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Original scientific paper

Diagnostic Accuracy of Ultrasound T-staging of the Urinary Bladder Cancer in Comparison with Histology in Elderly Patients

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ABSTRACT

Urinary bladder cancer (UBC) is dominantly the cancer of the elderly occurring primarily in the 6th, 7th and 8th decade of life. The aim of this study was to evaluate diagnostic accuracy of ultrasound T-staging (UTS) of UBC in the group of elderly patients. In 152 elderly patients referred to transabdominal ultrasound examination in two different facilities (76 each) due to various symptoms (primarily painless gross or microscopic haematuria) UBC was diagnosed. Initial UTS at the moment of detection was performed and compared with final histological T-staging (HTS). A high level of conformity between UTS and HTS was detected. In a total of 152 patients with UBC there were 115 (75.66%) patients with complete match between the UTS and HTS, 24 (15.79%) patients with minimal variation within one stage, and 13 (8.55%) patients with one stage difference between the UTS and HTS. The best result was established for the stage T1, where the accuracy was 94.5%. In other stages the accuracy was between 84.9% and 91.8%. The Youden's index for all the stages was over 0.6. UTS has a high diagnostic accuracy, especially for stages T1 and T2. It is extremely useful tool in differentiating the superficial UBC from the muscle-invasive one, being of significant importance in planning the further treatment of elderly patients and having important role in choosing appropriate surgical approach.

Key words: *cancer, T-staging, urinary bladder, ultrasound, elderly*

Introduction

Diagnostic accuracy of ultrasound T-staging (UTS) of the urinary bladder cancer (UBC) has permanently been a challenging issue in clinical practice, since the proper initial staging of the tumour is essential for further treatment[1]. Therefore, the comparison of initial UTS with the final histological T-staging (HTS) provides the best possible evaluation of the quality of initial UTS at the moment of detection of UBC. In this paper we report on the results of the retrospective study on diagnostic accuracy of UTS of UBC.

Materials and Methods

A sample of 152 patients with UBC examined at two different ultrasound diagnostic centres (76 in each) was analysed with respect to initial UTS and later HTS. All the patients (108 males and 44 females) were referred to transabdominal ultrasound examination due to various symptoms, primarily painless gross or microscopic haematuria in 60.52% and dysuria 28.94%. At the moment of detection of UBC all the patients underwent initial UTS of the tumour as illustrated in Figures 1 and 2. The postoperative histological findings were analysed and final HTS was compared with initial UTS at the moment of detection. The study was carried out in full accordance with ethical standards applicable in both institutions.

Statistics

The primary method in comparison of UTS and HTS was ROC analysis, where HTS was taken as reference diagnosis. The basic parameter for assessing the accuracy of diagnosis was the quotient calculated as the sum of true negative ones and true positive ones divided by the total

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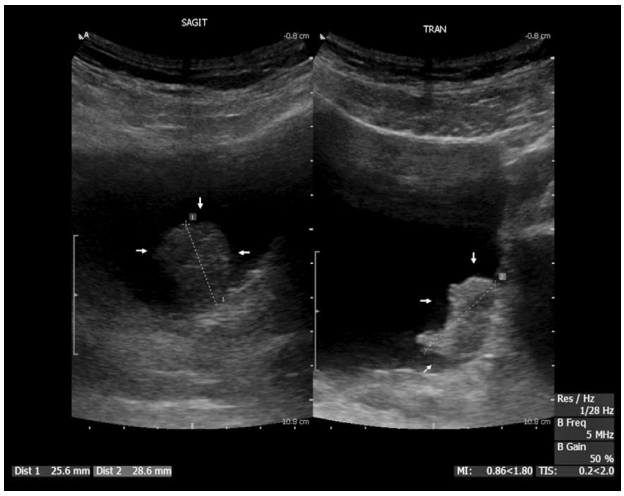

Fig. 1. Male, 62, with the only symptom being painless gross haematuria and with urinary bladder cancer on the left lateral wall of the bladder with superficial infiltration of the subepithelial connective tissue living intact muscle layer. The initial ultrasound T-staging at the moment of detection was T1. The final histological T-staging was pT1.

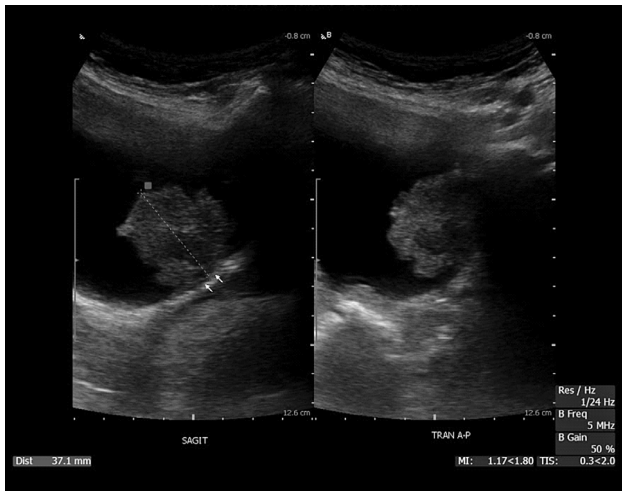

Fig. 2. Female, 58, with the only symptom being painless gross haematuria, and with urinary bladder cancer on the left lateral wall of the bladder, being muscle-invasive with initial infiltration of the inner half of the muscle layer (arrows). The initial ultrasound T-staging at the moment of detection was T2. The final histological T-staging was pT2.

number of patients. We also provided the other important parameters such as sensitivity, specificity, positive predictive accuracy and negative predictive accuracy. In order to study the overall performance of a test we provided kappa agreement measure and Youden's index. The quality of test was also tested with Chi-square test. The statistical analysis was performed by independent company, ID Consulting, Bribir, Croatia.

Results

In 152 patients both initial UTS and final HTS of UBC were determined. The findings were compared and the level of their match was determined as presented in Figure 3.

Comparative analysis of the above results shows that in 115 (75.66%) patients there was a complete match between the UTS and HTS, in 24 (15.79%) patients there was a minimal variation within one stage, and in 13 (8.55%) patients there was one stage difference between the UTS and HTS. In Table 1 statistical parameters are presented.

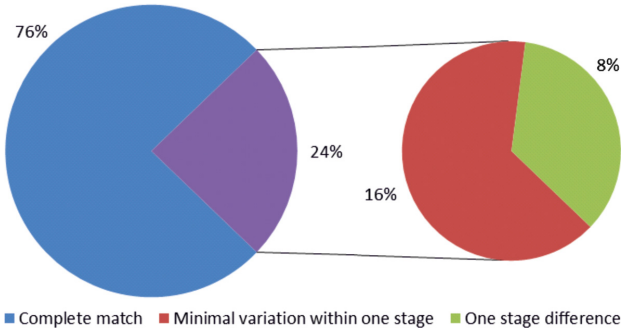

Fig. 3. Initial ultrasound T-staging and final histological T-staging of the urinary bladder cancer.

Diagnostic accuracy of UTS was rather high for stages T1 and T2, while it was slightly lower for the stages T3 and T4. Furthermore, diagnostic accuracy was particularly low for ultrasound differentiation between stages T3a and T3b. Nevertheless, diagnostic accuracy for common stage T3 was still sufficient enough in comparison with diagnostic accuracy for other stages. Therefore, the stages T3a and T3b shall not be taken into consideration separately in further discussion. Generally high specificity was accompanied with slightly lower sensitivity, especially for stage T1, but Youden's index in all cases is above satisfactory value of 0.6. Positive predictive accuracy was relatively lower for stage T2, and negative predictive accuracy was slightly lower for stage T3. For other stage these two parameters were relatively high, especially the negative predictive accuracy.

In all relevant cases Kappa agreement measure was above 0.65. Therefore, we have good agreement between provided diagnostic methods. Chi square test also showed that it was unlikely that the observed results were caused by chance.

Discussion

Rather high diagnostic accuracy for stages T1 and T2, and slightly lower accuracy for the stages T3 and T4 can be explained by the fact that deeper penetration of the tumour always involves obstacles in maintaining initial ultrasound precision of evaluation, particularly in assessing the penetration into surrounding structures. Particu-

TABLE 1

ACCURACY OF ULTRASOUND T-STAGING OF THE URINARY BLADDER CANCER IN COMPARISON WITH HISTOLOGICAL T-STAGING

Stages	T1	T2	T3a	T3b	T3	T4
Accuracy	0.945 95% CI: 0.898,0.992]	0.918 95% CI: [0.861, 0.975]	0.781 95% CI: [0.695, 0.866]	0.822 95% CI: [0.743, 0.901]	0.849 95% CI: [0.775, 0.923]	0.849 95% CI: [0.775, 0.923]
Kappa agreement measure	0.685 95% CI: [0.48,0.889]	0.653 95% CI: [0.447, 0.858]	0.36 95% CI: [0.154, 0.567]	0.383 95% CI: [0.187, 0.578]	0.685 95% CI: [0.48, 0.89]	0.681 95% CI: [0.476, 0.885]
Sensitivity	0.625 95% CI: [0.322,0.928]	0.778 95% CI: [0.533, 1.023]	0.533 95% CI: [0.306, 0.761]	0.375 95% CI: [0.161, 0.589]	0.742 95% CI: [0.603, 0.881]	0.88 95% CI: [0.765, 0.995]
Specificity	0.985 95% CI: [0.958,1.012]	0.938 95% CI: [0.884, 0.991]	0.845 95% CI: [0.761, 0.929]	0.947 95% CI: [0.895, 1]	0.929 95% CI: [0.858, 0.999]	0.833 95% CI: [0.738, 0.928]
Youden's J	0.61 95% CI: [0.306,0.913]	0.715 95% CI: [0.465, 0.966]	0.378 95% CI: [0.135, 0.621]	0.322 95% CI: [0.102, 0.543]	0.671 95% CI: [0.515, 0.826]	0.713 95% CI: [0.564, 0.862]
Positive predictive accuracy	0.833 95% CI: [0.564,1.102]	0.636 95% CI: [0.38, 0.893]	0.471 95% CI: [0.257, 0.685]	0.667 95% CI: [0.389, 0.944]	0.885 95% CI: [0.774, 0.995]	0.733 95% CI: [0.591, 0.876]
Negative predictive accuracy	0.955 95% CI: [0.911,1]	0.968 95% CI: [0.928, 1.007]	0.875 95% CI: [0.797, 0.953]	0.844 95% CI: [0.764, 0.924]	0.83 95% CI: [0.733, 0.927]	0.93 95% CI: [0.862, 0.999]
Chi square	70.185 (p<0.001)	63.087 (p<0.001)	19.08 (p<0.001)	24.023 (p<0.001)	69.936 (p<0.001)	69.108 (p<0.001)

larly low diagnostic accuracy between stages T3a and T3b can be explained partly by insufficient ultrasound differentiation of these two sub-stages of tumour penetration, and, in some cases, by time gap between initial ultrasound detection and final histological analysis. On the other hand, diagnostic accuracy for common stage T3 was sufficient to make this stage distinctive enough in comparison with other stages.

High specificity for stage T1 was accompanied with its relatively low sensitivity. Indeed, seeing the ultrasound difference between tumorous infiltration of the subepithelial connective tissue in T1 and initial tumorous infiltration of the muscular layer in T2 is possible in most of the cases with limited certainty (Fig. 1 & 2). On the other hand, detection of early forms, like Ta and T1, sometimes may be facing limitations due to insufficient visibility, which was also confirmed by Khan et al.[2].

However, insufficient visibility was a serious obstacle in certain number of cases. Therefore, a small number of tumours initially UTS classified as T1 were finally HTS classified as T2. In some case, time gap between UTS and HTS should be considered as a factor, as well. Slightly lower positive predictive accuracy for stage T2 can be explained by some borderline cases in which either final histological correction or progression of the finding took place till the moment of histological evaluation. After all, although operative treatment is always applied as soon as possible UTS and HTS are not simultaneous actions.

The slightly negative predictive accuracy for T3 can be explained by insufficient visibility in some cases that reduces the assessment of the extent of muscle infiltration versus T2 or extent of possibly deep penetration into surrounding structures versus T4, often accompanied by distant metastases[3]. Furthermore, Denkhaus et al. reported on sonographic staging being correct in 83% of all tumour stages but with the lowest value of 69% for T2/T3a tumours[4]. The latter one is particularly important from the surgical point of view because most of the patients undergoing radical surgical treatment are those with stages T3 and T2[5].

Although Tsakiris and de la Rosette[1] agree that proper staging of the tumour is essential for further treatment emphasising that the first aspect that has to be considered is whether the patient has a superficial or a muscle-invasive tumour, they find the role of imaging in T-staging being not that essential. On the contrary, the results of this study showed that preoperative UTS was extremely useful in determining further procedure being very accurate in making difference between stages T1 and T2. On the other hand, the results of this study confirmed low diagnostic accuracy of UTS in stages T3 and T4 because of the limited ability to evaluate the perivesical tissue, as earlier reported by Lantz and Hattery[6] and by Barentz et al.[7].

The results of this study are rather consistent with large study of Fang et al.8 comparing the UTS with HTS showing 78.5% of total accuracy. McLaughlin et al. also

confirmed a high degree of accuracy in staging by ultrasound[9]. The study of Caskurlu et al. found transabdominal ultrasound having sensitivity and specificity of 72.2% in the superficial tumours, and sensitivity of 65% and specificity of 70% for infiltrating tumours of the urinary bladder[10]. On the other hand, the overall accuracy of three-dimensional UTS reported by Wagner et al.[11] was 79%. The latest research of Masumbuko and Sydney[12] reported the overall sensitivity, specificity, positive predictive value, and negative predictive value of ultrasound in detection of UBC 83%, 93%, 89% and 89%, respectively.

Furthermore, recently published study of Xu et al.[13] on the use of flexible ultrasound bronchoscope (FUB) in bladder tumour staging had excellent results with overall accuracy (95.7%) and the specificity of muscle invasion detection of FUB (98.8%) being comparable to transurethral resection (overall accuracy 90.2% and specificity 100%), and with sensitivity of the muscle invasion detection of FUB being significantly higher than in initial TUR (72.7%VS18.2%). Moreover, the tumour's diameter could not affect the FUB's accuracy of muscle invasion detection. This promising new tool could be a break-through in future ultrasound staging of the primary tumour.

Conclusion

Diagnostic accuracy of UTS is high for stages T1 and T2, slightly lower for stages T3 and T4, and insufficient in differentiation between stages T3a and T3b. Therefore, it is extremely useful in initial assessment of newly detected UBC with respect to differing superficial tumour from the muscle-invasive one which is essential for planning the further treatment[14]. Furthermore, it is highly useful non-invasive tool for assessing the penetration of UBC into surrounding structures.

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DIJAGNOSTIČKA TOČNOST ULTRAZVUČNOG T-STUPNJEVANJA KARCINOMA MOKRAĆNOG MJEHURA U USPOREDBI S PATOHISTOLOŠKIM NALAZOM

SAŽETAK

Karcinom mokraćnog mjehura (KMM) je dominantno karcinom starije dobi koji se primarno razvija u 6., 7. i 8. desetljeću života. Cilj ovog istraživanja bio je procijeniti dijagnostičku točnost ultrazvučnog T-stupnjevanja (UTS) KMM-a u skupini starijih bolesnika. U 152 starijih bolesnika koji su upućeni na trasabdominalni ultrazvučni pregled u dvjema različitim ustanovama (76 u svakoj) zbog različitih simptoma (prvenstveno bezbolne makro- ili mikro- hematurije) dijagnosticiran je KMM. Početno UTS učinjeno je u trenutku otkrivanja i uspoređeno s konačnim histološkim T-stupnjevanjem (HTS). Nađena je visoku podudarnost između UTS-a i HTS-a. Od ukupno 152 pacijenata s KMM-om bilo je 115 (75,66%) bolesnika s potpunim podudaranjem UTS-a i HTS-a, 24 (15,79%) s minimalnim varijacijom unutar jednog stupnja i 13 (8,55%) pacijenata s razlikom od jednog stupnja između UTS-a i HTS-a. Najbolji rezultat je utvrđen za stupanj T1, gdje je točnost iznosila 94,5%. U drugim stupnjevima točnost se kretala između 84,9% i 91,8%. Yudenov indeks za sve stupnjeve iznosio je preko 0,6. UTS ima visoku dijagnostičku točnost, posebno za stupnjeve T1 i T2. Ono je izrazito korisno sredstvo u diferencijaciji površinskog KMM-a od mišićno-invazivnog i od velike je važnosti u planiranju daljnjeg liječenja pacijenata imajući važnu ulogu u odabiru pravilnog kirurškog pristupa.