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## Background

- Bladder cancer (BC) is the ninth most common cancer. Incidence rates are highest in Europe, the United States and Egypt with 430,000 new cases diagnosed in 2012 worldwide. Most BC patients (70%) present with NMIBC, between 50% and 70% of them do recur, and approximately 10% to 20% of them progress to muscle invasive disease (MIBC) (1).
- Until now, the standard non-invasive urinary marker is urinary cytology. This technique was more sensible in high-grade tumors than in low-grade ones, with an overall sensitivity ranging from 25–70% (2, 3).
- Investigators do their best to search for a non-invasive, highly sensitive and specific marker of BC. As urine is in contact with BC and can be collected non-invasively and in large amounts, urine-based assays are a natural and promising source for biomarkers.
- Micro-RNA155 (mir-155), MicroRNA-200b (mir-200b), human telomerase reverse transcriptase (hTERT), and E2F3 transcription factor had a role in BC pathogenesis.
- The objective of this study was to determine the ability of urine-based tumor markers in detection, staging, and grading of BC in a registered prospective trial.

## Methods

- A registered prospective trial (NCT03591367) for 64 NMIBC patients. From (50-100 mL) voided urine samples, total RNA extracted from sedimented urothelial cells were analyzed by a reverse transcriptase - polymerase chain reaction assay for the presence of mir-155, mir-200b, hTERT and E2F3 transcript.
- A receiver operating characteristics (ROC) was plotted in order to choose the best cut-off point. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each test.

## Results

- Patients demographic were comparable (table 1)
- The expression levels of the mir-155 didn't show difference between high grade (HG) and low grade (LG) (p=0.06) (table 1)
- Both mir-155 and mir-200b had the lowest AUC (table 2). E2F3 and hTERT expression in urine was higher in HG NMIBC group than in LG NMIBC (P<0.001) (table 1).
- The sensitivity, specificity, accuracy of E2F3 were 86%, 76.2%, and 82.8%, respectively. The sensitivity, specificity, accuracy of hTERT were 86%, 66.7%, and 79.7%, respectively (table 2 and figure 1).

## Results (continued)

Table 1: Baseline patient and urinary markers characteristics

Variable	LG N = 21	HG N = 43	P value
<b>Baseline patient characteristics (Mean ± SD)</b>			
Age (years)	56.57 ± 12.36	61.21 ± 10.18	0.12
Gender N <sup>0</sup> (%)			
Male	14 (66.7 %)	36 (83.7 %)	0.12
female	7 (33.3 %)	7 (16.3 %)	
BMI (kg/m <sup>2</sup> )	27.41 ± 3.62	26.14 ± 3.80	0.21
Serum creatinine (mg/dl)	1.37 ± 1.89	1.31 ± 1.13	0.89
Hemoglobin (gm/dl)	12.78 ± 1.66	12.68 ± 1.56	0.82
INR	1.07 ± 0.09	1.09 ± 0.09	0.53
<b>Baseline urinary markers characteristics (Mean ± SD)</b>			
Telomerase	5.46 ± .89	7.93 ± 1.70	< 0.001
E2F3	2.64 ± .45	4.89 ± 1.36	< 0.001
MIR-155	.48 ± .19	.58 ± .21	0.064
MIR- 200b	.28 ± .08	.54 ± .19	< 0.001

Table 2: urinary markers diagnostics of grade of NMIBC

Test	AUC	Cut off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	P value
mir-155	0.341	0.590	41.86	38.09	58.06	24.24	40.63	0.069
mir-200b	0.122	0.360	23.26	19.05	37.03	10.81	21.88	0.19
hTERT	0.872	5.605	86.05	66.67	84.09	70	79.69	< 0.001
E2F3	0.889	3.055	86.05	76.19	88.09	72.73	82.81	< 0.001

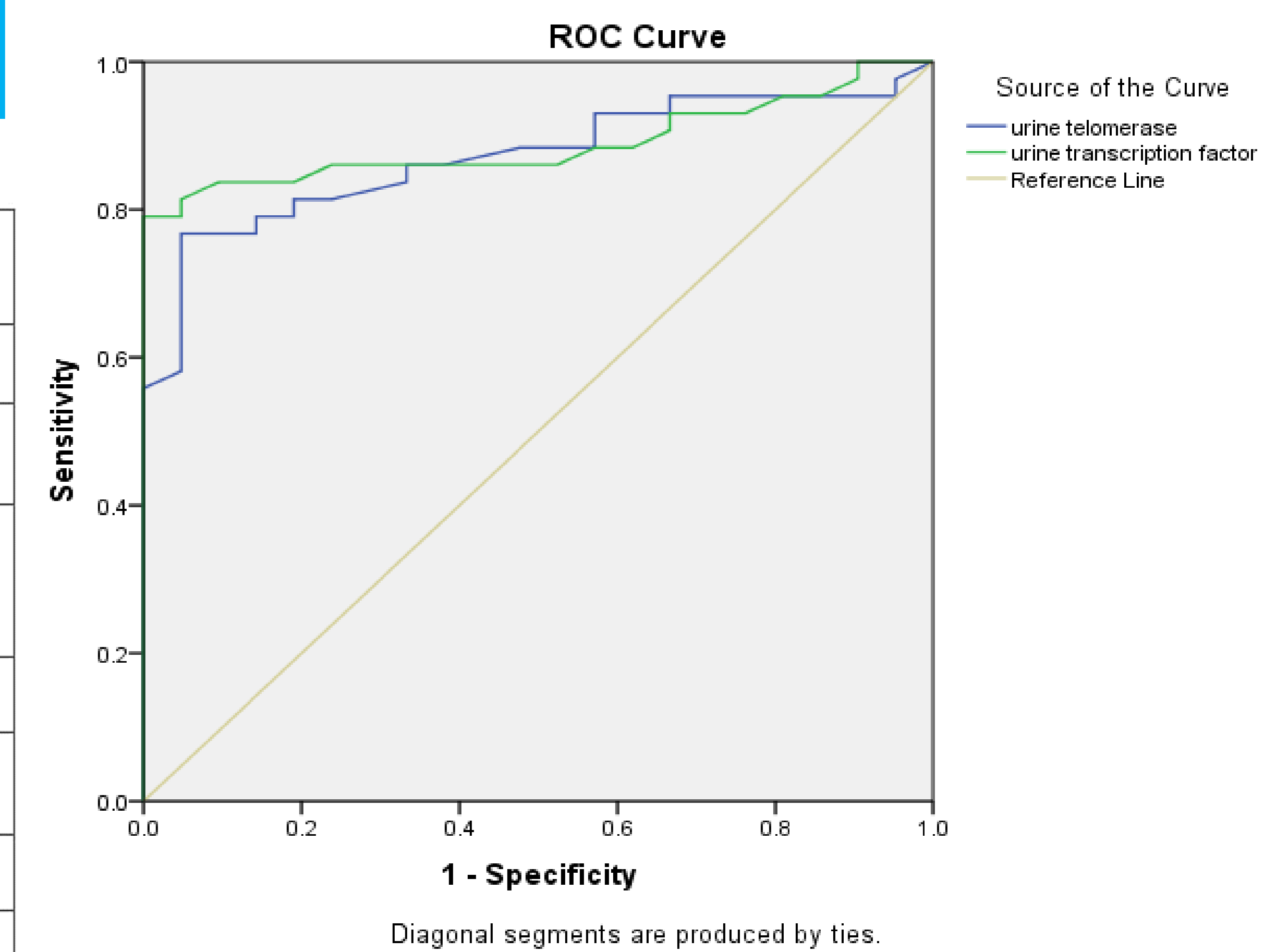


Figure 1: ROC curve of hTERT and E2F3 for discriminating NMIBC grades.

## Conclusion

As molecular urinary biomarkers ; **E2F3 and hTERT** have the highest potential for prediction of the grade of NMIBC to either low or high grade.

### References:

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