APOPTOSIS AND AUTOPHAGY AS DETERMINANTS OF OVARIAN RESERVE DECLINE FROM BIRTH TO REPRODUCTIVE AGE IN WOMEN UNDERGOING OVARIAN TISSUE CRYOPRESERVATION

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Abstract Body

Introduction: Apoptosis and autophagy are both known to be involved in follicle death as physiological mechanisms after damage to DNA or other cell compartments. However, their modulation throughout a woman's lifetime, especially in the presence of stressful events like cancer diagnosis and/or gonadotoxic chemotherapy (CHT), has still not been fully elucidated.

Objective: To determine how apoptosis and autophagy rates vary in women undergoing ovarian tissue cryopreservation at different ages and in case of previous CHT.

Materials and methods: Eighty-four patients (1-35 years) with ovarian tissue stored at the Université Catholique de Louvain (Belgium) for histological analyses at the time of cryopreservation were included in retrospective analyses. Ovarian fragments were investigated for (i) follicle count and classification, (ii) apoptosis (caspase3), and (iii) autophagy 2 (LC3B). All patients were stratified according to age, menarchal status (premenarchal 32/84; postmenarchal 52/84), diagnosis of malignancy (11/84), gonadotoxic CHT before cryopreservation (14/84), presence of endometriosis (6/52), and use of hormonal treatment (24/52).

Results: Premenarchal patients had a 5-fold larger follicle pool than postmenarchal subjects, characterized by significantly more morphologically abnormal and atretic follicles. Apoptosis rates did not depend on age, but autophagic death rates were 10 times higher prior to menarche. After CHT, significantly more apoptotic follicles were detected in premenarchal patients, while postmenarchal patients exhibited significantly accelerated follicle growth rates. Moreover, elevated autophagic activity was observed in case of malignant compared to benign conditions after menarche.

Conclusion: Although both of these cell death mechanisms play a role in ovarian reserve decline with increasing age, autophagy appears to be the determining factor in childhood and in the event of cancer. The effect of CHT appears to depend on age, with a direct impact on damaged follicle elimination before menarche, and a boost to follicle activation and growth after menarche.