

## COMPUTED TOMOGRAPHY OR MAGNETIC RESONANCE IMAGING – OUR EXPERIENCES IN DETERMINING PREOPERATIVE TNM STAGING OF BLADDER CANCER

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### Abstract

Bladder cancer is the ninth most common cancer diagnosis worldwide. Early detection of bladder cancer is important, since up to 47% of bladder cancer-related deaths might be avoided.

*Aim:* To show our experience in determining the staging of bladder cancer with multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI), making comparison of stage accuracy with contrast enhanced MDCT, conventional MR imaging and dynamic contrast-enhanced MR imaging on the one hand and pathoistological diagnoses after transurethral resection of the non-muscle invasive bladder cancers or radical cystectomy for patients with muscle-invasive bladder cancers.

*Materials and methods:* Ninety patients with histologically proved bladder cancer were prospectively examined with MDCT, conventional and dynamic MR imaging before tumour resection.

*Results:* Staging was correct in 55.6% with CT, 56.7% with conventional MRI and in 86.7% with dynamic MRI, which was highly significant compared with CT and conventional MRI. Overestimation for superficial tumors was high with CT (31.25%) and conventional MR imaging (25%), but was significantly reduced with dynamic MR imaging (8.3%). The percentages of underestimation in surgically proved invasive tumours (pT2- pT4) were lowest with dynamic MR imaging.

*Conclusion:* CT and MR imaging are less accurate in the evaluation of the depth of mural invasion and for both techniques overstaging is the most frequent error. Dynamic contrast-enhanced MRI with 87% of accuracy, 8.3% overestimation for superficial tumours and lowest underestimation for invasive tumours, make this imaging considerably more accurate.

**Key words:** bladder carcinoma, multidetector computed tomography, conventional magnetic resonance imaging, dynamic contrast enhanced imaging.

### Introduction

Carcinoma of the urinary bladder is a significant world health issue, since this disease is spreading more and more, both in the number of newly fallen ill and in the displacement of the age limit for the occurrence of the disease.

Bladder cancer is the ninth most common cancer diagnosis worldwide, with more than

330,000 new cases each year. At any point in time, 2.7 million people have a history of urinary bladder cancer [1]. It is the most common malignant tumour of the urinary tract and represents 4.5% of all new malignancies [2]. Urinary bladder carcinoma is the fourth most common cancer in males and the tenth most common cancer in females. It occurs three to four

times more frequently in men than in women [3]. The incidence increases with age; it is considered to be a disease of the elderly population, i.e. 80% of diagnosed patients are between 50 and 80 years of age, the peak incidence is in the 6<sup>th</sup> and 7<sup>th</sup> decades, but we more and more often bear witness to the displacement of such an age limit towards the younger population, which means that there is an increasing number of patients who present under the age of 40. Smoking, living in urban areas, diesel fumes, exposure to various aromatic amines causing an occupational hazard in the chemical, rubber, paint or leather industries increases the risk. There is also an association with long-term phenacetin use and cyclophosphamide treatment [4].

Considering present-day life with all the risk factors of modern civilization and the number of more than 130,000 fatalities annually world-wide [5], there is every reason for justification of the increased interest of medical science in a successful, timely diagnostics and treatment of carcinoma of the urinary bladder, because urinary bladder cancer has a high recurrence rate, necessitating long-term surveillance after initial therapy.

Early detection of bladder cancer is important, since up to 47% of bladder cancer-related deaths might have been avoided [6]. Although cystoscopy and pathological staging remain the standards of reference, in our days, multidetector CT and MR imaging are moderately accurate in the diagnosis and local staging of bladder cancer and can determine prognosis and provide information to assist with treatment selection.

Its treatment and prognosis are largely determined by the depth of tumour infiltration and the extent of metastases [7]. Therefore, exact staging is mandatory. To obtain a uniform staging system, the Union Internationale Contre le Cancer (UICC) proposed a clinical method for determining tumour, node, and metastasis (TNM) stages [8].

In bladder cancer, tumour stage is a more reliable prognosticator than is grade, and any evidence of muscle invasion markedly lowers survival. It is therefore essential, first to establish the stage of bladder tumours and select the appropriate treatment, and then to predict prognosis.

## Aim

The aim of this study is to show our experience in determining the staging of bladder cancer with MDCT and MRI, making a comparison of stage accuracy with contrast enhanced MDCT, conventional T1- and T2-weighted MR imaging and dynamic contrast-enhanced T1-weighted MR imaging on the one hand and pathohistological diagnoses after transurethral resection of the non-muscle invasive bladder cancers (TUR) or radical cystectomy for patients with muscle-invasive bladder cancers.

## Material and methodes

In the study we analysed 90 patients (71 men and 19 women) between 34 and 85 years of age, with macrohaematuria as the main clinical symptom. Cystoscopy with biopsy was previously made for all the patients studied, within 3 weeks before CT and MR studies, and all patients had histologically proved urinary bladder neoplasms.

After these radiological imaging procedures, histological staging was achieved with either transurethral deep tumour resection or radical cystectomy. The extent of tumour invasion was classified according to the system of the Union Internationale Contre le Cancer (UICC), (Table 1).

Table 1

### *T Staging for Bladder Cancer [8]*

Stage	Description
Tis	Carcinoma in situ
Ta	Papillary noninvasive tumor
T1	Tumor invades subepithelial connective tissue
T2a	Tumor invades superficial muscle
T2b	Tumor invades deep muscle
T3a	Tumor invades perivesical tissue microscopically
T3b	Tumor invades perivesical tissue macroscopically
T4a	Tumor invades prostate, uterus, or vagina
T4b	Tumor invades pelvic or abdominal wall

### *Preparation*

Patients were examined in a supine position. Adequate bladder distension is crucial for better bladder wall assessment, particularly for carcinoma staging, as both under and over dis-

tension can give erroneous false results. Asking patients to void and then not to void again for 2 hours (range of 1 to 3 hours) before examination, or clamping the Foley catheter for 2 hours, results in optimal bladder distension in most patients. All patients were asked not to eat for at least 4 hours before the examination, because of the administration of intravenous contrast. Bowel peristaltic artifact is reduced with anti-peristaltic agents – we used 1 mg glucagon or 20 to 40 mg Buscopan intravenously, administered immediately before scanning.

#### *CT Scanning*

CT studies were performed with a MDCT scanner. Siemens Volume Zoom – 4 Slices, SYNGO Software (Gantry rotation speed of 0.6s, tube voltage of 120 kV, tube current 280 mAs, collimation of 2.5 mm, and pitch of 1). Iodinated contrast material was administered intravenously as 80 ml of iodinated contrast (Omnipaque 300). Oral contrast material was administered as 500 ml of 2% solution of gastrographin, 30–60 min prior to the examination. Imaging of the urinary bladder was performed 60 sec after completion of contrast injection. Scanning started from the symphysis and upwards, in incremental contiguous sections of 3 mm.

#### *MR Imaging*

MR studies were performed at 1.5 T on a Magnetom Avanto (Siemens) with a phased-array pelvic coil. Conventional T1-weighted spin-echo images (TR/TE, 550/9; 512 × 192 matrix; 20 cm field of view; 6 mm section thickness; 2 mm intersection gap; 4 signals acquired) and T2-weighted fast spinecho images (TR range/TE range, 4.000–5.500/80–120; 256 × 256 matrix; 24 cm field of view; 6 mm section thickness; 2 mm intersection gap; 4 signals acquired) were obtained. Subsequently, fast multiplanar spoiled gradient-echo images with fat suppression (180–300/1.7–4.2; 70° flip angle; 512 × 92 matrix; 20 cm field of view; 6 mm slice thickness; 2 mm intersection gap; 2 signals acquired) were obtained in the axial plane after intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin). Imaging was repeated three times per 20 seconds at the same section, and the total imaging time of the dynamic study was approximately 1 minute. Sagittal and coronal gado-

linium-enhanced images were added if the tumour was located in the base or the dome of the bladder.

#### *Parameters*

Both T1 and T2-weighted sequences are necessary for complete examination. T1-weighted images are the best sequences for evaluating tumour extension into the adjacent bright fat, lymphadenopathy detection, and bone marrow involvement. There is better delineation of bladder cancer from urine with T2-weighted images. Presently, fast SE is state of the art for obtaining T2-weighted images of the pelvis. Coronal images are particularly useful in seminal vesicle and lateral wall neoplasm assessment, while sagittal images are useful in the assessment of posterior and anterior wall tumours.

Dynamic gadolinium-enhanced images should be performed in a plane perpendicular to the tumour-wall interface. Contrast administration and fast dynamic imaging improves the ability of MRI to detect and stage bladder cancers. Most carcinomas enhance intensely following intravenous contrast material administration, earlier than the muscle layer because the early distribution of contrast medium follows the abundance of vascular beds [9].

#### *Image Analysis*

Staging criteria similar to those described in the literature were used for CT (10–15) and MR imaging (13–19). For CT, a pedunculated lesion was classified as T<sub>i</sub>; a sessile lesion as T<sub>2</sub>; a sessile lesion with wall thickening but without perivesical infiltration as T<sub>3a</sub>; a lesion with an irregular, shaggy outer border and streaky areas of higher attenuation in perivesical fat as T<sub>3b</sub>; and an invasion of adjacent organs as T<sub>4</sub>. The same classifications were applied to T<sub>i</sub>-weighted MR images. For T<sub>2</sub>-weighted and contrast-enhanced MR images we used criteria based on the assessment of the linear hypointensity of the muscle layer. On dynamic MR images, bladder tumours, mucosa, and submucosa (lamina propria) are enhanced, but the muscle layer maintains its hypointensity immediately after gadopentetate dimeglumine injection. Thus an intact, low-signal-intensity muscle layer at the base of the tumour was classified as T<sub>i</sub>; an irregular inner margin of low-signal-intensity muscle layer was T<sub>2</sub>; a disrupted low-signal-intensity muscle layer without

perivesical infiltration was T3a, T3b lesions showing abnormal intensity in perivesical fat and invasion in adjacent organs is classified as T4. Lymph nodes were considered abnormal if the minimum transverse diameter was equal to or greater than 1 cm. Distant metastases were not evaluated in this study. A comparison of imaging findings and histopathologic staging (the extent of the bladder tumour was assessed by evaluation of the resected bladder and perivesicular tissues after total cystectomy and of tumour specimens with muscle structure after transurethral resection) was subsequently performed.

Statistical analysis and data processing was made based on the statistical program SPSS 13.0 for Windows. The distribution of the data

is presented in absolute and relative numbers. To test the differences between the three diagnostic methods we used the Chi-square test and tested for difference between two proportions. Values of  $p < 0.05$  were considered statistically significant and values of  $p < 0.01$  were considered as highly statistically significant.

The data are presented in tables and graphics.

### Results

Comparison of staging accuracies of contrast-enhanced CT, conventional MR imaging and dynamic MR imaging with histopathological findings, according to the level of the TNM staging system, is presented in Table 2.

Table 2

*Comparison of staging accuracies of contrast-enhanced CT, conventional MR Imaging, and dynamic MR imaging with histopathological findings, according to the level of the TNM Staging System*

Stage	HPF	CT	Conventional MRI	Dynamic MRI
pTa – pT1	48 (53.3%)	33/48 (68.8%)	32/48 (66.7%)	45/48 (93.7%)
pT2	20 (22.2%)	4/20 (20%)	7/20 (35%)	14/20 (70%)
pT3a	5 (5.5%)	0/5 (0)	0/5 (0)	2/5 (40%)
pT3b	9 (10%)	6/9 (66.7%)	5/9 (55.5%)	9/9 (100%)
pT4	8 (8.8%)	7/8 (87.5%)	7/8 (87.5%)	8/8 (100%)
All	90/90 (100%)	50/90 (55.6%)	51/90 (56.7%)	78/90 (86.7%)

Note-Numbers in parentheses are percentages.

As is shown, pTa and pT1 is a histopathological stage determined in 48 (53.3%) of the total number of patients evaluated in the study. This histopathological stage, was confirmed in 33 (68.8%) patients with CT, with conventional MRI was confirmed in 32 (66.7%) patients, and with dynamic MRI in 45 (93.7%) patients.

A histopathological stage pT2 was determined in 20 (22.2%) of the total number of patients evaluated in the study. This histopathological stage was confirmed in 4 (20%) patients with CT, with conventional MRI it was confirmed in 7 (35%) patients and with dynamic MRI in 14 (70%) patients.

A histopathological stage pT3a was determined in 5 (5.5%) of the total number of patients evaluated in the study. In our study, was not confirmed any patient with this histopatholo-

gical stage with CT and with conventional MRI, but with dynamic MRI, T3a was confirmed in 2 (40%) patients.

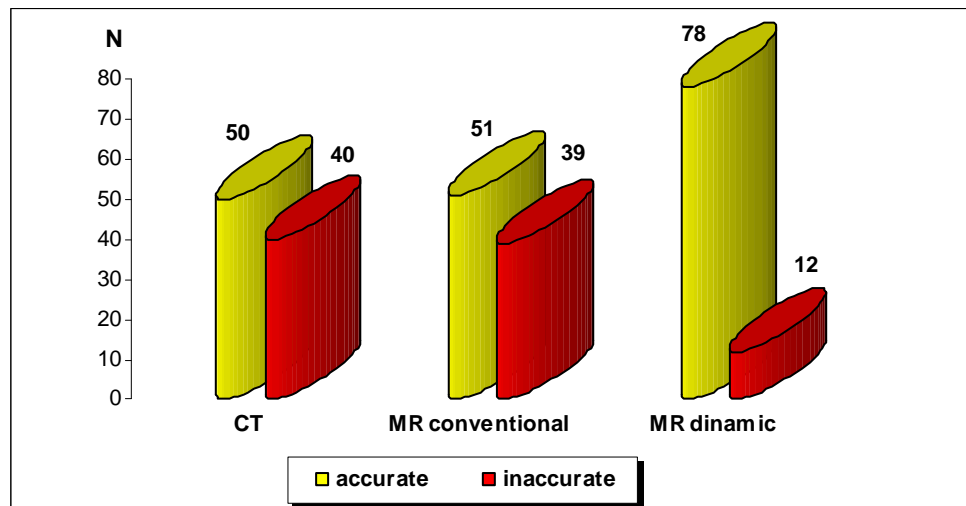
A histopathological stage pT3b was determined in 9 (10%) of the total number of patients evaluated in the study, with CT it was confirmed in 6 (66.7%), with conventional MRI it was confirmed in 5 (55.5%) patients and with dynamic MRI in 9 (100%) patients.

A histopathological stage pT4 was determined in 8 (8.8%) of the total number of patients evaluated in the study. This histopathological stage was confirmed in 7 (87.5%) patients with CT, with conventional MRI it was confirmed in 7 (87.5%) patients and with dynamic MRI it was confirmed in all 8 (100%) patients.

Dynamic MR imaging showed the best accuracy in all stages. It allowed total accuracy of 87% (78 of 90) in staging of bladder tu-

mours, which was highly significant compared with CT (55%; 50 of 90) ( $p < 0.001$ ) and compared with conventional MR imaging (57%; 51

of 90) ( $p < 0.001$ ). There was statistically no significance in the accuracy of CT /conventional MR ( $p > 0.05$ ) (Table 2 and Figure1).



CT / conventional MRI	Chi-square = 0.02	df = 1	p = 0.88	p > 0.05 N. Sig.
CT / dynamic MRI	Chi-square = 21.2	df = 1	p = 0.000004	p < 0,001
Conventional MRI / dynamic MRI	Chi-square = 19.95	df = 1	p = 0.000008	p < 0,001

Fig. 1 – Graphic presentation of accurate and inaccurate findings analyzed with contrast-enhanced CT, conventional MR Imaging, and dynamic MR imaging compared with hystopatological findings

To assess the contribution of each imaging method to staging, we also investigated the percentage of over- and underestimation, but the data were regrouped to evaluate the accuracy of each imaging in distinguishing superficial (pT1) from invasive (pT2-pT4) tumours with pathological confirmation as a gold standard. Overestimation of superficial tumours or under-estimation of invasive tumours should be particularly avoided, since only pT1 and less severe lesions can be treated with transurethral resection, and partial or total cystectomy and adjuvant therapies are usually intended for tumours beyond stage pT2.

In terms of surgically proved pT1 lesions, overestimation was high with CT (15 of 48; 31.25%) and conventional MR imaging (12 of 48; 25%), but was significantly reduced with dynamic MR imaging (4 of 48; 8.3%), with high significance  $p < 0.001$  ( $p = 0.0058$ ) for CT vs dynamic MRI and  $p < 0.05$  for conventional MRI /dynamic MRI ( $p = 0,027$ ). The percentages of underestimation in surgically proved invasive tumours (pT2- pT4) were lowest with dynamic MR imaging, with high significance  $p < 0.001$  for CT/dynamic MRI ( $p = 0.0006$ ) and  $p = 0.002$  for conventional MRI/dynamic MRI (Table 3).

Table 3

Over and underestimation findings with CT, Conventional MRI and Dynamic MRI in distinguishing superficial (pT1) from invasive (pT2-pT4) tumors

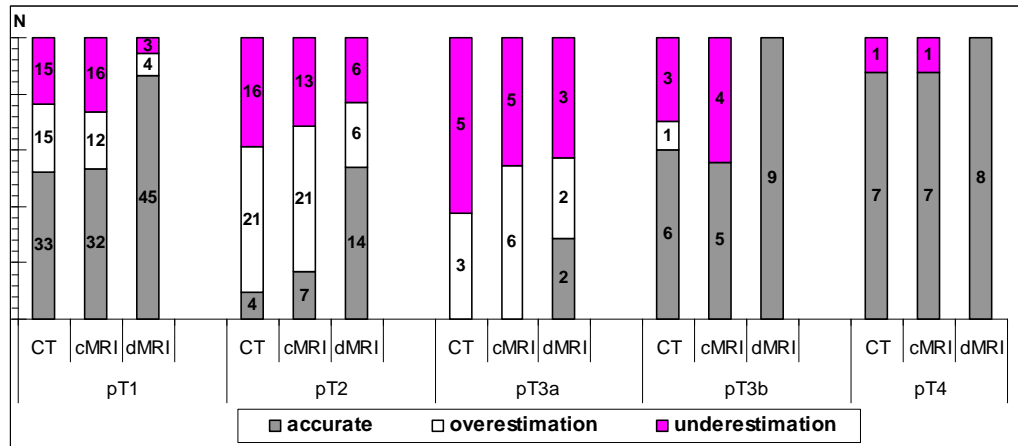
Imaging method	Overestimation of T1	Underestimation of T1
CT	15 / 48 (31.25%)	25 / 42 (59.5%)
Conventional MRI	12 / 48 (25.0%)	23 / 42 (54.8%)
Dynamic MRI	4 / 48 (8.3%)	9 / 42 (21.4%)

Figure 2 shows the number of accurate T stage, over- and underestimation with all three

radiological investigations. We can note a large number of over- and underestimation findings

with CT and conventional MRI in the determination of pT2 and pT3a stages, and very good results with all three investigations in determined pT3b, and especially pT4, where dynamic

MRI correctly determined all patients with perivesical infiltration and invasion into adjacent organs.



Note-N – number of radiological findings, with histopathologic confirmation as a gold standard

Fig. 2 – Staging accuracies of contrast-enhanced CT, conventional MR imaging (cMRI) and dynamic MR imaging (dMRI)

## Discussion

The results of our CT study, 55% accuracy for all stages, were mainly due to poor distinction between pT1, pT2 and pT3a lesions. It is generally accepted that CT fails to distinguish the intramural extent of bladder tumors [20]. Computed tomography is unable to differentiate between stages pTa to pT3a, but it is useful for detecting invasion into the perivesical fat (pT3b) and adjacent organs [21]. In our study, CT has a 31.2% overestimation of pT1 and 59.5% underestimation of pT2-pT4 stage, but correctly recognized 7 of 8 patients (87%) with pT4. The accuracy of CT in determining extravesical tumour extension varies from 55% to 92% [22] and increases with more advanced disease [23].

MR imaging has been shown to allow more accurate staging of bladder carcinomas than CT because of its high soft-tissue contrast resolution, multiplanar capability, and the possibility of dynamic contrast-enhanced MRI to differentiate bladder tumour from surrounding tissues because enhancement of the tumour occurs earlier than the normal bladder wall due to neovascularisation. The accuracy of MRI for primary tumour staging varies from 73% to 96%, and these values were 10–33% higher than those obtained with CT [24].

In our study, accuracy of staging with conventional MRI has no significant differences compared with CT ( $p > 0.05$ ), but accuracy of staging with dynamic contrast-enhanced MR imaging was significantly ( $p < 0.001$ ) increased and overestimation was significantly ( $p < 0.001$ ) decreased in comparison with accuracy with CT and conventional MR imaging, precisely because of the enhancement of bladder carcinomas, mucosa and submucosa earlier than the muscle layer which maintains its hypointensity and enhances late (60 sec after contrast injection) [25].

## Conclusions

Conventional CT and MR imaging are only moderately accurate in the diagnosis and local staging of bladder cancer; cystoscopy and pathologic staging remain the standards of reference.

CT and MR imaging are known to be relatively accurate in the evaluation of perivesical tumour extension (pT3b) and invasion into adjacent organs (pT4), but both modalities are less accurate in the evaluation of the depth of mural invasion and for both techniques overstaging is the most frequent error.

Dynamic contrast-enhanced MRI with 87% of accuracy, 8.3% overestimation for superfi-

cial tumours and lowest underestimation for invasive tumours, make this imaging considerably more accurate.

So, whole-body CT is the primary imaging technique for detecting metastases in affected patients, especially those with muscle-invasive disease, but MRI is a method of choice and promising technique for imaging bladder tumours, not only because of its high soft-tissue contrast resolution, spatial resolution, multiplanar capabilities, the availability of no ionizing radiation and a non-nephrotoxic contrast agent, but because performing dynamic contrast-enhanced images make it more so, respectively.

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Резиме

**КОМПЈУТЕРСКА ТОМОГРАФИЈА  
ИЛИ МАГНЕТНА РЕЗОНАНЦА  
– НАШИ ИСКУСТВА ВО ОДРЕДУВАЊЕТО  
НА ТНМ СТЕЈДИНГОТ  
НА КАРЦИНОМОТ НА МОЧНИОТ МЕУР**

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Карциномот на мочниот меур е деветта  
честа малигна дијагноза во светот. Раната дија-  
гноза на болеста е важна, бидејќи и до 47% од  
смртноста предизвикана од оваа болест може да  
биде избегната.

*Цел на истражувањето:* Да ги покаже нашите  
искуства во одредувањето на точноста на стеј-  
дингот на карциномот на мочниот меур со мул-  
тидетектор компјутерска томографија (МДКТ),  
конвенционална магнетна резонанца (МР) и ди-  
намична постконтрастна магнетна резонанца, од  
една страна и патохистолошката дијагноза по  
трансуретрална ресекција на неинвазивните карци-

номи на мочниот меур или по радикална цистек-  
томија кај пациенти со мускулна инвазија на  
карциномот.

*Материјал и методи:* Деведесет пациенти  
со хистолошки докажан карцином на мочниот  
меур беа прегледани со МДКТ, конвенционална  
МР и динамична постконтрастна МР пред ту-  
морската ресекција.

*Резултати:* Стејдингот беше потврден кај  
55,6% од пациентите со МДКТ, 56,7% со кон-  
венционална МР и кај 86,7% од пациентите со  
динамична постконтрастна МР, што е високо  
сигнификантна разлика компарирано со МДКТ  
и конвенционална МР. Преценетите наоди за  
суперфицијалните тумори беше висока со КТ  
(31,25%) и конвенционална МР (25%), но беше  
сигнификантно намалена со динамичниот МР  
имицинг (8,3%). Процентот на потценетост во  
однос на хируршки потврдените инвазивни ту-  
мори (pT2-pT4) беше најниска со динамичниот  
МР имицинг.

*Заклучок:* КТ и МР се методи со помала  
точноста во евалуацијата на длабочината на му-  
ралната инвазија и за двете техники на испиту-  
вање лажно позитивните резултати се честа  
грешка. Динамичниот постконтрастен МР со 87%  
точноста, 8,3% преценетост на резултатите за су-  
перфицијалните тумори и најмалку лажно нега-  
тивни резултати за инвазивните тумори, ја прави  
оваа метода значително потточна.

**Клучни зборови:** карцином на мочен меур, мулти-  
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