Medical Science

To Cite:
Włodarczyk M, Wójcikiewicz P, Zakrzewska G, Materek M, Kowalski K, Tarkowski R, Kułak K. Ovarian cancer or extraperitoneal tuberculosis? Is a fast and pertinent diagnosis possible?. *Medical Science* 2025; 29: e221ms3732
doi:

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Peer-Review History
Received: 16 July 2025
Reviewed & Revised: 03/August/2025 to 18/November/2025
Accepted: 25 November 2025
Published: 3 December 2025

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

Ovarian cancer or extraperitoneal tuberculosis? Is a fast and pertinent diagnosis possible?

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ABSTRACT

Extrapulmonary tuberculosis mimicking ovarian cancer poses a significant diagnostic problem. The intraoperative examinations determine diagnosis. Antituberculous drugs are initiated far too late. There is no factor differentiating these two diseases. Non-specific symptoms such as chronic lower abdominal pain, flatulence, nausea, vomiting, loss of appetite, and weight are common to both conditions, but do not raise the suspicion of tuberculosis in the first instance. Genital bleeding, fever, and increasing ascites, especially in patients with risk factors, should prompt a widening of the diagnosis to include a possible TB aetiology. An increase in CA-125 levels is also not tumour-specific. The presence of a lymphocytic exudate in the peritoneal fluid, the absence of malignant cells, and elevated ADA levels are essential clues in the diagnosis of peritoneal tuberculosis, even in the absence of bacteriological confirmation. A review of the available literature was conducted to identify factors that could suggest tuberculosis in these patients and allow for a precise preoperative diagnosis, thereby accelerating the initiation of anti-tuberculosis therapy. Laparoscopy enables the collection of biopsy samples and facilitates an accurate histopathological diagnosis. However, the question remains whether a tuberculous aetiology can be considered earlier to allow for timely treatment.

Keywords: tuberculosis, ovarian cancer, extraperitoneal tuberculosis

1. INTRODUCTION

Tuberculosis (TB) is a disease caused by an infection with *Mycobacterium tuberculosis*. It can spread to any organ system in the body, causing extrapulmonary TB (Rahlwes et al., 2023).

Genital tuberculosis (GTB) accounts for 9-15% of extrapulmonary TB cases. It is a significant cause of infertility in 5-20% of women struggling with this problem (Grace et al., 2017). Clinicians often detect female genital tuberculosis (FGTB) during infertility evaluations because of its asymptomatic course, which leads to an underestimation of its incidence. Incidence rates vary widely by geographical region: <1% in the USA, through 2% in Italy, 4% in Saudi Arabia, 7% in Yemen, 17% in Nigeria, 2%-20% in Pakistan, 6%-21% in South Africa, and up 3%-26% in India (Tzelios et al., 2022). FGTB carries complications, especially infertility, the incidence

of which ranges from 3 to 16% of cases in India. The only symptom of FGTB may be infertility, due to the presence of a small number of mycobacteria (Jirge et al., 2018).

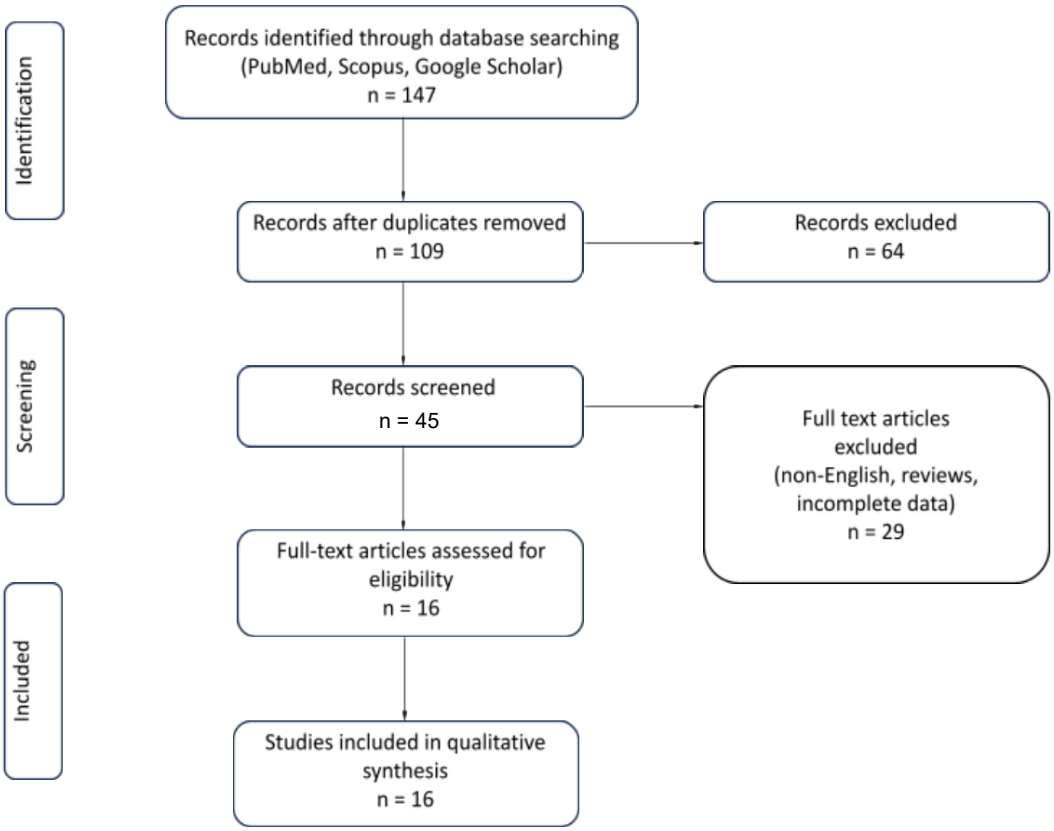
Ovarian tuberculosis accounts for 20-30% of cases. The diagnosis of FGTB is established by detecting acid-fast mycobacteria through microscopy or culture of endometrial biopsy specimens, or by identifying epithelial granulomas on histopathological examination. The polymerase chain reaction (PCR) carries a risk of a false-positive result and, therefore, is not sufficient on its own to establish the diagnosis. Laparoscopy and hysteroscopy are essential for the diagnosis (Sharma, 2015).

Ovarian cancer mimicking extrapulmonary tuberculosis is a major diagnostic problem. Interestingly, CA-125, which is a biomarker for ovarian cancer, among others, is also increased in benign diseases such as pulmonary and extrapulmonary TB, which can make differentiation difficult. In the present study, we analyzed papers describing cases of tuberculosis misdiagnosed as ovarian cancer (Rinaldi et al., 2022).

2. REVIEW METHODS

Studies included in this review were selected from PubMed, Google Scholar, and Scopus up to June 2025. The keywords used for the search included: “extraperitoneal tuberculosis” and “ovarian cancer”. A total of 147 records were initially identified. After removing 38 duplicates, 109 studies remained for screening. Based on titles and abstracts, 64 papers were excluded because they were not relevant to the topic. The full texts of the remaining 45 articles were assessed for eligibility. We included 16 articles that met all inclusion criteria, consisting of original research papers and case reports describing abdominal or genital tuberculosis mimicking ovarian malignancy. Articles not written in English, reviews, conference abstracts, and studies with incomplete data were excluded.

The selection process followed the PRISMA 2020 guidelines. The step-by-step inclusion and exclusion process is summarized in Figure 1.



*n - number of articles

Figure 1. PRISMA flow diagram.

3. RESULTS AND DISCUSSION

Maheshwari et al., (2021) analyzed the medical records of 120 female patients with peritoneal tuberculosis between 2009 and 2017. The mean age of the patients was 41 years. The most common symptoms reported by the patients were abdominal pain (88%), fever (30%), and weight loss (12.5%). A serum CA-125 level of more than 100 U/ml was found in 116 patients, indicating a result above normal. Cytological examination of peritoneal fluid was performed in 112 patients with ascites, but did not reveal the presence of malignant cells. Analysis of cytological smears showed a predominance of lymphocytes in the exudate in 103 patients, the presence of granulomas in 2 patients, reactive mesothelial cells in 4 patients, and acute inflammatory cells in 3 patients. Peritoneal fluid cultures for *Mycobacterium tuberculosis* in 59 patients identified only seven positive cases.

In 112 patients, 109 had ADA levels above the normal value (30 U/l), 107 had levels above 40 U/l (suggestive of possible tuberculosis), and 80 had levels above 60 U/l. Acid-fast staining (Ziehl-Neelsen) was performed in 62 patients and was positive in only four cases. The diagnosis of peritoneal tuberculosis was made based on histopathological biopsy (performed under image guidance) in 46 patients (38.3%) and surgical biopsy in eight patients (6.7%). In 66 patients (55%), clinicians established the diagnosis using clinical, radiological, and laboratory findings, while only eight (6.7%) required surgical biopsy. In the remaining cases, the diagnosis relied on image-guided biopsy or clinical and laboratory findings.

Oge et al., (2012) analysed 20 patients diagnosed with tuberculous peritonitis (TBP) mimicking ovarian cancer over a 10-years at a single centre. The researchers analysed retrospectively surgical and pathology reports of 20 patients whom physicians preoperatively suspected of having ovarian cancer but whose histopathological findings showed TBP out of 612 ovarian cancer surgeries. This study took place between 2000 and 2011 at a university clinic. Eleven, two, and seven patients underwent diagnostic laparotomy, laparoscopy, and Tru-Cut biopsy under ultrasound guidance. The patients ranged in age from 16 to 70 years. Abdominal pain (70%) and bloating (65%) were the most frequent symptoms. Sixteen patients (80%) had elevated CA 125 levels. On ultrasound and CT, ascites and a pelvic mass were detected in 19 patients (85%) and 12 patients (60%), respectively. Seven patients (35%) presented with suspected tuberculous peritonitis, and Tru-Cut biopsy under ultrasound guidance served as the preferred diagnostic approach. Eleven patients (55%) underwent surgery, during which surgeons observed extensive miliary nodules, diffuse adhesions, appendage masses, and necrotic serous substance. Patients underwent unilateral (27%) or bilateral (36%) salpingo-oophorectomy in 7 cases (63%). Tru-Cut biopsy under ultrasound guidance proved helpful in selected patients, and analysis of frozen sections avoided unnecessary radical surgery.

The study by Thomas et al., (2020) aimed to describe in detail the clinicopathological aspects in patients who were referred to the Gynaecology Oncology Unit between 2014 and 2017 with suspected ovarian cancer or primary peritoneal carcinomatosis and were eventually diagnosed with abdominal tuberculosis. In the study group, 23 patients were referred to the gynaecological oncology outpatient clinic for assessment of ascites, to rule out malignancy. The mean age of the patients was 35 years, and the mean CA 125 marker value was 333.5. Analysis of the peritoneal fluid revealed tuberculosis in 26% of the patients, while a net biopsy revealed tuberculosis in 69% of them. Diagnostic procedures, such as laparoscopy and laparotomy, were performed in 15 of 23 patients, achieving a 100% detection rate, which confirmed the diagnosis of TB. Peritoneal fluid and PCR results were not very sensitive - detection rates were 33% and 6%.

The study by Khoiwal et al., (2024) describes the case of a female patient. A 26-year-old woman presented with complaints such as abdominal bloating, nausea, vomiting, loss of appetite, and weight loss, which had lasted for three months. The patient was cachectic (BMI = 15 kg/m^2). The abdomen was uniformly distended and soft. CT scan revealed a thick-walled cystic lesion in the abdomen and pelvis, probably neoplasmic in nature - serous cystadenoma. The bilateral ovaries were not separately visible. Tumour markers were regular. They admitted the patient for laparotomy. During the operation, operators drained 7 litres of white, cloudy, non-stinking fluid from the peritoneal cavity. The frozen cyst wall and white debris over the base suggested chronic inflammation, but malignancy was excluded. Intraoperative examination indicated abdominal tuberculosis. Fluid analysis confirmed the diagnosis of TB (ADA = 78 u/L, LDH = 6940 u/L).

There was a retrospective analysis of 20 cases of APTB resembling advanced ovarian cancer. The main clinical manifestations were abdominal pain (45%) and bloating (45%). 18 patients had higher levels of CA125 (90.0%). Abdominal ultrasound showed ascites in 12 patients (60.0%). All bacteriological cultures and cytological tests were negative (10 cases, 100%). Laparotomy (17 cases) and laparoscopic evaluation (1 case) were with a presumptive diagnosis of advanced ovarian cancer, except for two patients treated with diagnostic anti-tumour chemotherapy. Frequent intra-operative findings were proliferative nodules (14 cases, 77.8%) and extensive

adhesions (10 cases, 55.6%). Intraoperatively, frozen sections were performed in 10 patients, and typical TB nodules were detected in all patients. This indicates that 100% of the patients had a diagnosis of APTB (Xi et al., 2010).

Data of 28 female patients with pelvic tuberculosis diagnosed with the disease between January 2000 and January 2010 at the gynaecology department of Nanjing Jinling Hospital were retrospectively analysed. The patients were 15-64 years. Elevated serum CA125 levels were found in 28/28 patients. Other common findings were ascites in 20 (20/28), pelvic tumour in 21 (21/28), mild fever with night sweats in 13 (13/28), cough and pleural effusion in nine (9/28), high fever above 39°C combined with abdominal pain and elevated white blood cell count in five (5/28), weight loss of more than 5 kg on admission in six (6/28). Diagnosis was based on biopsy from laparotomy in 14 patients, from laparoscopy in 9, from a diagnostic calpectomy for primary infertility in 2, and from clinical suspicion only in 3 patients. Histopathological examination revealed serous granulomatous lesions in 25 patients, and positive acid staining in 11 patients. A total of 26 patients successfully completed anti-tuberculosis therapy and became healthy; two patients died of their disease due to long-term use of an immunosuppressant (Liu et al., 2014).

In a clinical case report presented by Nissim et al., (2020), the case of a 42-year-old female patient who presented to the Gynaecological Oncology Outpatient Clinic with an image of an enlarged right ovary on CT scan and a CA-125 marker result of 1289 U/mL was presented. Women reported six-month abdominal discomfort and bloating, accompanied by night sweats, intermittent fevers, and unintentional weight loss. The patient presented with abdominal distension without increased muscle guarding. Physical examination of the external genitalia, vagina and cervix revealed no abnormalities. A transvaginal-rectal examination was performed, which also revealed no abnormalities.

A contrast-enhanced CT scan of the abdomen and pelvis was ordered, which revealed a moderate amount of fluid in the peritoneum, diffuse nodules in the greater omentum and enlarged right-sided extraperitoneal lymph nodes with a diameter of 1.2–1.4 cm. A biopsy of the omentum and abdominal wall revealed fibrous tissue with necrotic and non-necrotic granulomas, with no detection of acid-fast mycobacteria by modified Ziehl-Neelsen staining. A chest CT scan revealed a 4 mm nodule in the lower left lobe and single, small scars in the pleura. A tuberculin skin test (PPD) and QuantiFERON-TB Gold Plus test were performed, both of which were positive, ultimately confirming the diagnosis of tuberculosis. A four-week anti-tuberculosis chemotherapy (isoniazid, rifampin, pyrazinamide, ethambutol) was implemented. After four weeks of drug therapy, the CA-125 level dropped to 74 U/ml, and the woman's general condition improved significantly: her fever subsided, her appetite improved, and her body weight increased. After eight weeks of treatment, the pain completely disappeared, the patient's body weight increased from 56.6 kg to 62.1 kg, remission of changes in the omentum, disappearance of ascites and enlargement of lymph nodes was achieved, which was confirmed by a follow-up CT scan. Six months of anti-tuberculosis treatment led to complete resolution of clinical symptoms and changes visible in imaging tests (Nissim et al., 2022).

In a clinical case report presented by Yazdani et al., (2016), 32-year-old female G3P2L2 (Gavidity=3, Parity=2, Living child=2) who ended up to Ayatollah Rouhani Hospital in Babol with three months of increased lower abdominal pain and abnormal bleeding from the genital tract. Her history included monthly haemorrhages, episodes of fever with chills, and increasing ascites, which required hospitalisation. In addition, the patient had been addicted to opium for five years and remained on methadone substitution therapy. The general condition was assessed as relatively stable - vital signs normal, auscultation of the lungs clear, occasional temperature elevation to approximately 38 °C.

Ultrasonography revealed a single cyst measuring 53×65 mm in the area of the left ovary. The right ovary, uterus and abdominal organs - liver, kidneys and spleen were with normal morphology. Imaging tests confirmed the presence of fluid in the peritoneal cavity on imaging. Laparotomy revealed bilateral swollen fallopian tubes with multiple adhesions and scattered lumpy deposits on the peritoneum, omentum, and bowel surface; however, no separate focal mass was in the abdominal or pelvic cavity. Histopathological findings on samples taken from the uterus, fallopian tubes, omentum, and liver, and bowel fragments indicated peritoneal tuberculosis. Based on the confirmed diagnosis, standard quadruple antimicrobial chemotherapy - isoniazid, pyrazinamide, ethambutol, and rifampin - was initiated. Therapy resulted in resolution of general symptoms, regression of peritoneal lesions, and improvement in the patient's nutritional status.

In a clinical case report presented by Jiandani et al., (2023), there was a 22-year-old woman with monthly pain and a feeling of abdominal distension and concomitant dysuria. On physical examination, the patient had a slim figure (40 kg; BMI 16.2 kg/m^2). Ultrasonography of the abdomen and pelvis revealed a large, well-demarcated cyst (29 × 25 × 25 cm), with uniformly thickened walls (3.3 mm), located in the right adnexa and lacking echogenic structures internally. The initial diagnosis was based on the suspicion of an ovarian lesion, which was in magnetic resonance imaging - it showed a unifocal, cystic lesion of an appendiceal nature, originating

from the right ovary. Laboratory investigations revealed severe anaemia (Hb 8.2 g/dl; normal 12-16 g/dl), leucocytosis (10 950/mm³; normal 4 500-10 500/mm³) and a significant elevation of the CA-125 marker to 523 U/ml (normal 0-35 U/ml). Due to clinical and radiological features suggestive of malignant proliferation of the ovary, an exploratory laparotomy was performed. The operation revealed a thickened peritoneum, closely fused to the omentum, and multiple papular lesions on the posterior peritoneal surface. Histopathological examination of omental sections and peritoneal fluid revealed a picture of granulomatous inflammation with necrotic changes, characteristic of extrapulmonary tuberculosis.

Chest X-ray excluded pulmonary lesions. The patient had peritoneal tuberculosis, and started a short-term observational treatment programme (DOTS), followed by standard four-drug anti-tuberculosis chemotherapy. Monitoring of the course of therapy was with monthly ultrasound examinations and periodic determination of CA-125 levels, which decreased to 38 U/ml after 2 months, 12 U/ml after 4 months, and 8 U/ml after 6 months of treatment. The patient achieved complete remission of clinical symptoms and resolution of imaging abnormalities after completion of the 6-month treatment plan (Jiandani et al., 2023).

A study by Lee et al., (2023) describes the case of a 56-year-old woman. The woman had been complaining of abdominal fullness for 3 months. She had ascites, normocytic anaemia (Hb = 10.3 g/dl) and elevated CA-125 levels. CT of the abdomen and pelvis exposed multilevel ascites, peritoneal thickening, tangles in the omentum, small mesenteric nodules, enlarged mesenteric lymph nodes and paraortic nodes, as well as markedly enlarged ovaries and dilated fallopian tubes. There were no soft tissue tumours in the ileum. A primary diagnosis was ovarian cancer with peritoneal metastases. The patient underwent an exploratory laparotomy. Surgery revealed small nodules in the peritoneum, omentum, small bowel loops, uterus, and fallopian tubes. Moreover, there were multiple adhesions between the bowel loops, left ovary, and pelvic sidewall. It was peritoneal carcinomatosis, so the patient had a salpingo-oophorectomy, enterolysis, and peritoneal biopsy. A contrast-enhanced CT scan of the abdomen and pelvis revealed changes suggestive of bilateral salpingitis. With the presence of free fat in the abdominal cavity, it can suggest the possibility of infection. A contrast-enhanced CT scan also showed nodules in the omentum and localised ascites. A coronal contrast CT scan showed a disproportionately large mass in the left ovary and the presence of diffuse ascites, which differed from the typical signs of ovarian cancer. A biopsy confirmed tuberculous peritonitis. The ovary, fallopian tube and peritoneum microscopically revealed tuberculosis.

The intraoperative image and histopathological findings, confirming granulomatous lesions without a neoplastic focus, suggest that tuberculosis should be considered in the differential diagnosis (Oge et al., 2012; Liu et al., 2014). In many of the cases analysed, the diagnosis was made only after invasive procedures such as laparotomy or laparoscopy (Khoiwal et al., 2024; Xi et al., 2010; Liu et al., 2014; Yazdani et al., 2016).

Biopsies were important in diagnosis, as were histopathological examinations, which revealed the presence of granulomas with serous necrosis (Jiandani et al., 2023). It is worth noting that standard microbiological tests (cultures, Ziehl-Neelsen staining, PCR) had low sensitivity, confirming the limited value of these methods in cases of extrapulmonary TB (Nissim et al., 2022). Table 1 shows a comparison of prevalence, typical age, and risk groups in extraperitoneal tuberculosis and ovarian cancer.

Table 1. A comparison of prevalence, typical age, and risk groups in extraperitoneal tuberculosis and ovarian cancer

Feature	**Extraperitoneal tuberculosis**	**Ovarian cancer**
Prevalence	<1 / 100 000 per year in developed countries; higher in endemic countries	10-15 / 100 000 women per year (statistics from 2020 year)
Typical age of disease	Mostly 20-40 years old (young women)	Mostly >50 years (post-menopausal)
Risk groups	HIV, immunosuppression, contact with tuberculosis, poverty	BRCA1/2 mutations, childlessness, obesity, older age

The level of ADA in the peritoneal fluid was also helpful in laboratory diagnosis - values above 40-60 U/l showed a correlation with TB. In addition, confirmation of TB was obtained in some patients by immunological tests such as QuantiFERON-TB Gold or PPD (Khoiwal et al., 2024).

The presence of granulomatous lesions and positive tests for tuberculosis points to peritoneal tuberculosis as a rare but important cause of symptoms mimicking malignancy. The efficacy of antituberculous treatment, was evidenced by the rapid resolution clinical symptoms and the normalisation of the radiological picture, underscores the need to include tuberculosis in the differential diagnosis in patients with an atypical course of the disease and an elevated CA-125 level (Nissim et al., 2022). Differences between ovarian cancer and extraperitoneal tuberculosis were shown in Table 2.

Table 2. Extraperitoneal tuberculosis vs ovarian cancer - clinical and diagnostic comparison.

Category	Extraperitoneal	Category
Clinical picture	Abdominal pain, ascites, genital bleeding, fever, general symptoms	Abdominal pain, ascites, genital bleeding, fever, general symptoms
CA-125	Often significantly elevated, it may suggest cancer	Usually significantly elevated but not specific
Peritoneal fluid	Lymphocytic exudate, no tumour cells, high ADA level (>40-60 U/l)	Presence of tumour cells (sometimes), absence of typical inflammatory features
Microbiological tests	Often negative (low sensitivity), confirmation rare	Not applicable
Diagnostic imaging	Nonspecific lesions - often resembling peritoneal carcinomatosis	Ovarian tumour, cystic/solid lesions, infiltrates
Laparoscopy	Helpful - allows diagnosis and biopsy from granulomatous foci	Used for tumour staging and confirmation

4. CONCLUSION

TBP can very effectively mimic ovarian cancer in both clinical and radiological features. Symptoms such as abdominal pain, ascites, and genital bleeding, often interpreted as typical of cancer, can also occur in the course of TB. When CA-125 levels are elevated, physicians should consider extrapulmonary tuberculosis as a differential diagnosis of ovarian cancer, especially in countries with a high incidence of tuberculosis. The presence of a lymphocytic exudate in the peritoneal fluid, the absence of malignant cells, and elevated ADA levels are essential clues in the diagnosis of peritoneal TB, even in the absence of bacteriological confirmation. Laparoscopy is the best method for differentiating peritoneal tuberculosis, peritoneal carcinomatosis, and advanced ovarian cancer. Benefits include direct visualization and the possibility of taking biopsies for histological examination. Effective anti-tuberculosis treatment leads to a rapid improvement in patients' clinical status, normalization of CA-125 levels, and resolution of lesions seen on imaging.

Acknowledgments

The authors have no acknowledgments to disclose.

Author Contribution

Miłosz Włodarczyk, Patrycja Wójcikiewicz, Gabriela Zakrzewska, and Maria Materek performed the literature search, collected and compiled data, and drafted the manuscript. Kajetan Kowalski assisted with organizing the reviewed studies, editing, and formatting

the manuscript. Rafał Tarkowski and Krzysztof Kułak conceived the idea for the review, supervised the project, provided critical revisions to the manuscript, and approved the final version. All authors read and approved the final manuscript.

Informed consent
Not applicable.

Ethical approval
Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Funding
This research did not receive any external funding like specific grant from funding agencies in the public, commercial, or nonprofit sectors.

Conflict of interest
The authors declare that they have no conflicts of interests, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability
All data associated with this work are present in the paper.

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