

Analysis of prognostic factors in patients diagnosed with bladder cancer complicated by hemorrhage treated by drug-eluting bead embolization

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Background: Transcatheter bladder arterial chemoembolization (TACE) is an alternative treatment used to control bladder cancer (BC) with bleeding, especially in older adult patients with comorbidities. This retrospective observational study evaluated the effect and prognostic factors of transcatheter drug-eluting bead (DEB) embolization in patients with advanced BC.

Methods: We assessed 39 patients diagnosed with BC with hemorrhage who were either inoperable or unwilling to undergo surgery at our hospital between January 2018 and October 2022. All patients underwent TACE by DEB loaded with epirubicin and imaging scans after 2 months to evaluate the curative effect according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) standard to determine treatment. Re-examination and follow-up were performed every 3–6 months to observe hematuria recurrence and the curative effect.

Results: A total of 95 interventional treatments were performed in 39 patients, and all participants achieved complete hemostasis within 5 days after the first intervention. Computed tomography or magnetic resonance imaging showed that the total effective rate [complete response (CR) + partial response (PR)] was 64.1%, and the disease benefit rate (CR +PR + stable disease) was 79.5%. A total of 30 patients (76.9%) had no hematuria recurrence. Logistic regression analysis indicated that the type of blood supply in BC may relate to whether the patients benefited from the intervention. Hematuria recurrence was significantly associated with the total number of tumors and the type of blood supply (P<0.05).

Conclusions: Superselective embolization of bladder arteries with DEB can be used to treat BC with hemorrhage. However, hypovascular tumor blood supply may result in poor postoperative efficacy and hematuria recurrence. Additionally, multiple bladder tumors may be a risk factor for hematuria recurrence.

Keywords: Drug-eluting bead (DEB); bladder cancer (BC); hemorrhage; superselective embolization; prognostic factors

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Introduction

Background

Bladder cancer (BC) is the most common neoplasm of the urinary system, with the global incidence ranking fourth among malignant tumors in males and seventh for mortality (1). Over 70% of all bladder tumors may present with hematuria nowadays. Most patients with BC complicated with gross hematuria have muscle-invasive BC (MIBC) and are thus unsuitable for treatment with transurethral resection of bladder tumor (TURBT) alone. Imaging usually indicates the cancer is in stage T2-T4. Therefore, radical cystectomy is standard treatment. However, due to surgical morbidity, a high recurrence rate, and potential decline in quality of life postoperatively, patients and physicians are faced with a challenge concerning the benefit of surgical resection (2). Transcatheter bladder arterial chemoembolization (TACE) is an alternative treatment used to control hematuria from BC, especially in elderly patients or those with multiple underlying diseases. Currently, short-term hemostasis in the treatment of BC by embolization using common embolic agents has been reported to have an effective rate of 75-100% (3). However, during the treatment period, it may be necessary to repeatedly intervene with embolization in a short period of time to improve the control over the bladder tumor and to prolong the control of hematuria. Multiple intubations can lead to bladder arterial injury, affecting follow-up interventional therapy. Drug-eluting

Highlight box

Key findings

• Superselective embolization of bladder arteries with drugeluting bead (DEB) can be used to treat bladder cancer (BC) with hemorrhage. However, the hypovascular type of tumor blood supply may result in poor postoperative efficacy and hematuria recurrence. Additionally, multiple bladder tumors may be a risk factor for hematuria recurrence.

What is known and what is new?

- Superselective embolization of bladder arteries was widely used to treat BC with hemorrhage.
- DEB-transcatheter bladder arterial chemoembolization is safe and effective in BC, however, few such cases have been reported in clinic currently.

What is the implication, and what should change now?

• Superselective embolization of bladder arteries with DEB can be used to treat BC with hemorrhage.

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beads (DEBs) loaded with epirubicin have been widely used in the embolization of solid tumors and have achieved good results owing to the dual effects of embolization and chemotherapy (4,5).

Rationale and knowledge gap

DEBs are regarded as a new type of embolization agent. They can be loaded with chemotherapy drugs that are slowly released after being administered to tumor blood vessels via catheters. Simultaneously, local highconcentration chemotherapy drugs remain in prolonged contact with tumor cells rather than entering the systemic circulation. This improves the anti-tumor effect and reduces the adverse reactions caused by the administration of chemotherapy drugs. Therefore, DEB has been widely used in solid tumors such as primary liver cancer and has achieved good therapeutic response for dual effects of embolization and chemotherapy (4,6). However, it is currently uncommon to use DEB in BC. In this study, we administered DEB to patients with advanced BC accompanied by hematuria, aiming to control hematuria as well as tumor progression and provide a palliative alternative for clinical treatment.

Objective

This study aimed to analyze the beneficial effects of DEB embolization in patients with advanced BC to identify factors affecting prognosis and better guide clinical treatment. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-506/rc).

Methods

General information

Thirty-nine patients with BC complicated by hematuria and who successfully underwent DEB-TACE between January 2018 and October 2022 were included in this study. All patients underwent a pelvic magnetic resonance imaging (MRI) or computed tomography (CT) plain scan, enhanced examination, and obtained informed consent prior to the interventions. Inclusion criteria: (I) preoperative CT or MRI scan and pathology showed BC; (II) Complicated by hematuria; (III) refused surgical treatment; (IV) none of the patients had a history of bladder radiotherapy, chemotherapy, immunotherapy, or treatment with traditional Chinese medicine prior to DEB embolization. Exclusion criteria: (I) tumor cachexia; (II) severe organ insufficiency; (III) allergic to contrast media; (IV) a mental disorder resulting in failure to cooperate with treatment. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Affiliated Hospital of Putian University (No. 2022079). Informed consent was taken from all the patients.

Study methods

Interventional procedures

DEB-TACE was only considered for the included patients when the patient, urologist and family members agreed that no surgical intervention was possible. The groin was disinfected and draped, the femoral artery sheath was locally anesthetized with 2% lidocaine, and the modified Seldinger technique was used to puncture the femoral artery. A 5-F arterial sheath was placed, and the guide wire was introduced into a 4-F Robert uterine artery catheter or 4-F catheter under fluoroscopy. Cobra catheters were superselectively inserted into the anterior trunk of the bilateral internal iliac arteries. Following the angiographic confirmation, 40-60 mg cisplatin was cautiously administered for chemotherapy infusion (specific dose was based on the body surface area), considering the superior gluteal artery localization. DC Bead embolization microspheres sized 100-300 µm (1 bottle of drug-loaded microspheres loaded with 75 mg epirubicin) were selected for chemoembolization. After perfusion chemotherapy, a 2.1-F microcatheter (Ept) was used to superselect the supplying artery of the bladder tumor under the guidance of the road map, and the drug-loaded microspheres with epirubicin were slowly injected under fluoroscopy at an injection speed of 1-2 mL/min until the tumor was displayed. The embolization endpoint was defined by the disappearance of the tumor staining or the slow disappearance of the injected contrast agent after 5 cardiac cycles.

Postoperative follow-up and analysis of influencing factors

CT or MRI scan was performed 2 months after the first interventional treatment, and the curative effect was evaluated by the modified Response Evaluation Criteria in Solid Tumors (mRECIST) standard. If the response was 1699

found to be a progressive disease (PD) or the lesion was still significantly enhanced on imaging, re-intervention treatment was considered. Thereafter, a re-examination was performed every 3-6 months. We determined the next step of treatment by repeating follow-up visits to observe the recurrence of hematuria and therapeutic effect (Figures 1,2). We recorded the factors that may affect BC prognosis after intervention, including age, sex, comorbidity, hydronephrosis, tumor size, number of lesions, T stage, pelvic lymph node metastasis, pathological type, and tumor blood supply type. For the latter, the imaging diagnostic criteria of hypovascular BC [i.e., the digital subtraction angiography (DSA)-guided bladder arteriography imaging] was evaluated by at least two physicians ranked above the deputy director of intervention department with more than 10 years of working experience at our hospital. If the target lesions showed no obvious radiological staining or mild staining and the supplying arteries were thin and few, the diagnosis could be made.

Efficacy evaluation

According to the mRECIST evaluation criteria for solid tumors, the measurable lesions of BC that were evaluated by re-examination using MRI or CT were categorized as follows: (I) complete response (CR): the arterial phase enhancement imaging of all target lesions disappeared; (II) partial response (PR): the sum of long diameters of target baseline lesions (or arterial phase enhancement imaging) decreased by \geq 30%; (III) stable disease (SD): reduction did not reach PR or increase did not reach PD; (IV) PD: the sum of long diameters of the target lesion (or arterial phase enhancement imaging) increased by $\geq 20\%$ or new lesions appeared. A finding of (CR + PR) was considered effective, and (CR + PR + SD) was regarded as able to control the bladder tumor and benefit the patient. To evaluate the control of hematuria, complete hemostasis was noted when gross hematuria disappeared.

Statistical methods

The statistical software SPSS 19.0 (IBM Corp., Armonk, NY, USA) was used to process the data. The measurement data conforming to the normal distribution was calculated as mean \pm standard deviation ($\overline{x} \pm s$). The measurement data with non-normal distribution were expressed as median (25th percentile, 75th percentile) [M (P25, P75)]. Count data were expressed as case numbers or rates. Binary chi-square test of the prognosis factors was used for single factor

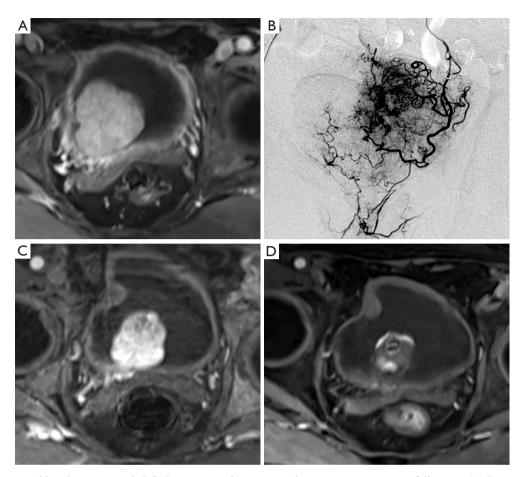


Figure 1 An 82-year-old male patient with BC. Interventional imaging and postoperative imaging follow-up. (A) Preoperative enhanced MRI showing a bulky soft tissue shadow protruding into the bladder cavity with uniform enhancement. (B) The microcatheter superselecting the bladder artery, and anteroposterior angiography showing a tumor with typical radiation staining and thickened tortuous tumor vessels. Subsequently, embolization therapy was provided with DEB. (C) MRI re-examination 2 months postoperatively showing that the lesion was significantly reduced, but the tumor was still considerably enhanced on the arterial phase, warranting re-interventional treatment. (D) Three months after the second intervention, re-examination using MRI showing that the lesion was further reduced, and imaging enhancement was not noticeable. Further, TURBT was evaluated after consultation with the department of urology. BC, bladder cancer; MRI, magnetic resonance imaging; DEB, drug-eluting bead; TURBT, transurethral resection of bladder tumor.

analysis, then the related indicators in single-factor analysis were brought into multi-factor logistic regression analysis. All tests were two-sided, and P<0.05 was considered statistically significant.

Results

Postoperative curative effect

All 39 patients in this study successfully underwent interventional embolization, with a 100% success rate. All patients were aged between 53 and 91 years (mean,

77.9±9.4 years). There were 32 males and 7 females. The imaging findings revealed local pelvic lymph node metastasis (8 patients), moreover single BC (26 patients) and multiple BC (13 patients). Tumor size (T) of tumor-node-metastasis (TNM) staging system was classified as [T2b (7 patients), T3a (12 patients), T3b (12 patients), and T4 (8 patients)] with imaging. Vesical arteriography showed that 12 patients had poor blood supply, whereas 27 patients had a rich blood supply to the tumor. The pathological types were urothelial carcinoma (32 patients) and others (7 patients). The comorbidities included hypertension (23 patients), diabetes (8 patients), cerebral infarction (2 patients), coronary

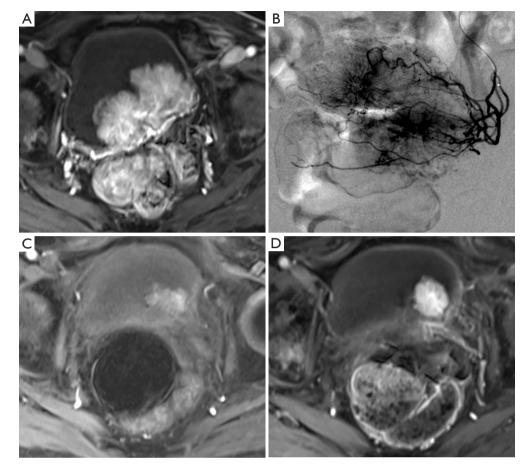


Figure 2 A 76-year-old male with BC. Interventional imaging and postoperative imaging follow-up. (A) Preoperative enhanced MRI showing a cauliflower-like soft tissue shadow in the bladder that protruded into the cavity, exhibiting uniform enhancement. (B) The microcatheter superselecting the bladder artery, and anteroposterior angiography showing a tumor with thickened tortuous tumor vessels and typical radiation staining. Subsequently, embolization therapy was provided with drug-loaded microspheres. (C) MRI re-examination 2 months postoperatively showing that the lesion was significantly reduced, and the tumor margin was slightly enhanced on the arterial phase. (D) Re-examination with MRI 5 months postoperatively showing homogeneous enhancement of the lesion on the arterial phase; DEB-TACE was performed again. BC, bladder cancer; MRI, magnetic resonance imaging; DEB-TACE, drug-eluting bead-transcatheter bladder arterial chemoembolization.

heart disease (8 patients), renal insufficiency (7 patients), arrhythmia (4 patients), hydronephrosis (10 patients), and chronic obstructive pulmonary disease (8 patients). Gross hematuria disappeared in all patients within 5 days after the operation, with a 100% hemostasis rate. Among them, 33 patients expressed clear urine from the urinary catheter within 24 hours after intervention, but 6 patients required continuous bladder irrigation due to intermittent hematuria (considered related to hemorrhage in the bladder). However, clear urine was noted in these patients within the following 5 days. CT or MRI imaging data 2 months after the operation showed that the total effective rate (CR + PR) was 64.1%, and the disease benefit rate (CR + PR + SD) was 79.5%.

Postoperative adverse reactions and treatment

None of the patients had serious complications related to DEB-TACE during treatment. No significant deterioration of renal function was observed with postoperative therapies such as intravenous fluid, diuretic and using kidney-protecting drugs after local artery infusion with cisplatin. However, mild adverse reactions were observed, mainly including post-embolism syndrome [n=12 patients (30.8%)],

nausea and vomiting [n=16 patients (41.0%)], and bladder irritation [n=24 patients (61.5%)]. Nonetheless, all reactions disappeared 2–5 days after symptomatic treatment, such as antiemetics, analgesia.

Follow-up and analysis of prognostic factors

The postoperative follow-up period was 2-40 (18.4±11.3) months. The 39 patients underwent 95 embolizations, with an average of 2.0 (2.0, 3.0) procedures per patient. Among the participants, 6 received 1 interventional treatment, 16 received 2 interventional treatments, and 17 received more than 3 interventional treatments. A total of 30 patients (76.9%) had no recurrence of hematuria during the follow-up period. Age, sex, comorbidity, hydronephrosis, tumor size, number of lesions, T stage, pelvic lymph node metastasis, and pathological type had no significant correlation with postoperative efficacy (P>0.05). Additionally, age, sex, comorbidity, hydronephrosis, tumor size, T stage, pelvic lymph node metastasis, and pathological type also had no significant correlation with postoperative hematuria recurrence (P>0.05). Tumor blood supply type, however, was an influencing factor on efficacy and hematuria recurrence in patients with MIBC (P<0.05). The number of tumor lesions was also related to the recurrence of hematuria (P<0.05) (Tables 1,2).

Multivariate regression analysis

Logistic regression analysis revealed hypovascular tumor blood supply was a negative factor affecting treatment effect (P<0.05). Hypovascular blood supply and multiple bladder tumors were both revealed as significant factors for postintervention hematuria recurrence (P<0.05) (*Table 3*).

Discussion

BC complicated by hemorrhage often indicates that the tumor extends to involve at least the muscular layer of the bladder. Patients with MIBC generally have a poor prognosis (7), and TURBT has been shown to be unsuccessful in completely removing such lesions. Therefore, radical cystectomy combined with pelvic lymph node dissection is the choice of treatment. With this standard procedure, the 5-year survival rate post-surgery is 43–57% (8). However, patients who are elderly, have underlying comorbidities or poor cardiopulmonary function

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may not be able to tolerate this operation. The procedure is often traumatic, with a relatively high incidence rate of postoperative complications. Furthermore, the need for urinary diversion leads to decreased quality of life and makes many patients unwilling to accept this approach. Therefore, some clinical centers have adopted different interventional techniques using embolic agents and chemotherapy drugs, with satisfactory results (9,10). In this study, most of the patients with advanced BC were elderly and had underlying diseases, while DEB-TACE achieved good results. The disease benefit rate (CR + PR + SD) could reach 79.5%. Some patients even achieved CR results and tumor downstaging, then were successfully treated with TURBT. The short-term hemostasis rate reached 100%, and the hemostasis rate could still reach 76.9% during the limited follow-up period. Compared with previous research (11), 36 out of 44 patients were successfully hemostatic, with an effective rate of 82%. In long-term follow-up, 43% of patients had no rebleeding within 10.5 months.

Embolic agents such as polyvinyl alcohol (PVA) granules, gelatin sponge granules, N-butyl cyanoacrylate (NBCA) embolic agents, and iodized oil are currently used clinically and achieve good curative effects in a short time. In most cases, no serious complications occur after embolization with meticulous superselection (12-14). This provides a theoretical basis for the precise superselective embolization of the bladder vascular supply using drug-loaded microspheres in this study. However, this method remains worthy of consideration by clinicians to further improve its palliative effect and reduce hematuria recurrence. The factors including age, sex, comorbidity, hydronephrosis, tumor size, number of lesions, T stage, pelvic lymph node metastasis, pathological type, and tumor blood supply type were analyzed to further explore the correlation with treatment prognosis. The results of the univariate analysis showed that tumor blood supply type impacts oncologic effect, and hematuria recurrence is associated with the number of bladder tumors and the type of blood supply. In addition, multivariate regression analysis showed that tumor blood supply may be the key factor for efficacy benefit and recurrence of hematuria. The effect of interventional therapy in patients with hypervascularity was significantly better than that of those with hypovascularity. Among the limited number of patients, those with hypervascularity were more likely to achieve benefit above PR (Figures 1,2). This may be a consequence of more DEBs being injected into the tumor-feeding artery, so a high concentration of drugs

Table 1 Anal	vsis of relevant	influencing facto	rs for the curative	effect 2 months	nostoneratively
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Factors	Cases (n=39)	Disease benefit rate, n (%)	χ²	P value
Age (years)			1.64	0.323
≤70	8	5 (62.5)		
>70	31	26 (83.9)		
Sex			1.44	0.617
Male	32	26 (81.3)		
Female	7	5 (71.4)		
Comorbidity			1.23	0.997
Yes	33	26 (78.8)		
No	6	5 (83.3)		
Hydronephrosis			2.05	0.653
Yes	10	9 (90.0)		
No	29	22 (75.9)		
Tumor size (cm)			2.46	0.682
≥3	27	22 (81.5)		
<3	12	9 (75.0)		
Number of lesions			2.67	>0.99
Single	26	21 (80.8)		
Multiple	13	10 (76.9)		
T stage			3.9	0.451
T2b-T3a	19	14 (73.7)		
T3b-T4	20	17 (85.0)		
Pelvic lymph node metastasis			1.64	0.658
Yes	8	6 (75.0)		
No	31	25 (80.6)		
Pathological type			1.44	0.617
Urothelial carcinoma	32	26 (81.3)		
Others	7	5 (71.4)		
Tumor blood supply type			2.46	0.006*
Rich blood supply	27	25 (92.6)		
Poor blood supply	12	6 (50.0)		

*, indicates significant differences with P<0.05.

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Table 2 Analysis of relevant influencing factors for postoperative hematuria recurrence

Factors	Cases (n=39)	Disease benefit rate, n (%)	χ^2	P value
Age (years)			1.85	0.355
≤70	8	3 (37.5)		
>70	31	6 (19.4)		
Sex			1.62	>0.99
Male	32	8 (25.0)		
Female	7	1 (14.3)		
Comorbidity			1.38	0.305
Yes	33	9 (27.3)		
No	6	0 (0.0)		
Hydronephrosis			2.31	0.400
Yes	10	1 (10.0)		
No	29	8 (27.6)		
Tumor size (cm)			2.77	0.416
≥3	27	5 (18.5)		
<3	12	4 (33.3)		
Number of lesions			3	0.039*
Single	26	3 (11.5)		
Multiple	13	6 (46.2)		
T stage			4.38	0.716
T2b-T3a	19	5 (26.3)		
T3b-T4	20	4 (20.0)		
Pelvic lymph node metastasis			1.85	0.355
Yes	8	3 (37.5)		
No	31	6 (19.4)		
Pathological type			1.62	0.319
Urothelial carcinoma	32	6 (18.8)		
Others	7	3 (42.9)		
Tumor blood supply type			2.77	0.014*
Rich blood supply	27	3 (11.1)		
Poor blood supply	12	6 (50.0)		

*, indicates significant differences with P<0.05.

Factors	β	SE	Wald χ^2	P value	OR	95% CI
Tumor blood supply type [†]	2.526	0.935	7.305	0.007	12.5	2.002-78.051
Tumor blood supply type [‡]	-2.228	0.957	5.422	0.02	0.108	0.017-0.703
Number of lesions [‡]	-2.041	0.957	4.546	0.033	0.13	0.02-0.848

Table 3 Multivariate regression analysis to examine the statistically significant factors above in single-factor analysis

[†], multivariate analysis of curative effect 2 months postoperatively; [‡], multivariate analysis of hematuria recurrence. SE, standard error; OR, odds ratio; CI, confidence interval.

was able to reach the tumor and render a therapeutic effect. The patients with hypovascularity were also more likely to have recurrent hematuria, which may be related to poor lesion control. Moreover, patients with multiple bladder tumors were more likely to have hematuria recurrence than those with single tumors. The reason might be related to the multifocal characteristics of the tumor. As mentioned in the previous study (15), multifocal bladder tumors were a high-risk factor for recurrence. Thus, it may be easy for the tumor to invade the surrounding bladder tissue and urethra, eventually leading to a higher recurrence of hematuria.

As an important interventional therapy in treating solid tumors, DEB-TACE has been widely used in liver cancer and other solid tumors. However, the use of DEB-TACE in BC has been rarely reported, according to a systematic literature search of peer-reviewed papers in China and internationally in recent decades (3). Currently, in DEB-TACE treatment of primary liver cancer, excessive embolization occasionally leads to the aggravation of the tumor and ischemic necrosis of the surrounding hepatic duct. Subsequently, this often results in liver abscesses and other complications (16). Thus, clinicians are reminded to pay attention to the degree of embolization to the bladder vascular supply and control of the embolization range. Our interventional experience is summarized as follows: (I) BC is more common in older patients with poor vascular health. The opening of the superior vesical artery was often complicated by stenosis and occasionally had an ectopic opening. Thus, it generally requires reliance on DSA multi-angle angiography, with some cases even requiring the use of three-dimensional (3D)-DSA and DynaCT to reconstruct scans to find the opening of the bladder artery. Afterward, microcatheters are finely superselected to the supply artery of the bladder tumor. However, surgeons need to consciously avoid blood vessels, such as the internal pudendal artery and the penile artery to prevent skin necrosis caused by ectopic embolization. (II) During the procedure, low pressure and slow pulse injection under DSA fluoroscopy are used to avoid reflux. The injection is then stopped strictly by the standard of embolization endpoint. None of the patients in this study had serious complications such as bladder necrosis and skin necrosis. However, some patients often had symptoms of bladder irritation, pain in the lower abdomen, low-grade fevers, and other complications that resolved within a week after symptomatic treatment. Therefore, we believe that embolization of DEB in the treatment of BC is safe and effective on the condition of being strict on grasping embolization after fine superselection and the end point of embolization.

Key findings

Most of the patients in this study were elderly, with 37 (94.8%) of them over 60 years old and the highest age of 91 years old. A total of 33 patients (86.8%) had different comorbidities such as hypertension, diabetes, and coronary heart disease. Thus, most of them would not be able to tolerate surgery, but successfully completed interventional embolization of bladder tumors by DEB-TACE. Reliable results were achieved in a limited number of cases, with some patients achieving CR results and tumor downstaging, after which they were transferred to the department of urology for further TURBT treatment.

In this study, 39 patients diagnosed with BC with hematuria were treated with DEB-TACE. The hemostasis rate of 100% was achieved in a short period of time with no serious postoperative complications. During the limited follow-up period after the operation, 9 patients (23.1%) were found to have recurrent hematuria, all of whom were sent for re-embolization to control the bleeding. Although this procedure exhibited some therapeutic benefits, there were still some cases of PD during curative effect evaluation, and some patients with recurrence of hematuria during follow-up resulting from this palliative treatment method.

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Strengths and limitations

DEB-TACE is not only minimally invasive and safe, but also can achieve good efficacy without increasing the number of interventional therapies because of the characteristics of DEB. This approach is a good choice for advanced-BC patients who are elderly, frail, or affected by other underlying diseases. However, this study had certain limitations. It was a retrospective study with a limited number of cases and a short follow-up time. Therefore, validation of these results is required via multi-center randomized controlled trials with a larger sample size.

Comparison with similar studies

In this study, cisplatin administration by internal iliac artery infusion and DEB loaded with epirubicin chemoembolization were performed to treat BC with hemorrhage. The disease benefit rate was 79.5%, which further confirmed the satisfactory curative effect of chemotherapy drugs on BC (10). The short-term hemostatic rate of hematuria could reach 100%, which was comparable to the short-term hemostatic success rate previously reported by simple superselective arterial embolization (2). However, the recurrence rate of hematuria was 33.1% with the average follow-up (18.4 \pm 11.3 months), which was better than the rate of 50% with an average follow-up of 10 months noted elsewhere (11).

Explanations of findings

Most BCs are sensitive to chemotherapeutics such as epirubicin and can be treated effectively. The principle of DEB-TACE is to inject DEBs loaded with chemotherapeutics (epirubicin in this study) into tumor blood vessels, which slowly release the drugs to maintain a high local concentration within a few weeks. Thus, most patients can obtain a good therapeutic effect. Furthermore, some patients may even achieve downstaging and possibly become eligible for TURBT.

Implications and actions needed

This study confirmed the efficacy and safety of DEB-TACE and further analyzed the factors affecting prognosis, which enriched the means of interventional therapy for BC with hematuria. Thus, it is worthy of reference for clinicians. However, this was a retrospective study with a short followup duration to observe whether the survival benefit was

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achieved or not. Future multi-center participations are required to set up case-control studies.

Conclusions

Superselective embolization of bladder arteries with DEB can be used in the treatment of BC patients with hemorrhage. The procedure can preserve bladder function to the greatest extent and help stop bleeding. Additionally, some patients may experience downstaging and be offered TURBT. However, the type of tumor blood supply characterized by hypovascularity may be a risk factor for poor curative effect postoperatively and recurrence of hematuria. Moreover, multiple bladder tumors may be a risk factor for hematuria recurrence. Nonetheless, patients should be informed of the high cost of DEB and its experimental use for BC treatment. This study clarified the timing and indications of interventional therapy to guide clinicians in successfully determining clinical treatment and to select cases for DEB embolization appropriately.

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Footnote

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The other authors have no conflicts of interest to declare.

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References

- Sharma JD, Kataki AC, Barman D, et al. Cancer statistics in Kamrup urban district: Incidence and mortality in 2007-2011. Indian J Cancer 2016;53:600-6.
- Abt D, Bywater M, Engeler DS, et al. Therapeutic options for intractable hematuria in advanced bladder cancer. Int J Urol 2013;20:651-60.
- 3. Chen C, Kim PH, Shin JH, et al. Transcatheter arterial embolization for intractable, nontraumatic bladder hemorrhage in cancer patients: a single-center experience and systematic review. Jpn J Radiol 2021;39:273-82.
- Sottani C, Poggi G, Quaretti P, et al. Serum pharmacokinetics in patients treated with transarterial chemoembolization (TACE) using two types of epirubicinloaded microspheres. Anticancer Res 2012;32:1769-74.
- Shang B, Li J, Wang X, et al. Clinical effect of bronchial arterial infusion chemotherapy and CalliSpheres drugeluting beads in patients with stage II-IV lung cancer: A

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prospective cohort study. Thorac Cancer 2020;11:2155-62.

- Baur J, Ritter CO, Germer CT, et al. Transarterial chemoembolization with drug-eluting beads versus conventional transarterial chemoembolization in locally advanced hepatocellular carcinoma. Hepat Med 2016;8:69-74.
- Tomioka M, Yoneyama T, Tobisawa Y, et al. Ghrelin after chemotherapy as a prognostic predictor of progressionfree survival in patients with muscle-invasive bladder cancer. Transl Androl Urol 2021;10:1192-201.
- Resnick MJ, Bassett JC, Clark PE. Management of superficial and muscle-invasive urothelial cancers of the bladder. Curr Opin Oncol 2013;25:281-8.
- Liu Z, Ye Y, Li X, et al. The effects of intra-arterial chemotherapy on bladder preservation in patients with T1 stage bladder cancer. World J Urol 2018;36:1191-200.
- Yoshioka H, Shimbo T, Yoshida K, et al. Treatment Results of Radiotherapy Combined with Balloon-occluded Arterial Infusion Chemotherapy for Invasive Bladder Cancer. Anticancer Res 2016;36:731-6.
- 11. Liguori G, Amodeo A, Mucelli FP, et al. Intractable haematuria: long-term results after selective embolization of the internal iliac arteries. BJU Int 2010;106:500-3.
- 12. Loffroy R, Pottecher P, Cherblanc V, et al. Current role of transcatheter arterial embolization for bladder and prostate hemorrhage. Diagn Interv Imaging 2014;95:1027-34.
- Tsitskari M, Spiliopoulos S, Konstantos C, et al. Longterm results of super-selective trans-catheter embolization of the vesical arteries for the treatment of intractable bladder haematuria. CVIR Endovasc 2020;3:97.
- Delgal A, Cercueil JP, Koutlidis N, et al. Outcome of transcatheter arterial embolization for bladder and prostate hemorrhage. J Urol 2010;183:1947-53.
- Daza J, Grauer R, Chen S, et al. Development of a predictive model for recurrence-free survival in pTa lowgrade bladder cancer. Urol Oncol 2023;41:256.e9-256.e15.
- Kallini JR, Gabr A, Abouchaleh N, et al. New Developments in Interventional Oncology: Liver Metastases From Colorectal Cancer. Cancer J 2016;22:373-80.