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**Associations of hormonal exposures with grip strength among women: data from the CONSTANCES French cohort study**

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**ABSTRACT**

**CONTEXT** - Increasing life expectancy in developing countries makes healthy ageing a major public health issue. Physical performance has been shown to predict unfavorable outcomes, such as frailty, hospital stays, disability, and death. Hand-grip strength (GS) is currently the recommended and easiest method to assess muscle strength. Beneficial effects of estrogens on several biological mechanisms, as muscular mass maintenance, bone resorption inhibition or neuro- and cardio-protection, could be implicated in the inter-individual variability in muscle strength among women. In agreement with this hypothesis, previous studies showed that postmenopausal women and those with artificial or premature menopause had lower muscle strength than others. However, the association with other reproductive life characteristics has been little investigated with inconclusive results. **OBJECTIVE** - To explore the association of endogenous and exogenous lifetime hormonal exposures with maximal GS in women. **METHODS** - Between 2012 and 2020, the Constances French prospective cohort study included 37,935 women aged  $\geq 45$ y, who self-reported lifetime hormonal exposure and underwent functional tests, including GS, by trained neuropsychologists at a Health Center. After multiple imputation of missing values, linear mixed models with a random intercept for the centers were used to estimate the association of hormonal exposures with GS, adjusted for a wide range of confounders, including age, education, health behaviors, depression, cognition, and cardiovascular disease. **RESULTS** - Women were 57.1y old on average. Mean GS was 26.6 kg. GS increased with age at menarche ( $\beta +1$  year=0.06; 95% Confidence Interval [CI]= 0.02 to 0.10) and lifetime duration of breastfeeding ( $\beta \geq 12$  vs  $< 3$  months=0.45; 95% CI: 0.19 to 0.70, p-trend $< 0.01$ ). Compared to premenopausal women, perimenopausal and postmenopausal women had lower GS ( $\beta = -0.55$ ; 95% CI: -1.03 to -0.07 and  $\beta = -0.85$ ; 95% CI: -1.04 to -0.66, respectively) while age at and type of menopause were not associated with GS. Longer duration of contraceptive pill use was associated with worse GS ( $\beta \geq 5$  years vs  $< 1$  year=-0.31; 95% CI: -0.57 to -0.05, p-trend $< 0.01$ ) as well as past use of HT ( $\beta = -0.24$ ; 95% CI: -0.42 to -0.07). GS was positively associated with current use of HT among postmenopausal women ( $\beta = 0.23$ ; 95% CI: 0.04 to 0.42). **CONCLUSION** - Hormonal exposures through women's reproductive life play a role in maintaining muscle strength after midlife.

**KEYWORDS:** -

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