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Expert Opinion

Reconsidering Routine Appendectomy in Ovarian Neoplasms: Implications for Diagnostic Staging

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Abstract

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Quick Response Code:

Dear Editor,

Although the current International Federation of Gynecology and Obstetrics (FIGO) guidelines permit omitting appendectomy if the organ appears macroscopically normal,[1] this "*visual-only*" assessment lacks diagnostic validity in complex ovarian neoplasms. Preserving the appendix creates a "*diagnostic vacuum*", resulting in under-staging and diagnostic uncertainty. Amidst the ongoing debate regarding appendectomy during gynaecological surgeries, the necessity of an appendectomy is often unknown until the final pathology report. [2,3] This letter highlights two scenarios where its absence almost hindered a definitive diagnosis.

Brief Background and Guidelines on the Current FIGO Recommendation on Cancer of the Ovary, Fallopian Tube, and Peritoneum: 2025 Update

In 2025, Renz *et al.* established the current global benchmark for staging ovarian, fallopian tube, and primary peritoneal cancers,[1] shifting towards selective surgery to minimize morbidity. Under these standards, appendectomy is indicated only for mucinous tumours, pseudomyxoma peritonei, or grossly abnormal appendix (defined by increased diameter, discoloration, or visible nodules). [4] This conservative posture relies on the statistically low rate of occult (microscopical) primary appendiceal tumours in a macroscopically normal appendix. [5]

However, a critical clinical gap exists where intra-operative frozen section is unavailable. Without real-time histology, surgeons are unable to definitively distinguish mucinous from non-mucinous ovarian epithelial tumours during primary surgery. Omitting appendectomy based on a "*grossly normal"* appearance frequently necessitates a second, avoidable surgery for diagnostic validation and staging if a mucinous morphology is later confirmed. Consequently, lack of immediate diagnostics transforms conservative surgery into a pathway of increased morbidity and delayed staging, often leaving the primary site as "*undesignated*" when definitive identification is impossible. [4,6,7]

Brief Background of the College of American Pathologists (CAP) Current Cancer Protocol (2024) for the Examination of Specimens from Patients with Primary Tumours of the Ovary, Fallopian Tube, or Peritoneum.

The College of American Pathologists (CAP) Cancer Protocol (Version 1.5.0.0, June 2024), aligned with National Comprehensive Cancer Network [NCCN] guidelines, establishes the mandatory framework for pathological evaluation and synoptic reporting of ovarian, fallopian tube, and primary peritoneal neoplasms. Central to this protocol is the requirement that the "*Primary Site***"** (Note C) be explicitly identified. [8] The guidelines acknowledge a significant historical shift in diagnostic practice, where the determination of the primary site was often based simply on the "*dominant mass*" encountered during surgery. However, the CAP protocol emphasizes that this historical reliance on organ size frequently resulted in extra-ovarian primary sites, such as those originating in the appendix or other gastrointestinal primaries, being mistakenly identified as primary ovarian or peritoneal neoplasms. The most dangerous diagnostic hurdle in ovarian mucinous neoplasms is the "*maturation phenomenon"* or "*mimicry study,*" where metastatic low-grade appendiceal mucinous neoplasm (LAMN) to the ovary histologically mimics a primary ovarian mucinous cystadenoma or carcinoma. [9,10] These cases are often missed without examining the appendiceal source. For the pathologists, the absence of the appendix, the most common site of metastatic origin for most pelvic tumours presents a critical diagnostic and documentation challenge. While CAP technically allows for "*undesignated"* or "*unknown"* primary site categories, it strongly advises against their use. Instead, CAP protocol encourages using validated algorithms and criteria such as the Seidman or Yemelyanoava Algorithms, and Hart- Norris Criteria in differentiating primary bilateral ovarian tumours from metastatic ovarian tumours. [11, 12, 13] In the absence of a histological negative from the appendix, pathologists are unable to fulfill the mandate for a primary definitive site with absolute certainty. (Table 1) shows a comparison of recommendations and protocols for Appendectomy in ovarian neoplasms.

Table 1: Comparison of the Recommendations for Appendectomy in Ovarian Neoplasms

S/No	Feature	FIGO (Surgical/Clinical Recommendations) [1]	CAP v1.5.0.0 (Pathological Protocol) [8]
1	Primary Focus	**Clinical/Surgical Staging and Management Protocol** (focuses on the extent of spread to determine the FIGO stage, immediate treatment and survival)	**Diagnostic Validation** (determining definitive site of origin for accurate synoptic report)
2.	Evaluation Method of the Appendix	**Gross/Visual Inspection** (decisions are made based on the intra-operative gross appearance of the appendix)	**Microscopical Validation** (requires histological evidence to rule-out mimics and avoid the undesignated label)
3.	Determination of Origin or Primary Site	**Pre-operative Imaging and Intra-operative findings** (often relies on pre-operative images and intra-operative examination especially the "*dominant mass*" to decide the surgical approach)	**Disagrees with the Historical "*Dominant Mass*" Rule** (requires microscopical proof to avoid misidentifying appendiceal or GI metastases as ovarian primaries)
4.	The Role of Appendectomy	**Selective** (viewed as an extra procedure. Appendectomy is performed only if it appears grossly abnormal or the presence of histologically confirmed ovarian mucinous neoplasms via frozen section or presence pseudomyxoma peritonei to avoid unnecessary morbidity)	**Diagnostic Proof** (viewed as the necessary "*negative control*" to "rule-out" metastases and fulfill the mandate of ruling out a GI primary and avoiding the "*undesignated*" label)
5.	Significance of Bilaterality	**Stage IB indicator or Possible Metastases** (seen as a sign of advanced stage disease or appendiceal and other GI metastases)	**Bilateralism as a Major "*Red Flag*"** (seen as a sign of possible metastases especially in ovarian mucinous neoplasms, making microscopical examination of appendix a functional necessity for a definitive primary search)
6.	Maturation Phenomenon	**Not Factored** (normal looking appendix is assumed to be disease free)	**Major Diagnostic Pitfall** (Recognizes that metastatic appendiceal tumours can mature into benign looking cystic ovarian mass such as ovarian mucinous cystadenoma)
7.	Handling Uncertainty	**Clinically Acceptable** (to treat based on the most likely origin)	**Strongly Advised Against** (protocol advises pathologists to avoid the "*undesignated*" or "*unknown*" primary category)
8.	End Goal	Optimizing patient survival and treatment protocol.	To provide a validated and definitive primary site for accurate synoptic reporting and cancer registry data.
9.	Consequence of Omission	No immediate surgical consequence if the patient is staged based on visible disease.	The pathologists are prevented from fulfilling the mandate to definitively rule out an appendiceal primary.

**Abbreviations*: College of American Pathologists– CAP, Gastrointestinal – GI, International Federation of Gynecology and Obstetrics- FIGO.

Diagnostic Challenges in Ovarian Mucinous and Seromucinous Tumours

The diagnostic intersection of the ovary and appendix remains one of the most significant challenges in surgical pathology and gynaecological oncology. When a mucinous tumour is identified, the pathologist must determine if it is a primary ovarian neoplasm or a metastasis from a LAMN or other gastrointestinal sources. A multidisciplinary diagnostic gap lies between the coordination of the gynaecological oncologists and the pathologists.

The Morphological Ambiguity: A histomorphological overlap makes primary ovarian and metastatic mucinous/seromucinous tumours indistinguishable histologically. Primary ovarian mucinous tumours typically show a "benign- to-borderline-to-invasive" progression; without these precursor areas, extensive sampling or appendectomy is required. Appendiceal metastasis often presents as bilateral ovarian surface

implants with signet ring cells. [11] Also, a histological challenge is the concept of stromal invasion, while expansile/confluent (non-destructive) invasion suggests a primary tumour, infiltrative (destructive) stromal invasion with associated stromal desmoplasia is typical of metastasis. [11, 12, 14, 15] Furthermore, right-sided LAMN may mimic an ovarian mucinous borderline tumour (OMBT) histologically, necessitating an appendectomy. Some appendiceal tumours may have endocervical-like cells rather than the classical intestinal-type, and this may mimic a seromucinous carcinoma. [16]

The Clinical and Algorithmic challenge: In situations where morphology is not sufficient, surgeons and pathologists rely on validated algorithms, especially for mucinous tumours such as the Seidman Algorithm (macroscopical) that utilizes the rule of bilateralism, size and presence of ascites. While seromucinous carcinomas are biologically mullerian, they present a significant intra-operative diagnostic challenge due to their frequent bilaterality, involvement of the ovarian surface and smaller sizes, which is a feature shared with metastatic appendiceal neoplasms. [15, 16] The lack of performing an appendectomy based on the preliminary suspicion of a seromucinous differentiation may lead to the risk of missing an occult appendiceal primary.

Illustrative Cases Highlighting the Problem

Case 1 (The Mucinous Morphology): A 65-year-old grand multiparous, postmenopausal woman presenting with a five-month history of abdominal pain, swelling, easy satiety, and significant weight loss. Clinical examination confirmed gross abdominal distension and bilateral mobile adnexal masses. Computed tomography scan revealed multiloculated hypodense ovarian masses and a normal gastrointestinal tract, including the appendix, even though imaging does not definitively exclude a microscopical or occult appendiceal primary. Patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy without an appendectomy. Intra-operatively, massive ascites and omental metastasis were observed. Gross examination revealed massive 19 cm and 12 cm ovarian tumours. Histological confirmation of primary bilateral low-grade ovarian mucinous carcinoma required extensive sampling to identify precursor areas and morphological algorithms. Patient is currently on follow-up, and information on chemotherapy is unavailable at the time of this report.

Case 2 (The Seromucinous Morphology): A 55-year-old grand multiparous, postmenopausal, known diabetic woman who presented with an eight-month history of abdominal swelling, pain and weight loss. She had no history suggestive of endometriosis or family history of gynaecological malignancy. Clinical examination revealed a wasted patient with gross abdominal distension, while an ultrasound scan showed complex adnexal masses. The Cancer Antigen 125 (CA125) level was markedly elevated [110μ/ml -normal reference value = 0-35 μ/ml]. Patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy without an appendectomy. Intra-operatively, bilateral solid-to-cystic masses, multiple peritoneal nodules, and massive serous ascites were observed. Gross examination revealed 9 x 7 x 6 cm and 9.5 x 8 x 6 cm multilocular cystic masses with excrescences. Histological confirmation of primary bilateral seromucinous ovarian carcinoma required extensive sampling to identify precursor areas. The patient had an uneventful postoperative recovery, and she is on follow-up to commence platinum-based chemotherapy. Figure 1 shows the histological features of these tumours.

Implications for Staging and Treatment

Routine appendectomy is a surgical necessity for precise staging and treatment of ovarian neoplasms. Histologically excluding an appendiceal primary resolves diagnostic uncertainty and ensures the correct management path. [11,12] Staging accuracy depends on distinguishing primary ovarian tumours from appendiceal metastasis; a macroscopically normal appendix may harbor microscopical disease, leading to the risk of under-staging a metastatic cancer as a Stage I ovarian primary. [17,18] Accurate staging dictates therapeutic decisions, as ovarian and appendiceal malignancies require different chemotherapy regimens. [19,20] Initial appendectomy prevents the morbidity of secondary surgeries and eliminates treatment delays, ensuring patients receive effective, site-specific therapy immediately for optimal outcomes.

Suggested Reconsideration of Appendectomy Practice in Ovarian Neoplasms

The surgical management of ovarian neoplasms necessitates a formal reconsideration of appendectomy practice, transitioning the procedure from an elective adjunct to a mandatory histologically negative control. This proposed procedural shift is clinically paramount to achieve definitive diagnostic validation and ensure therapeutic precision in accordance with NCCN and European Society of Medical Oncology (ESMO) guidelines. Standardizing routine appendectomy as a primary surgical requirement effectively prevents the risk of misclassifying the primary origin and under-staging. Finally, the appendix acts as a "*pathological anchor*" and a critical negative control required to exclude a gastrointestinal primary with certainty.

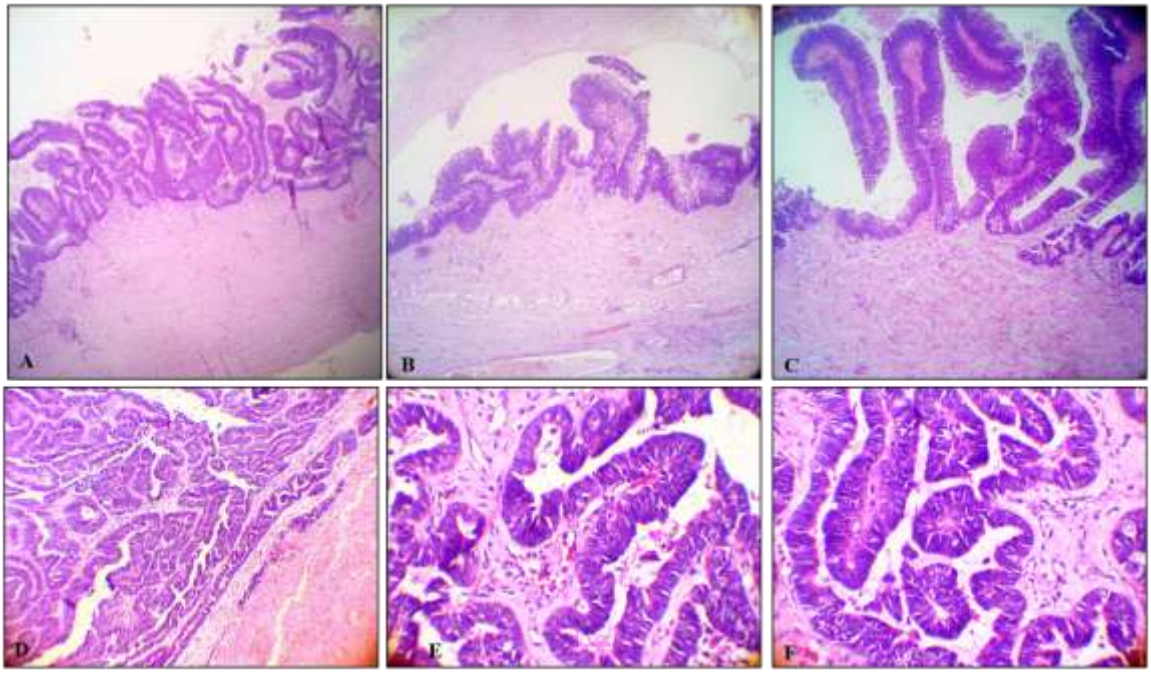

Figure 1 [A, B, C, D]: Haematoxylin and Eosin-Stained Histological Features of Mucinous and Seromucinous Ovarian Carcinomas

Legend: (A) Photomicrograph showing borderline precursor areas with tufts and villi lined by neoplastic cells in ovarian mucinous carcinoma- H&E x40. (B) Photomicrograph showing villi lined by dysplastic intestinal-like epithelium with goblet cells seen in ovarian mucinous carcinoma- H&E x100. (C) Photomicrograph showing intraepithelial carcinoma within ovarian mucinous carcinoma- H&E x100. (D) Photomicrograph showing the complex hierarchical true papillary architecture of seromucinous ovarian carcinoma- H&E x40. (E) & (F) Photomicrographs showing true papillary fronds and tufts lined by markedly pleomorphic endocervical type cells and ciliated cells with oedematous and fibrosed stromal cores showing few inflammatory cells in a seromucinous ovarian carcinoma.

**Abbreviation:* H&E- Haematoxylin and eosin stained

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