IMPACT OF DIFFERENT DNA PLOIDY PATTERNS ON ENDOMETRIAL CARCINOMAS BASED ON IMAGE CYTOMETRY

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Worldwide, endometrial cancer is one of the most frequently diagnosed malignancies in women and a notable cause of death. The aim of this study was to perform image cytometric DNA ploidy analysis on a prospective material of endometrial adenocarcinomas in order to determine potential correlation between ploidy status and their histological features. The analysis was carried out in fresh tissue samples resected by implementing complete hysterectomy in a series of patients (n = 126). We found that ploidy status using image cytometry correlate with histologic type, grade and stage in endometrial cancer and aneuploid tumor samples are associated with aggressive phenotype statistics. Furthermore, DNA ploidy should be used as a reliable and applicable prognostic marker in the routine clinical practice.

Key words: *DNA ploidy, Image cytometry, diploid, aneuploidy, endometrial carcinoma.*

ВИЯВЛЕННЯ ВПЛИВУ РІЗНИХ МОДЕЛЕЙ ПЛОЇДНОСТІ ДНК НА КАРЦИНОМИ ЕНДОМЕТРІЮ ЗА ДОПОМОГОЮ ЦИТОМЕТРІЇ З ВІЗУАЛІЗАЦІЄЮ

У всьому світі рак ендометрію є однією з найчастіше діагностованих злоякісних пухлин та значною причиною смерті жінок. Мета цього дослідження полягала в проведенні цитометричного аналізу плоїдності ДНК з візуалізацією, використовуючи передбачуваний матеріал ендометріальних аденокарцином, щоб визначити можливу кореляцію між статусом плоїдності та їхніми гістологічними характеристиками. Проводили аналіз свіжих зразків тканин, отриманих резекцією під час повної гістеректомії у пацієнток (n=126). Ми виявили, що статус плоїдності, виявлений за допомогою цитометрії з візуалізацією, корелював із гістологічним типом, ступенем та етапом раку ендометрію, а зразки пухлин із анеуплоїдними клітинами пов'язані зі статистикою агресивного фенотипу. Плоїдність ДНК потрібно використовувати як надійний та застосовний прогностичний маркер у звичайній клінічній практиці.

Ключові слова: плоїдність ДНК, цитометрія з візуалізацією, диплоїд, анеуплоїдія, карцинома ендометрію.

REFERENCES

Baak JP, Snijders W, van Diermen B, van Diest PJ, Diepenhorst FW, Benraadt J (2003) Prospective multicenter validation confirms the prognostic superiority of the endometrial carcinoma prognostic index in international Federation of gynecology and obstetrics stage 1 and 2 endometrial carcinoma. J Clin Oncol 21(22):4214–4221. https://doi.org/10.1200/JCO.2003.02.087

Bishop R (2010) Applications of fluorescence in situ hybridization (FISH) in detecting genetic aberrations of medical significance. Bioscience Horizons 3 (1):85–95. https://doi.org/10.1093/biohorizons/hzq009

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68(6):394–424. https://doi.org/10.3322/caac.21492

Danielsen HE, Pradhan M, Novelli M (2016) Revisiting tumour aneuploidy - the place of ploidy assessment in the molecular era. Nat Rev Clin Oncol 13(5):291–304. https://doi.org/10.1038/nrclinonc.2015.208

Davoli T, de Lange T (2011) The causes and consequences of polyploidy in normal development and cancer. Annu Rev Cell Dev Biol 27:585–610. https://doi.org/10.1146/annurev-cellbio-092910-154234

Haroske G, Giroud F, Reith A, Bцcking A (1998) 1997 ESACP consensus report on diagnostic DNA image cytometry. Part I: basic considerations and recommendations for preparation, measurement and interpretation. European Society for Analytical Cell Pathol Anal Cell Pathol 17(4):189–200. https://doi.org/10.1155/1998/390837

Hecht JL, Ince TA, Baak JP, Baker HE, Ogden MW, Mutter GL (2005) Prediction of endometrial carcinoma by subjective endometrial intraepithelial neoplasia diagnosis. Mod Pathol 18(3):324–330. https://doi.org/10.1038/modpathol.3800328

Kildal W, Micci F, Risberg B, Abeler VM, Kristensen GB, Heim S, Danielsen HE (2012) Genomic imbalances in endometrial adenocarcinomas – comparison of DNA ploidy, karyotyping and comparative genomic hybridization. Mol Oncol 6(1):98–107. https://doi.org/10.1016/j.molonc.2011.10.002

Korabiowska M, Ruschenburg I, Schlott T, Kubitz A, Brinck U, Droese M (2001) Relation between DNA ploidy status and the expression of the DNA-mismatch repair genes MLH1 and MSH2 in cytological specimens of melanoma lymph node and liver metastases. Diagn Cytopathol 24(3):157–162. https://doi.org/10.1002/1097-0339(200103)24:3<157::aid-dc1033>3.0.co;2-a

Koskas M, Amant F, Mirza MR, Creutzberg CL (2021) Cancer of the corpus uteri: 2021 update. Int J Gynaecol Obstet 155(Suppl. 1):45–60. https://doi.org/10.1002/ijgo.13866

Kurman RJ, Blaustein's Pathology of the Female Genital Tract (Springer, New York, 2011)

Lax SF, Pizer ES, Ronnett BM, Kurman RJ (1998) Comparison of estrogen and progesterone receptor, Ki-67, and p53 immunoreactivity in uterine endometrioid carcinoma and endometrioid carcinoma with squamous, mucinous, secretory, and ciliated cell differentiation. Hum Pathol 29(9):924–931. https://doi.org/10.1016/s0046-8177(98)90197-6

Lax SF, Pizer ES, Ronnett BM, Kurman RJ (1998) Clear cell carcinoma of the endometrium is characterized by a distinctive profile of p53, Ki-67, estrogen, and progesterone receptor expression. Hum Pathol 29(6):551–558. https://doi.org/10.1016/s0046-8177(98)80002-6

Liu FS (2007) Molecular carcinogenesis of endometrial cancer, *Taiwan J.* Obstet Gynecol 46(1):26–32. https://doi.org/10.1016/S1028-4559(08)60102-3

Lundgren C, Auer G, Frankendal B, Moberger B, Nilsson B, Nordstrцm B (2002) Nuclear DNA content, proliferative activity, and p53 expression related to clinical and histopathologic features in endometrial carcinoma. Int J Gynecol Cancer 12(1):110–118. https://doi.org/10.1046/j.1525-1438.2002.01079.x

Mauland KK, Wik E, Salvesen HB (2014) Clinical value of DNA ontent assessment in endometrial cancer. Cytometry B Clin Cytom 86(3):154–163. https://doi.org/10.1002/cyto.b.21164

Mauland KK, Wik E, Hoivik EA, Kusonmano K, Halle MK, Berg A, Haugland HK, Шуап AM, Kalland KH, Stefansson IM, Akslen LA., Krakstad C, Trovik J, Werner HM, Salvesen HB (2017) Aneuploidy related transcriptional changes in endometrial cancer link low expression of chromosome 15q genes to poor survival. Oncotarget 8(6):9696–9707. https://doi.org/10.18632/oncotarget.14201

Mutter GL, Baak JP, Crum CP., Richart RM, Ferenczy A, Faquin WC (2000) Endometrial precancer diagnosis by histopathology, clonal analysis, and computerized morphometry. J Pathol 190(4):462–469. https://doi.org/10.1002/(SICI)1096-9896(200003)190:4<462::AID-PATH590>3.0.CO;2-D

Nordström B, Strang P, Lindgren A, Bergström R, Tribukait B (1996) Carcinoma of the endometrium: do the nuclear grade and DNA ploidy provide more prognostic information than do the FIGO and WHO classifications? Int J Gynecol Pathol 15(3):191–201. https://doi.org/10.1097/00004347-199607000-00002

Oehler MK, Brand A, Wain GV (2003) Molecular genetics and endometrial cancer. J. Br Menopause Soc 9(1):27–31. https://doi.org/10.1258/1362180003100322116

Origoni M, De Marzi P, Almirante G, Ottolina J, Frigerio L, Carnelli M, Gelardi C, Candiani M (2013) The Prognostic Value of DNA Ploidy Determination in Endometrial Cancer. J Clin Exp Oncol 2(1). https://doi.org/10.4172/2324-9110.1000105

Pradhan M, Abeler VM, Danielsen HE, Sandstad B, Tropй CG, Kristensen GB, Risberg BE (2012) Prognostic importance of DNA ploidy and DNA index in stage I and II endometrioid adenocarcinoma of the endometrium. Ann Oncol 23(5):1178–1184. https://doi.org/10.1093/annonc/mdr368

Pradhan M, Abeler VM, Danielsen HE, Tropé CG, Risberg BA (2006) Image cytometry DNA ploidy correlates with histological subtypes in endometrial carcinomas. Mod Pathol 19(9):1227–1235. https://doi.org/10.1038/modpathol.3800641

Prat J (2004) Prognostic parameters of endometrial carcinoma. Hum Pathol 35(6):649–662. https://doi.org/10.1016/j.humpath.2004.02.007

Salvesen HB, Akslen LA (2002) Molecular pathogenesis and prognostic factors in endometrial carcinoma. APMIS 110(10):673–689. https://doi.org/10.1034/j.1600-0463.2002.1101001.x

Sasaki K, Kurose A, Miura Y, Sato T, Ikeda E (1996) DNA ploidy analysis by laser scanning cytometry (LSC) in colorectal cancers and comparison with flow cytometry. Cytometry 23(2):106–109. https://doi.org/10.1002/(SICI)1097-0320(19960201)23:2<106::AID-CYTO3>3.0.CO;2-I

Susini T, Amunni G, Molino C, Carriero C, Rapi S, Branconi F, Marchionni M, Taddei G, Scarselli G (2007) Ten-year results of a prospective study on the prognostic role of ploidy in endometrial carcinoma:

DNA aneuploidy identifies high-risk cases among the so-called 'low-risk' patients with well and moderately differentiated tumors. Cancer 109(5):882–890. https://doi.org/10.1002/cncr.22465

Terada K (2012) DNA ploidy in endometrial cancer: unfinished business? Ann Oncol 23(5):1083–1084. https://doi.org/10.1093/annonc/mdr549

Uharcek P (2008) Prognostic factors in endometrial carcinoma. J Obstet Gynaecol Res 34(5):776–783. https://doi.org/10.1111/j.1447-0756.2008.00796.x

WHO Classification of Tumours Editorial Board. Female Genital Tumours (IARC, Lyon, 2020)

Wik E, Trovik J, Iversen OE, Engelsen IB, Stefansson IM, Vestrheim LC, Haugland HK, Akslen LA, Salvesen HB (2009) Deoxyribonucleic acid ploidy in endometrial carcinoma: a reproducible and valid prognostic marker in a routine diagnostic setting. Am J Obstet Gynecol 201(6):603.e1–7. https://doi.org/10.1016/j.ajog.2009.07.029

Wimberger P, Hillemanns P, Kapsner T, Hepp H, Kimmig R (2002) Evaluation of prognostic factors following flow-cytometric DNA analysis after cytokeratin labelling: II. Cervical and endometrial cancer. Anal Cell Pathol 24(4–5):147–158. https://doi.org/10.1155/2002/346969

Zaino RJ, Davis AT, Ohlsson-Wilhelm BM, Brunetto VL (1998) DNA content is an independent prognostic indicator in endometrial adenocarcinoma. A Gynecologic Oncology Group study. Int J Gynecol Pathol 17(4):312–319. https://doi.org/10.1097/00004347-199810000-00004

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