

ABSTRACT**APOPTOSIS, CATALASE,
HEAT SHOCK PROTEIN 70, CYTOKERATIN 19 AND
PHOSPHATIDYLINOSITOL TRIPHOSPHATE EXPRESSION
RELEVANCE WITH RADIOTHERAPY RESISTANCE
OF CERVICAL CANCER****Poedjo Hartono**

Background : The huge number of cervical cancer cases diagnosed in advanced stages are huge problem in many developing countries like Indonesia. With radiotherapy as main therapy, there were many cases of radioresistance that were not responding or relapsing post treatment. Radiosensitivity rely on resistant subpopulation of cells. By identifying indicators of radioresistant cells, we expect to investigate the resistance mechanism in order to evaluate and treat radioresistant cervical cancer better.

Objective : To investigate relationship between radiotherapy resistance in cervical cancer with apoptosis, *catalase* (CAT), *heat shock protein* (Hsp) 70, *cytokeratin* (CY) 19 and *Phosphatidylinositol Triphosphate* (PIP3) expressions.

Method : Anaytic observasional, cross sectional study performed on 40 cervical cancer patients stage IIB-III received external beam radiotherapy 35 times and divided into 20 radioresistant and 20 radiosensitive sample groups. Radiotherapy resistance was determined from clinical evaluation with histopathological confirmation of cancer cells, three months after last radiotherapy. Cervical biopsy was performed to investigate apoptotic cells, the expression of CAT, Hsp70, CY19 and PIP3 by immunohistochemistry examination.

Result : All 40 patients had mean age of 50.93 years with 60% were *squamous* histopathologically. There was a significant difference between radiotherapy resistance with the histopathology type ($p=0.01$), no difference with age ($p=0.95$) nor stage ($p=0.57$). This study revealed lower apoptotic cells with higher in CAT, Hsp70, CY19 and PIP3 expressions significantly ($p<0.001$) in radioresistant cervical cancers compared with the radiosensitive ones. All variables were performed discriminant analysis and can be used as radiotherapy sensitivity indicators, with PIP3 expression was the most dominant and Hsp70 had the least role among them.

Conclusion : There was a lower in apoptotic cells with a higher in CAT, Hsp70, CY19 and PIP3 expressions in radioresistant cervical cancer.

Keywords : Cervical cancer, radiotherapy, radioresistant

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Gambar 5.3 Perbandingan Sel Apoptosis antara Kanker Serviks Radioresisten dan

DAFTAR SINGKATAN



APAF	<i>Apoptotic Protease Activating Factor</i>
BAD	<i>B-cell Lymphoma-2-associated death promoter</i>
BAK	<i>B-cell lymphoma antagonist killer</i>
Bax	<i>B-cell Lymphoma-2 protein-associated X protein</i>
Bcl-xl	<i>B-cell lymphoma extra large</i>
Bcl-2	<i>B-cell lymphoma 2</i>
BER	<i>Base excision repair</i>
BSA	<i>Bovine Serum Albumin</i>
CAT	<i>Catalase</i>
CIN	<i>Cervical Intraepithelial Neoplasia</i>
CY	<i>Cytokeratin</i>
cyto C	<i>Cytochrome C</i>
DAB	<i>Diaminobenzidine</i>
dATP	<i>deoxyadenosine Triphosphate</i>
DNA	<i>Deoxyribonucleid Acid</i>
DSB	<i>Double strand break</i>
EBRT	<i>External beam radiation therapy</i>
FasL	<i>Fas Ligand</i>
FIGO	<i>Federation Internationale de Gynecologie et d'Obstetrique</i>

FOXO	<i>forkhead family of transcription factor</i>
GPx	<i>glutathione peroxidase</i>
GSH	<i>Glutathione</i>
Gy	<i>Gray</i>
H ₂ O ₂	<i>Hidrogen peroksida</i>
HEJ	<i>Homologous end join</i>
HPV	<i>Human Papilloma Virus</i>
HRP	<i>Horseradish peroxidase</i>
Hsp	<i>Heat Shock Protein</i>
IAP	<i>Inhibitory of anti apoptosis</i>
JNK	<i>c-Jun N-terminal kinases</i>
Mab	<i>Monoclonal antibody</i>
MDA	<i>Malondialdehyde</i>
MMR	<i>Mismatch repair</i>
NER	<i>Nucleotide excision repair</i>
NF-κβ	<i>Nuclear Factor-kb</i>
NHEJ	<i>Non homologous end join</i>
O ₂	<i>Oksigen</i>
O ₂ *	<i>Anion superoksid</i>
OH*	<i>Radikal hidroksil</i>
p27Kip1	<i>cyclin-dependent kinase inhibitor 1B</i>
p53	<i>Protein 53</i>
PARP	<i>Poly ADP-ribose polymerase</i>