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REVIEW

Imaging approaches for the diagnosis of genetic diseases affecting the female reproductive organs and beyond

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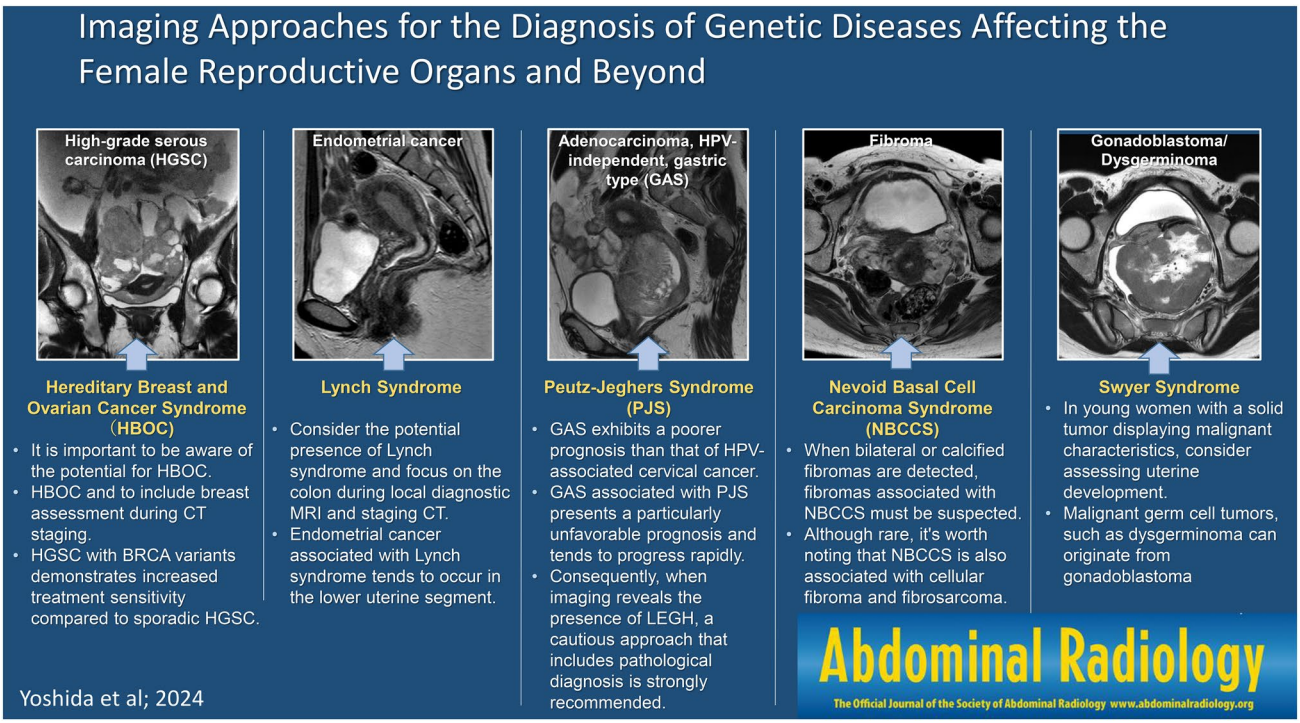
Abstract

This review aims to provide an overview of neoplastic lesions associated with genetic diseases affecting the female reproductive organs. It seeks to enhance our understanding of the radiological aspects in diagnosing genetic diseases including hereditary breast and ovarian cancer syndromes, Lynch syndrome, Peutz-Jeghers syndrome, nevoid basal cell carcinoma syndrome, and Swyer syndrome, and explores the patterns and mechanisms of inheritance that require elucidation. Additionally, we discuss the imaging characteristics of lesions occurring in other regions due to the same genetic diseases.

Graphical abstract



Keywords Uterus · Ovary · Tumor · Hereditary · Inheritance · Gene

Extended author information available on the last page of the article

Introduction

Hereditary gynecological tumors present a complex and challenging field in clinical management, but advancements in medical imaging and genetic research have led to improved understanding and characterization of these conditions. Radiologists play a crucial role in this domain, utilizing their expertise to estimate tumor histology and contribute significantly to patient care. However, radiologists often face knowledge gaps between their specialty and other fields, and understanding the genetic patterns of these diseases may still be incomplete.

This review not only focuses on well-known hereditary conditions such as hereditary breast and ovarian cancer syndromes and Lynch syndrome, but also on diseases encountered in routine practice, including benign ones. By understanding these genetic patterns and grasping the differences in imaging and clinical characteristics between hereditary and sporadic tumors, we aim to provide deeper diagnoses and appropriate investigative plans based on imaging and patient/family history.

Inheritance pattern

Although various genetic patterns exist, many of the diseases discussed in this review follow an autosomal dominant inheritance pattern. This implies that when one parent has a mutated gene on an autosome (non-sex chromosome), their child has a 50% chance to inherit this gene.

Swyer syndrome is associated with various genetic inheritance patterns beyond autosomal dominant inheritance. Among these patterns, Y-linked inheritance is a major one. This pattern involves genes located on the Y chromosome. Thus, diseases or conditions linked to these genes are exclusive to males. Another pattern is a sex-limited autosomal recessive pattern. This involves autosomal genes (non-sex chromosome), which express traits or conditions specifically in one sex, even though both sexes can carry these genes. In this pattern, an individual inherits two copies of a recessive gene, one from each parent, to express a trait or condition. However, owing to factors such as hormonal differences, anatomical variances, or other sex-specific influences, the trait or condition may manifest solely in one sex. [1].

Table 1 summarizes the causative genes and inheritance patterns for each genetic disease.

Hereditary breast and ovarian cancer syndrome (HBOC)

Hereditary breast and ovarian cancer syndrome (HBOC) is a condition characterized by an increased risk for breast and ovarian cancers. HBOC occurs in approximately 1 in 400–500 individuals, accounting for approximately 5% of breast cancers and 15% of ovarian cancers. People with HBOC are often diagnosed with cancer before the age of 50, with high-grade serous carcinoma (HGSC) being the

Table 1 Summary of the related genes, inheritance patterns, and characteristics of associated gynecologic tumors for each genetic disease

Genetic disease	Related gene	Inheritance pattern	Characteristics of associated gynecologic tumor
HBOC	*BRCA1*	Autosomal dominant	High-grade serous carcinoma: associated with HBOC demonstrates increased treatment sensitivity compared to sporadic cases
	BRCA2	Autosomal dominant	
Lynch syndrome	*MLH1*	Autosomal dominant	Endometrial carcinoma: associated with Lynch syndrome tends to occur in the lower uterine segment Ovarian cancer: various histological subtypes can occur
	MSH2	Autosomal dominant	
	MSH6	Autosomal dominant	
	PMS2	Autosomal dominant	
	EPCAM	Autosomal dominant	
PJS	*STK11*	Autosomal dominant	Lobular endocervical glandular hyperplasia Adenocarcinoma, HPV-independent, gastric type: associated with PJS presents a particularly unfavorable prognosis and tends to progress rapidly Sex cord tumor with annular tubules of the ovary: associated with PJS tends to be bilateral or very small compared to sporadic cases Mucinous tumor of the ovary
NBCCS	*PTCH1*	Autosomal dominant	Fibroma: associated with NBCCS tends to be bilateral or calcified compared to sporadic cases
Swyer syndrome	*SRY*	Y-linked	Gonadoblastoma: can originate from dysgenetic gonads Dysgerminoma: can originate from gonadoblastoma
	MAP3K1	Autosomal dominant	
	NR5A1	Autosomal dominant	
	DHH	Autosomal recessive	

HBOC Hereditary breast and ovarian cancer syndromes; *PJS* Peutz-Jeghers syndrome; *NBCCS* Nevoid basal cell carcinoma syndrome

most prevalent type of ovarian cancer associated with this syndrome [2, 3]. HBOC should be suspected in individuals with a personal or family history (Table 2) [2–4]. Serous tubal intraepithelial carcinoma (STIC) is also acknowledged as an early form of HGSC [5]. Despite being named ovarian cancer syndromes, many of these cancers are fallopian tube carcinomas rather than ovarian carcinomas [5].

It is inherited in an autosomal dominant manner, mainly due to mutations in *BRCA1* and *BRCA2*, which play crucial roles in DNA repair. *BRCA1* is a large gene located on chromosome 17q21, and its function is primarily associated with DNA integrity. It plays a significant role in the homologous recombination repair of DNA double-strand breaks, as well as in regulating cell cycle checkpoints and functioning as a co-factor for numerous transcription factors. It also controls cellular proliferation by regulating cell death (apoptosis). *BRCA2* is located on chromosome 13q12-13, and it is functionally associated with the homologous recombination repair of DNA double-strand breaks [3]. When functioning properly, these genes assist in repairing DNA breaks via homologous recombination. However, this repair mechanism is impaired in cancer cells harboring *BRCA1* or *BRCA2* variants, making the cells more vulnerable to cancer development. Conversely, these variants render cancer cells sensitive to poly (ADP-ribose) polymerase (PARP) inhibitors. PARP inhibitors block base excision repair by converting single-stranded breaks into double-stranded breaks. Therefore, *BRCA1* and *BRCA2* variant-positive cancers exhibit heightened sensitivity to platinum-based agents and PARP inhibition owing to defective homologous recombination in tumor cells [6].

HGSC is characterized by a higher incidence of bilateral disease, smaller tumor size, higher signal intensity on diffusion-weighted imaging, and more advanced stage at presentation than other epithelial ovarian cancers [7]. Further, HGSCs with *BRCA1* variants (Fig. 1a and b) are larger and more intensely enhanced, have higher levels of the tumor marker CA125, and exhibit lymph node metastases more frequently than those with *BRCA2* variants [8]. Additionally, HGSCs without *BRCA* variants typically display an infiltrative pattern within the peritoneal cavity, which can obscure the tumor margins and reduce visibility. These tumors are also more likely to spread to inaccessible sites such as the lesser sac, complicating the surgical procedure of primary debulking [9].

Regarding breast cancer, individuals with *BRCA1* variants typically develop the disease at a younger age and may initially present with more benign features (circumscribed margins, oval shapes, and posterior acoustic enhancement). However, these cancers tend to be more aggressive, have a poorer prognosis, and often exhibit a triple-negative phenotype (Fig. 1c and d), than breast cancer with *BRCA2* variants. The MRI findings characteristic of triple-negative breast cancer included pronounced rim enhancement and internal necrosis. In contrast, breast cancers associated with *BRCA2* variants resemble more spontaneous forms and are often linked to the luminal B phenotype and ductal carcinoma in situ (DCIS) [10].

Lynch syndrome

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, significantly increases the risk for various cancers, particularly colorectal and endometrial cancers. Approximately 1 in 300 individuals have Lynch syndrome. This results in extensive genetic alterations, particularly in repetitive DNA sequences. Individuals with this syndrome are often diagnosed with cancer before the age of 50. In addition to colorectal and endometrial cancers, it is associated with cancers of the ovary, stomach, small intestine, hepatobiliary tract, prostate, brain, pancreas, and urothelial

Table 2 Personal and family histories (first-, second-, or third-degree relative in either lineage) indicative of suspected hereditary breast and ovarian cancer

Personal/Family history
Breast cancer diagnosed at or before age 50 years
Ovarian cancer at any age
Multiple primary breast cancers in either one or both breasts
Male breast cancer
Triple-negative (estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2-negative) breast cancer
The combination of pancreatic cancer and/or prostate cancer (metastatic or Gleason score ≥ 7) with breast cancer and/or ovarian cancer
Breast cancer diagnosed at any age in an individual of Ashkenazi Jewish ancestry
Two or more relatives with breast cancer, one diagnosed at or before age 50 years
Three or more relatives with breast cancer at any age
A family member with a known BRCA1 or BRCA2 variant

Petrucelli et al. [2]

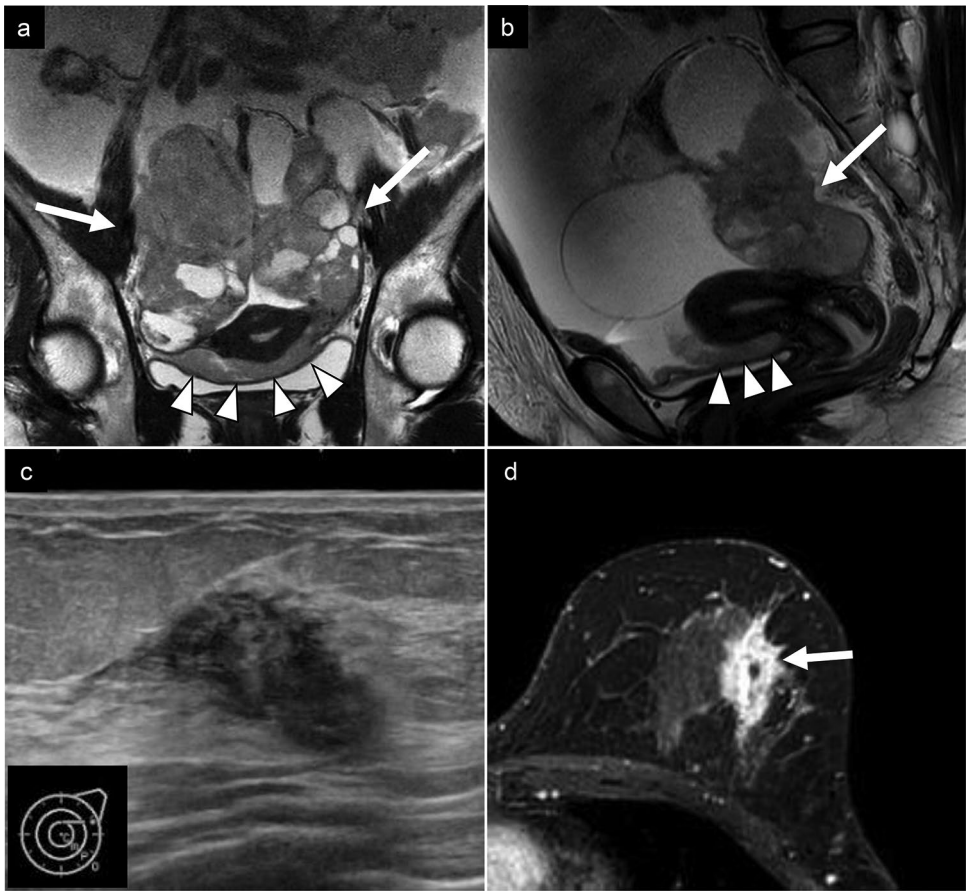


Fig. 1 A woman in her 40 s with a *BRCA1* variant and a family history of reproductive cancer, with ovarian cancer diagnosed in her mother, breast cancer in her aunt, and prostate cancer in her uncle. **a**, **b** Coronal and sagittal T2-weighted imaging showed solid and cystic tumors located in the bilateral adnexa (arrows) with an elevation of CA125 (4749 U/mL). Massive ascites and peritoneal metastasis (arrowheads) were also observed, and the staging was classified as IIIC. After a total abdominal hysterectomy and bilateral salpingo-oophorectomy, bilateral adnexal tumors were identified in the ovaries and fallopian tubes to be pathologically diagnosed as high-grade serous carcinoma (HGSC) originating from the left fallopian tube. The patient received paclitaxel and carboplatin therapy, and no recurrence of HGSC was observed in the past five years. **c** A hypoechoic mass with an irregular margin and attenuated posterior acoustic enhancement was observed on the US after three years. **d** Fat-saturated contrast-enhanced T1-weighted imaging confirmed the presence of a spiculated mass (arrow) in the left C region and was pathologically diagnosed as invasive ductal carcinoma, specifically of the scirrhous type with a triple-negative profile

tract [11, 12]. The Amsterdam II Criteria are commonly used to diagnose Lynch syndrome (Table 3) [13].

Lynch syndrome is inherited in an autosomal dominant manner. Characteristically, Lynch syndrome tumors exhibit defects in DNA mismatch repair (MMR), leading to microsatellite instability (MSI). Microsatellites are short sequences that are typically composed of repeated base units within DNA and should be copied faithfully. MSI refers to the condition in which microsatellites are not accurately replicated. Normally, when a mismatch in DNA is detected,

Table 3 Amsterdam II Criteria for Lynch syndrome

There should be at least 3 relatives with any Lynch syndrome-associated cancer (colorectal endometrial, small bowel, ureter, or renal pelvis): all of the following criteria should be present
One should be a first-degree relative of the other two
At least two successive generations should be affected
At least one should be diagnosed before age 50 years
Familial adenomatous polyposis should be excluded in the colorectal cancer case
Tumors should be verified by pathologic examination

Vasen et al. [13]

specific enzymes remove the incorrect base insert the correct one, and prevent gene mutations and the development of cancer; during MSI, these repeated regions are replicated incorrectly, leading to gene mutation and cancer development [14]. Lynch syndrome is diagnosed when pathogenic variants are identified in MMR genes, specifically *MLH1* or *MSH2*, and sometimes *MSH6*, *PMS2*, or *EPCAM*. The diminished MMR function increases the likelihood of changes occurring in repeat sequence regions in the coding regions of genes involved in tumor suppression, cell proliferation, DNA repair, apoptosis, and other aspects of carcinogenesis. The accumulation of abnormalities in these genes is believed to contribute to tumor initiation and growth. The cumulative lifetime risk for endometrial cancer is reportedly up to 26% in individuals with a mutation in *MSH6* and up to 15% in those with a mutation in *PMS2*. Mutations in *MLH1* and *MSH2* confer a 25–60% increase in risk, which is substantially higher than the 2.9% lifetime risk for endometrial cancer in the general population [14].

Unlike sporadic cancers, endometrial cancers linked with Lynch syndrome (Fig. 2) are more commonly found in the lower uterine segment. These cancers typically display endometrioid histological features similar to those observed in a broader population. Lynch syndrome-associated endometrial cancers often present with characteristics such as stage I disease, endometrioid differentiation, low-grade lesions, peritumoral lymphocytes, and lymphovascular invasion. A notable high-risk molecular marker of these cancers is the presence of *MSH2*/*MSH6* abnormalities [15–17].

In a comprehensive analysis of ovarian cancers associated with Lynch syndrome, there was a notable increase in the incidence of non-serous histological subtypes (Fig. 3). This study identified mixed ovarian carcinoma, including mucinous, endometrioid, and clear cell types, as the most prevalent, accounting for 33% of cases. This was followed by endometrioid carcinoma (25%) and serous carcinoma (22%) [18, 19].

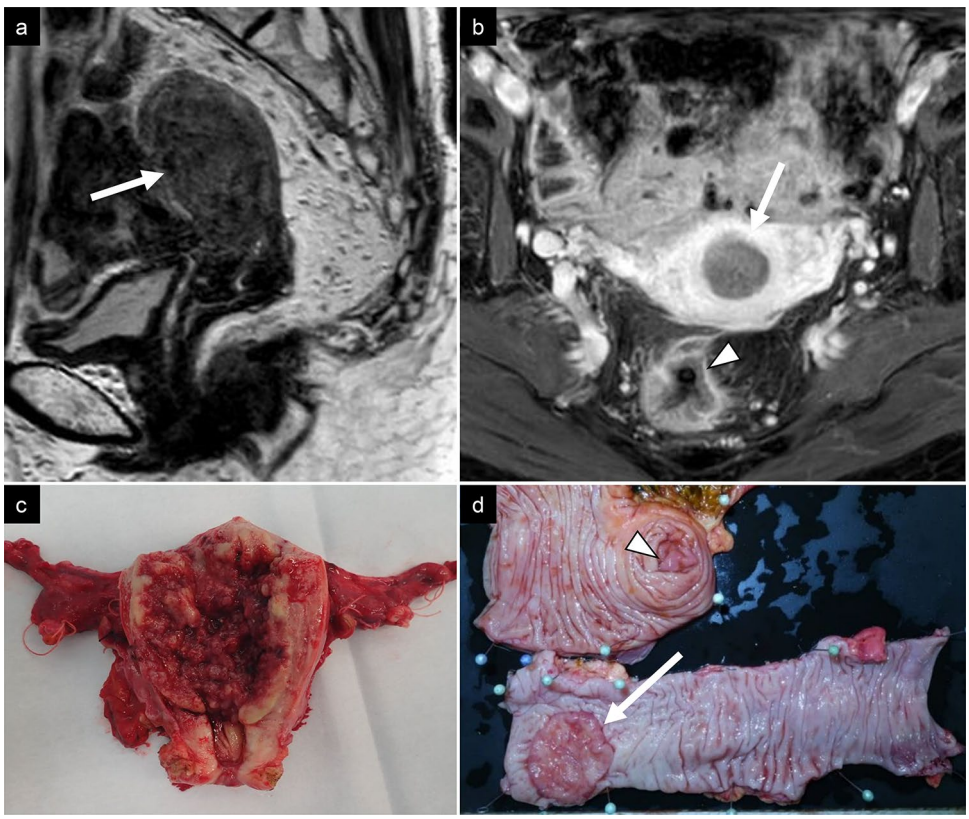


Fig. 2 A woman in her 60 s with Lynch syndrome and a family history of colon cancer in her daughter, uterine and gastric cancer in her sister, and colon cancer in her nephew. **a** A tumor with low signal intensity on T2-weighted imaging occupies the endometrial cavity, with deep myometrial invasion extending beyond half of the anterior myometrium (arrow), resulting in the indistinctness of the junctional zone. **b** On fat-saturated contrast-enhanced T1-weighted imaging, endometrial and rectal cancers showed hypo enhancement relative to the myometrium. **c** Endometrial cancer was diagnosed as grade 1 endometrioid carcinoma, stage IB with myometrial invasion measuring 12/13 mm. **d** The rectal cancer was identified as type 2 tubular adenocarcinoma with infiltration beyond the muscularis propria (arrow). Furthermore, the lesion at the cecum was diagnosed as an intramucosal carcinoma (arrowhead). Both cancers have not recurred, and the patients are undergoing regular checkups

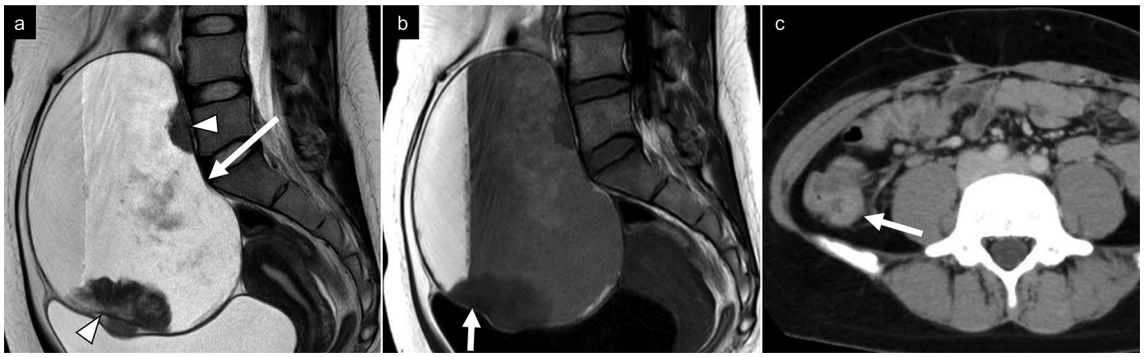


Fig. 3 A woman in her 20 s with Lynch syndrome and a family history of colon cancer in her mother and brother. **a** On T2-weighted imaging, a unilocular cystic tumor (arrow) displayed high signal intensity. Papillary projections (arrowheads), situated on the wall with low signal, indicated a malignant tumor. **b** On T1-weighted imaging the abdominal side showed high intensity. In contrast, the dorsal side showed low signal intensity, creating a fat-fluid level (arrow), indicative of a teratoma, and pathologically diagnosed as a mucinous carcinoma associated with mature teratoma. **c** Three years later, localized wall thickening with contrast enhancement (arrow) was seen in the ascending colon on contrast-enhanced CT, indicative of colorectal cancer. Pathologically, type 2 tubular adenocarcinoma had infiltrated the submucosal layer. Both cancers have not recurred, and the patients are undergoing regular checkups

Table 4 Diagnostic criteria for Peutz-Jeghers syndrome

Diagnosed when at least two of the following three clinical criteria are met
Family history
Multiple dark blue to brown pigmented (macules) lesions on the mucous membranes and skin are most often intraoral on the buccal mucosa or gingiva, lips, perioral, fingertips, palms, and soles
Hamartomatous intestinal polyps

Wu, Krishnamurthy [21]

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome (PJS) is a genetic disorder characterized by melanotic macules, intestinal polyps, and an elevated lifetime risk for malignancies in the uterus, ovary, breast, colon, stomach, small intestine, pancreas, lungs, and testicles. The frequency of PJS carriers is approximately 1 in 100,000 individuals [20]. The diagnostic criteria for PJS are listed in Table 4 [21].

PJS is inherited in an autosomal dominant manner, and arises from mutations in *STK11*, a tumor suppressor serine/threonine kinase gene previously called *LKB1*, on chromosome 19p. *STK11* is activated in response to metabolic stress and hypoxic conditions caused by energy deficiency within tumors. Its related pathways include gene expression (transcription) and regulation of TP53 activity. *STK11* plays a role in various processes such as cell metabolism, cell polarity, apoptosis, and the DNA damage response [22].

In terms of associated malignancies, PJS is linked to human papillomavirus (HPV)-independent gastric-type adenocarcinoma of the uterine cervix (GAS) (Fig. 4), which is found in 11–17% of female patients with PJS. Lobular endocervical glandular hyperplasia (LEGH) is often identified as a precursor to GAS. In a review of patients with PJS, the median age at diagnosis was 17 years in those with LEGH and 35 years in those with GAS [23]. Typically, GAS has a worse prognosis than HPV-associated adenocarcinomas [5]. Furthermore, patients with GAS associated with PJS tend to have worse outcomes and shorter progression-free and overall survival than those with sporadic cancers [23]. Infiltrative growth patterns, intratumoral cyst formation, and heterogeneous enhancement are characteristic MRI findings in GAS [24]. The shape of LEGH on MR images has been divided into two patterns: "cosmos pattern" [25] or "flower-type" [26], which comprised numerous small cysts surrounded by several larger cysts, and 2) lesions with "microcystic pattern" [27] or "raspberry-type" [26], which consisted of a close aggregation of numerous tiny cysts. In addition, most tumors are located in the upper portion of the cervical canal, the entire cervix, or in the endocervix.

PJS is also commonly associated with ovarian tumors such as sex cord tumors with annular tubules (SCTATs) (Fig. 5a) and Sertoli cell tumors. Mucinous tumors (Fig. 5b and c) are another ovarian neoplasm linked to the PJS. SCTATs are distinctive ovarian neoplasms featuring nests of cells that form ring-like structures surrounding basement membrane-like materials. Diseases associated with PJS often present as benign, multifocal, and bilateral, with very small or even microscopic tumors showing signs of calcification. Patients may also experience hyperestrogenism symptoms. In contrast, SCTATs that occur independent of the PJS tend to be unilateral and significantly larger, sometimes extending beyond the ovary [28].

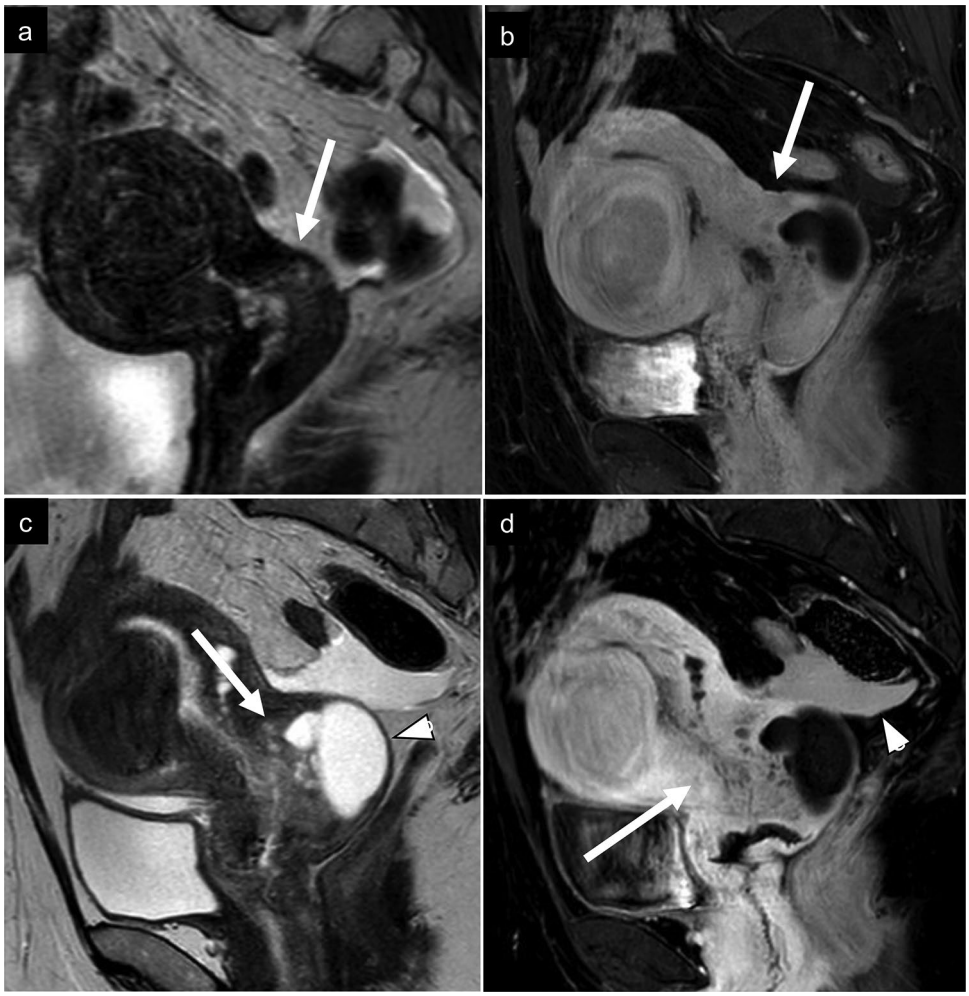


Fig. 4 A woman in her 50 s with Peutz-Jeghers syndrome and a family history of lung and esophageal cancer in her father. **a** Scattered small cysts with a "microcystic pattern" in the cervix (arrow) were observed on T2-weighted imaging and was diagnosed with lobular endocervical glandular hyperplasia. **b** Solid component was not apparent on fat-saturated contrast-enhanced T1-weighted imaging (FS-CE-T1WI). **c** Eight months later, the cysts in the cervix enlarged (arrowhead), with a surrounding solid component exhibiting intermediate T2-weighted signal intensities (arrow). **d** The solid part appeared as low signals on FS-CE-T1WI (arrow). HPV-independent, gastric-type adenocarcinoma was confirmed by biopsy. High signal intensity on fat-suppressed T1-weighted imaging indicates the presence of hemoperitoneum (arrowhead), leading to a diagnosis of peritoneal dissemination. Consequently, the patient underwent concomitant chemoradiotherapy but experienced a recurrence, culminating in death. Simultaneously, there were multiple polyps in the small intestine, a finding consistent with Peutz-Jeghers syndrome

Nevoid basal cell carcinoma syndrome

Nevoid basal cell carcinoma syndrome (NBCCS), commonly known as the Gorlin syndrome, is a genetic disorder characterized by multiple basal cell carcinomas on the skin, cysts in the jaw, small pits on the palms and soles, calcium deposits in the brain, developmental disabilities, and skeletal abnormalities [29]. The diagnostic criteria for NBCSS are listed in Table 5 [30]. Owing to the increased risk for multiple skin cancers, individuals with NBCCS are advised to avoid radiation therapy because it can increase the risk for basal cell skin cancer.

NBCCS typically follows an autosomal dominant inheritance pattern; however, approximately 30% of the cases arise without a known family history [29]. This syndrome is mainly associated with mutations in *PTCH1*, which has been identified as the gene responsible for NBCCS as well as some related sporadic tumors. *PTCH1* has been mapped to 9q22.3-31 and dysregulation of signaling caused by the inactivation of *PTCH1* has been implicated in the development of NBCCS and some related sporadic tumors, supporting the hypothesis that *PTCH1* is a tumor suppressor gene in this syndrome [31].

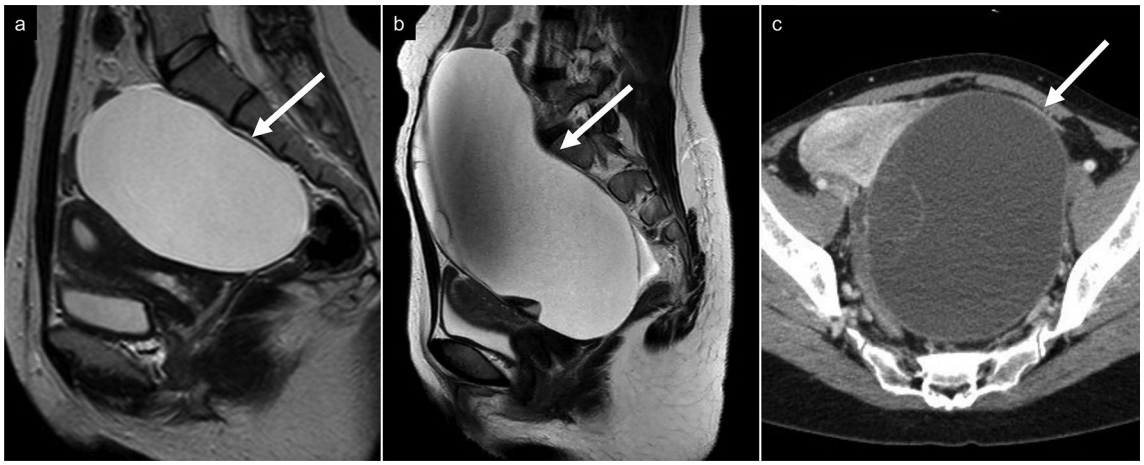


Fig. 5 A woman in her 20 s with Peutz-Jeghers Syndrome and a family history of colon cancer in her grandmother. **a** A cyst displaying a uniform signal was observed behind the uterus (arrow) on T2-weighted imaging (T2WI), with no enhancing solid components. Enucleation was performed, and sex cord tumors with annular tubules of the bilateral ovaries were diagnosed. **b** Nine years later, a large cyst with multiple septations (arrow) and protein-rich contents exhibited pronounced low signal intensities on T2WI, with no enhancing component. A mucinous cystadenoma of the left ovary was diagnosed by enucleation. **c** Another five years later, a cystic tumor with septations (arrow) was observed on contrast-enhanced CT in the left ovary. Another mucinous cystadenoma of the left ovary was diagnosed by enucleation. However, no recurrence of the ovarian tumor has been observed since then, and she has been undergoing regular checkups. Repeated resections of small intestine and colon polyps were also performed simultaneously

Table 5 Diagnostic criteria for nevoid basal cell carcinoma syndrome

Diagnosed by meeting the following two major criteria or one major and two minor criteria
Major Features
Multiple basal cell skin cancers that appear earlier in life than is usual
Increased calcium deposits in the head that can be seen on an x-ray
Jaw or bone cyst(s)
Three or more pits on the palms of the hands or soles of the feet
A parent, sibling, or child with NBCCS
Minor Features
Medulloblastoma
Increased head size and large forehead
Cleft lip or palate, extra fingers or toes
Abnormal shape of the ribs or spinal bones
Eye problems such as cataracts, small eyes, or tumors in the iris
Fibromas, meaning benign fibrous tumors, of the ovaries or heart
Abdominal cysts

Veenstra-Knol et al. [30]

Ovarian fibromas are prevalent in 25% of patients with NBCCS. Ovarian fibromas associated with NBCCS (Fig. 6) are commonly bilateral (75%) and often exhibit calcification and a nodular appearance. In contrast, ovarian fibromas not associated with this syndrome are typically unilateral, with calcification occurring in only 10% of cases [32]. Ovarian fibromas tend to show markedly low T2-weighted signals and are occasionally mistakenly diagnosed as calcified uterine leiomyomas. NBCCS is also associated with various forms of ovarian fibromas and fibrosarcomas. Cellular fibrous tumors with moderate to high nuclear atypia are classified as fibrosarcomas, whereas those with high mitotic activity but lacking severe atypia are categorized as mitotically active cellular fibromas [32, 33] (Fig. 7).

Swyer syndrome

Swyer syndrome, also known as XY gonadal dysgenesis, is a rare developmental disorder in which individuals with an XY chromosome pair, typically females, experience abnormal development of their sex glands. In this condition, the gonads are underdeveloped and non-functional and are often described as streak gonads [34, 35].

Swyer syndrome is frequently associated with mutations in *SRY*, *MAP3K1*, *NR5A1*, and *DHH*. Mutations in the *MAP3K1* or *DHH* genes result in 18% of cases, while 15% of cases are due to mutations in the *SRY* or *NR5A1* genes. Other cases occur due to certain non-genetic factors, such as hormonal medications administered during pregnancy. The *SRY* gene encodes a protein that regulates the start of male sex determination by activating the gene encoding the Müllerian inhibitory substance. Most cases of *SRY*-related are not inherited. However, some individuals inherit an altered *SRY* gene with a Y-linked inheritance pattern. *MAP3K1* encodes a protein that helps regulate signaling pathways controlling various processes in the body, including those that determine sexual characteristics before birth. *NR5A1* encodes a transcription factor, which helps control the activity of several genes related to the development of the gonads

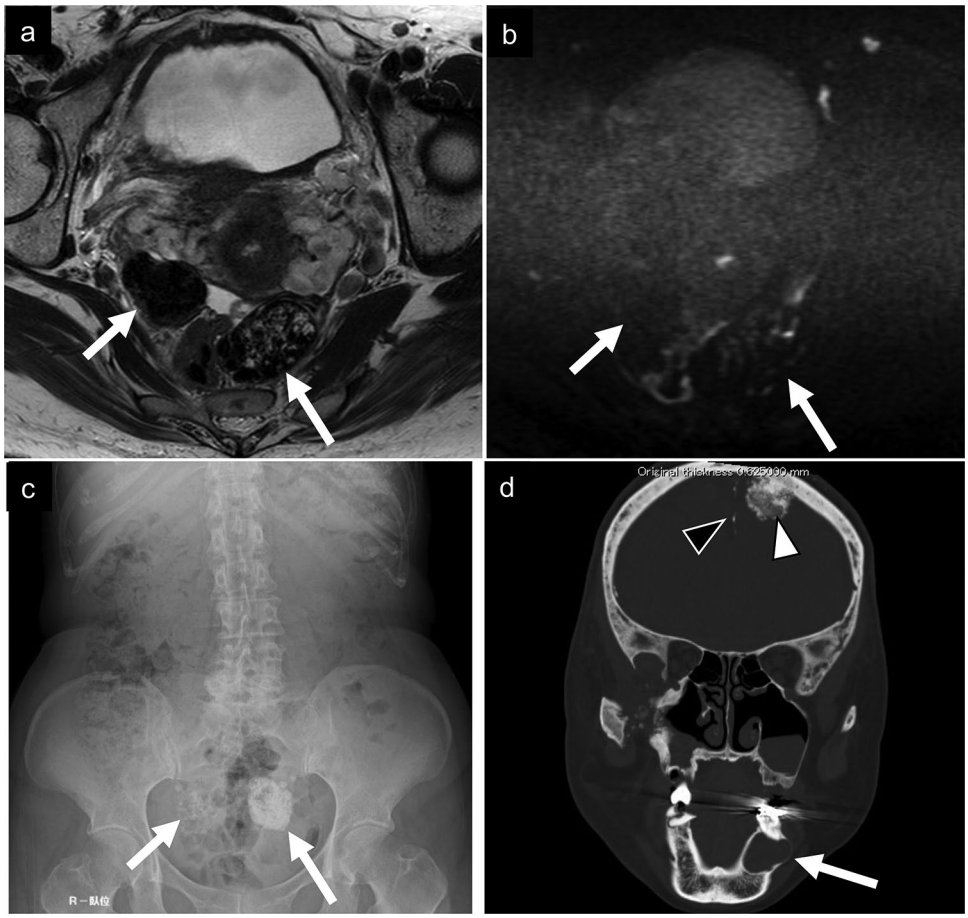


Fig. 6 A woman in her 40 s with nevoid basal cell carcinoma syndrome and no known family history. **a** T2-weighted imaging showed bilateral ovarian masses (arrows) with lower signal intensities than those in the skeletal muscle, with mottled high signal intensities in the left mass. **b** Both masses had no restricted diffusion on diffusion-weighted imaging (arrows), suggesting fibromas. **c** Radiograph showed diffuse calcification consistent with masses (arrows). The patient was diagnosed with bilateral ovarian fibromas. **d** Simultaneously, CT of the same patient showed cysts in the jaw (arrow), calcification of the cerebral sickle (black arrowhead), and calcification consistent with left frontal meningioma; an nevoid basal cell carcinoma syndrome (NBCCS)-related tumor (white arrowhead). These findings were consistent with NBCCS

and adrenal glands. *MAP3K1*- or *NR5A1*-related Swyer syndrome is often non-inherited but may follow an autosomal dominant pattern. Genetic changes in *DHH* affect sexual differentiation, and *DHH*-related Swyer syndrome is inherited in a sex-limited autosomal recessive manner, indicating that both copies of the gene in each cell carry this variant [35].

A major concern in Swyer syndrome is the high risk for gonadoblastoma. Therefore, early diagnosis is imperative owing to the elevated risk for gonadoblastoma and germ cell malignancies, necessitating timely gonadectomy [36]. Gonadoblastomas can vary in size, with some growing up to approximately 8 cm. However, many are small, ranging from a few to approximately a dozen millimeters when examined under a microscope [36]. These tumors are often unexpectedly discovered in specimens obtained during prophylactic gonadectomy. Punctate calcifications are observed on CT scans [36] and may even be identifiable on plain radiographs because of their coarse appearance [37]. While there are no comprehensive reports on MRI-based diagnosis, some studies have suggested that gonadoblastomas exhibit low signal intensities on both T1- and T2-weighted imaging [38]. Malignant germ cell tumors that occur during adolescence are believed to originate from late primordial germ cells. Among these tumors, precursor lesions include gonadoblastoma and germ cell neoplasia in situ (GCNIS) [39]. In 20–30% of Swyer syndrome cases, malignant germ cell tumors, including dysgerminoma (seminoma-like tumors) (Fig. 8), can develop, often affecting both sides. Dysgerminomas are frequently divided into lobules that enhance the septa. They typically exhibit low or isointense signals on T2-weighted imaging and are often associated with elevated levels of human chorionic gonadotropin (HCG) and lactate dehydrogenase (LDH) [40, 41].

Conclusion

The accurate diagnosis of hereditary gynecological tumors requires a multifaceted approach that integrates patient age, medical history, and family history, along with a deep understanding of the imaging characteristics specific to these tumors. The importance of knowing not only the imaging characteristics but also the genetic predisposition and associated tumors is emphasized in order to implement this approach. This comprehensive strategy is essential to achieve an accurate diagnosis that goes beyond a localized evaluation and is critical to evaluate and manage hereditary gynecologic tumors and ensure effective patient care.

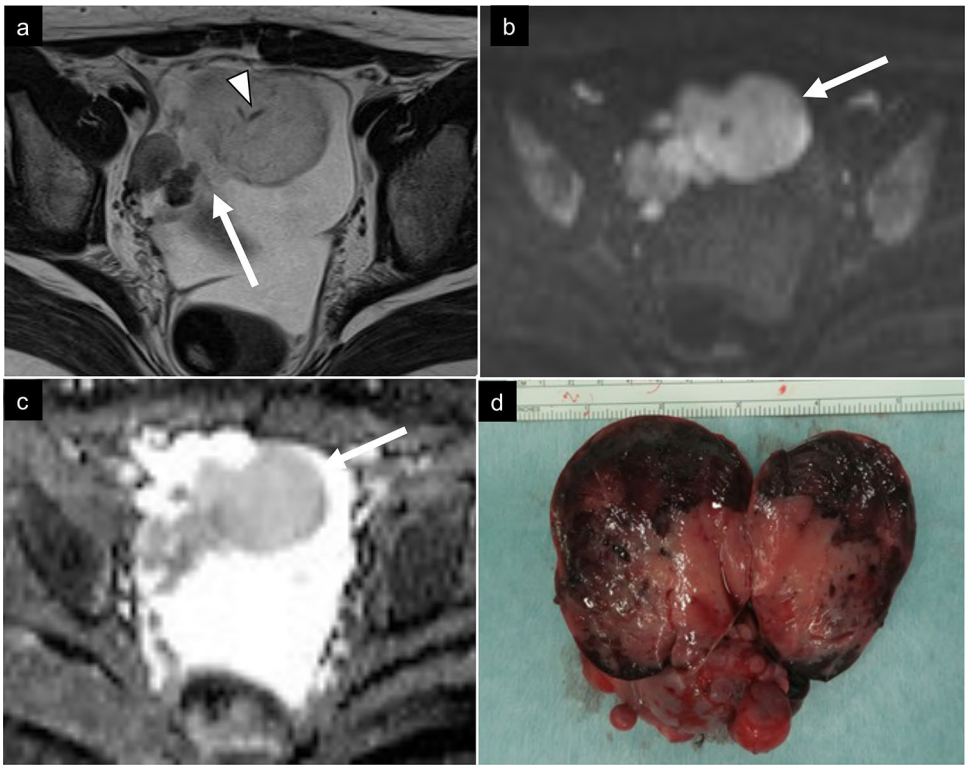


Fig. 7 A teenage girl with a history of a medulloblastoma of the brain and a fibroma of the left ovary and a family history of colon cancer in her grandmother and breast cancer in her aunt, diagnosed with nevoid basal cell carcinoma syndrome. **a** In the right adnexal region, there was a multi-nodular tumor (arrow) displaying a wide range of signals on T2-weighted imaging (T2WI), ranging from fairly high to low intensities. Vascular structures (arrowhead) were observed within the areas of prominent high signal intensity on T2WI, suggesting a solid tumor rather than cystic lesions. **b** On diffusion-weighted imaging, the tumor exhibited high signal intensities (arrow). **c** No signal decrease was observed on the apparent diffusion coefficient map (arrow), indicating the absence of diffusion restriction. **d** A right salpingo-oophorectomy was performed, and a solid tumor with dark red hemorrhage was pathologically diagnosed as a mitotically active cellular fibroma. Since then, there has been no recurrence of the ovarian tumor, and she has been undergoing regular checkups

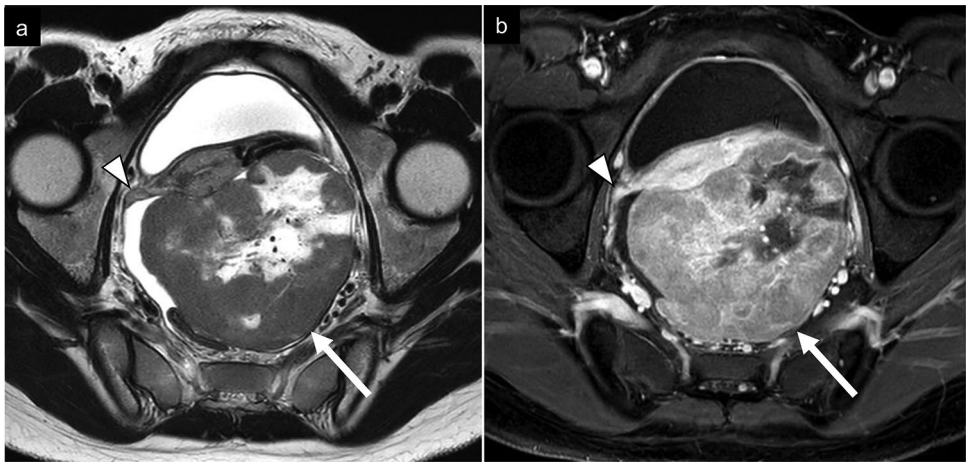


Fig. 8 A teenage girl diagnosed with Swyer syndrome, no known family history. **a** T2-weighted imaging demonstrated a solid tumor on the left ovary (arrow). The uterus was smaller than expected for a late teenager. **b** On fat-saturated contrast-enhanced T1-weighted imaging, the left adnexal tumor (arrow) presented with predominantly enhanced regions at the periphery, alongside non-enhancing areas suspected of necrosis within the tumor. Within the tumor, linear strong enhancement effects indicative of fibrovascular septations were observed. A left gonadectomy was performed, and a dysgerminoma/seminoma was diagnosed. Subsequently, a chromosomal test revealed that she was an XY female, further confirmed by genetic tests. Thus, Swyer syndrome was diagnosed. The right ovary (arrowheads in **a** and **b**) was identifiable but appeared small, with no visible follicles, suggestive of a streak gonad. A few months after the surgery for a left ovarian tumor, a right gonadectomy was performed, and gonadal dysgenesis of the right ovary was diagnosed

However, for individuals with genetic conditions associated with gynecologic cancers, currently there are no effective screening tests for ovarian cancer, and some screening for uterine cancer is conducted using transvaginal ultrasound, but its utility remains unknown [42].

Author contributions The study conception and design performed by TS. Literature search and data collection were performed by MY, TS, TI, KM, MS, SS, SK, YF and TS. Supervision was performed by TN. The first draft of the manuscript was written by MY and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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