

Imaging Manifestations and Clinical Analysis of 12 Cases of Anorectal Malignant Melanoma

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AIM: To investigate the computed tomography (CT) and magnetic resonance imaging (MRI) features and clinical characteristics of primary anorectal malignant melanoma (ARMM).

METHODS: This retrospective analysis was conducted on the clinical, imaging and pathological data of 12 patients with pathologically confirmed ARMM admitted to The First Affiliated Hospital, Zhejiang University School of Medicine between March 2021 and December 2024, and the relevant literature was reviewed and summarized.

RESULTS: All patients underwent CT and MRI examinations. Among the 12 patients, 5 were male and 7 were female; their ages ranged from 37 to 78 years, with a median age of 65 years. The clinical manifestations were diverse, with bloody stool being the most common (58.3%), followed by anal pain (16.7%) and polypoid vegetation prolapsing from the anus (16.7%). Typical anal pigmentation with pruritus was rare (8.3%). Gross pathological examination revealed a polypoid tumor in 7 cases and an ulcerative or infiltrative growth pattern in 5 cases. Immunohistochemical staining results showed that 12 cases were positive for human melanoma black-45 (HMB-45) and Melan-A, and 9 cases were positive for S-100. On imaging, plain CT scan showed that the tumors were predominantly isodense or slightly hyperdense, with a maximum diameter of approximately 2–5 cm. The enhancement patterns varied, but the tumors predominantly demonstrated marked heterogeneous enhancement. On MRI, most lesions were isointense on T1WI (10/12); 11/12 lesions were slightly hyperintense on T2WI, and hyperintense on diffusion-weighted images (DWI). After enhancement, most tumors exhibited marked heterogeneous enhancement.

CONCLUSIONS: Most of the ARMM lesions in this group demonstrated atypical MRI signal characteristics, making diagnosis challenging. When an anorectal tumor exhibits iso- or hypointensity on T1WI and hyperintensity on T2WI, ARMM should be considered in the differential diagnosis. The CT manifestations lack specificity, and clinical symptoms may mimic those of benign lesions. ARMM may show involvement of the perirectal fat plane on imaging and regional lymph node metastasis and generally shows limited sensitivity to radiotherapy and chemotherapy, contributing to low therapeutic efficacy and poor prognosis. The definitive diagnosis of ARMM depends on histopathological examination, with immunohistochemical staining for S-100, HMB-45 and Melan-A can provide supportive information for the diagnosis of ARMM.

Keywords: melanoma; anal canal; rectum; magnetic resonance imaging; computed tomography

Introduction

Anorectal malignant melanoma (ARMM) is a relatively rare but highly malignant tumor, accounting for approximately 0.4%–1.6% of all melanomas and around 0.05% of all colorectal malignancies. The anorectal region is

the most common site of primary malignant melanoma in the digestive tract, and its incidence is increasing over time [1,2]. This malignancy exhibits distinct demographic characteristics, with a higher prevalence among older women and a reported male-to-female ratio of approximately 1:4. Common clinical manifestations include non-specific symptoms, such as bloody stools, anorectal pain, protruding anal masses, and tenesmus. Approximately 30%–40% of ARMM cases lack typical pigmentation, and early endoscopic examination may lead to misdiagnosis as hemorrhoids or polyps [3,4]. At the time of diagnosis, most patients have already developed distant metastases, most commonly involving the liver, lungs and brain, with an average 5-year survival rate of about 10%–22% [5,6]. Definitive diagnosis of ARMM relies on immunohistochemical examination, with positivity for S-100, human melanoma

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black-45 (HMB-45), and Melan-A serving as important diagnostic markers [7,8].

Imaging investigations primarily include computed tomography (CT) and magnetic resonance imaging (MRI), which enable early tumor screening, determination of the specific location, size and morphology of the tumor, and detection of regional lymph node metastasis, forming a crucial step in the diagnosis, staging and prognosis assessment of ARMM [9,10]. Surgical resection is the standard treatment for ARMM, with two primary approaches: wide local excision (WLE) and abdominoperineal resection (APR). However, the optimal surgical approach remains controversial. Recent studies have shown that there is no significant difference in overall survival (OS) between patient cohorts receiving WLE and APR [11,12,13]. Adjuvant therapies primarily include radiotherapy, chemotherapy and immunotherapy, with those involving anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA-4) and anti-programmed cell death protein 1 (anti-PD-1) representing current areas of clinical research [14,15,16]. In this retrospective analysis, we analyzed 12 patients with pathologically confirmed ARMM treated at our hospital. By combining CT and MRI findings, clinical characteristics and pathological results, we aimed to explore the imaging features, clinical characteristics, and treatment outcomes of ARMM, with the goal of improving imaging-based diagnosis and clinical management.

Methods

Study Population

This study employed a continuous enrollment approach and retrospectively collected data from patients admitted to The First Affiliated Hospital, Zhejiang University School of Medicine between March 2021 and December 2024. The inclusion criteria were as follows: (i) completion of pelvic CT (non-contrast and contrast-enhanced) and MRI (non-contrast and contrast-enhanced) examinations within the same time period (no more than 4 weeks apart), with complete and clear imaging data that met the requirements for subsequent analysis; and (ii) pathologically diagnosed ARMM based on surgical resection or biopsy. All cases were comprehensively evaluated based on detailed clinical data (e.g., medical history, physical examination, colonoscopy, and abdominal ultrasound or whole-abdominal CT imaging). In accordance with current diagnostic and treatment guidelines, primary tumors originating from other anatomical sites were ruled out. A total of 12 patients who ultimately met the above criteria were included in the study cohort. The collected data included clinical symptoms, CT and MRI findings, and immunohistochemical staining results. Of the 12 patients, 11 underwent surgical resection, and 1 patient was diagnosed with multiple distant intracranial metastases, sacrum, and liver at the time of diagnosis and therefore underwent rectal tumor biopsy without surgical treatment.

CT and MR Image Acquisition and Imaging Evaluation

Patients were instructed to fast from both food and water for 6 hours before imaging. To reduce gastrointestinal motility, 10 mg of racemic anisodamine hydrochloride (Hangzhou Minsheng Pharmaceutical Co., Ltd., Hangzhou, China; batch NO. 2109033) was administered intravenously 15–20 minutes before the examination. Contrast-enhanced MRI and whole-abdominal enhanced CT scans were performed using multiple MRI and CT scanners, respectively; the imaging protocols followed consistent acquisition principles across all devices. The CT scanners included the Philips Brilliance iCT 256-slice CT system (software v4.1, Philips) and the GE Healthcare's Revolution Frontier (software v21BW26.X, www.gehealthcare.com), Optima CT540 (software v20BW15.x), and Revolution CT systems (software v23MW17.18). MRI examinations were performed using the GE Healthcare 1.5T Optima MR360 (software vSV20.3), 3.0T SIGNA Architect (software vDV29.5), and 1.5T SIGNA Voyager (software vVX29.1), as well as the United Imaging 3.0T uMR 880 (United Imaging, www.united-imaging.com).

The MRI scanning protocols were based on standardized guidelines [17]. The scanning sequences included: (1) sagittal, oblique coronal (parallel to the long axis of the rectal tumor) and oblique axial (perpendicular to the long axis of the rectal tumor) T2-weighted high-resolution spin echo sequences (slice thickness of 3 mm, slice spacing of 0; repetition time [TR]: 2500 ms to 6000 ms, echo time [TE]: 90 ms); (2) T1 cross-section: TR 570 ms, TE 13.5 ms, slice thickness 3 mm; (3) diffusion-weighted images (DWI) sequence (slice thickness [SL] of 3 mm, slice spacing of 0; TR: 3000–8000 ms, TE set to the shortest TE value; low b-value = 50 s/mm², high b-value = 1000 s/mm²), with the distribution map of apparent diffusion coefficient (ADC) determined; (4) contrast-enhanced sequences that acquire T1-weighted images in the sagittal, oblique coronal and oblique axial planes (SL of 2 mm, inter-slice spacing of 0; TR: 300–700 ms, TE set to the shortest TE value; flip angle is 12°). Gadolinium contrast agent (Gadopentetic Acid Dimeglumine Salt 0.2 mL/kg up to a maximum of 15 mL or gadobutrol 0.1 mL/kg up to a maximum of 7.5 mL, at a flow rate of 2.0–2.5 mL/s) was intravenously injected, followed by flushing with 20 mL of physiological saline.

The acquisition parameters for the CT plain scan sequence are as follows: iCT256: kV = 120, mAs = 277, SL = 5 mm, iterative reconstruction technique (iDose) = 3, window width (WW) = 200 Hounsfield unit (HU), window level (WL) = 40 HU, display field of view (DFOV) = 36.4 cm × 36.4 cm; Revolution Frontier: kV = 120, mAs = 29, SL = 5 mm, WW = 200, WL = 40, DFOV = 37 cm × 37 cm, Smart Prep Series; Revolution CT: kV = 120, mAs = 200, SL = 1.25, WW = 200, WL = 40, DFOV = 39.5 cm × 39.5 cm, Abdomen C+1.25 mm P; Optima CT540: kV = 120, mAs = 32, SL = 5 mm, WW = 200, WL = 40, DFOV = 30.7 cm × 30.7 cm.

The enhanced CT scanning protocol is as follows: Patients were instructed to assume a supine position and hold their breath during the scan, with the scanning range extending from the diaphragmatic dome to the lower edge of the pubic symphysis. During the contrast-enhanced scan, non-ionic contrast agent iodixanol (iodine content 320 mgI/mL) or iopamidol (iodine content 350 mgI/mL) was administered via high-pressure injection into the cubital vein. The total contrast agent dose for iodixanol (320 mgI/mL) is 1.3 mL/kg up to a maximum of 100 mL, and that for iopamidol (350 mgI/mL) is 1.2 mL/kg up to a maximum of 100 mL, with a flow rate of 2–3 mL/s. Scan parameters are as follows: tube voltage of 120 kVp, using automatic tube current modulation technology; noise index set to 8; slice thickness and slice spacing both 5 mm; and pitch of 0.992:1. Thin-slice reconstruction was performed at 0.625 mm for the arterial phase, and coronal and sagittal multiplane reconstruction (MPR) was conducted at a slice thickness of 2 mm. For the arterial phase, a bolus-tracking method was used to automatically trigger image acquisition. The venous phase was acquired 60 seconds after completion of the arterial phase scan.

CT and MR images of all enrolled patients were independently reviewed and evaluated in a blinded manner by two radiologists. The two radiologists had 5 years (attending physician) and 10 years (associate chief physician) of experience in abdominal and pelvic imaging, respectively. Both radiologists were blinded to the patients' clinical and pathological information during image evaluation. Each radiologist independently assessed the radiological features and provided an interpretation. When the interpretations were concordant, that result was accepted directly. In cases of discrepancy, consensus was reached through joint discussion and consultation. If consensus could not be reached after discussion, the assessment of the associate chief physician was adopted as the final interpretation. Tumor maximum diameter was measured on the largest cross-sectional image available on CT or MRI. Given the limited number of cases in this group, no statistical tests were performed to assess inter-reader agreement.

The operational definitions of the various parameters used for image interpretation are as follows: (1) density/signal intensity assessment (using adjacent normal muscle tissue as a reference): On CT, "isodense" indicates that the density of the lesion is similar to that of adjacent normal muscle (such as the obturator internus or gluteus maximus); "hypodense" indicates that the density of the lesion is lower than that of adjacent normal muscle; and "hyperdense" indicates that the density of the lesion is higher than that of adjacent normal muscle. On MRI, isointense, hypointense, and hyperintense signals refer to the lesion's signal intensity being the same as, lower than, or higher than that of adjacent normal muscle, respectively (assessed separately on T1-weighted images (T1WI), T2-weighted images (T2WI), and DWI sequences). (2) Contrast-enhanced

imaging findings: "Marked enhancement" refers to a degree of enhancement significantly higher than that of adjacent normal muscles following intravenous administration of contrast agent (qualitative assessment); "homogeneous enhancement" refers to uniform density/signal distribution within the lesion after enhancement, with no obvious regional differences; "inhomogeneous enhancement" refers to the presence of marked density/signal differences within the lesion after enhancement, with patchy, nodular, or linear areas of low or no enhancement visible. (3) Regional lymph node metastasis refers to the presence of any of the following findings in regional lymph nodes within the pelvis (including pararectal, obturator, internal iliac, and external iliac lymph nodes): (1) shortest diameter ≥ 10 mm; (2) shortest diameter < 10 mm, but accompanied by malignant features such as irregular shape, blurred margins, internal necrosis, annular enhancement, or a tendency toward fusion. (4) Blurring of the perirectal fat refers to the presence of cord-like, reticular, or patchy abnormal soft tissue shadows within the perirectal fat space, or increased fat density/signal intensity, with indistinct space boundaries and marked asymmetry compared to the normal side, suggesting tumor invasion or a local inflammatory reaction.

Pathological Analysis

Histological specimens from 12 patients were examined using routine tissue sectioning and hematoxylin and eosin (H&E) staining, followed by evaluation under light microscopy. Immunohistochemical detection was performed using a fully automated immunohistochemistry instrument (Ventana BenchMark XT Autostainer, Roche Ventana Company), with diaminobenzidine (DAB) counterstaining for visualization. The immunohistochemistry system was operated using Ventana Software Suite (VSS), version 12.5 (Ventana Medical Systems Inc). The immunohistochemical panel included HMB-45, Melan-A, S-100, SRY-box transcription factor 10 (SOX10), Ki-67, pan-cytokeratin (CKpan), chromogranin A (CgA), synaptophysin, and leukocyte common antigen (LCA). All antibodies were purchased from Fuzhou Maxin Biotechnology Development Co., Ltd (Fuzhou, China; product/catalog numbers as follows: HMB-45, MAB-0098; Melan-A, MAB-0275; S-100, Kit-0007; SOX10, RMA-0726; Ki-67, MAB-0672; CKpan, MAB-0051; CgA, MAB-0707; Syn, MAB-0742; LCA, MAB-0552). The primary antibodies were used as working solutions (without additional dilution). Sections were incubated with the primary antibodies at room temperature for 20–30 min, followed by visualization with DAB. The antibody clones and positive staining localizations were as follows: HMB-45 (HMB45, cytoplasm), Melan-A (A103, cytoplasm), S-100 (4C4.9, nucleus/cytoplasm), SOX10 (EP268, nucleus), Ki-67 (MIB-1, nucleus), CKpan (AE1/AE3, cytoplasm), CgA (MX018, cytoplasm), Syn (SP11, cytoplasm), and LCA (PD7/26, membrane/cytoplasm). Positive immunoreactivity was de-

fined as the presence of brownish-yellow granules in the corresponding cellular compartments. Both positive and negative controls were included in each staining procedure.

Data Analysis and Follow-up

Follow-up was initiated from the date of the first definitive diagnosis. The primary endpoints were recurrence-free survival (RFS), defined as the time from diagnosis to the first occurrence of local recurrence or distant metastasis, and overall survival (OS), defined as the time from diagnosis to death from any cause. Since only one death occurred in this cohort, it was not statistically feasible to perform reliable Kaplan–Meier survival analysis or Cox regression analysis. Continuous variables were presented as mean $\pm$ standard deviation (SD) or median (range), as appropriate. Therefore, follow-up outcomes were summarized using descriptive statistics, including median, range, and frequency, without between-group significance testing. For patients who were lost to follow-up, survival data were censored at the date of the last known follow-up.

Results

Clinical Features

The cohort comprised 5 males and 7 females, with ages ranging from 37 to 78 years (median, 65 years). The primary tumor was located in the anal canal in 3 cases, the lower rectum in 6 cases, and involved both the lower rectum and anal canal in 3 cases. Clinical manifestations were diverse and non-specific, with bloody stool being the predominant symptom. Seven patients presented with hematochezia bloody stool as the initial symptom, two with anal pain, and two with a polypoid vegetation prolapsing from the anus. Only one patient presented with typical anal pigmentation accompanied by pruritus. Preoperative quantitative tumor marker testing revealed carcinoembryonic antigen (CEA) positivity in one patient (6.4 ng/mL; reference range 0–5.0 ng/mL) and carbohydrate antigen 125 (CA125) positivity in one patient (41.6 U/mL; reference range 0–35 U/mL). All patients had carbohydrate antigen 19-9 (CA19-9) levels within the normal range. The clinical characteristics of the patients are shown in Table 1.

Pathological Examination

Gross pathological examination revealed a polypoid tumor morphology in 7 cases, whereas the remaining 5 cases exhibited an ulcerative or infiltrative growth pattern. Immunohistochemical staining showed that all 12 patients were positive for HMB-45 and Melan-A. S-100 expression was positive in 9 patients, negative in 2, and not tested in 1 patient. Pathological examination confirmed malignant tumors of the rectum or anal canal, with immunohistochemical findings consistent with malignant melanoma (Fig. 1). Among the immunohistochemical markers evaluated in this study, HMB-45, Melan-A, and S-100 were considered the melanocyte-specific markers that play a key role

Table 1. Clinical characteristics of the 12 patients with anorectal malignant melanoma.

Clinicopathological features	<i>n</i>
Gender	
Male	5
Female	7
Age of onset (years), mean $\pm$ SD	64.6 $\pm$ 10.8
Tumor anatomical site	
Rectum	6
Anal canal	3
Rectum and anal canal	3
Initial clinical symptoms	
Bloody stool	7
Anal pain	2
Polypoid vegetation prolapsing from the anus	2
Anal pigmentation with pruritus	1
Metastasis	
Liver	3
Intracranial	1
Sacrum	1
Regional lymph node	4
Follow-up	
Survival	10
Death	1
Lost to follow-up	1

in the definitive diagnosis of ARMM. The remaining markers, namely SOX10 and Ki-67, were primarily used for differential diagnosis. However, given the small cohort size of 12 patients and the absence of statistical analysis, immunohistochemical findings concerning SOX10 and Ki-67 were of limited analytical value; therefore, only the results for HMB-45, Melan-A, and S-100 are reported.

Imaging Manifestation

Among the 12 lesions, 11 demonstrated intestinal wall thickening, including 2 cases presented with uniform thickening and 9 with non-uniform thickening. Of the 2 cases with uniform thickening, 1 was accompanied by circular calcification. Among the 9 cases with non-uniform thickening, 7 exhibited circumferential thickening. The remaining lesion presented as a solitary polypoid lesion. Three patients had distant metastases, including 2 with liver metastases and 1 with intracranial metastases, sacrum, and liver. Regional lymph node metastases were identified in 4 patients. No obvious signs of intestinal obstruction were observed in all 12 patients. On plain CT scans, 6 lesions appeared isodense, 4 slightly hyperdense, and 2 demonstrated mixed isodensity and hyperdensity. Following contrast administration, 3 cases showed marked homogeneous enhancement, whereas 9 demonstrated marked heterogeneous enhancement. The fat planes around the intestine were well-defined in 6 cases and indistinct in 6 cases, while enlarged peri-intestinal lymph nodes were observed in 5

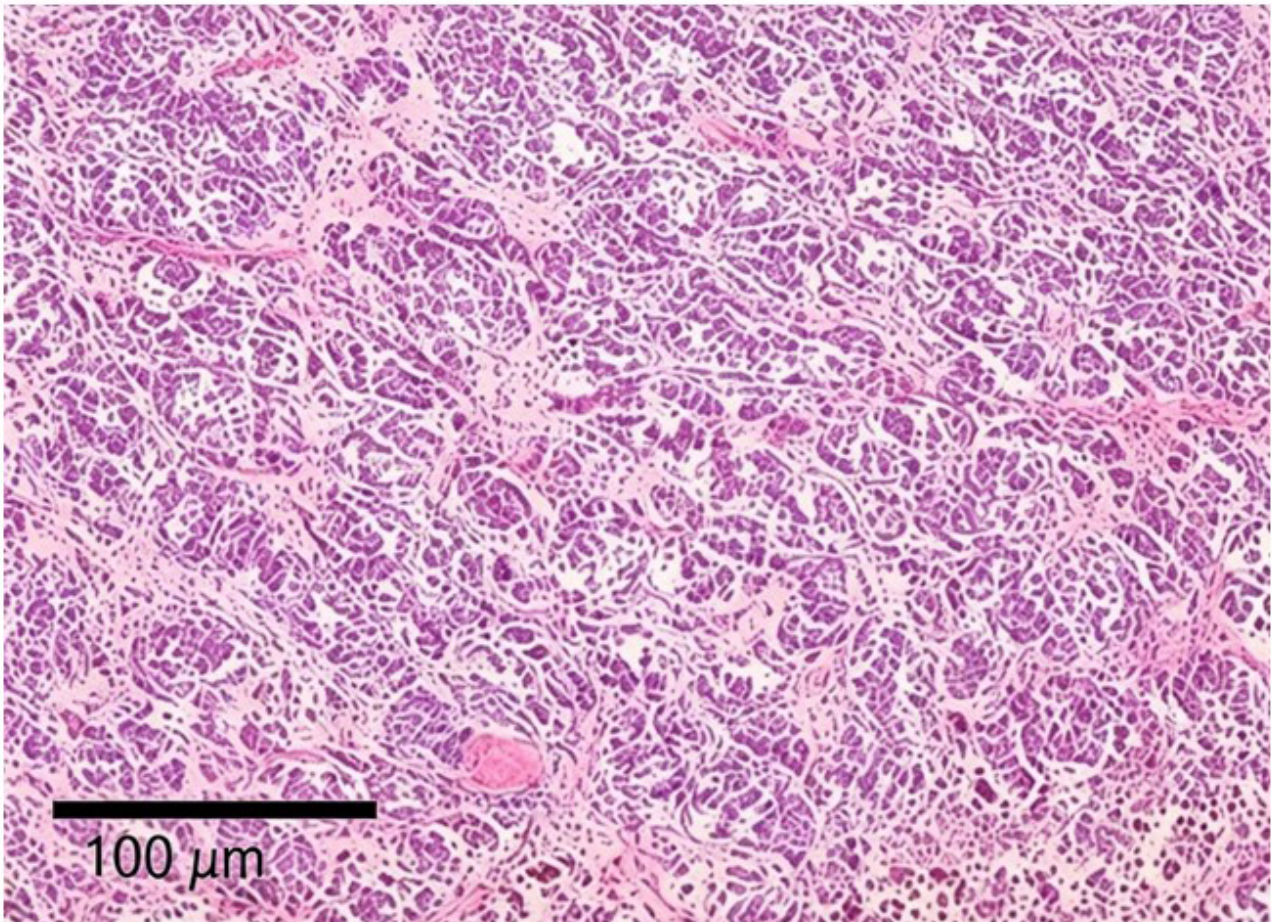


Fig. 1. Microscopic findings from a hematoxylin and eosin (H&E) staining tissue section of a 64-year-old male patient with anorectal malignant melanoma (ARMM) (magnification 40×). The tumor cells show a diffuse infiltrative growth pattern in nests and sheets, with significant cellular atypia and prominent nucleoli. Some cells contain focal melanin deposition and adjacent mucosa shows extensive necrosis.

cases (Fig. 2). None of the 12 patients showed clear CT signs of intestinal obstruction.

On MRI, 10 lesions demonstrated isointense signal intensity on T1WI, 1 showed mixed high and low signal intensity, and 1 showed slightly hyperintense signal intensity. On T2WI, 11 lesions appeared slightly hyperintense and 1 was isointense. All cases demonstrated high signal intensity on DWI. Following contrast administration, all lesions showed marked enhancement, including homogeneous enhancement in 3 cases and heterogeneous enhancement in 9 cases. Enlarged peri-intestinal lymph nodes were observed in 4 cases, with signal characteristics similar to those of the primary tumors (Fig. 3).

Treatment and Follow-up

In this cohort, 7 patients underwent APR and 4 underwent WLE. One patient presenting with multiple distant metastases at the time of consultation and refusing surgical treatment was diagnosed with malignant melanoma following biopsy of a rectal tumor. Subsequently, the patient received

four cycles of targeted therapy (dabrafenib combined with trametinib) and anti-PD-1 therapy. Postoperative adjuvant therapy was administered to 6 of the 11 patients who underwent surgery, with radiotherapy in one patient, chemotherapy in one patient, immunotherapy in three patients, and chemotherapy combined with immunotherapy in one patient. Adjuvant radiotherapy, chemotherapy, immunotherapy and targeted therapy are hereinafter referred to as adjuvant therapy.

All follow-up data in this study were derived from the patients' routine outpatient follow-up records. All patients returned to the hospital periodically for imaging and laboratory tests in accordance with the postoperative follow-up plan outlined in their discharge summaries or the scheduled cycles of their established chemotherapy regimens. The frequency and scope of these follow-up visits adhered to standard clinical management protocols and did not involve any additional study-related contacts. Of the 12 patients in the group, 1 (Case 1) was lost to follow-up approximately 2 months after the clear diagnosis was made (censored at the

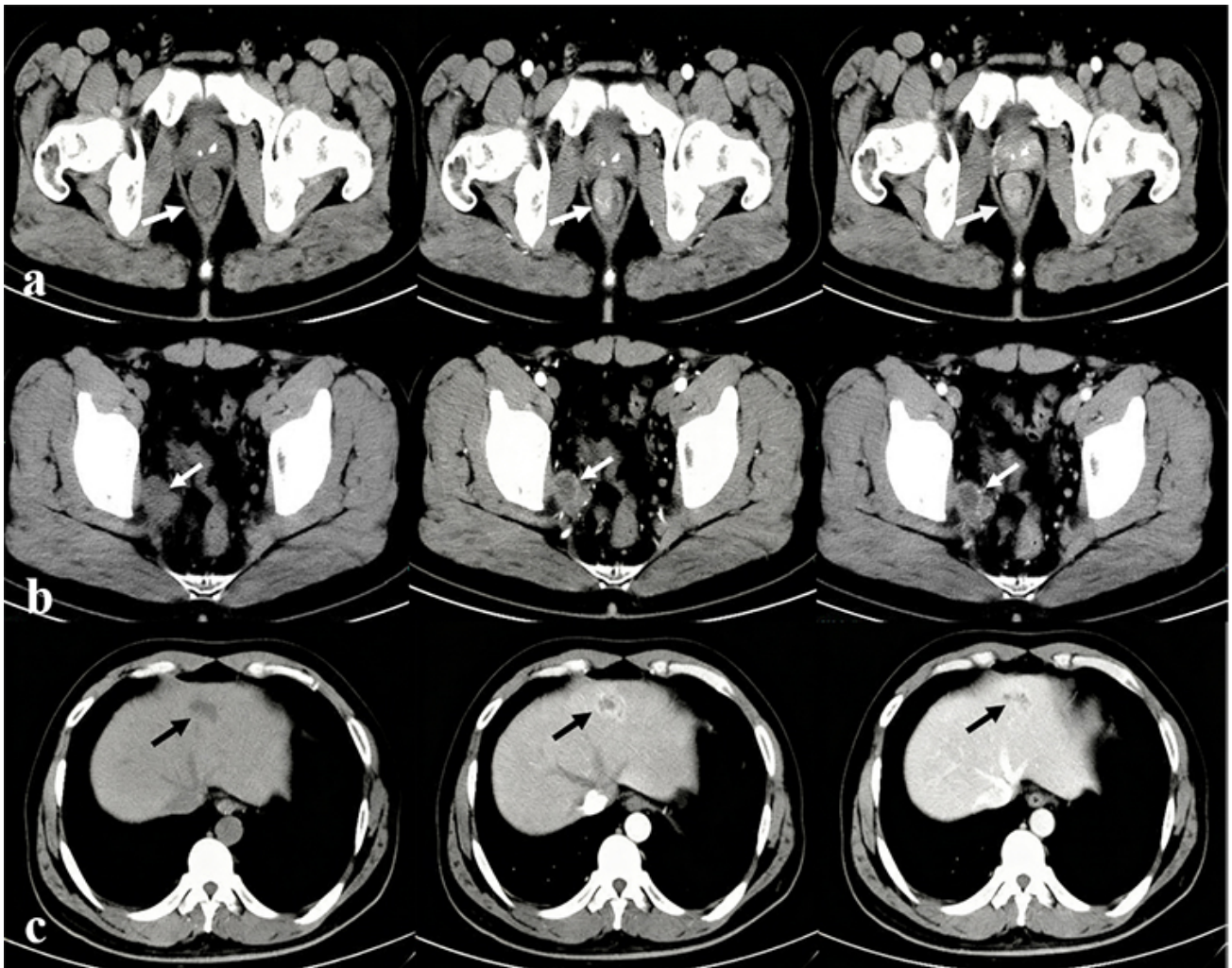


Fig. 2. Contrast-enhanced computed tomography (CT) scan of the whole abdomen of a 37-year-old male patient. The images from left to right are plain scan, arterial phase, and venous phase. (a) A polypoid mass protruding into the rectal lumen is observed (thick white arrows). On plain CT scan, the mass appears isodense with relatively homogeneous density, and the corresponding intestinal lumen appears narrowed. On contrast-enhanced images, the mass demonstrates marked heterogeneous enhancement. (b) Enlarged lymph nodes are visible on the right side of the pelvis (thin white arrows). On the contrast-enhanced scan, the lesions show ring-like enhancement, suggesting metastatic lymph nodes. (c) In segment II of the liver, a slightly hypodense nodule (thick black arrows) is seen. The “target sign” can be observed in both the arterial phase and venous phase, suggesting a metastatic tumor.

time of the last follow-up). The median follow-up duration for the remaining 11 patients was 18 months (range: 6–36 months). As of the last follow-up, 10 patients were alive; 1 patient (Case 4) died approximately 3 months after undergoing Gamma Knife surgery for intracranial metastases. During follow-up, 2 patients experienced recurrence or metastasis. Of these 2 patients, 1 patient—who had not received adjuvant therapy—developed distant metastases (involving the liver and lungs) 14 months after the definite diagnosis, whereas the other patient—who had received 8 cycles of chemotherapy following APR—developed local pelvic peritoneal metastases. Due to significant heterogeneity between the two groups in terms of baseline disease staging (localized vs. metastatic) and subsequent treatment regimens, as well as the small number of events, this

study did not perform a statistical comparison of the efficacy of adjuvant therapy. Owing to the retrospective design and the long interval since treatment in some cases, certain treatment details (e.g., product name of PD-1 inhibitor, exact dosage, and radiotherapy fractionation) were not fully available in the medical records. Only information that was available in the medical records, such as detailed follow-up durations, recurrence status and sites, and survival status, is presented in Table 2.

Discussion

Clinical and Pathological Characteristics of ARMM

Melanoma primarily occurs in the skin, while a small number of cases (approximately 0.8%–3.7%) may occur in other parts, with mucosal sites being the most common, includ-

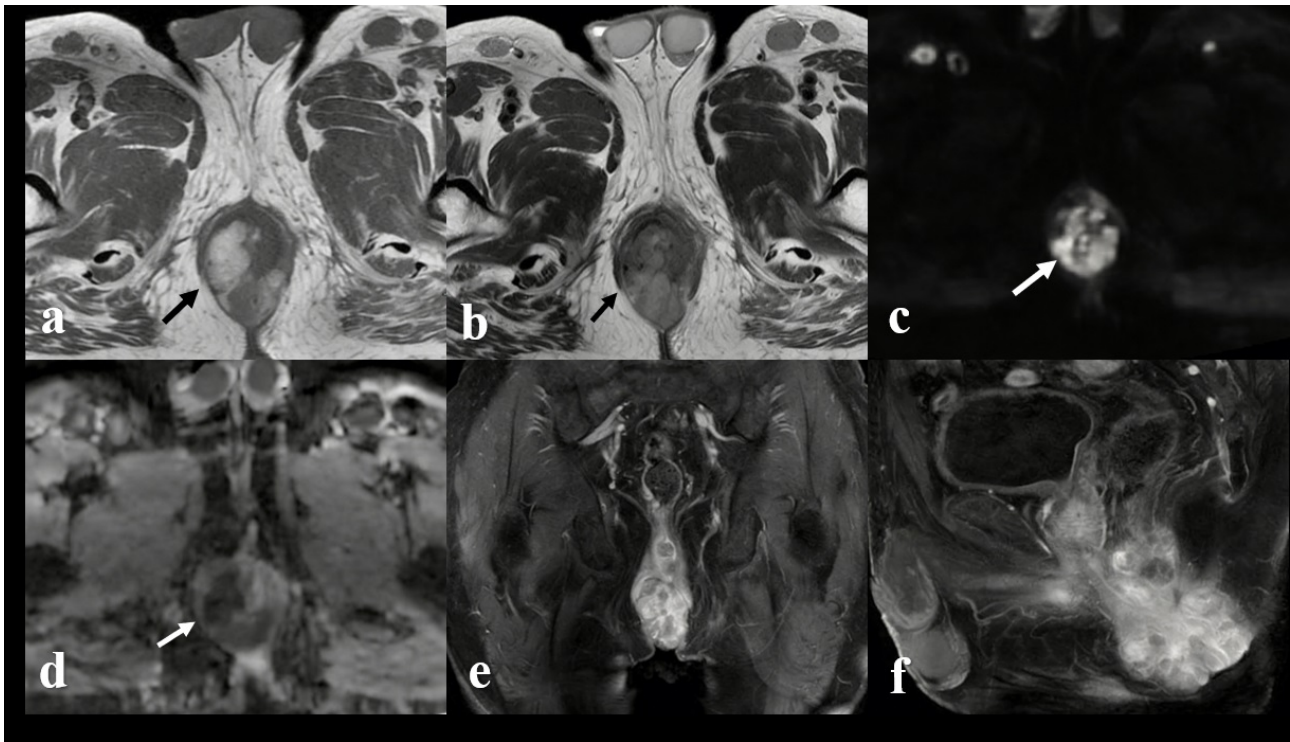


Fig. 3. Plain and contrast-enhanced magnetic resonance imaging (MRI) images of the rectum of a 64-year-old male patient. (a,b) Axial T1-weighted images (T1WI) (thick black arrow) and T2-weighted images (T2WI) (thick black arrow) show a polypoid mass filling the rectal lumen. (c,d) Diffusion-weighted images (DWI) sequence with b-value = 1000 (thick white arrow) shows increased signal intensity of the mass, and the corresponding apparent diffusion coefficient (ADC) value (thin white arrow) is decreased. (e,f) Coronal and sagittal fat-suppressed sequences of T1-weighted enhanced scan demonstrate marked heterogeneous enhancement of the mass. The lesion involves the rectum and anal canal, with loss of the normal architecture of the mucosal and muscular layers in the rectum and anal canal. The serosal surface appears irregular, and the surrounding fat planes are indistinct.

ing the nasopharynx, oral cavity, vagina, rectum and anus. Compared with cutaneous melanoma, mucosal melanoma has a poorer prognosis [18,19]. ARMM has an insidious onset and non-specific clinical presentation. Most ARMM cases mimic other benign lesions of the rectum and anus, representing one of the most common reasons for delayed diagnosis. In some advanced-stage patients, local symptoms caused by metastatic lesions constitute some of the initial manifestations [20]. In this study, the median age of patients was 65 years, ranging from 37 to 78 years. We also observed a slight gender predominance, with female patients accounting for 58.3% (7/12) of cases, slightly higher than males, consistent with previous reports that ARMM is more common in older women [21,22,23]. In our cases, lesions involving only the rectal area accounted for 50% (6/12), while 50% (6/12) involved the anal canal and rectal-anal junction. This finding is slightly inconsistent with a previous large-scale study [24] reporting that most ARMM lesions were located in the anal or junctional area (66%). This discrepancy may be attributable to the smaller sample size of this study. None of the 12 patients in this cohort exhibited obvious signs of intestinal obstruction, consistent with the finding of Santhalia et al. [25], who reported that ARMM often presents as a large, intraluminal poly-

poid mass without causing any obstruction. In this study, only one lesion was accompanied by anal pigmentation and pruritus, suggesting that it is unreliable to make a diagnosis solely based on the typical signs of pigmentation. Diagnosis of this disease requires careful morphological observation combined with relevant imaging studies, with a definite diagnosis ultimately established through immunohistochemical staining and molecular pathology.

Grossly, ARMM tumors can be divided into three types: polypoid, ulcerative, and infiltrative. The polypoid type is more common, presenting as a polypoid protrusion into the intestinal lumen, accompanied by bleeding and ulceration. With well-defined margins, a polypoid tumor can easily be mistaken for a rectal polyp [26]. In this cohort, the polypoid type was the most common macroscopic pathological presentation (7/12), which is consistent with previous findings. Malignant melanoma is characterized by the presence of brown-black pigment granules within the cytoplasm of tumor cells, but some tumors do not produce distinct melanin. The diagnosis must be confirmed by immunohistochemical staining. The immunohistochemical staining showed that HMB-45 and Melan-A were positive or focally positive in all 12 patients, and S-100 was positive in 9 cases (negative in 2 cases and not tested in 1 case). Melanoma cells

Table 2. Surgical methods, follow-up details and outcomes, and adjuvant treatment regimens in 12 patients.

Case	Surgical method	Follow-up start date	Follow-up duration (months)	Recurrence/metastasis (with location)	Time of first recurrence (months after diagnosis)	Status as of the last follow-up	Adjuvant therapy
1	APR	2021-3	2	Lost	Lost	Lost	Lost
2	WLE	2021-5	36	None	None	Survived and in good condition	Anti-PD-1 therapy for 4 cycles
3	WLE	2021-6	24	None	None	Survived and in good condition	None
4	None	2021-10	8	/	/	Died about 3 months after undergoing Gamma Knife surgery for intracranial metastatic tumor	Targeted therapy (dabrafenib + trametinib) and anti-PD-1 therapy for 4 cycles
5	APR	2022-1	36	None	None	Survived and in good condition	None
6	APR	2022-6	12	None	None	Survived and in good condition	None
7	APR	2021-3	16	Pelvic peritoneal metastasis	9	Survived	Chemotherapy (dacarbazine + temozolomide) for 8 cycles
8	APR	2022-8	18	Recurrence accompanied by hepatic and pulmonary metastasis	14	Survived	None
9	WLE	2023-3	36	None	None	Survived and in good condition	Conventional fractionated radiotherapy for 1 cycle
10	APR	2023-3	24	None	None	Survived; right-sided urinary tract infection developed after last immunotherapy (about 1-year post-surgery) and improved with symptomatic treatment	Anti-PD-1 therapy for 10 cycles
11	APR	2024-8	10	None	None	Survived and in good condition	Chemotherapy and immunotherapy (cisplatin plus temozolomide plus toripalimab) for 1 cycle, and then oral temozolomide for 5 cycles
12	WLE	2024-12	6	None	None	Survived and in good condition	Anti-PD-1 therapy for 4 cycles

APR, abdominoperineal resection; WLE, wide local excision; PD-1, programmed cell death protein 1.

exhibited positive reactivity to S-100, HMB-45, Melan-A, Ki-67, vimentin, and tyrosinase. HMB and Melan-A are specific markers for malignant melanoma, but their sensitivity is decreased in advanced diseases and cannot be used as an indicator for distinguishing between malignant and non-malignant melanocytic lesions. S-100 shows a high but non-specific sensitivity for ARMM. The proliferative marker Ki-67 is present at very low levels in common nevi but is found in 30%–100% of melanoma cells. The level of Ki-67 may be correlated with tumor recurrence, lymph node metastasis, and poor prognosis [19,27]. In recent years, it has been proposed that MART-1 could serve as a marker for the presence of melanoma cells in lymph nodes [28].

Imaging Manifestations of ARMM

MRI provides superior soft tissue contrast and enables detailed assessment of local tumor characteristics, making it the optimal imaging modality for local staging of rectal and anal canal malignancies [29]. CT can be used for the screening and detection of lesions, and contrast-enhanced CT can clearly depict lesion characteristics and local findings [25]. ARMM most commonly presents as a large, polypoid mass protruding into the intestinal lumen, with a maximum diameter often exceeding 3 cm, almost filling the lumen, yet rarely causing intestinal obstruction. This may be related to the tumor's tendency to grow along the longitudinal axis of the intestinal lumen, with the lumen expanding as the tumor grows [25,30]. In this cohort, 58.3% (7/12) of cases presented as polypoid masses, with a maximum diameter of approximately 2–5 cm. On plain CT scans, the lesions appeared isodense or slightly hyperdense, with mostly homogeneous density, and calcification was rarely observed. Among the patients in this cohort, 4 cases exhibited regional lymph node metastasis, and 3 cases had distant liver metastasis. In this cohort, there were 4 cases of regional lymph node metastasis, 3 cases of distant metastasis occurred in the liver, 1 case in the head, and 1 case in the sacrum.

The typical signal features of melanoma on MRI exhibit a certain specificity: high signal intensity on T1WI and low signal intensity on T2WI. This is due to the paramagnetic effect of melanin, which shortens both T1 and T2 relaxation times. In this study, only two lesions exhibited high signal intensity on T1WI, and the majority displayed atypical signal features, leading to diagnostic difficulties. This finding is consistent with the results of previous studies [31,32]. Atypical signal characteristics are associated with the content and distribution of melanin within the lesion, and may also be related to intratumoral hemorrhage and liquefactive necrosis. Hemorrhage at different stages presents with varying signal characteristics on MRI, which may contribute to the atypical and heterogeneous signal appearances of ARMM. On contrast-enhanced MRI scans, ARMM frequently shows moderate or marked heterogeneous enhancement. Both CT and MRI examinations can indicate lymph node metastasis. The most commonly affected sites are the

perirectal lymph nodes, and MRI provides a clearer view of the lymph nodes. In this group, CT scans showed perirectal lymph node enlargement in 5 cases, while MRI scans showed perirectal lymph node enlargement in 4 cases, and their signal characteristics were consistent with those of the primary lesion. Postoperative pathologic examination confirmed that four of these abnormalities were regional lymph node metastases.

Treatment and Prognosis of ARMM

Currently, there is no standard treatment protocol for ARMM established by the American Joint Committee on Cancer (AJCC). Clinically, surgery is the treatment of choice for disease control [2]. There remains controversy regarding the optimal surgical approach. Wide local excision (WLE) preserves sphincter function but carries a risk of positive surgical margins and is generally considered suitable for patients with early-stage disease [33]. Although abdominoperineal resection (APR) improves local control, it requires a permanent stoma and is more suitable for patients with larger lesions and a wider extent of invasion [34]. Some studies suggest that there is no significant difference between the two procedures in terms of prognosis and survival rates [35,36]. However, several studies have indicated that surgical resection alone may not yield significant survival benefits in patients with advanced ARMM [37,38]. Consequently, a comprehensive approach combining surgery with adjuvant therapy is the primary strategy for managing advanced ARMM [20,39].

Research at the molecular level has driven the development of postoperative adjuvant immunotherapy and other targeted therapies for unresectable advanced melanoma. V-raf murine sarcoma viral oncogene homologue B1 (*BRAF*) is the most common genetic mutation in melanoma, with *BRAF* mutations present in approximately 50% of melanoma cases. Several studies have shown that compared to the high frequency of *BRAF* mutations in cutaneous melanoma, the frequency of *BRAF* mutations in mucosal melanoma is lower. Nevertheless, *BRAF* remains an important target for clinical targeted therapy in ARMM [11,40,41,42]. In this cohort, one patient with a *BRAF* p.G466E mutation received a therapy combining a *BRAF*/Mitogen-Activated Protein Kinase Kinase (MEK) inhibitor with anti-PD-1 therapy. Currently, there is a lack of large-scale evidence regarding the efficacy of targeted therapy for non-V600 *BRAF* mutations, and since this cohort included only one such case, it is not possible to assess the efficacy of this combination regimen based on the available data.

Although numerous studies in recent years have demonstrated that drugs such as *BRAF*/MEK inhibitors and tyrosine kinase inhibitors have significantly improved treatment outcomes for cutaneous melanoma, ARMM exhibits low sensitivity to radiotherapy and chemotherapy due to differences in genomic expression profiles, and the efficacy

of immune checkpoint inhibitors and targeted therapies is limited [43,44,45,46]. The 5-year survival rate of ARMM patients in stage IV according to AJCC statistics is approximately 15%–20% [47]. At present, standard adjuvant chemoradiotherapy and some targeted and immunotherapy regimens are still unable to effectively improve the long-term prognosis of high-risk patients following surgical resection of ARMM. Thus, there is an urgent need to explore more precise molecular stratification markers and develop novel combination adjuvant therapies and personalized treatment strategies to overcome the current therapeutic bottlenecks. The multidisciplinary collaborative approach to disease diagnosis and treatment and the integration of multimodal treatment strategies represent important future directions in the management of ARMM [37].

Advantages and Limitations

This study has several strengths. First, it focuses on ARMM, a clinically rare tumor with unique biological behavior. Given the limited number of case reports concerning this tumor, the 12 consecutive cases included in this study provide real-world diagnostic and treatment data from a provincial-level class A tertiary hospital in Zhejiang Province, China, and are thus representative of the region to a certain extent. Second, this study systematically describes and compares paired CT and MRI imaging features in a synchronized manner. Notably, it was found that the majority of lesions in this cohort exhibited isointense signal intensity on T1WI, rather than the classic melanin-like hyperintensity. This finding adds to the atypical imaging patterns of ARMM and provides new reference criteria for clinical imaging differential diagnosis. Third, this study adopted a continuous enrollment strategy, enrolling all eligible confirmed cases between March 2021 and December 2024 without selective exclusion. This approach helped mitigate the selection bias commonly associated with retrospective studies to a certain extent and enhanced the completeness of the case cohort. Furthermore, all patients had relatively comprehensive clinical, pathological, and follow-up data, providing a useful foundation for future multicenter studies.

Several limitations of this study should be highlighted. First, this was a single-center, retrospective case series. Although all eligible cases from 2021 to 2024 were consecutively enrolled to minimize selection bias, the total sample size was only 12 cases, resulting in limited statistical power, which restricts the generalizability and robustness of the conclusions. Second, although the follow-up period ranged from 6 to 36 months, the median follow-up duration was relatively short, and one patient was lost to follow-up. These factors may have limited the accurate assessment of long-term survival and recurrence patterns. Third, there was significant heterogeneity in treatment strategies, including variations in surgical techniques, adjuvant therapy, and the regimens and durations of palliative systemic therapy. Fur-

thermore, only one patient underwent next-generation sequencing; the remaining cases lacked molecular typing data for driver genes such as *BRAF*, *c-KIT*, and *NRAS*. Consequently, it was not possible to conduct meaningful association analyses between molecular characteristics and imaging findings or prognosis. Fourth, regarding radiological assessment, this study did not perform quantitative measurements of CT values for lesions, nor did it conduct quantitative or semi-quantitative analyses of ADC values or layer-by-layer delineation of regions of interest (ROI). All radiological findings were based on visual, qualitative interpretation, lacking objective quantitative metrics, which may affect the reproducibility of the results. The aforementioned limitations require validation in future prospective, multicenter, large-sample studies incorporating quantitative imageomics.

Conclusions

In summary, ARMM is a rare malignancy characterized by atypical clinical manifestations, tumor aggressiveness, and poor prognosis. The therapeutic effects of conventional adjuvant radiotherapy and chemotherapy, as well as targeted and immunotherapy regimens, remain uncertain in ARMM. On imaging, ARMM commonly presents as a polypoid mass protruding into the intestinal lumen. On plain CT scans, the lesion usually appears homogeneous and isodense or mildly hyperdense. On MRI, ARMM generally exhibits atypical signal characteristics, with predominantly isointense signals on T1WI and slightly hyperintense signals on T2WI. Post-contrast enhancement shows moderate to marked heterogeneous enhancement. Imaging examinations can provide valuable information for the diagnosis, staging, and prognostic assessment of ARMM. However, definitive diagnosis requires pathological examination supplemented by immunohistochemical staining. Owing to the rarity of ARMM and the small sample size reported in this paper, continued reporting and accumulation of ARMM cases are necessary to improve clinical and imaging understanding of this malignancy and to strengthen differential diagnosis for space-occupying lesions of the anorectal region.

Availability of Data and Materials

The data analyzed are available from the corresponding authors upon reasonable request.

Author Contributions

PZ and LC were responsible for the overall design of the research and determining the research direction. FC acquired and provided clinical and imaging data. LC and JD were responsible for collecting the clinical and radiological data and drafted the manuscript. LM and CD analyzed the data. PZ and FC supervised the study. All authors have been involved in revising the manuscript critically for important

intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy and integrity.

Ethics Approval and Consent to Participate

This study has received approval from the Ethics Committee of The First Affiliated Hospital, Zhejiang University School of Medicine (approval number: [2026B] No. 0513). The study is in line with the Declaration of Helsinki. According to the Declaration of Helsinki, in the case that informed consent is unavailable or impractical, such as in retrospective research on previously archived materials, informed consent may be exempted after examination and approval by the Ethics Committee. This study is a retrospective study that collects only patients' historical clinical data. All data used have been anonymized, do not involve personally identifiable information, and do not cause any intervention or harm to patients. Due to its retrospective nature, this study is exempt from requiring patients to sign informed consent forms.

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Conflict of Interest

The authors declare no conflict of interest.

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