

Detection of early DJ-stent encrustation by sonographic twinkling-artifacts – a pilot study

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Introduction Ureter obstruction caused by a retro-peritoneal tumor is treated by inserting an indwelling ureter splint (DJ-stent). Indwelling duration is limited by cumulative crystalline deposits into the splint, eventually causing the repeated impairment of urine flow. Deciding when a DJ-stent must be replaced is important since belated removal can be accompanied by severe complications. X-ray or conventional sonography do not allow satisfactory evaluation of early incrustation, therefore, the use of sonographic twinkling artifacts (TA) to provide accurate stent surveillance was investigated.

Material and methods 26 patients with indwelling ureter splints carrying a high risk of developing tumor lysis syndrome (TLS), which is often accompanied by early splint incrustation, were investigated utilizing TA the day after DJ-stent implantation and weekly thereafter. Serum creatinine, uric acid, and urine pH were measured at all TA exams.

Results Early incrustation of the ureter splint was detected by TA in all patients 1–4 weeks after implantation. Incrustation occurred sooner with increased uric acid levels, and high creatinine or acidic urine accelerated early implant incrustation.

Conclusions TA can be used to monitor early crystalline deposits in implanted ureter splints, before they can be detected by conventional sonography or X-ray imaging and before complications occur.

Key Words: twinkling-artifact ↔ DJ-stent ↔ stent incrustation ↔ encrusted urologic implant
↔ color Doppler ↔ tumor lysis syndrome ↔ hydronephrosis

INTRODUCTION

Impaired upper urinary tract urine flow is often caused by ureter obstruction due to retro-peritoneal metastatic cancer. Obstruction generally begins with pain, then with loss of renal function due to long-lasting congestion, acute or chronic renal insufficiency and/or hydronephrosis of the infected kidneys and may end with generalized sepsis. Indwelling ureter splints consisting of polyurethane, silicon, or other polymers are placed to restore urine flow from the renal pelvis to the bladder

but gradually become encrusted with crystalline deposits, which can ultimately result in renewed flow obstruction.

Routinely, indwelling ureter splints are monitored sonographically or by X-ray to detect renewed urinary congestion due to stent obstruction by crystalline deposits. However, early crystalline implant deposits cannot be detected by X-ray, presumably due to low spatial resolution and radiolucency of the deposited material. Conventional ultrasonography also does not allow satisfactory evaluation of early incrustation. Severe complications of ‘for-

gotten' incrustrated DJ-stents have been described and continuous monitoring of implanted material and removal or exchange as early as possible is recommended [1].

In vascular Doppler sonography, the 'glittering artifact' (= twinkling artifact, TA) appears as a color Doppler signal at atheromatous plaque, calcified cardiac valves [2, 3], and also at other calcified body structures. Here, the Doppler signal falsely indicates turbulent current, thus limiting the correct assessment of vascular circulation. However, twinkling artifacts were employed in 2013 to detect early incrustation of a nephrostomy catheter by TA [4] and, with minor sonographic parameter modification in the color Doppler mode, they can be used to detect minimal ureter splint incrustation.

Ureter splints are particularly susceptible to crystalline deposits in patients with tumor lysis syndrome (TLS). During TLS the high filtration rate of uric acid exerts a severe burden on the kidneys and becomes a decisive factor contributing to impaired renal function that can culminate in renal failure. Clinically manifested TLS is a life-threatening complication of tumor chemotherapy and results in a high dialysis rate [5]. One option of lowering uric acid is to inhibit xanthine oxidase with allopurinol, as far as the nephrotoxicity of allopurinol will allow, at which point the allopurinol dosage must be reduced. Another option is to employ rasburicase, a synthetic recombinant urate oxidase, transforming uric acid into the more water-soluble allantoin. In 2001, a randomized study [6] demonstrated higher rasburicase efficacy compared to that of allopurinol. Although treatment with rasburicase significantly reduces renal complications, including the necessity for dialysis [7], the high therapeutic cost of rasburicase limits preventive application prior to the occurrence of TLS. Therefore, an easily applied, inexpensive technique to identify stent incrustation in time to prevent complications is important.

The present study aimed to employ TA to detect early ureter splint incrustation in oncologic patients and to follow blood and urine parameters, which might correlate with ureter splint incrustation.

MATERIAL AND METHODS

Material

Twenty-six oncologic patients with implanted DJ stents (DJ-stent; 7/28 DJ, Optimed, Ettlingen, Germany) and receiving chemotherapy or combined radio/chemotherapy and at high risk for developing tumor lysis syndrome (TLS) were included

in the investigation. The patients were hospitalized due to routine change of their ureter splints or to change their ureter splints because of presenting complications such as flank pain. Sonographic examination employing twinkling artifacts took place the day after implantation and then at weekly intervals. Serum creatinine and uric acid as well as urine pH were also measured on the day of stent implantation and weekly thereafter. Patients with initially evident TLS, increased blood levels of uric acid (>6 mg/dl) or manifest symptoms of TLS were excluded from the study. Removal of the newly implanted stent was not influenced by the detection of TAs, but was initiated according to customary diagnostic procedure. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this retrospective type of study formal consent was not required.

Twinkling artifact ultrasonography

Ultrasonography was carried out with an Acuson Sequoia 512™ ultrasound system with the following transducers: 4V1™ (range 4/3/1.75), 4C1™ (range 4/3/1.75), 6C2™ (range 5/3.5/2.5 used for very slim patients) (Siemens, München, Germany) (normal frequency on color Doppler in MHz). The following defined parameters and structured procedure ensured targeted, reproducible TAs, which could be distinguished from signals stemming from blood flow. 'Velocity' instead of 'power mode' was chosen for color Doppler imaging (CDI). Depending on the transducer, the nominal frequency was selected at the lowest possible MHz level. A high pulse repetition frequency (PRF, cm/sec) was selected on the velocity scale. Signal gain uptake was enhanced for all frequencies. Transmitting focus on a particular site is essential at highest acoustic energy and post-processing with color variance (CDVV) must be turned on to distinguish TA arising from blood vessels. These parameters were not only employed for implanted stents in patients, but also in a water bath for new, unused DJ-stents and stents after removal from the urinary tract.

Infrared spectroscopy

Infrared spectroscopy (FT/IR 4100, Jasco, Groß-Umstadt, Germany) was used to analyze the incrustation material scratched from ureter splints after explantation.

Statistics

The command variable (time for twinkling artifacts to appear after implantation, revealing incrustation) and cause variables (sex, age, pH of urine, uric acid and creatinine) were correlated by Spearman correlation and nonparametric biserial correlation (sex) [8]. Since three censored data existed (time to appearance of incrustation >12 weeks after implantation) the significance of the five cause variables was calculated by Cox-regression including backward elimination (Wald-statistics). The criterion of elimination was 10% [9].

RESULTS

No twinkling artifacts were detected in new, unused DJ-stents investigated in a water bath. After incrustated implanted stents had been removed from the urinary tract and were investigated in a water bath, TAs exclusively and reproducibly were visible where crystals had been deposited and did not appear on the stent material itself (Figures 1A and 1B).

One to four weeks after implantation minimal TA activity was apparent at the indwelling splints in all patients (Figure 1B). None of the patients developed clinically manifest TLS with the need for dialysis. Incrustation was rapidly progressive in patients with increased serum uric acid and creatinine. A further predictive factor for stent incrustation was acidic urine (Table 1).

Extremely early incrustation of the ureter splint was found in one patient (metastasizing urothelial carcinoma) with uric acid increased to 11.7 mg/dL, slightly acidic urine (pH 6.0) and compensated renal insufficiency of a single kidney with serum creatinine of 2.9 mg/dL. After one week of implantation, the indwelling ureter splint already displayed distinct TAs at the distal end of the stent inside the bladder and in the intramural course of the ureter (Figure 1C). This ureter splint required change at this time, since renewed obstruction of the upper urinary tract was diagnosed with conventional ultrasonography.

Incrustations scratched from the ureter splints were predominantly identified as phosphates (struvite, apatite), uric acid and oxalates (whewellite, weddellite). Mixed deposits were also found. Struvite deposits often occurred with concomitant infection of the urinary tract (biomatrix). Xanthine or cystine incrustation was not found in any of the patients.

Repeated X-ray examination of clearly incrustated stents, which had been explanted, revealed no deposits. Incrustation had previously been identified by TA while these splints were indwelling (example: Figures 1D, 1E).

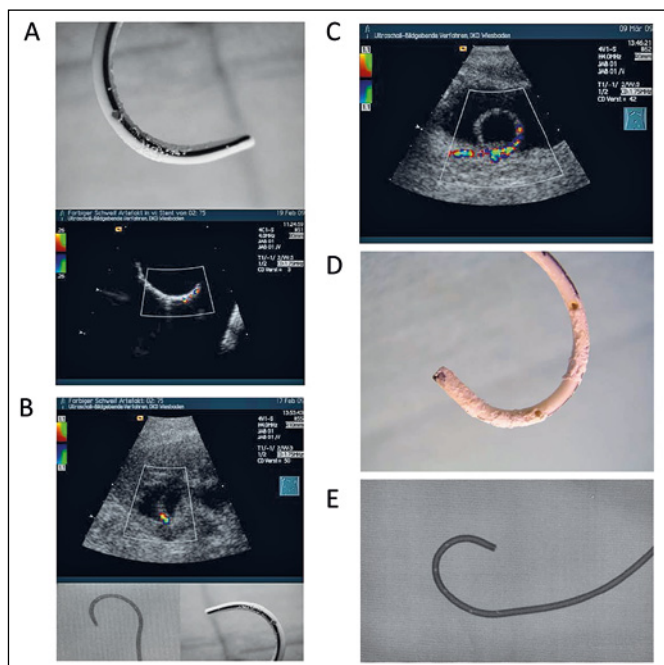


Figure 1. Minor stent incrustation at the distal end (urinary bladder) of a DJ-stent, removed six weeks after implantation (upper picture). Twinkling artifacts (TAs) appear as colored spots on the pigtail, but not on the polyurethane stent itself (lower picture). Sonography in water bath. B. Minimal stent incrustation of intra-renal pigtail (upper picture). Lower picture, right shows stent after explantation. Lower picture left, is X-ray image of the same explanted stent. Incrustation is not apparent. C. Distinct TA at the distal intra-vesical pigtail of the ureter splint (urinary bladder) with detectable incrustation in the intramural course of the ureter (extra-luminal). D. Explanted ureter splint with massive incrustation (primarily phosphates). E: X-ray image of the same explanted ureter splint (D) showing no visible incrustation.

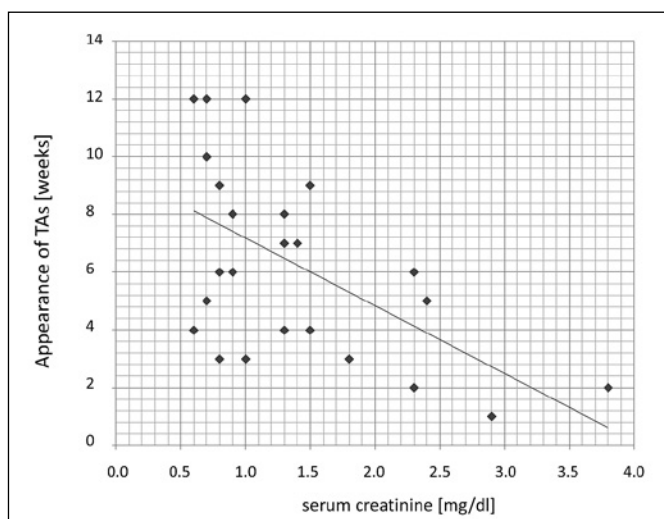


Figure 2. Time between stent placement and appearance of twinkling artifacts (TAs) as a function of serum creatinine.

A significant correlation was apparent between the serum creatinine level and the time it took after stent implantation for TAs to appear, indicating incrustation (correlation coefficient of -0.54) (Figure 2). Creatinine was the only significant variable ($p = 0.000386$). All other cause variables had no significant influence on the time it took after stent implantation to identify incrustation by TAs.

DISCUSSION

Conventional X-ray imaging cannot be used to detect stent incrustation since uric acid crystals are X-ray translucent. Conventional sonographic monitoring of the kidneys in patients with an indwelling stent

can only differentiate between renewed urinary congestion due to obstruction by stent incrustation or manifest urolithiasis. During conventional color Doppler sonography it was noted that colored spots, dubbed twinkling artifacts, appeared on crystalline surfaces such as arterial plaque or kidney stones [5, 10, 11]. These artifacts are common enough to cause considerable misinterpretation of flow where atheromatous vascular plaque occurs [3]. However, with specific defined sonographic parameter selection it is possible to utilize twinkling artifacts to locate even minor incrustation in indwelling ureter splints. Patients with impaired urine flow of the upper urinary tract and severe tumor load, require ureter splint implantation, and face increased risk

Table 1. Appearance of twinkling artifacts (TAs) in indwelling ureter splints as well as urine pH and serum levels of uric acid and creatinine

Male	Female	Age (years)	Disease	TA-appearance (weeks after implantation)	pH of urine	Uric acid [mg/dL]	Creatinine [mg/dL]
X		33	seminoma	3	5.0	6.2	1.0
X		45	seminoma	7	6.5	6.6	1.4
X		54	RCC, c.a. KTX	5	6.0	9.6	2.4
X		58	RCC	6	7.5	7.1	2.3
X		75	urothel-Ca	4	5.0	4.1	0.6
	X	62	ovarial-Ca	3	6.0	7.2	0.8
	X	64	ML	5	5.5	6.8	0.7
X		77	bronchial-Ca	8	6.5	7.3	0.9
X		73	ALL	10	5.5	6.7	0.7
X		53	CLL	>12	7.0	7.4	0.7
	X	85	NHL	8	6.5	5.1	0.9
X		65	CUP	4	7.5	10.2	1.3
	X	56	vaginal-Ca	>12	7.0	5.8	0.6
X		76	colon-Ca	3	5.5	7.8	1.8
X		66	GIST	4	5.5	7.2	1.5
	X	68	CUP	8	7.0	6.3	1.3
X		71	GIST	7	8.0	7.2	1.3
	X	59	CUP	10	5.5	6.2	0.7
X		60	colon-Ca	2	7.0	9.7	3.8
X		77	AML	>12	6.5	5.8	1.0
X		66	CUP	9	5.5	7.4	1.5
	X	56	vaginal-Ca	6	6.0	2.3	0.8
X		73	urothel-Ca	1	6.5	11.7	2.9
	X	86	NHL	2	6.0	5.5	2.3
	X	57	ovarial-Ca	6	7.0	6.2	0.9
	X	48	NHL	9	5.5	4.7	0.8

RCC – renal cell carcinoma; c.a. KTX – condition after kidney transplantation; Ca – carcinoma; leukemias (among others), ML, ALL, CLL, NHL, AML; CUP – cancer of unknown primary; GIST – gastrointestinal stroma tumor

of splint incrustation. Tumor lysis syndrome (TLS), resulting from the breakdown of dying cells induced by successful cancer treatment manifests itself with high phosphate and uric acid levels in both blood and urine. Resulting splint incrustation from crystalline deposits can lead to severe urinary tract complications, including lumen obstruction and renewed kidney congestion. Incrustation and protein precipitates in the implant can also lead to an infected biomatrix, possibly causing a urinary tract infection culminating in sepsis, particularly in immunocompromised patients.

This investigation shows that serum creatinine negatively correlates with the time it takes for TAs to become apparent during examination of the ureter stent: the higher the creatinine, the less time it takes for TAs revealing incrustation to appear. This implies that patients with normal kidney function have a significantly lower risk for DJ-stent incrustation, while patients with renal insufficiency could require more frequent monitoring by means of TA.

A DJ-stent should be removed before the stent becomes highly incrustated. Removing a highly incrustated DJ-stent can cause complications including mechan-

ical strain to the urothelium, injuries, consecutive strictures, bleeding, impossible stent removal or ureter avulsion [12]. Since TAs appear as a result of minute incrustation, but minute incrustation does not obstruct urine flow, identification and establishment of the rate of increase can facilitate decisions about removal, so that complications do not become manifest.

CONCLUSIONS

This investigation shows that the use of sonographic twinkling artifacts may be especially useful in cases where a high rate of ureter stent incrustation can be expected, such as in patients at risk for tumor lysis syndrome.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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