



# The Mystery Behind the Mechanisms of Appendix Cancer

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Out of all the organs in the body, one of the most understudied is the appendix. The appendix was first identified when the infamous Charles Darwin<sup>1</sup> proposed that a “pouch-like” structure existed in the human body extending off of the colon<sup>2</sup>. Darwin predicted that the appendix was a vestigial structure<sup>3</sup> that helped our herbivorous ancestors break down plants. This hypothesis has persisted until the 21st century as some people are born without an appendix and removal of the appendix (appendectomy) does not result in any adverse<sup>4</sup> side effects. Still, research regarding appendix-related diseases must be studied as appendicitis<sup>5</sup> and cancers that develop near the appendix are still identified within the human population. This summary will investigate and discuss the current research surrounding appendiceal neoplasms<sup>6</sup>.

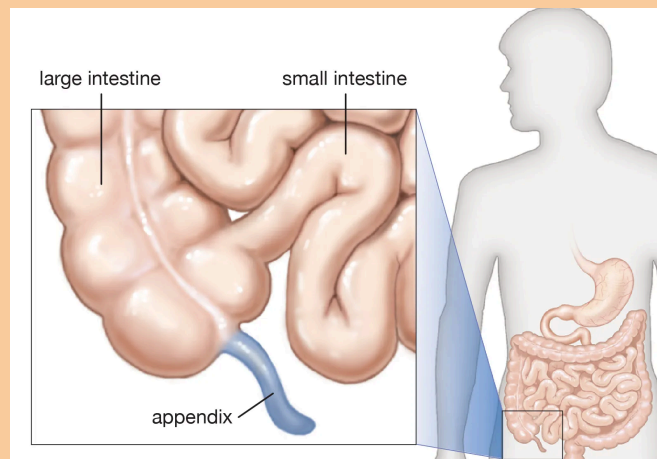


Figure 1 - Diagram of the appendix and surrounding organs (Britannica, 2024)

Appendiceal neoplasms are found in around 0.9-1.4% of appendiceal specimens and have increased in incidence over the past few decades. These neoplasms do not have to originate from the appendiceal cells themselves. Instead, many neoplasms can originate from appendicitis, regions in the colon near the appendix, or metastasize from local organs such as the liver or lymph nodes. The two major types of appendiceal neoplasms are

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<sup>1</sup> Naturalist and explorer

<sup>2</sup> Another term for the long intestine

<sup>3</sup> A part of the body that is had a function in ancestors, but has no function in the modern human

<sup>4</sup> Unfavorable or disadvantageous

<sup>5</sup> Inflammation of the appendix

<sup>6</sup> Another term for tumor



epithelial<sup>7</sup> and nonepithelial. One of the major subtypes of epithelial neoplasms is mucinous, meaning that they lead to the excessive spread of mucin, proteins that are involved in the formation of mucus. In non-epithelial neoplasms, the cancer arises from neuroendocrine<sup>8</sup> cells, mutations of B lymphocytes, or other sources that do not fit into a specific epithelial neoplasm subtype. However, while there are these categories for different appendiceal neoplasms, many neoplasms are asymptomatic<sup>9</sup> or have variable symptoms leading to different diagnoses. In addition, current imaging techniques and surgery intervention approaches such as appendectomy or right hemicolectomy<sup>10</sup> can only be used for specific subtypes of appendix cancer. Chemotherapy approaches are subtype-specific as well. However, even with these limitations surrounding appendix cancer research, appendix cancer is considered to be biologically indolent<sup>11</sup> and is considered less aggressive compared to colon cancer. These findings suggest that further inquiry into appendiceal neoplasms is warranted.

In the past decade, researchers from across the globe have embarked on a journey to learn more about this puzzling organ and the diseases affecting it. A group of researchers in Istanbul, Turkey, performed a study to explore the prevalence and characteristics of appendix tumors in over 2,800 hospital patients who had appendicitis. In addition to this, the study aimed to identify the most suitable form of surgery that can be used to investigate and diagnose these neoplasms. By performing operations such as appendectomies and laparoscopic appendectomies<sup>12</sup>, collecting patients' medical records, and using CT<sup>13</sup> and abdominal ultrasonography scans<sup>14</sup>, the researchers found that 1.06% of their patients had appendix neoplasms. After performing histopathological<sup>15</sup> examinations and patient check-ups, they found that the majority of patients either had adenocarcinomas or neuroendocrine tumors. Ultimately, the researchers concluded that it is crucial to perform histopathological examinations for patients experiencing any form of discomfort from their appendix because most tumors are not recognized through surgical procedures.

Similarly, through different pathological methods of examination, McCusker and colleagues conducted a study analyzing the epidemiology of primary malignant appendiceal neoplasms using malignancy cases reported to the SEER program. They categorized appendix tumors into several types, including colonic type adenocarcinoma, mucinous adenocarcinoma, signet ring cell carcinoma, goblet cell carcinoid, and malignant

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<sup>7</sup> Referring to the inner lining of the appendix

<sup>8</sup> Hormone-secreting

<sup>9</sup> Showing no symptoms

<sup>10</sup> Removal of the entire right side of the colon

<sup>11</sup> Lazy, or less likely to metastasize

<sup>12</sup> Surgical procedure that uses a long tube with a camera called a laparoscope to view abdomen

<sup>13</sup> Computed tomography scan that images patient's body

<sup>14</sup> Ultrasound done on the abdomen that views the liver, gallbladder, pancreas, and spleen

<sup>15</sup> Branch of medicine studying the cell and tissue changes characteristic of disease



carcinoid. Afterward, they compared different demographic characteristics of each group, as well as incidence and survival rates. Comparing the different variations of appendiceal cancer allowed the researchers to understand that survival rates differed depending on the tumor type and the extent of disease spread at diagnosis by their results, discovering that patients with signet ring cell carcinoma had notably worse survival outcomes. In contrast, those with malignant carcinoids had better survival rates. The results of this study revealed adenocarcinoma's rarity and low incidence, with only about 0.12 new cases of appendix cancer being diagnosed each year for every 1,000,000 people.

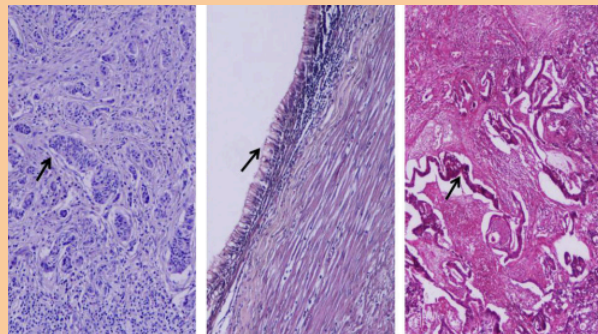


Figure 2 - Histological specimens of appendix neoplasms, manifesting as either neuroendocrine tumors or mucinous neoplasms (Yıldırım et al., 2021)

These studies highlight the uncertainty surrounding appendiceal cancer, emphasizing the need to further investigate this disease and identify potential therapies. With the study done in Turkey, researchers identified that histopathological examinations, pre-operative and post-operative check-ups, and certain procedures such as colonoscopies were crucial in detecting and classifying specific tumors. However, as previously noted, some of these procedures only help in locating certain appendiceal cancers, making it difficult to detect other malignant ones. Likewise, McCusker et al.'s pathological study using patient cases, statistical software, and mathematical models (such as the Cox proportional hazards model and Pearson's chi-square test), shines a light on characteristics and data (oncologically and demographically) on different kinds of adenocarcinoma, which allows for subtype-specific treatments to be developed for this form of cancer. Most of the research done on appendix cancer is gathering data and statistical analysis from patient diagnoses. Both the study done in Turkey and McCusker et al. classify forms of adenocarcinoma and provide insight into them. Despite their insight, research still needs to be conducted to find other ways to detect tumors that can not otherwise be identified by CTs or be treated with chemotherapy. Through detection, classification, and treatment, researchers can develop more effective strategies for dealing with appendix cancer - those that are tailored to each tumor type and improve patient outcomes.



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