

ABSTRAK

Latar belakang: Peningkatan ketahanan hidup pasien kanker mendorong perhatian lebih terhadap dampak fungsi reproduksi pada paparan agen kemoterapi dan radioterapi terutama pada pasien perempuan muda dan anak-anak. Upaya preservasi fertilitas pada perempuan diantaranya adalah kriopreservasi jaringan ovarium. Kriopreservasi jaringan ovarium dan transplantasi adalah prosedur bertingkat dimana masing-masing langkah memiliki dampak terhadap kelangsungan hidup folikel dalam irisan korteks ovarium. Kehilangan folikel primordial dapat terjadi saat pengambilan jaringan, transportasi jaringan, preparasi jaringan, prosedur kriopreservasi, dan transplantasi jaringan.

Tujuan: Untuk mengetahui perbedaan ukuran jaringan terhadap *burnout* folikel pascavitrifikasi dan transplantasi jaringan ovarium melalui jalur PI3K-PTEN-AKT-FOXO3-mTOR dan jalur Hippo *signaling* dengan berbagai parameter pewarnaan immunohistokimia.

Metode: Penelitian ini merupakan studi eksperimental menggunakan 32 sampel jaringan korteks ovarium yang didapat dari 5 pasien dengan diagnosis berbeda dan diindikasikan menjalani kistektomi/ooforektomi di RSUP Dr. Sardjito. Sampel dibagi menjadi 8 kelompok perlakuan: *fresh*, *fresh* transplantasi, vitrifikasi, vitrifikasi transplantasi dengan ukuran 0,4x0,4x0,1 cm dan 0,8x0,8x0,1 cm. Sampel dinilai secara mikroskopis setelah dilakukan pewarnaan hematoksin eosin untuk mengetahui persentase folikel primordial dan imunohistokimia untuk menilai ekspresi anti-CD34, anti-caspase-3, anti-Ki67, anti-p-Akt, anti-FOXO3a, anti-YAP1, dan anti-CCN2.

Hasil: Pada ukuran jaringan 0,4x0,4x0,1 cm, persentase ekspresi anti-CD34 lebih tinggi secara signifikan pada kelompok vitrifikasi transplantasi dibanding kelompok vitrifikasi non transplantasi ($p=0,036$). Pada kelompok vitrifikasi transplantasi, jaringan berukuran 0,4x0,4x0,1 cm memiliki ekspresi anti-caspase-3, anti-Ki67, anti-p-Akt, dan anti-YAP1 lebih tinggi secara tidak signifikan dibandingkan ukuran 0,8x0,8x0,1 cm. Persentase folikel primordial, ekspresi anti-CCN2 pada jaringan berukuran 0,4x0,4x0,1 cm lebih rendah secara tidak signifikan dibanding ukuran 0,8x0,8x0,1 cm.

Kesimpulan: Ukuran jaringan korteks ovarium lebih kecil tampaknya memiliki ketahanan hidup pascatransplantasi yang lebih baik namun aktivasi folikel primordial lebih tinggi dibandingkan dengan ukuran lebih besar berdasarkan parameter IHK anti-CD34, persentase folikel primordial, anti-Ki67, anti-caspase3, anti-p-Akt, dan anti-YAP1.

Kata kunci: Kriopreservasi jaringan ovarium, jalur Hippo *signaling*, jalur PI3K/PTEN/Akt, membran korioalantois, ukuran fragmen korteks ovarium

ABSTRACT

Background: Increased survival of cancer patients has prompted more attention to the impact of reproductive function on exposure to chemotherapy and radiotherapy agents, especially in young women and children. Efforts to preserve fertility in women include cryopreservation of ovarian tissue. Ovarian tissue cryopreservation and transplantation are stratified procedures where each step has an impact on the viability of the follicles in the ovarian cortex slices. Loss of primordial follicles can occur during tissue collection, tissue transport, tissue preparation, cryopreservation procedures, and tissue transplantation.

Objective: This study aims to determine differences in tissue size on follicular burnout post vitrification and transplantation through the PI3K-PTEN-AKT-FOXO3-mTOR pathway and the Hippo signaling pathway using various immunohistochemical staining.

Method: This experimental study used 32 ovarian cortical tissue samples obtained from 5 patients with different diagnosis and underwent cystectomy/oophorectomy at Dr. Sardjito General Hospital. Tissue samples were distributed equally into 8 groups: fresh tissue, fresh-transplanted tissue, vitrified tissue, and vitrified-transplanted tissue, with 0.4x0.4x0.1 cm and 0.8x0.8x0.1 cm size in each group. Tissue samples were evaluated microscopically after haematoxylin eosin and immunohistochemical staining for anti-CD34, anti-caspase-3, anti-Ki67, anti-p-Akt, anti-FOXO3a, anti-YAP1, and anti-CCN2 expressions.

Results: In 0.4x0.4x0.1 cm sized tissue, the expression of anti-CD34 percentage was significantly higher in vitrified-transplanted group compared to vitrified group ($p=0.036$). In vitrified-transplanted group, 0.4x0.4x0.1 cm sized tissue showed higher expression of anti-CD34, anti-caspase-3, anti-Ki67, anti-p-Akt, and anti-YAP1 without significant difference compared to 0.8x0.8x0.1 cm sized tissue. Meanwhile, percentage of primordial follicle and expression of anti-CCN2 of 0.4x0.4x0.1 cm sized tissue were lower compared to 0.8x0.8x0.1 cm sized tissue.

Conclusion: Smaller ovarian cortical tissue size seems to have better post-transplantation survival, but higher primordial follicle activation compared to larger ovarian cortical tissue size based on the parameters of anti-CD34, percentage of primordial follicles, anti-Ki67, anti-caspase3, anti-p-Akt, and anti-YAP1.

Keywords: ovarian tissue cryopreservation, Hippo signaling pathway, PI3K/PTEN/Akt pathway, chorioallantoic membrane, ovarian cortical fragment size