

# Ultrasonografi sebagai prediktor diagnosis reseptivitas endometrium pada masa jendela implantasi embrio perempuan infertil sindrom ovarium polikistik = Ultrasound as diagnostic predictor for endometrial receptivity assessment during embryo implantation window period in infertile female with polycystic ovary syndrome

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## Abstrak

Sindrom Ovarium Polikistik (SOPK) saat ini merupakan salah satu kelainan dengan keberhasilan kehamilan terendah di antara berbagai penyebab infertilitas. Penelitian ini bertujuan untuk menilai ultrasonografi (USG) sebagai prediktor diagnosis reseptivitas endometrium perempuan infertil Sindrom Ovarium Polikistik. Penelitian ini merupakan studi diagnostik observasional dengan disain potong lintang. Tiga puluh empat perempuan usia reproduksi ( $32,5 \pm 3,8$  tahun), mengalami infertilitas primer  $4,9 \pm 3,1$  tahun dengan siklus anovulasi mendapat klomifen sitrat 100 mg perhari H2?6; perkembangan folikel dan ovulasi dikonfirmasi dengan pemeriksaan ultrasonografi (USG) H12?17. Pemeriksaan USG yang diikuti biopsi endometrium dan hormon progesteron dilakukan pada H19?21 atau pasca ovulasi H+5?+7. USG digunakan untuk menilai Zona Vaskularisasi menurut kriteria Sonai, Volume Endometrium menurut kriteria Zollner, dan Indeks Vaskularisasi-Arus Darah menurut kriteria Wu. Biopsi endometrium dinilai berdasarkan penanggalan histopatologis menurut kriteria Noyes, dan pemeriksaan imunohistokimia VEGF dan VEGFR-1 dengan penilaian secara H-Score. Kadar VEGF serum diperiksa dengan metode Elisa. Analisis statistik menggunakan uji chi-square, uji-t dan nilai ROC. Dihasilkan titik potong komposit endometrium sebagai baku emas reseptivitas endometrium berdasarkan pemeriksaan penanggalan histopatologis endometrium. Pemeriksaan USG berdasarkan pemeriksaan komposit endometrium ini akhirnya menghasilkan baku emas USG penetapan reseptivitas endometrium. Pemeriksaan USG H19?21 menunjukkan rerata tebal endometrium  $10,47 \pm 1,85$  mm, Volume Endometrium  $3,70 \pm 1,31$  ml, Indeks Vaskularisasi?Arus Darah Indeks Vaskularisasi?Arus Darah 0,08 (0,00-3,21) dan Zona Vaskularisasi di lapis 1,2,3 dan 4 masing-masing 14,7%, 41,2%, 35,3% dan 8,8%. Pemeriksaan histopatologis endometrium mendapatkan 58,8% in-phase dan 41,2% out-phase. Pemeriksaan VEGF endometrium mendapatkan ekspresi tertinggi di endotel ( $2,34 \pm 0,26$ ), kemudian di epitel luminal ( $2,23 \pm 0,37$ ), sel stroma ( $2,1 \pm 1,9$ ), terendah di epitel kelenjar ( $2,00 \pm 0,68$ ). VEGFR-1 endometrium tertinggi di epitel kelenjar ( $2,85 \pm 0,30$ ), diikuti di epitel luminal ( $2,83 \pm 0,54$ ), endotel ( $2,70 \pm 0,42$ ) dan terendah di sel stroma ( $2,58 \pm 0,42$ ). Secara statistik, ditemukan hubungan bermakna antara Zona Vaskularisasi dengan VEGF sel stroma ( $p = 0,018$ ), Volume Endometrium dengan VEGF endotel ( $p = 0,000$ ), epitel luminal ( $p = 0,029$ ) dan total sel ( $0,043$ ) serta Penanggalan Histologis Endometrium dengan VEGFR-1 sel stroma ( $p = 0,009$ ). Penetapan reseptivitas endometrium hasil penilaian Komposit USG berdasarkan baku emas komposit endometrium adalah ditemukannya Zona Vaskularisasi lapis 3?4, Volume Endometrium 3,090 ml dan Indeks Vaskularisasi-Arus Darah 0,253 yang menunjukkan spesifisitas 77,4%. Ultrasonografi dapat digunakan sebagai prediktor diagnosis reseptivitas endometrium masa jendela implantasi embrio perempuan infertil SOPK.

.....Polycystic ovary syndrome has been recognized as one of the lowest successful pregnancy rates in infertile women. This studi aimed to assess ultrasound as predictor of endometrial receptivity in PCOS

infertile women.

Diagnostic observational study in cross sectional design was conducted. Thirty-four subjects suffered anovulatory cycles in a average  $32,5 \pm 3,8$  years of age and primary infertility for  $4,9 \pm 3,1$  years, receiving 100 mg/d clomiphene citrate therapy on D2?6 . Follicular development and ovulation were confirmed by transvaginal USG examination on D12?17 . Repeated USG procedures followed by endometrial biopsy and serum progesterone test were conducted on either D 19?21 or D+5?+7 post ovulatory. The use of USG was to assess Vascularization Zone by Sonai criteria, Endometrial Volume by Zollner criteria and Vascularization Flow Index (VFI) by Wu criteria. Endometrial biopsy was performed and dated, based on endometrial histological dating by Noyes criteria. Immunohistochemistry of VEGF and VEGFR-1 were done and counted by H-Score formula. VEGF serum was tested by Elisa method. Statistical analysis of Chi-square test, student t-test and ROC value were used. Immunohistochemistry composite formation was based on histological dating of endometrium. Ultrasound composite based on immunohistochemistry composite was finally resulting the new cut-off of endometrial receptivity. Ultrasound findings on D19?21 showed the average endometrial thickness  $10,47 \pm 1,85$  mm, Endometrium Volume  $3,70 \pm 1,31$  ml, Vascularization?Flow Index (VFI)  $0,08 (0,00?3,21)$  and Vascularization Zone (ZV) of zone 1,2,3 and 4 were 14,7%, 41,2%, 35,3% and 8,8%. Endometrial dating was 58,8% in-phase and 41,2% out-phase. Endometrial VEGF staining showed the highest expression in endothel ( $2,34 \pm 0,26$ ), followed by luminal epithelium ( $2,23 \pm 0,37$ ), stromal cells ( $2,1 \pm 1,9$ ) and the lowest in glandular epithelial ( $2,00 \pm 0,68$ ); meanwhile the highest VEGFR-1 expression was seen in glandular epithelial ( $2,85 \pm 0,30$ ), followed by luminal epithelial ( $2,83 \pm 0,54$ ), endothelial ( $2,70 \pm 0,42$ ) and the lowest at the stromal cells ( $2,58 \pm 0,42$ ). Statistically, ZV was correlated to the VEGF stromal cells ( $p = 0,018$ ) and Endometrial Volume was correlated to VEGF endothelial ( $p = 0,000$ ) and VEGF luminal epithelium ( $p = 0,029$ ) and VEGF total cells ( $p = 0,043$ ); meanwhile Histological Dating of Endometrium was correlated to VEGFR-1 stromal cells ( $p = 0,009$ ). Endometrial receptivity predictor determined by Ultrasound Composite based on immunohistochemistry composite was Vascularization Zone of layer 3?4, Endometrial Volume of 3,090 ml and endometrial VFI of 0,253 with a specificity of 77,4%. Ultrasound was the useful tools for diagnostic predictor of endometrial receptivity diagnosis during the implantation windows period of PCOS infertile female.