

Age-dependent bone mineral density responses to GAHT: a one-year prospective study



A. Scala^{1,2}, C. Ceolin^{2,3}, M. Dall'Agnol³, G. Casali¹, G. Termini³, M.V. Papa³, A. Bertocco³, S. Giannini^{2,4}, A. Ferlin^{1,3}, G. Sergi^{2,3}, M. De Rui³, A. Garolla^{1,2}



¹Unit of Andrology and Reproductive Medicine, DIMED, University of Padua, Italy

²Regional Reference Center for Gender Incongruence (CRRIG), University Hospital of Padua, Italy

³Geriatrics Division, DIMED, University of Padua, Italy

⁴Internal Medicine 1, DIMED, University of Padua, Italy

BACKGROUND

Bone mineral density (BMD) acquisition peaks during adolescence and early adulthood. Transgender and gender-diverse (TGD) individuals, particularly those assigned male at birth (AMAB), may present with reduced BMD before gender-affirming hormone therapy (GAHT). Evidence on the skeletal effects of GAHT across different age groups remains limited.

AIM

To evaluate changes in BMD after one year of GAHT in TGD individuals compared with age-matched cisgender controls, with an age-stratified approach to assess whether skeletal responsiveness to GAHT differs across age groups.

MATERIALS AND METHODS

We present a prospective observational study including 162 TGD adults (96 AFAB, 66 AMAB) and 107 cisgender controls (56 AFAB, 51 AMAB) evaluated at the University Hospital of Padua between 2020–2024. Clinical evaluation and DXA was performed at lumbar spine and femoral sites at baseline and after one year of GAHT. Age-stratified analyses (<20, 20–30, >30 years) and linear regression models were used to assess predictors of BMD change.

RESULTS

In the TGD AFAB group, mean age was 24.2 (SD 5.9) years and mean BMI was 24.5 (SD 7.2) kg/m²; one-third were active smokers.

Among TGD AMAB individuals, mean age was 24.8 (SD 7.6) years and mean BMI was 21.8 (SD 3.6) kg/m²; a quarter were active smokers.

At baseline, TGD individuals exhibited significantly lower BMD across all skeletal sites. Vitamin D levels were low compared with cisgender controls, especially in AMAB individuals.

After one year of GAHT, skeletal responses differed according to sex assigned at birth and age (**Fig. 1**).

In AMAB individuals, lumbar spine BMD increased significantly, with the greatest improvement observed in participants younger than 20 years, suggesting a favorable effect of estrogen therapy during the period of ongoing bone mass accrual.

In contrast, AFAB individuals showed stable BMD at the lumbar spine and total femur, but a modest yet significant reduction at the femoral neck, particularly in the 20–30-year age group, potentially indicating a temporary rearrangement of trabecular bone during the first year of testosterone.

Age-stratified analyses showed significant BMD gains in younger participants (<20 years) of both groups, whereas individuals aged ≥20 years exhibited stable or declining femoral BMD. Linear regression confirmed age as an independent negative predictor of BMD change at femoral sites in both AFAB and AMAB individuals.

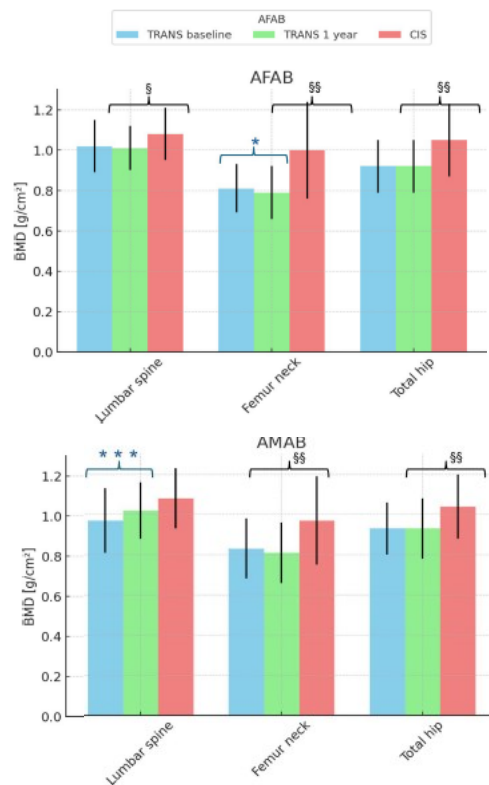


Fig. 1. Changes in BMD values in transgender individuals after one year of GAHT

CONCLUSIONS

GAHT induces age- and sex-specific skeletal responses. Early initiation of GAHT appears to favor bone accrual, particularly in AMAB individuals, whereas AFAB individuals may experience site-specific femoral bone loss during testosterone therapy, probably due to transitory rearrangement of trabecular bone. These findings highlight the importance of age-tailored bone health monitoring in transgender care.