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Musculoskeletal response to hormonal therapies is influenced by CYP19A1

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Polymorphisms of the CYP191A1 which encodes aromatase, the enzyme that converts testosterone to estradiol, are reported to influence the skeletal phenotypes in both men and postmenopausal women. We reported that the rs700518 polymorphism (G to A) of the CYP19A1 was associated with differences in bone loss and body composition changes among women with estrogen receptor positive breast cancer given aromatase inhibitors (AIs). Women with the AA genotype had significant bone loss in the spine and total hip compared to women with the G allele (GA+GG genotypes) after 1-year AI treatment. Meanwhile, women with the GG genotype had significant loss in fat-free mass (FFM) and gain in trunk fat mass (TFM) compared to women with the A allele (AA+GA) who had no loss in FFM but had significant loss in TFM. These findings suggest that women with the GA genotype have the best side effect profile to AIs. Using the same concept in hypogonadal men treated with testosterone for 18 months shows that although there were no inter-genotype differences in bone mineral density changes (hip and spine) for both rs700518 and rs1062033, the GG genotype (G to C) for rs1062033 experienced significant improvement in bone geometry parameters (total bone and cortical area) compared to GC+CC genotypes. Moreover, total fat and TFM decreased more in AA than GA+GG and in CC than GC+GG in rs700518 and rs1062033, respectively. Lean mass increased more in AA than GA+GG and in CC than GC+GG in rs700518 and rs1062033, respectively. We found no inter-genotype differences in adverse effects on the hematocrit and the prostate. A difference in CYP19A1 expression in the fat was observed in rs1062033 variants. Rs700518 and rs1062033 are in partial linkage in our sample. Thus, we conclude that CYP19A1 polymorphisms influences response to hormonal therapies and should be considered in treatment decision-making.

Biography

Villareal has established herself as a respected patient-oriented researcher studying the genetic determinants of estrogen metabolism and bone biology. She obtained RO3, R21, and VA Merit Award support for her research program. She left Washington University to become an Associate Professor of Medicine at the New Mexico VA Health Care System and the University of New Mexico School of Medicine. There, she served as the Chief of the Endocrinology Division. Recently, she joined the faculty at Baylor Medical College of Medicine as an Associate Professor of Medicine. She has a VA Merit Award to support work on the role of sex steroids to augment lifestyle in obese, elderly patients.

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