

Comparative evaluation of the bladder cancer antigen and telomerase activity in the detection of primary and recurrent bladder tumor

Thesis

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Abstract

Purpose:

The diagnostic efficacy of telomerase activity and urinary cancer bladder antigen was evaluated in a trial to assess their value in the detection of bladder cancer and to compare it to that of routine urine cytology.

Subjects and Methods:

The study included 50 bladder cancer patients diagnosed by cystoscopy and histopathological typing, in addition to 20 benign bladder lesions patients and 20 healthy volunteers as a control group. Thirty three of cancer patients were of grades I & II while 17 were grade III. Twenty six patients were of stages I & II while 24 patients were of stages III & IV. Twenty one patients were papillary superficial and 29 were invasive TCC. Twenty patients had bilharziasis. A single freshly voided urine sample ($\approx$ 100ml) was collected from each patient and control subject and aliquoted for each test. All assays were conducted according to the manufactures guidelines and the results were compared to those of urine cytology.

Results:

The optimal cutoffs for UBC antigen and telomerase activity were calculated by ROC curves were 3.315 ug/l and 0.256 (Ratio) respectively. The level of the UBC antigen were significantly higher in the malignant group compared to the normal control group (P-value <0.001). However, its level was not significantly different between the benign bladder lesions group and the bladder cancer group. The level of telomerase activity was significantly higher in the malignant group compared to either the benign group or normal group (P-value <0.001). The overall sensitivity of UBC, telomerase and cytology was 84.0%, 80.0% and 36.0% respectively. Sensitivity of UBC, telomerase and cytology was 96.9%, 75.9% and 41.4% respectively for invasive and it was 61.9%, 76.19% and 28.57% respectively for papillary. Sensitivity of UBC, telomerase and cytology was

75.75%, 81.81% and 33.33% respectively for grade I and II and it was 100%, 82.4% and 41.2% respectively for grade III. Sensitivity of UBC, telomerase and cytology was 73.07%, 80.76% and 30.76% respectively for stage T1 and T2 and it was 95.8%, 83.3% and 41.7% respectively for stage T3 and T4. Sensitivity of UBC, telomerase and cytology was 95%, 80% and 45% respectively for bilharziasis and it was 76.6%, 83.3% and 30% respectively for non bilharziasis. The overall specificity of UBC, telomerase and cytology was 75.0%, 75.0% and 100.0% respectively. Double or triple combinations of the assayed markers with each other or with cytology did not improve the sensitivity over each parameter individually.

Conclusion:

Our data indicate that UBC and telomerase had superior sensitivities compared to voided urine cytology. It can be concluded that UBC and telomerase have enough potential for future clinical use, although UBC showed slightly better diagnostic performance than telomerase regarding the pathological subtypes, grade and stage of bladder cancer.

Keywords: bladder cancer, tumor markers, UBC, telomerase, urine cytology.

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LIST OF ABBREVIATIONS

A	: Absorbance
aa	: Amino acid
AJCC	: American Joint Committee on Cancer
ALT	: Alternative lengthening of telomeres
AUC	: Area under the curve
BTA	: Bladder Tumor Antigen
CD	: Cluster of Differentiation
cDNA	: Cyclic DNA
CIS	: Carcinoma in situ
CK	: Cytokeratin
DA	: Diagnostic Accuracy
DCIS	: Ductal Carcinoma in situ
DIG	: Digoxigenin
DNA FCM	: DNA flow cytometry
DNA	: Deoxyribonucleic acid
EGF	: Epidermal Growth Factor
ELISA	: Enzyme linked immunosorbent assay
FDA	: Food and Drug Administration
FDP	: Fibrin degradation product
FISH	: Fluorescent in situ hybridization technique
HA	: Hemagglutinin
HA	: Hyaluronic acid
HAse	: Hyaluronidase
HCC	: Hepatocellular carcinoma
HMK	: High molecular weight keratin
HPV	: Human Papilloma Virus
HRP	: Horseradish peroxidase
hTERC	: human Telomere RNA Component
hTERT	: human Telomere Reverse Transcriptase
hTR	: RNA subunit of telomerase
IS	: Internal standard
KDa	: Kilo dalton
LMK	: Low molecular weight keratin
M	: metastasis
Mcm5	: Minichromosome maintenance
m-RNA	: Messenger-RNA
MTP	: Microtitre plate
N	: regional lymph node
NCI	: National Cancer Institute

NMP-22	: Nuclear Matrix Protein-22
NPV	: Negative Predictive Value
nt	: Nucleotides
p123	: Protein 123
P21	: Protein 21
P53	: Protein 53
PCNSL	: Primary central nervous system malignant lymphoma
PPV	: Positive Predictive Value
PRB	: Retinoblastoma pretein
Rb	: Retinoblastoma
RCA	: Regulators of complement activators
RNA	: Ribonucleoprotein acid
ROC curve	: Receiver operating characteristic curve
rpm	: Revolution per minute
RT	: Room temperature
RTA	: Relative telomerase activity
RT-PCR	: Real time-polymerase chain reaction
<i>S. cerevisiae</i>	: <i>Saccharomyces cerevisiae</i>
SCC	: Squamous cell carcinoma
sno RNA	:Small nucleolar RNA
T	: tumor
TCC	: Transitional cell carcinoma
TMB	: Tetramethyl benzidine
TNM	: Tumor-node-metastasis staging system
TRAP	: Telomere repeat amplification protocol
UBC	: Urinary bladder cancer antigen
UICC	: Union International Contre Cancer
VUC	: Voided urine cytology
WHO	: World Health Organization

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**INTRODUCTION
AND
AIM OF WORK**