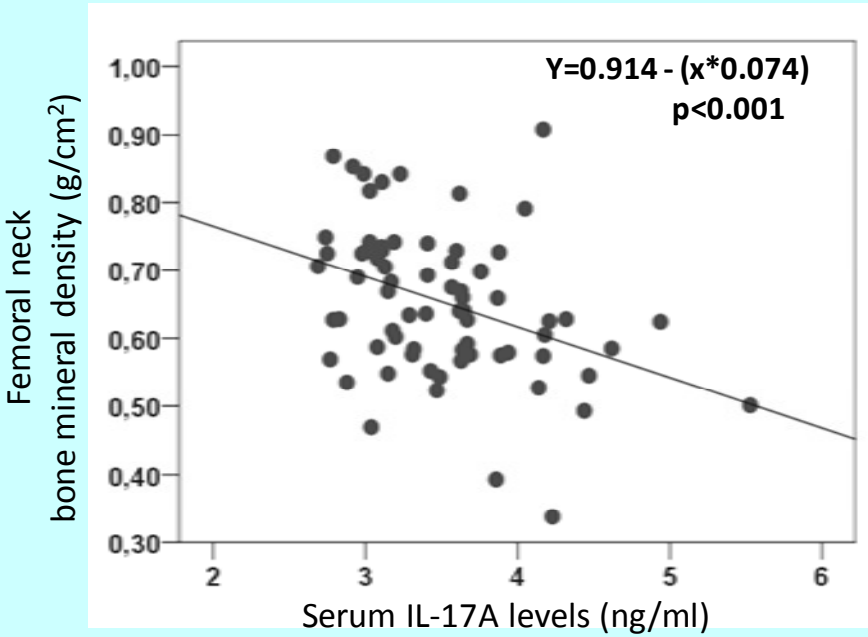
Figure 14

Serum IL-17A levels correlated inversely with bone mineral densities in postmenopause.



Lumbar region





Femoral regions

Figure 15

Relationship between serum IL-17A and sRANK ligand or OPG levels.

Increased serum IL-17A and sRANK ligand levels were detected in osteoporotic women.

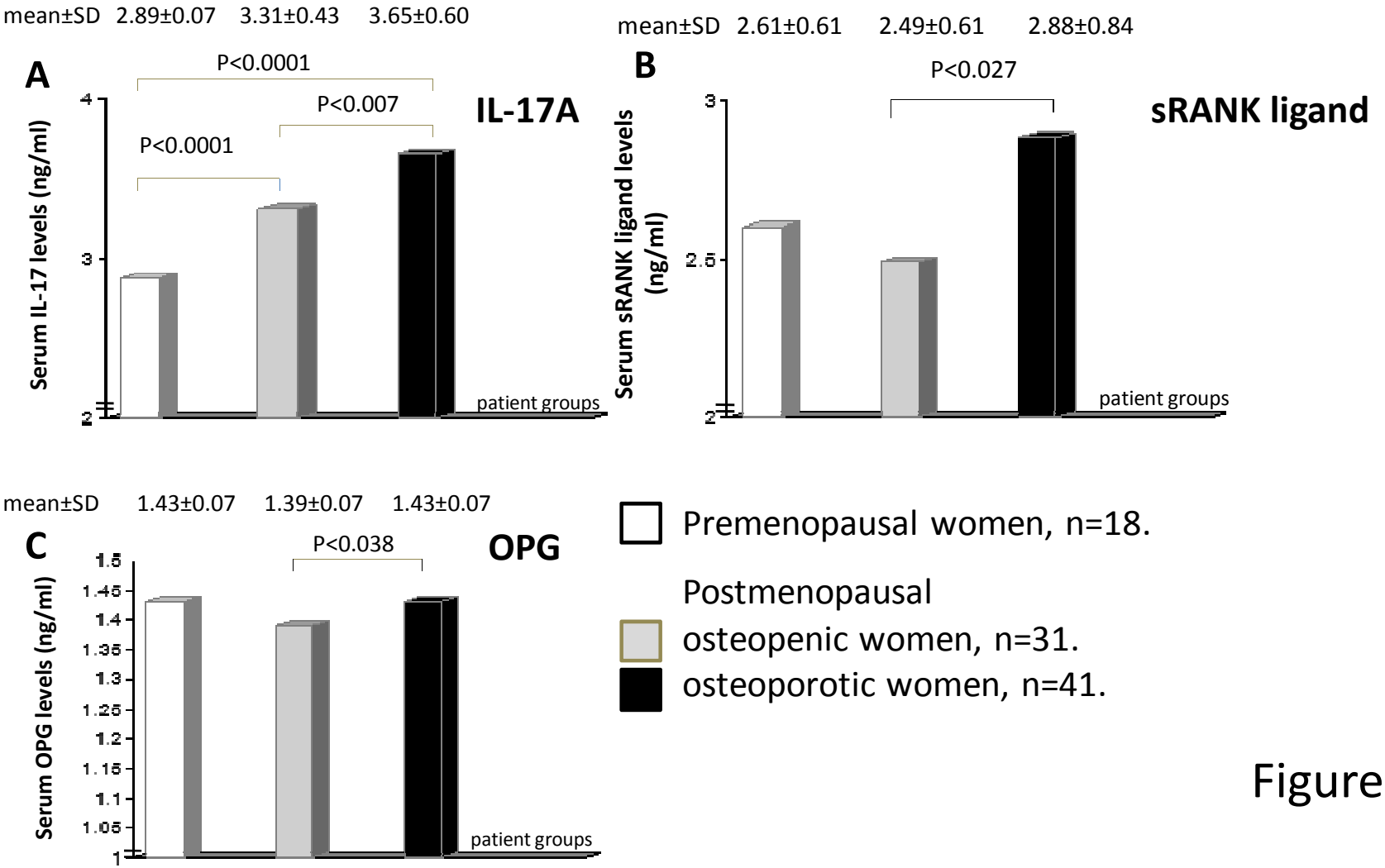


Figure 17

Serum IL-17A levels correlated positively with sRANK ligand and did not with OPG serum levels, but with the ratio of sRANK ligand and OPG serum levels.

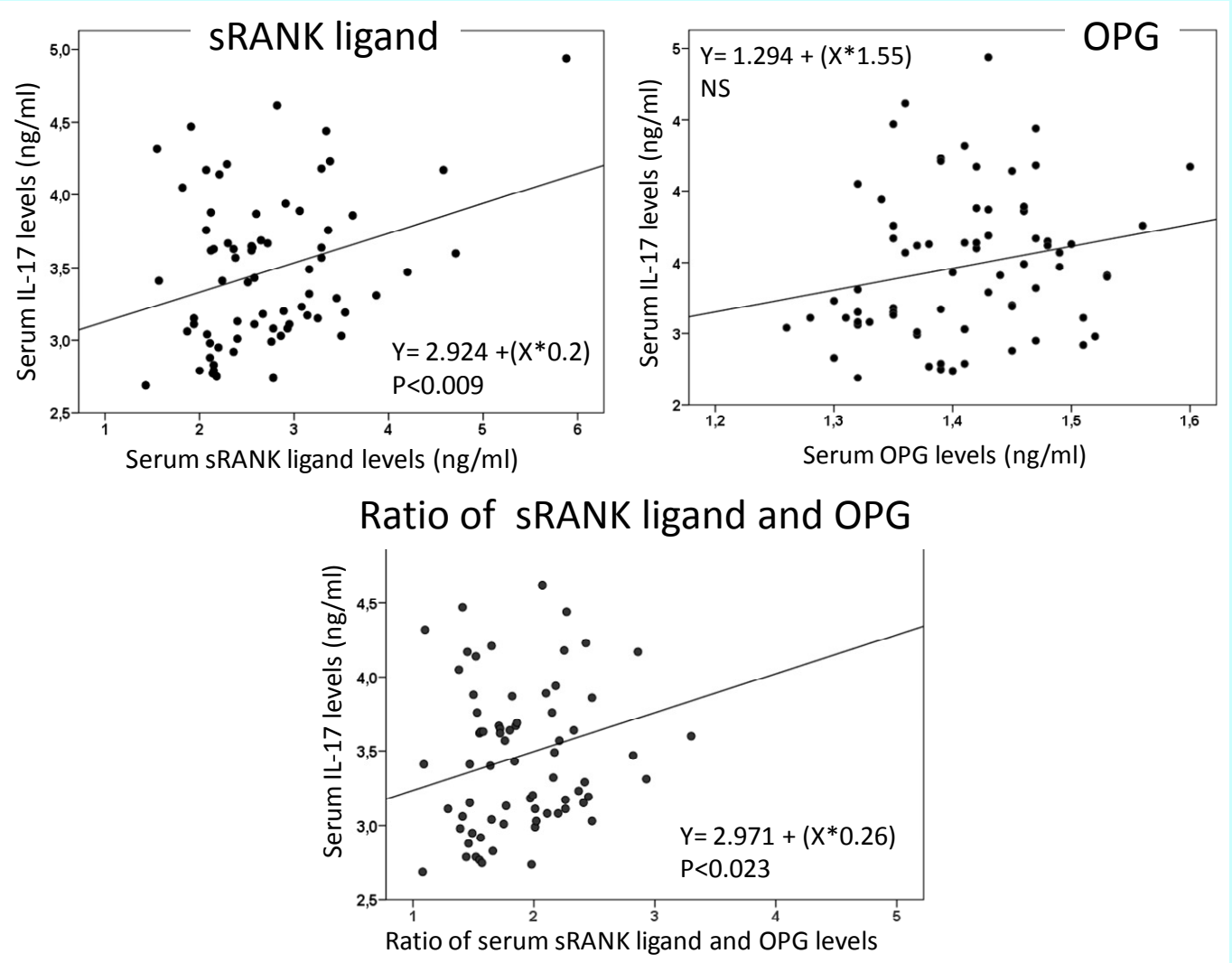


Figure 18

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Vitamin D_3 deficiency and serum IL-17A levels.

Serum IL-17A levels were significantly higher in post-menopausal women with vitamin D_3 deficiency.

Parameters	Vitamin D_3 deficiency (n=18) <50 nmol/l	Vitamin D_3 insufficiency (n=25) 51-75 nmol/l	Vitamin D_3 sufficiency (n=11) >75 nmol/l	P-values
Age (years)	59±17	61±13	61±12	
BMI* (kg/m^2)	29±5	29±6	29±6	
Vitamin D_3 (nmol/l)	16,84±6,06	35,08±5,79	68,95±44	
IL-17A (ng/ml)	13,35±2,9 °	12,07±2,61	11±1,9 °	0.033
MCP-1** (ng/ml)	17,35±2,9	16,62±2,07	16,18±1,23	
IL-6 (ng/ml)	26,11±12,66	26,25±12,23	22,68±13,52	

Table 1

*Body mass index (BMI) **Monocyte chemoattractant protein-1 (MCP-1)

Serum IL-17A levels correlated inversely with vitamin D_3 serum levels in postmenopause.

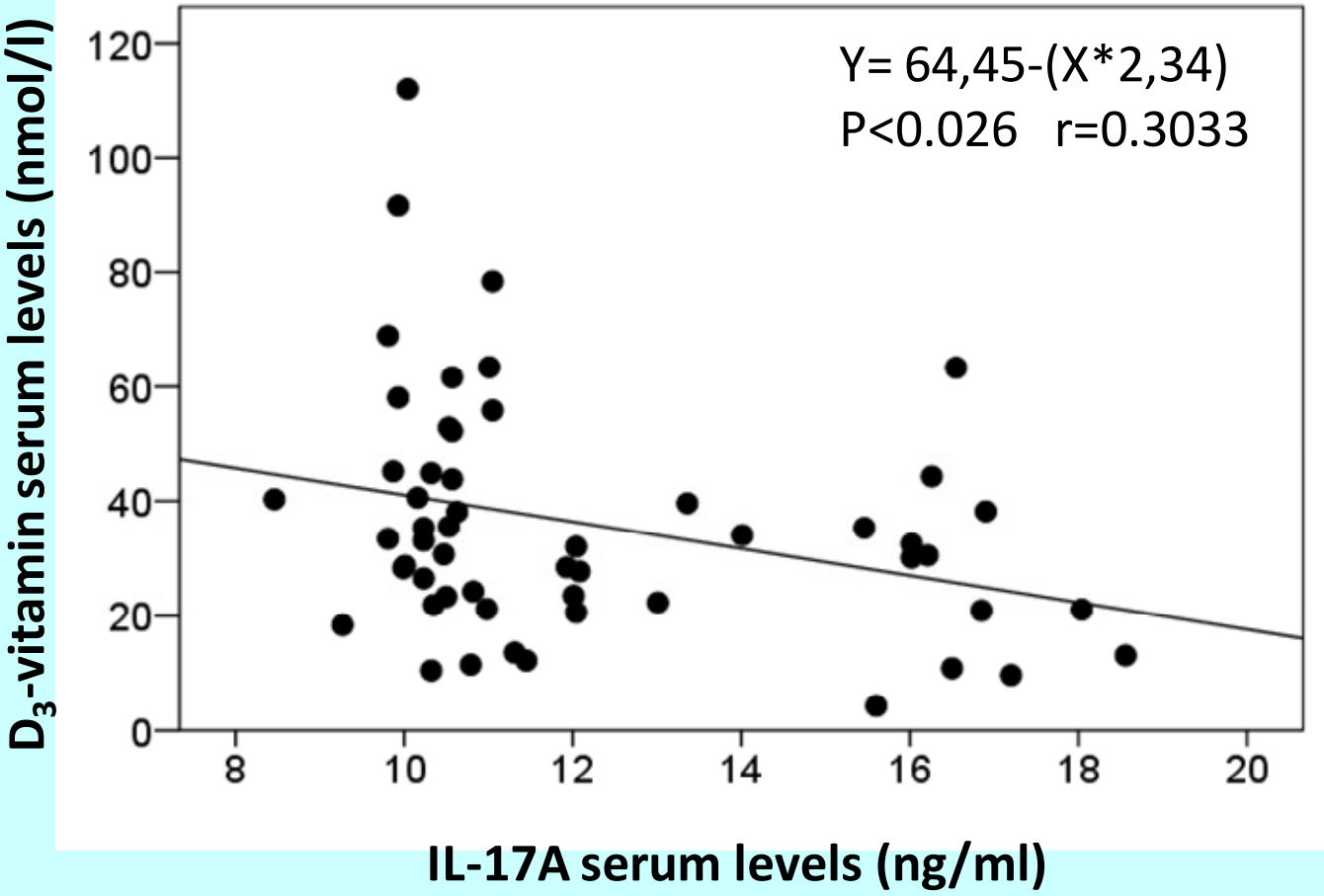

Figure 20

Relationship between serum IL-17A and IL-6 or MCP-1 levels.

Serum IL-17A levels correlated positively with serum MCP-1 levels in postmenopause.

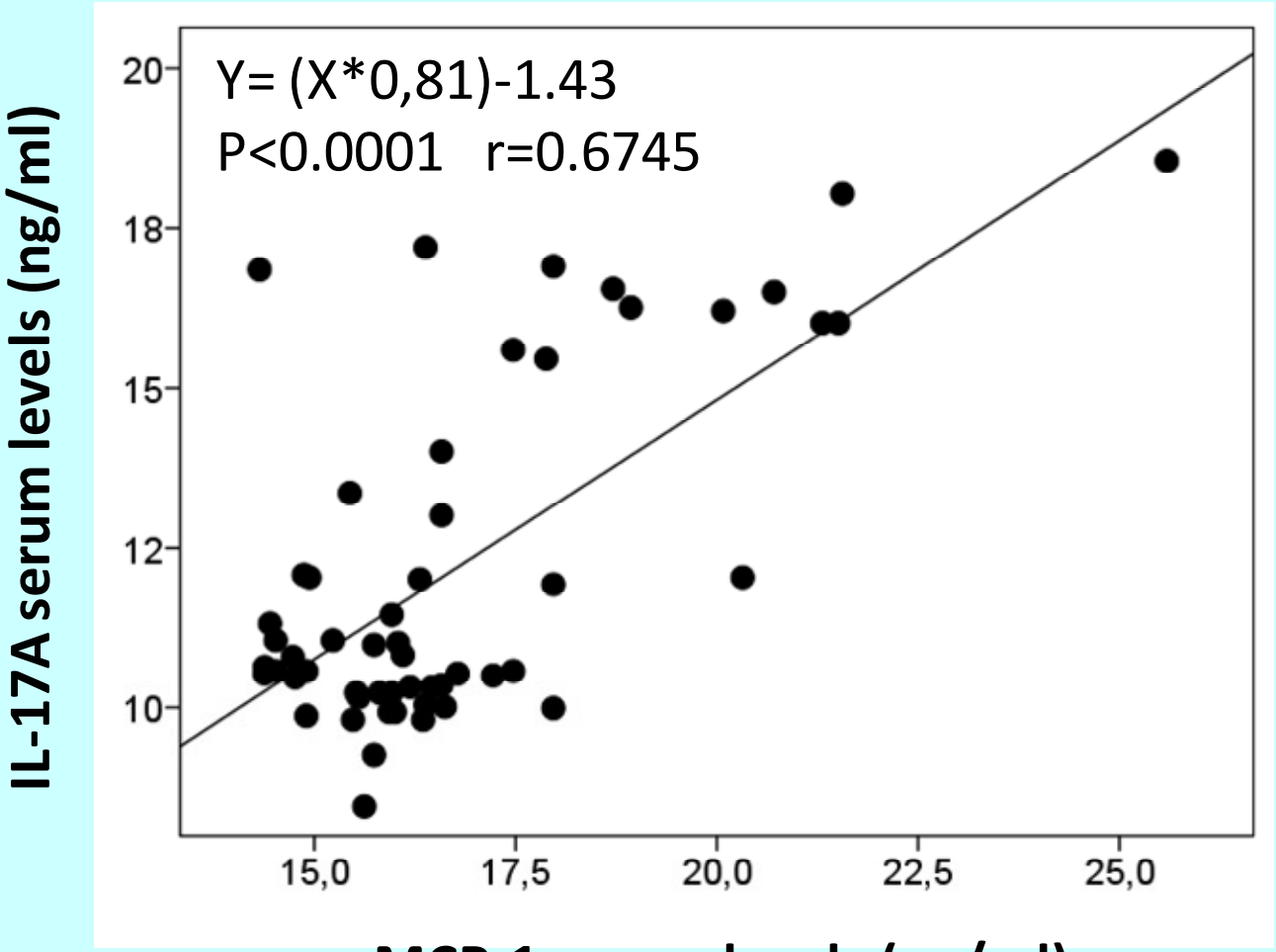

Figure 22

Serum IL-17A levels correlated positively with serum IL-6 levels in postmenopause.

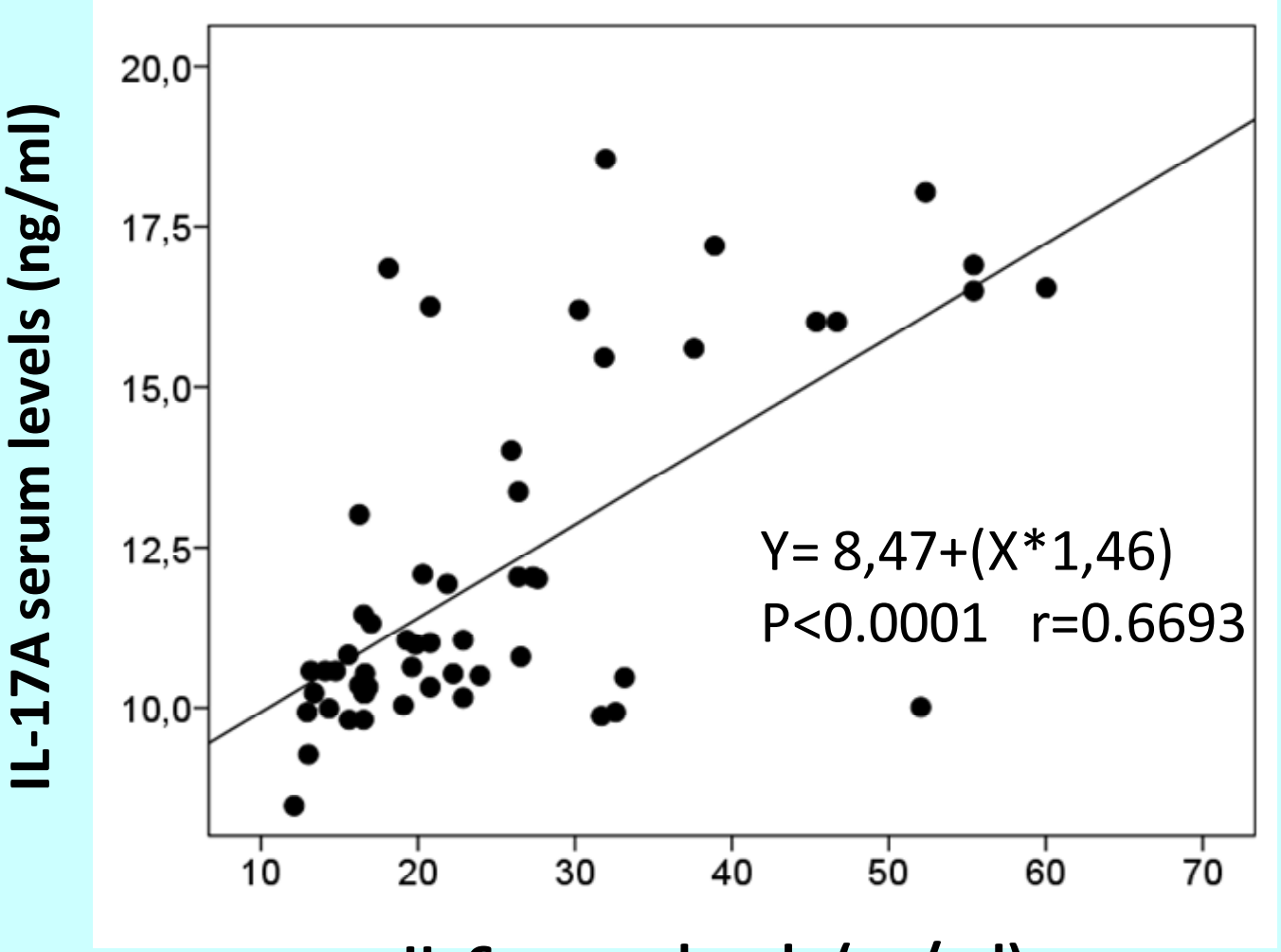

Figure 23

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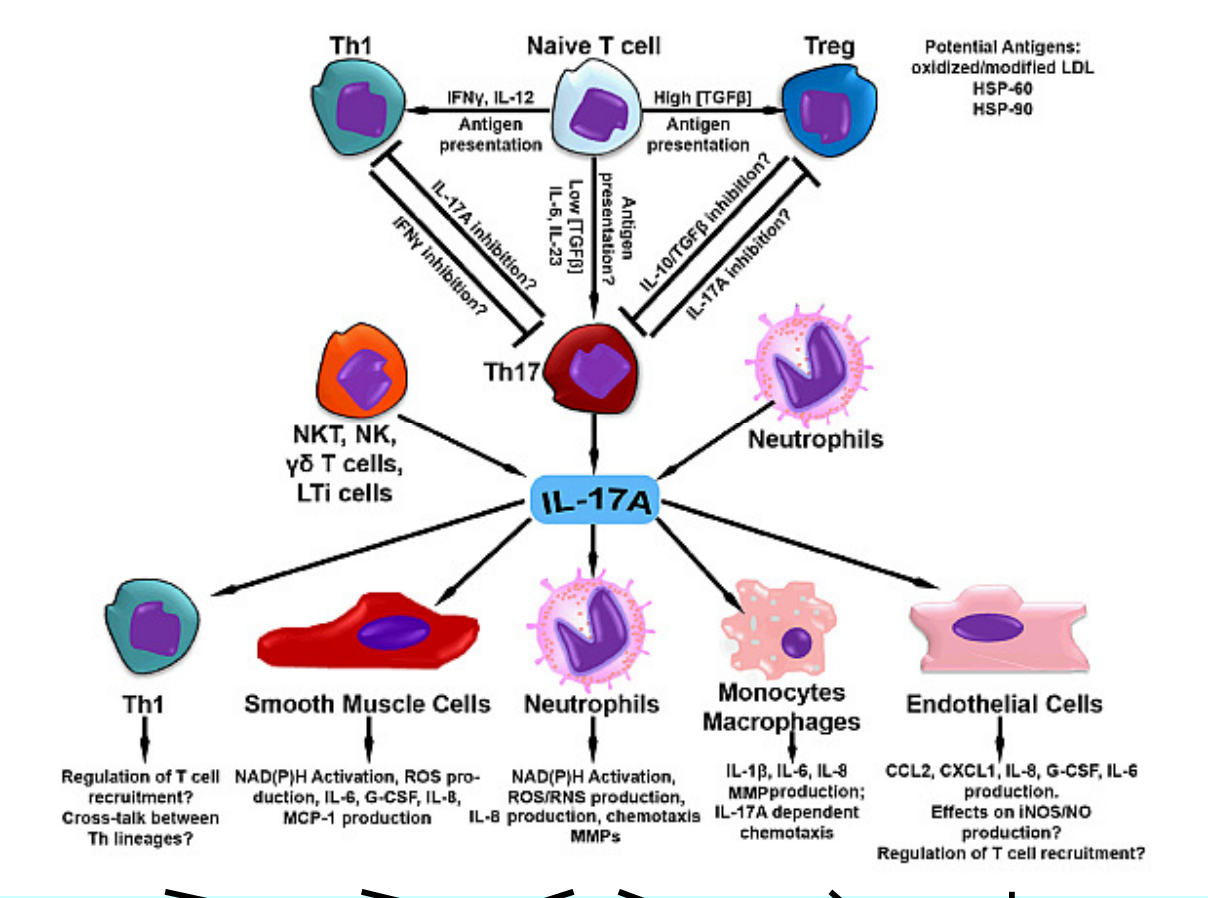
Synergism between bone loss and arteriosclerosis via IL-17 cytokine.



From Butcher M and Galkina EV , Thromb Haemost, 2011, 106(5): 787-795.

Figure 24

bone loss

arteriosclerosis

Conclusions

- The high prevalence of **increased serum IL-17A levels** was connected to postmenopausal **estrogen deficiency** and showed a postmenopausal period-related dependency.
- Postmenopausal **osteoporosis** was associated with **increased** serum **IL-17A** and **sRANK ligand** levels, but only weakly increased serum OPG levels.
- **Vitamin D_3 deficiency** was associated with **higher** serum **IL-17A** levels in postmenopause.
- The strong **correlation between** serum **IL-17A and IL-6 or MCP-1** highlighted the **relationship** between **osteoporosis and arteriosclerosis**, as well as cardio-vascular diseases.

Thank you for your attention!

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