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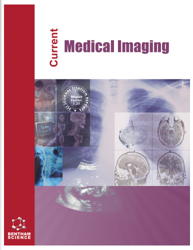

RESEARCH ARTICLE

Clinical Outcomes of Transcatheter Arterial Embolization in Patients with High-grade Gross Hematuria

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Abstract:

Introduction:

To investigate factors influencing the effectiveness and safety of super-selective embolization in patients with high-grade gross hematuria.

Materials and Methods:

This retrospective, single-center study included 19 consecutive cancer patients (12 men and 7 women, mean age of 72.3 years) who had undergone TAE for intractable hematuria between January 2008 and February 2024. Factors such as technical and clinical success rates, embolized vessels, embolic agents used, and complications were evaluated. This study specifically focused on patients with severe hematuria (grade 3 or above) and examined the effects of super-selective embolization, hematuria grade, and embolic agents on patient outcomes.

Results:

Technical success was achieved in all 23 angiography procedures performed, with a clinical success rate of 56.5%. Clinical success was significantly correlated with hematuria grade, super-selectivity of the procedure, and type of embolic agent used. Multivariate logistic regression analysis revealed that the embolic material, specifically tris-acryl gelatin microspheres (TAGM), was an independent factor that significantly affected clinical outcomes. No major complications were reported.

Conclusion:

TAGM for supers-elective embolization in patients with massive gross hematuria is both effective and safe. However, the effectiveness of TAE may decrease in patients with severe hematuria, highlighting the need for combination therapies.

Keywords: Hematuria, Embolization, Microsphere, Bladder cancer, Cystitis, Angiography.

Article History	Received: September 24, 2024	Revised: October 30, 2024	Accepted: November 01, 2024

1. INTRODUCTION

Primary or metastatic tumors or hemorrhagic cystitis often predispose to intractable hematuria originating from the urinary bladder [1]. Traditional conservative treatments like bladder irrigation with formalin, silver nitrate, or alum, intravesical hydrostatic pressure, hyperbaric oxygen therapy, and endoscopic diathermy have been largely ineffective [2, 3]. Surgical interventions such as internal iliac artery (IIA) ligation and cystectomy are the last resort but come with high operative risks, mortality, and morbidity, especially in older adults with poor health [4 - 6].

Transcatheter arterial embolization (TAE) is recommended when conventional methods fail, offering a minimally invasive alternative that avoids the disadvantages of aggressive surgery [5 - 9]. TAE has multiple advantages over IIA ligation, including its minimally invasive nature, preventing collateral circulation activation, reduced analgesia, sustained bleeding control, and improved quality of life through reduced blood transfusions and fewer repeat cystoscopies [6, 8, 9]. First described in 1974 for bladder haemorrhage [10], TAE has advanced significantly through the strategic selection of embolic vessels, including the IIA and its anterior division to the vesical artery [11 - 13].

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DOI: 10.2174/0115734056359111241202170209, XXXX, *XX*, e15734056359111

Our study aims to summarize our experiences at a tertiary referral hospital, focusing on intractable massive hematuria management, analyzing technical and clinical success rates, specific vessels embolized, types of embolic agents used, and complications encountered.

2. METHODS

2.1. Patient Population

This retrospective, single-center study was approved by the institutional review board, and the need for informed consent was waived owing to the study design (approval no. EUMC-2024-03-004). All methods were performed in accordance with the relevant guidelines and regulations. Between January 2008 and February 2024, 19 consecutive cancer patients (12 men and 7 women) with a mean age of 72.3 years (range, 53–87 years) who underwent TAE for intractable bladder hematuria were identified from the hospital information system. Electronic medical records and images were reviewed. TAE was performed based on clinical and laboratory evidence of continued bleeding despite adequate conventional therapy. All patients with gross hematuria due to malignancy or hemorrhagic cystitis required continuous bladder irrigation (CBI) with Foley catheter insertion. Patients for whom conventional treatments failed and those needing transfusions due to hemoglobin (Hb) decrease were candidates for TAE. Patients with hematuria due to blunt trauma, biopsy, or other iatrogenic injuries, those with mild hematuria (grade 1 or 2), and those not requiring transfusions were excluded.

2.2. Procedure

The right common femoral artery was accessed under local anesthesia, and a 5-F Cobra catheter (Cook, Bloomington, IN, USA) was advanced using a 0.035-inch hydrophilic guidewire (Radifocus; Terumo, Tokyo, Japan) for selective contralateral IIA catheterization and the ipsilateral IIA was selected using the same Cobra catheter after forming a Waltman loop. If selection using the Waltman loop technique was not possible due to iliac artery tortuosity, an Omni Catheter (Cook) was used. The 5-F catheter was placed in the bilateral IIAs for DynaCT imaging, confirming the origin of the bilateral vesical or prostatic arteries using DynaCT 3-D angiography. The contrast agent was injected to enhance the visualization of the vascular architecture, including the vesical or prostatic arteries, tumors, or urinary bladder wall. Based on the angiographic and DynaCT findings, supers-elective catheterization of the feeding arteries to the bladder was performed using a 1.7–2.0 Fr coaxial microcatheter (Progreat; Terumo, Tokyo, Japan or Veloute; ASHAI INTECC, Aichi, Japan).

The feeding arteries were subsequently embolized until blood flow stasis or disappearance of the bleeding focus was observed. Embolic agents included tris-acryl gelatin microspheres (TAGM; Embosphere®; Merit Medical Systems, South Jordan, UT, USA), nonspherical polyvinyl alcohol (PVA; Contour; Boston Scientific, Marlborough, MA, USA) and gelatin sponge particles (GSP; EG-gel, Engain, Seongnam, South Korea) or their combinations. Embolic materials were selected intraoperatively on a case-by-case basis at the discretion of the interventional radiologist. Subsequently, a final arteriography was performed to confirm the successful occlusion of the target vessel.

2.3. Study Endpoints

Technical success was defined as the cessation of extravasation and/or occlusion of the targeted vessel on postembolization arteriography. Clinical success was defined as no recurrence of bleeding within 1 month after embolization or before radical cystectomy with urinary diversion for bladder cancer. Recurrence of bleeding was defined as the recurrence of hematuria requiring additional treatments after successful cessation of bleeding. The severity of hematuria was assessed based on the gross hematuria scale for patients who had undergone CBI [14 - 16]. The visual scale for gross hematuria was categorized as follows: grade 1 (urine appears clear), if the patient is on clamp CBI, continue with the clamp if CBI is still running; grade 2 (clear pink urine), decrease the rate of irrigation if CBI is still running or maintain the clamp; grade 3 (pink), maintain the current rate of CBI running, or keep clamped; grade 4 (bloody urine), increase the rate of CBI, restart CBI if clamped; grade 5 (frank bloody), increase the rate of CBI if the color does not change, obtain a bladder scan and perform hand irrigation, and notify the provider. Complications were classified into minor and major categories according to the Society of Interventional Radiology criteria [17].

2.4. Statistical Analysis

To investigate the factors related to clinical success, categorical variables such as sex, underlying disease, oral anticoagulation therapy, hematuria grade, embolic materials, patient survival, and whether the procedure was super-selective were analyzed using Fisher's exact test, whereas continuous variables such as age, Hb, packed red blood cell (pRBC) transfusion, systolic blood pressure, heart rate, platelet count, and international normalized ratio (INR) were compared using the Mann–Whitney U test. Univariate and multivariate logistic regression analyses of the independent factors for clinical failure after TAE were performed. Two-sided tests were used, and $p < 0.05$ indicated statistical significance. All statistical analyses were performed using SPSS 18.0 statistical software (SPSS, Chicago, IL, USA).

3. RESULTS

The baseline demographic and clinical data of the included patients are presented in Table **1**. During the study period, 23 angiography procedures were performed, including reinterventions and embolization of severe intractable bladder hematuria in 19 patients. Four patients underwent a subsequent TAE because of persistent hematuria following the initial TAE. Primary bladder cancer was identified as the most common cause of bladder hemorrhage in 12 patients, followed by hemorrhagic cystitis in 5 patients. Additionally, one patient had prostate cancer, and the other had sigmoid colon cancer with urinary bladder invasion. Oral anticoagulation therapy was administered to 7 of the 19 patients (36.8%). All 23 patients exhibited grade 3 or higher hematuria, with grade 3 in 8 (34.8%), grade 4 in 10 (43.5%), and grade 5 in 5 patients (21.3%).

Table 1. Patients characteristics, computed tomography findings, and baseline laboratory finding.

Patient no.	Age/Sex	Underlying Disease	Anticoa-gulation	Hematuria Grade	RBC Transfusion (unit)	Hb (g/dL)	Platelet ($x10^3$/dL)	Angiographic Finding	Embolic Materials	Emblized Vessel	Technical Success	Clinical Success	Complication	Remarks
1	M/87	Bladder cancer	Y	4→ 3	0 → 4	8.5 → 7.0	224	Mild tumor staining with hypervascularity	GSP+TAGM → TAGM	Anterior division of right IIA → Both vesical artery	Y	N → Y	N	Transiently clinical improvement, but hematuria recurrence within 2 weeks → Clinically improved within 1 day after 2nd EMB
2	M/59	Bladder cancer	Y	4	2	8.0	125	No hypervascularity	TAGM	Both vesical artery	Y	Y	N	Clinically improved within 1 day. Radical cystectomy → 5 days after EMB
3	F/74	Bladder cancer	Y	3	1	7.7	422	Tumor staining with hypervascularity	TAGM	Both vesical artery	Y	Y	N	Clinically improved within 2 days. Radical cystectomy → 6 days after EMB
4	M/80	Bladder cancer	Y	3	4	8.4	105	Tumor staining with hypervascularity	TAGM	Both vesical artery	Y	Y	N	Clinically improved within 1 day. Radical cystectomy → 10 days after EMB
5	M/77	Bladder cancer	Y	5	1	7.8	116	Tumor staining with hypervascularity	TAGM + GSP	Both vesical artery	Y	Y	N	Clinically improved within 1 day. Radical cystectomy → 4 days after EMB
6	M/73	Bladder cancer	N	4	4	6.9	209	Tumor staining with hypervascularity	TAGM	Both vesical artery	Y	Y	N	Decreased tumor on POD 3 days follow-up CT Radical cystectomy → 6 days after EMB
7	M/84	Prostate cancer	Y	5 → 4	4 + 6	6.1 → 5.4	149	No hypervascularity	GSP → TAGM	Both prostatic, vesical artery	Y	N → Y	N	No clinical improvement after 1st EMB → 2nd embolization on POD 3 days Decreased tumor on POD 8 days follow-up CT
8	F/80	Hemorrhagic cystitis	N	4	1	7.3	463	Slightly hypervascularity	GSP	Both vesical artery	Y	Y	N	Immediately improvement after EMB
9	M/58	Bladder cancer	N	4	7	5.7	267	Tumor staining with hypervascularity	TAGM	Both vesical artery	Y	Y	N	Radical cystectomy → 4 days after embolization

(Table 1) contd.....

Patient no.	Age/Sex	Underlying Disease	Anticoa-gulation	Hematuria Grade	RBC Transfusion (unit)	Hb (g/dL)	Platelet ($x10^3$/dL)	Angiographic Finding	Embolic Materials	Emblized Vessel	Technical Success	Clinical Success	Complication	Remarks
10	F/81	Hemorrhagic cystitis	N	3 → 4	3 + 4	7.6 → 7.6	81	Slightly hypervascularity	GSP → GSP	Both vesical artery	Y	N → N	N	No clinical improvement after 1st EMB → 2nd embolization on POD 12 days → Expire 3days after 2nd EMB
11	F/74	Hemorrhagic cystitis	N	3	6	5.7	56	Slightly hypervascularity	GSP	Both vesical artery	Y	Y	N	Clinical improvement and expire 4 months after EMB due to deterioration of the general condition
12	M/53	Sigmoid colon cancer	N	4	2	7.4	273	Tumor staining with hypervascularity	PVA	Anterior division of right IIA	Y	Y	N	No clinical improvement after EMB → subsequent TURB.
13	M/58	Hemorrhagic cystitis	N	5	7	7.2	40	Slightly hypervascularity	PVA	Both vesical artery	Y	N	N	No clinical improvement and expires 4 months after EMB
14	M/64	Bladder cancer	N	5 → 4	8 + 6	6.0 → 5.6	176	Tumor staining with hypervascularity	GSP → PVA	Both vesical artery	Y	N → N	N	No clinical improvement after 1st EMB → 2nd embolization on POD 4 months → Expire 2 months after 2nd EMB
15	M/74	Bladder cancer	N	4	7	6.5	100	Tumor staining with hypervascularity	PVA	Anterior division of right IIA	Y	N	N	s/p radical cystectomy and orthotopic neobladder 1 year ago. Expires 8 days after EMB.
16	F/57	Bladder cancer	N	4	10	6.7	50	Tumor staining with hypervascularity	PVA + GSP	Anterior division of both IIA	Y	N	N	No clinical improvement after EMB → Expire 45 days after EMB
17	M/70	Bladder cancer	N	5	11	5.4	40	No hypervascularity	GSP	Anterior division of both IIA	Y	N	N	No clinical improvement after EMB → Expire 12 days after EMB
18	F/85	Hemorrhagic cystitis	Y	3	4	6.6	205	Tumor staining with hypervascularity	GSP	Both vesical artery	Y	Y	N	Clinically improved within 1 day → No additional massive hematuria within 2.5 years follow-up
19	F/86	Bladder cancer	N	3	2	8.1	273	Tumor staining with hypervascularity	GSP	Left vesical artery	Y	Y	N	Immediately improvement after EMB

Abbreviations: * Hb, Hemoglobin; GSP, gelatin sponge particles; TAGM, tris-acryl gelatin microspheres; PVA, nonspherical polyvinyl alcohol; IIA, internal iliac artery; EMB, embolization.

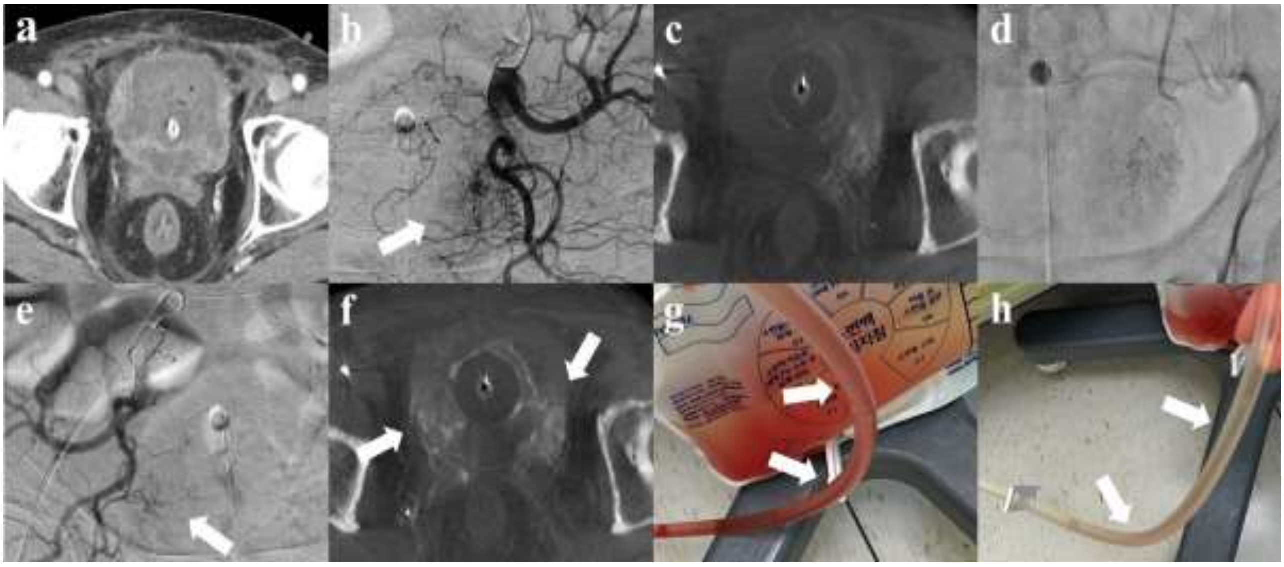

Fig. (1). An 80-year-old man with massive hematuria caused by bladder cancer underwent abdominopelvic computed tomography (CT) a day before transcatheter arterial embolization (TAE). (**a**) The CT revealed an enhancing lesion at the posterior aspect of the urinary bladder, suggestive of probable bladder cancer with a high-density lesion, raising the possibility of a hematoma within the urinary bladder. (**b**) A left internal iliac angiogram showed prominent tumor staining (arrow) on the left side of the urinary bladder. (**c**) Dyna CT showed significant staining of the left posterior aspect of the urinary bladder, with blood supply identified from the left vesical artery. (**d**) Following the successful super-selection of the left vesical artery, embolization was performed using a gelatin sponge particle (GSP). (**e**) A right internal iliac angiogram revealed prominent tumor staining (arrow) on the right side of the urinary bladder. (**f**) After successfully super-selection of the right vesical artery, embolization was performed using GSP. Subsequent cone beam CT demonstrated contrast retention within the tumor (arrow) at the posterior aspect of the urinary bladder. (g, h) Through a Foley catheter, the gross hematuria scale showed a pinkish appearance (arrow), rated as grade 3 before the procedure (**g**), but appeared clear (arrow), improving to grade 1 after the procedure (**h**).

Angiography revealed hyper-vascular tumor staining in the urinary bladder in 83.3% of patients (10/12) with bladder cancer and diffuse increased pelvic vascularity/neovascularity in all patients with hemorrhagic cystitis (5/5). In addition, hyper-vascular tumor staining was observed in one of the two patients with other malignancies involving urinary bladder invasion; however, this was not observed in patients with prostate cancer. Bladder catheterization was maintained, and the catheter was removed after an average of 1.7 days once clear urine was confirmed. The technical success rate was 100% (23/23 cases); however, despite multiple attempts, catheterization of the vesical artery was not achieved in five cases (21.7%) owing to its small size and tortuosity. Therefore, selective proximal GSP embolization of the anterior division of the internal iliac artery was performed. Super-selective distal embolization of the vesical arteries was performed in 18 of the 23 patients (78.3%). The embolic materials used included GSP (n = 9), TAGM (n = 7), PVA (n = 4), TAGM + GSP (n = 2), and PVA + GSP (n = 1) (Fig. **1**).

The clinical success rate was >56.5% (13/23 cases) 68.4% (13/19 patients). >To analyze the factors affecting patients' clinical success, Fisher's exact test and the Mann-Whitney U test were used. These tests helped identify which factors had a significant impact on clinical success. According to Fisher's exact test, clinical success was significantly associated with the hematuria grade ($p = 0.049$), super-selectivity of the procedure ($p = 0.024$), and type of embolic agent used ($p = 0.031$). The Mann-Whitney U test revealed that transfusion (pRBC) ($p = 0.041$) and platelet count ($p = 0.025$) were statistically significant (Table **2**).

A multivariable logistic regression analysis was performed to investigate independent risk factors associated with clinical failure. Univariate logistic regression analysis identified transfusion (pRBC), hematuria grade, and embolic materials as risk factors associated with clinical failure in patients with massive hematuria (transfusion, odds ratio (OR) and 95% confidential interval (CI): 1.559 (1.030–2.358), $p = 0.036$; hematuria grade, – OR(95% CI): 28.000 (1.350–580.591), $p = 0.031$ in grade 5; embolic materials, OR(95% CI): 0.069 (0.007–0.727), $p = 0.026$ in TAGM). However, embolic materials were the only independent risk factors associated with clinical failure in the multivariate logistic regression analysis (OR[95% CI]: 0.040 [0.002–0.928], $p = 0.045$) (Table **3**). No major complications or bladder or sexual dysfunction were reported. Only minor complications, including mild fever, were observed in five patients (21.7%), which improved following conservative treatment within 2–3 days postoperatively.

4. DISCUSSION

TAE for bladder hemorrhage has demonstrated high technical and clinical success rates of 99.0% and 80.9%, respectively, with a minimal complication rate of 5.5%, highlighting its commendable safety profile [5 - 9, 18]. These investigations were mostly retrospective cohort studies and case series, which can be attributed to the rarity of this condition.

Table 2. Factors influencing clinical outcomes in patients who underwent transcatheter arterial embolization for massive hematuria.

-	Clinical Success		*p* value
	Yes (n=13)	No (n=10)	
Sex	-	-	0.999
Male	8 (61.5)	7 (70.0)	-
Female	5 (38.5)	3 (30.0)	-
Age	76.6 ± 11.3	72.0 ± 11.0	0.597
Anticoagulation	-	-	0.197
Yes	7 (53.8)	2 (20)	-
No	6 (46.2)	8 (80)	-
Underlying	-	-	0.341
Malignancy*	11	6 (60)	-
Cystitis	2	4 (40)	-
Hematuria grade	-	-	0.049
3	7 (53.8)	1 (10)	-
4	5 (38.5)	5 (50)	-
5	1 (7.7)	4 (40)	-
Transfusion (pRBC)	3.31 ± 2.18	6.10 ± 3.48	0.041
Hemoglobin (g/dL)	7.08 ± 0.98	6.72 ± 0.99	0.336
Systolic blood pressure (mmHg)	119.9 ± 13.1	125.2 ± 16.7	0.535
Heart rate	84.7 ± 20.4	88.0 ± 21.7	0.877
Platelet count (x10^3/uL)	218.7 ± 122.9	122.9 ± 85.2	0.025
International normalized ratio	1.31 ± 0.52	1.17 ± 0.20	0.495
Superselective	-	-	0.024
Yes	13 (100)	6 (60)	-
No	0 (0)	4 (40)	-
Embolic materials	-	-	0.031
TAGM	8 (61.5)	1 (10)	-
GSP	1 (7.7)	4 (40)	-
PVA	4 (30.8)	5 (50)	-
Survival (%)	-	-	0.002
Yes	13 (100)	4 (40)	-
No	0 (0)	6 (60)	-

Note: * malignancy includes primary bladder cancer, sigmoid colon cancer, and prostate cancer.
** pRBC, packed red blood cell; TAGM, tris-acryl gelatin microspheres; GSP, gelatin sponge particles; PVA, nonspherical polyvinyl alcohol.

Table 3. Multivariable logistic regression analysis of independent factor for primary clinical failure after transcatheter arterial embolization in patients with massive hematuria.

Characteristics	Univariate		Multivariate	
	OR(95% CI)	p	OR(95% CI)	p
Sex	-	-	-	-
Male	1.458(0.252-8.429)	0.673	-	-
Female	-	-	-	-
Age	-	-	-	-
<70	1	-	-	-
70-79	0.375(0.039-3.605)	0.396	-	-
≥80	0.500(0.070-3.550)	0.488	-	-
Underlying	-	-	-	-
Malignancy*	0.273(0.038-1.951)	0.196	-	-
Cystitis	-	-	-	-
Superselective	-	-	-	-
Yes	<0.001	0.999	-	-

(Table 3) contd.....

Characteristics	Univariate		Multivariate	
	OR(95% CI)	p	OR(95% CI)	p
No	-	-	-	-
Anticoagulation	-	-	-	-
Yes	0.214(0.032-1.425)	0.111	-	-
No	-	-	-	-
Transfusion (pRBC, unit)	1.559(1.030-2.358)	0.036	1.158(0.690-1.942)	0.579
Hematuria grade	-	-	-	-
3	1	-	-	-
4	7.000(0.613-79.871)	0.117	17.362(0.655-460.392)	0.088
5	28.000(1.350-580.591)	0.031	40.785(0.633-2627.534)	0.081
Embolic materials	-	-	-	-
TAGM	0.069(0.007-0.727)	0.026	0.040(0.002-0.928)	0.045
Others**	-	-	-	-
Platelet count (x10^3/uL)	0.990(0.980-1.001)	0.067	-	-

Note: * Malignancy includes primary bladder cancer, sigmoid colon cancer, and prostate cancer.
** Others include gelatin sponge particles and nonspherical polyvinyl alcohol.
*** pRBC, packed red blood cell; TAGM, tris-acryl gelatin microspheres.

Intractable hematuria originating from the bladder or prostate is potentially fatal with substantial therapeutic hurdles. The clinical efficacy of TAE in managing hematuria is influenced by several factors. For instance, higher success rates have been associated with bilateral embolization [18], super-selective embolization [7, 8], and the treatment of radiation cystitis [7]. Additionally, most cases involve older patients living in suboptimal conditions, which correlates with increased morbidity from surgical intervention [9, 19].

Our current study reported that TAE for high-grade gross hematuria achieved effective temporary hemostasis, with technical and clinical success rates of 100% and 56.5%, respectively. The lower clinical success rate observed in this study may be attributable to differences in patient characteristics and the severity of hematuria compared to other reports. Patients with mild hematuria or those exhibiting a prompt therapeutic response typically achieve resolution more rapidly, whereas patients with more severe or refractory cases often require extended interventions and demonstrate delayed outcomes [19]. Our study specifically focused on a cohort with high-grade hematuria (grade 3 or higher), with a substantial subset (69.6%, 16 out of 23) presenting with grades 4 and 5 hematuria. This cohort represents a population with progressively worsening, uncontrolled hematuria, refractory to conservative management. Additionally, the mean hemoglobin level of 6.92 ± 0.98 g/dL highlights the severity of anemia and the advanced disease state within this group. This level of clinical deterioration likely impacted the success rates of TAE, as more aggressive disease states are generally associated with higher rates of therapeutic resistance. While direct comparisons with other studies are challenging due to differences in patient populations and hematuria grading criteria, the severity of cases included in this study likely contributed to the lower clinical success rates observed, underscoring the complexities in achieving hemostasis in high-grade, refractory hematuria cases.

The effect of embolic agent type on clinical outcomes remains controversial. Because most previous studies included only a small number of patients, identifying optimal embolic agents remains inconclusive [5, 7, 20]. The current preference leans towards permanent particulate embolic agents, such as nonspherical PVA or TAGM. Multivariate logistic regression analysis revealed that only TAGM significantly reduced clinical failure rates, marking it as an independent influential factor (OR[95% CI] = 0.040 [0.002–0.928], $p = 0.045$). GSP induces recanalization within 2–3 weeks following TAE [1, 21], remains proximal to the arterioles, and does not interfere with capillary circulation [22]. Because of their irregular shapes and wide range of sizes, the degree of arterial occlusion obtained using nonspherical PVA particles could not be predicted [23]. This is attributed to the uneven obstruction and proximal embolization, mostly caused by particles sticking together [24]. However, compared to other similar products, TAGM, a polymeric microsphere composed of trisacryl gelatin, exhibits deeper penetration and more effective embolization of smaller vessels because of its non-aggregating nature, smooth hydrophilic surface, and deformability [25]. The uniform size and spherical shape of the TAGM prevent proximal aggregation and promote more efficient distal embolization [26]. These characteristics may elucidate the better clinical outcomes with TAGM observed in our study than with other embolic materials, suggesting a superior distal embolic effect. Additionally, TAGM is easier to inject and less likely to cause catheter occlusion than PVA [27]. To minimize clumping, PVA was diluted with a greater volume of normal saline and contrast than required for TAGM, which consequently increased the contrast volume used in the PVA group [28], highlighting another advantage of TAGM over nonspherical PVA particles.

Although not related to hematuria, a previous study on gastrointestinal hemorrhage in gastric cancer patients treated with TAE showed that active bleeding ($p = 0.044$) and higher transfusion requirements (3.3 unit ± 2.6 *vs*. 1.8 unit ± 1.7; $p = 0.039$) were associated with TAE failure [29]. Hematuria caused by malignancy or cystitis typically presents with abnormal hypervascularity or even a mass on angiography; however, visualization of extravasation is rare [30], which is consistent with our findings, with no evidence of contrast media extravasation on angiography. However, consistent with the aforementioned study, univariate logistic analysis revealed that an increase in transfusion (pRBC) increased the likelihood of clinical failure (OR[95% CI]: 1.559 (1.030–2.358), p = 0.036). Additionally, our findings identified hematuria grade as a factor affecting clinical failure in univariate logistic regression analysis (OR[95% CI]: 28.000 (1.350–580.591), p = 0.031 for grade 5). A clinically useful gross hematuria scale that improves communication and minimizes ambiguous language among providers with varying levels of experience has been previously developed [16]. In this retrospective analysis, we assessed hematuria grade based on existing records of urine color and CBI. Of the five patients with a hematuria grade of 5, only one (20%) achieved clinical success, and the majority experienced clinical failure, with three expiring within 4 months. Because patients with high-grade gross hematuria are likely to have poor overall health conditions, aggressive treatments, including TAE combined with surgery, may be necessary to improve clinical outcomes, underscoring the need for further research in this area.

In our study, the clinical outcome was significantly influenced by whether embolization was super-selective, as determined by Fisher's exact test (p = 0.024). In addition, no major complications were reported in our study, with only mild fever observed as a minor complication in five patients (21.7%), which resolved within 2–3 days. To more easily and quickly achieve super-selection of the vesical or prostatic artery, we utilized Dyna CT imaging and employed small caliber microcatheters, ranging from 1.7 to 2.0 Fr in our study. Super-selective embolization, the most widely performed procedure, demonstrated high initial clinical success rates with relatively low complication rates of approximately 10%, underscoring its effectiveness and safety [7, 8]. Concurrent with previous studies, our study indicates that super-selective embolization is crucial for improving clinical outcomes and reducing complications. However, when super-selection of the vesical or prostatic artery is virtually impossible, especially when the embolization level is at the anterior division of the IIA, the GSP approach may be more suitable [18]. Before employing GSP, it is advisable to protect the distal arterial territory by placing coils immediately distal to the branches that require embolization. This strategy is particularly useful in cases where a tumor has recruited several small collateral feeding vessels from the branches of the internal iliac artery, as it helps prevent ischemic complications [1].

This study had some limitations. Owing to its retrospective, non-randomized nature, there was heterogeneity in the patient group, tumor characteristics, and angiographic findings, with potential confounding factors. The selection of the target vessel and embolic agent varied and depended on the operator's preference, which could have affected the outcomes. This could be attributed to the smaller sample size and the retrospective study design. Furthermore, we focused on patients with massive hematuria of grade 3 or above, which resulted in poor clinical success. Some patients who showed favorable outcomes underwent radical cystectomy combined with TAE a few days after the procedure, making it impossible to assess long-term patency. Despite variations in the severity of hematuria among patients, there was a noticeable difference in the clinical outcomes with the use of TAGM.

CONCLUSION

Our study supports the use of TAGM for super-selective embolization in patients with massive gross hematuria, which is effective and safe. However, the effectiveness of TAE may decrease in patients with high-grade gross hematuria, suggesting the need for more aggressive treatment, including combination with other therapies.

AUTHORS' CONTRIBUTION

C.H.O.: Study conception and design; H.J.L.: Writing - Original Draft Preparation; S.C.L.: Writing - Reviewing and Editing. All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

TAGM	=	Tris-Acryl Gelatin Microspheres
IIA	=	Internal Iliac Artery
TAE	=	Transcatheter arterial embolization
CBI	=	continuous bladder irrigation
pRBC	=	packed red blood cell

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Medical Ethics Committee of the Ewha Womans University Mokdong Hospital, republic of Korea (EUMC- 2024-03-004).

HUMAN AND ANIMAL RIGHTS

All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

As this is a retrospective study, informed consent was waived owing to the study design.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Loffroy R, Pottecher P, Cherblanc V, *et al.* Current role of transcatheter arterial embolization for bladder and prostate hemorrhage. Diagn Interv Imaging 2014; 95(11): 1027-34. [http://dx.doi.org/10.1016/j.diii.2014.03.008] [PMID: 24746761]

[2] Choong SKS, Walkden M, Kirby R. The management of intractable haematuria. BJU Int 2000; 86(9): 951-9. [http://dx.doi.org/10.1046/j.1464-410x.2000.00900.x] [PMID: 11119085]

[3] Capelli-Schellpfeffer M, Gerber GS. The use of hyperbaric oxygen in urology. J Urol 1999; 162(3 Part 1): 647-54. [http://dx.doi.org/10.1097/00005392-199909010-00002] [PMID: 10458334]

[4] Abt D, Bywater M, Engeler DS, Schmid HP. Therapeutic options for intractable hematuria in advanced bladder cancer. Int J Urol 2013; 20(7): 651-60. [http://dx.doi.org/10.1111/iju.12113] [PMID: 23387805]

[5] Nabi G, Sheikh N, Greene D, Marsh R. Therapeutic transcatheter arterial embolization in the management of intractable haemorrhage from pelvic urological malignancies: preliminary experience and long□term follow□up. BJU Int 2003; 92(3): 245-7. [http://dx.doi.org/10.1046/j.1464-410X.2003.04328.x] [PMID: 12887476]

[6] 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(4): 500-3. [http://dx.doi.org/10.1111/j.1464-410X.2009.09192.x] [PMID: 20128777]

[7] Delgal A, Cercueil JP, Koutlidis N, *et al.* Outcome of transcatheter arterial embolization for bladder and prostate hemorrhage. J Urol 2010; 183(5): 1947-53. [http://dx.doi.org/10.1016/j.juro.2010.01.003] [PMID: 20303518]

[8] Prasad V, Sacks BA, Kraus S, Clouse ME. Embolotherapy for lower urinary tract hemorrhage. J Vasc Interv Radiol 2009; 20(7): 965-70. [http://dx.doi.org/10.1016/j.jvir.2009.04.048] [PMID: 19501528]

[9] Korkmaz M, Şanal B, Aras B, *et al.* The short- and long-term effectiveness of transcatheter arterial embolization in patients with intractable hematuria. Diagn Interv Imaging 2016; 97(2): 197-201. [http://dx.doi.org/10.1016/j.diii.2015.06.020] [PMID: 26489590]

[10] Hald T, Mygind T. Control of life-threatening vesical hemorrhage by unilateral hypogastric artery muscle embolization. J Urol 1974; 112(1): 60-3. [http://dx.doi.org/10.1016/S0022-5347(17)59642-1] [PMID: 4835080]

[11] Giuliani L, Carmignani G, Belgrano E, Zambelli S, Puppo P, Cichero A. Total pelvic arterial embolization in a case of massive vesical and vaginal bleeding by pelvis carcinomatosis. Eur Urol 1979; 5(3): 205-7. [http://dx.doi.org/10.1159/000473107] [PMID: 446495]

[12] Pontin AR, Barnes RD, Young CJ. Radiation induced vesical arterial aneurysm cured by selective embolization. BJU Int 1999; 84(6): 743-4. [http://dx.doi.org/10.1046/j.1464-410x.1999.00299.x] [PMID: 10510132]

[13] Kobayashi T, Kusano S, Matsubayashi T, Uchida T. Selective embolization of the vesical artery in the management of massive bladder hemorrhage. Radiology 1980; 136(2): 345-8. [http://dx.doi.org/10.1148/radiology.136.2.7403507] [PMID: 7403507]

[14] Olliff S, Thomas S, Karani J, Walters H. Superselective embolization using a co-axial catheter technique. Br J Radiol 1990; 63(747): 197-201. [http://dx.doi.org/10.1259/0007-1285-63-747-197] [PMID: 2334831]

[15] Hays MC, Wilson NM, Page A, Harrison GSM. Selective embolization of bladder tumours. Br J Urol 1996; 78(2): 311-2. [http://dx.doi.org/10.1046/j.1464-410X.1996.16235.x] [PMID: 8813940]

[16] Stout TE, Borofsky M, Soubra A. A visual scale for improving communication when describing gross hematuria. Urology 2021; 148: 32-6. [http://dx.doi.org/10.1016/j.urology.2020.10.054] [PMID: 33285214]

[17] Angle JF, Siddiqi NH, Wallace MJ, *et al.* Quality improvement guidelines for percutaneous transcatheter embolization: Society of Interventional Radiology Standards of Practice Committee. J Vasc Interv Radiol 2010; 21(10): 1479-86. [http://dx.doi.org/10.1016/j.jvir.2010.06.014] [PMID: 20870162]

[18] 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(3): 273-82. [http://dx.doi.org/10.1007/s11604-020-01051-y] [PMID: 33030650]

[19] Carnevale FC, Antunes AA, da Motta Leal Filho JM, *et al.* Prostatic artery embolization as a primary treatment for benign prostatic hyperplasia: preliminary results in two patients. Cardiovasc Intervent Radiol 2010; 33(2): 355-61. [http://dx.doi.org/10.1007/s00270-009-9727-z] [PMID: 19908092]

[20] Appleton DS, Sibley GNA, Doyle PT. Internal iliac artery embolisation for the control of severe bladder and prostate haemorrhage. Br J Urol 1988; 61(1): 45-7. [http://dx.doi.org/10.1111/j.1464-410X.1988.tb09160.x] [PMID: 3342300]

[21] Loffroy R, Guiu B, Cercueil JP, Krausé D. Endovascular therapeutic embolisation: an overview of occluding agents and their effects on embolised tissues. Curr Vasc Pharmacol 2009; 7(2): 250-63. [http://dx.doi.org/10.2174/157016109787455617] [PMID: 19356008]

[22] Higgins CB, Bookstein JJ, Davis GB, Galloway DC, Barr JW. Therapeutic embolization for intractable chronic bleeding. Radiology 1977; 122(2): 473-8. [http://dx.doi.org/10.1148/122.2.473] [PMID: 834898]

[23] Kwak BK, Shim HJ, Han SM, Park ES. Chitin-based embolic materials in the renal artery of rabbits: pathologic evaluation of an absorbable particulate agent. Radiology 2005; 236(1): 151-8. [http://dx.doi.org/10.1148/radiol.2361040669] [PMID: 15987971]

[24] Laurent A. Microspheres and nonspherical particles for embolization. Tech Vasc Interv Radiol 2007; 10(4): 248-56. [http://dx.doi.org/10.1053/j.tvir.2008.03.010] [PMID: 18572137]

[25] Vaidya S, Tozer KR, Chen J. An overview of embolic agents. Semin Intervent Radiol 2008; 25(3): 204-15. [http://dx.doi.org/10.1055/s-0028-1085930]

[26] Lee SH, Lin CY, Hsu YC, Liu YS, Chuang MT, Ou MC. Comparison of the efficacy of two microsphere embolic agents for transcatheter arterial chemoembolization in hepatocellular carcinoma patients. Cancer Res Treat 2020; 52(1): 24-30. [http://dx.doi.org/10.4143/crt.2019.018] [PMID: 31048665]

[27] Spies JB, Allison S, Flick P, *et al.* Polyvinyl alcohol particles and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a randomized comparative study. J Vasc Interv Radiol 2004; 15(8): 793-800. [http://dx.doi.org/10.1097/01.RVI.0000136982.42548.5D] [PMID: 15297582]

[28] Han K, Kim SY, Kim HJ, *et al.* Nonspherical polyvinyl alcohol particles *versus* tris-acryl microspheres: Randomized controlled trial comparing pain after uterine artery embolization for symptomatic fibroids. Radiology 2021; 298(2): 458-65. [http://dx.doi.org/10.1148/radiol.2020201895] [PMID: 33350893]

[29] Park S, Shin JH, Gwon DI, *et al.* Transcatheter arterial embolization for gastrointestinal bleeding associated with gastric carcinoma: Prognostic factors predicting successful hemostasis and survival. J Vasc Interv Radiol 2017; 28(7): 1012-21. [http://dx.doi.org/10.1016/j.jvir.2017.03.017] [PMID: 28483303]

[30] Taha DE, Shokeir AA, Aboumarzouk OA. Selective embolisation for intractable bladder haemorrhages: A systematic review of the literature. Arab J Urol 2018; 16(2): 197-205. [http://dx.doi.org/10.1016/j.aju.2018.01.004] [PMID: 29892482]