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THE CURRENT LANDSCAPE OF MANAGEMENT OF LOW GRADE MUCINOUS APPENDICEAL ADENOCARCINOMA

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Appendiceal cancer is a rare disease with reported age-adjusted incidence rates ranging from 0.12 to 4 cases per 1,000,000, but it presents with a wide range of histologic subtypes that carry different prognostic implications [1,2]. Given the rarity and heterogeneity of the disease, there is little evidence to support best treatment practices [3]. There are many different subtypes of appendiceal cancer, and their classification and terminology have been a source of debate and confusion in the past [4]. While some epithelial tumors of the appendix can behave similarly to those found in colonic primary sites, the majority of appendiceal adenocarcinomas are of the mucinous histologic subtype [2]. These tumors can produce abundant intraabdominal mucin, and are further defined by

their differentiation level, or grade [4]. Tumor grade has significant implications on both clinical predilections and survival in this patient population [4,5]. Low grade appendiceal mucinous adenocarcinomas tend to evolve into peritoneal metastases rather than distant metastases, but are a distinct entity from low grade appendiceal mucinous neoplasms (LAMN), which do not invade beyond the lamina propria [4,6]. Here, we will discuss the management of low grade mucinous appendiceal adenocarcinomas.

Many cases of appendiceal adenocarcinoma are discovered incidentally on pathologic review of appendectomy specimens resected for presumed acute appendicitis, with approximately 1% of appendectomy specimens revealing malignancy [7]. While a right hemicolectomy was originally proposed as treatment for appendiceal cancer, the question of whether it is necessary for all appendiceal cancers remains unclear [8]. Sugarbaker reviewed a series of 299 patients with mucinous appendiceal neoplasms, and found patients with low or moderately differentiated tumors had a low incidence of lymph node positivity (6%) compared to patients with high grade disease (29%), and concluded that hemicolectomy should only be performed for patients with high grade disease [9]. Similarly, a recent study evaluating patients with non-metastatic low grade mucinous appendiceal cancers found that there was no survival benefit to performing hemicolectomy over a margin-negative appendectomy alone [10]. However, over 67.2% of these patients underwent colonic resection beyond appendectomy, suggesting that while there may be little evidence to support the practice of performing a right hemicolectomy, many providers continue to perform this practice [10].

For patients with metastatic low grade mucinous appendiceal adenocarcinoma, cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy (HIPEC) is the primary modality in management of the disease [6]. An important part of the preoperative workup is cross sectional imaging to determine resectability of the intracellular mucin, and to estimate the peritoneal carcinomatosis index (PCI) [6]. For patients who have disease that is deemed resectable, cytoreduction with removal of visible gross disease or with residual tumor that is no greater than 2 mm thick to allow penetration of HIPEC [6]. While some small retrospective studies show improved survival of cytoreduction with HIPEC over cytoreduction alone, there remains some controversy over the utility of HIPEC use in patients with this disease [11]. Even with debulking and HIPEC, recurrence is frequently seen with reported median disease free survival of 38.1 months [3]. However, due to the indolent nature of low grade disease, median 5 year survival remains at 75–81% [3].

Systemic chemotherapy has also been suggested as an adjunct therapy for patients with metastatic low grade mucinous appendiceal adenocarcinoma, especially in cases deemed to be unresectable [3]. However, some studies have shown that systemic chemotherapy use in this particular subset of patients is not

associated with improved survival [12,13]. This is hypothesized to be related to the indolent nature of low grade disease, as chemotherapy agents tend to target disrupting cell replication [3]. While some aspects of best treatment practices of metastatic low grade appendiceal mucinous adenocarcinoma remain unclear, it is important to note that these patients should all be referred to palliative care within eight weeks of diagnosis; this is in accordance to the American Society of Clinical Oncology guidelines released in 2012 regarding integration of palliative care with standard oncologic treatment [14].

While appendiceal cancers are a rare disease, the incidence is increasing [2]. Low grade appendiceal mucinous adenocarcinomas are a unique subtype that tends to have a more indolent natural history but is unfortunately often diagnosed in late stages [10]. Although there is limited data supporting treatment for this disease, surgical resection remains a critical component of management.

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