Original Article

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Appendiceal tumours as incidental findings in patients undergoing emergency appendicectomy: A retrospective, single-center study and a brief overview of current practice standards

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ABSTRACT

Introduction: Primary cancers of the appendix are very rare and most of them are usually found accidentally on appendectomies performed for appendicitis. Although these tumours are rare, there is a diverse histology.
Methods: We conducted a single-center retrospective study of patients undergoing appendectomy at our institution for the suspended diagnosis of appendicitis. From January 2003 to December 2018 a total of 1809 patients underwent appendectomy under general anaesthesia. Patient demographics, type of procedure, and tumour histology were recorded.
Results: The mean age of patients was 32 years (range, 14 to 85). Of these patients, 821 (45.38%) were female, and 988 (54.62%) were male. In total 959 (53.01%) underwent laparoscopic appendectomy and 850 (46.99%) underwent open appendectomy. An appendiceal neoplasm was found in 17 patients (0.94%). Of these 17 patients, four (23.53%) were reported to have benign tumours, while 13 (76.47%) were reported to have malignancies. The most frequent appendiceal tumour was carcinoid, which was detected in 10 patients (58.82%).
Conclusion: Tumours of the appendix are very rare and the majority of them are malignancies. Early recognition is very important. There is no standard of care due to the rare frequency of these tumours.

Key Words: *Appendiceal tumours; appendicitis; laparoscopic appendectomy; open appendectomy*

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INTRODUCTION

Primary appendiceal tumours consist of rare entities that occur in less than 2% of all performed appendicectomies, irrespective of preoperative diagnosis, and in about 0.7% to 1.7% of appendiceal specimens retrieved from patients with a preoperative diagnosis of acute appendicitis [1–3]. Pathological classification of appendiceal tumours has seen multiple revisions and re-classifications. The current practice consensus is focused around the revised

WHO 2019 classification, as well as the consensus statement issued by the Peritoneal Surface Oncology Group International (PSOGI) Executive Committee regarding mucinous appendiceal neoplasms and pseudomyxoma peritonei [1,4–8].

The small patient number in reported cohorts of appendiceal tumour patients, as well as the lack of RCTs largely owed to the incidental nature of this condition, has been a hurdle in the development of guidelines for their detection, management, and follow-up. The presence of diverse histological subtypes with differentiating predictive characteristics has further complicated the process. Appendiceal tumours can be broadly split into epithelial and neuroendocrine neoplasms [1–3,8]. Mucinous appendiceal tumours form a distinct subtype of the former, which is most commonly described using the PSOGI classification as the golden standard for pathological classification. The 2019 WHO classification, splits epithelial tumours of the appendix into the following categories: Hyperplastic polyp, Sessile serrated lesion with or without dysplasia, low-grade appendiceal mucinous neoplasm (LAMN), high grade appendiceal mucinous neoplasm (HAMN), adenocarcinoma, undifferentiated carcinoma, Goblet cell adenocarcinoma and neuroendocrine tumours (well- or poorly differentiated). A study reported a cumulative five-year survival rate of 83% for patients with any type of appendiceal tumour, indicating acceptable survival rates as a whole, but with many variations regarding different subtypes. Due to the scarcity and heterogeneity of reports on appendiceal tumours, estimates of the incidence rates of histological subtypes are also difficult to obtain [4–7,9]. The most common subtype of appendiceal tumours are neuroendocrine appendiceal neoplasms, with an incidence rate ranging from 35% to 85% of all appendiceal tumours (as identified by the largest patient series available through the SEER database), while other studies mention that adenocarcinoma of the appendix makes up for almost 60% of appendiceal tumours [4,9]. A recent study showed that patients that underwent interval appendicectomy after a case of appendicitis that was managed nonoperatively, had a pooled prevalence of 11% for appendiceal malignancies.

The primary clinical manifestation of appendiceal tumours is often non-specific and can vary between patients. Chronic distention of the appendix due to mucin accumulation might cause non-specific right lower quadrant pain, although this can also often be a late finding of advanced disease. Weight loss and chronic iron deficiency anaemia are also symptoms associated with appendiceal tumours. The most often acute presentation of appendiceal tumours is invariably acute appendicitis, caused by luminal obstruction evident by RLQ abdominal pain, elevation in inflammatory markers, anorexia etc. [4,9–16].

Although a number of retrospective reviews have presented several patient cohorts, there is still a scarcity of data regarding appendiceal tumours and their histopathological subtypes. This retrospective, single-center cohort study presents data on patients that were taken to the operating theatre with a diagnosis of acute appendicitis, underwent emergency appendicectomy and appendiceal tumours were found as the final diagnosis.

METHODS

We conducted a systematic, retrospective search of our institution's database for patients that underwent emergency laparoscopic or open appendicectomy due to acute appendicitis over a period of 16 years. Patient inclusion criteria included the following: 1) Definitive sonographic or CT-confirmed diagnosis of acute appendicitis preoperatively, 2) Presence of a finalised pathological report for the extracted specimen, 3) Patients that underwent emergency appendicectomy due to acute appendicitis either with a laparoscopic or open approach and 4) Patients that underwent surgery from January 1st 2003 to December 31st 2018. Patients with no definitive pathological report, patients that underwent interval appendicectomy, patients undergoing palliative surgery for known malignancies of the appendix (e.g. advanced stage pseudomyxoma peritonei with complications) and patients with a preoperative diagnosis of appendiceal neoplasm were excluded from the study.

After identifying qualifying patients for inclusion in the study, we tabulated the demographics of those that were ultimately diagnosed with appendiceal tumours vs patients without further appendiceal pathology. Statistical processing of the data utilised the Student's t-test for continuous variables and chi-squared two-sided tests for comparing proportions.

RESULTS

In total, 1809 patients that underwent emergency appendicectomy during the specified time period were identified. The mean patient age was 32.6 years (range 15 – 85). Of these patients, 821 (45.38%) were female and 688 (54.6%) were male. In total, 959 patients (53.01%) underwent laparoscopic appendicectomy and 850 (45.99%) underwent open appendicectomy. Appendiceal neoplasms were found intraoperatively in 17 patients in total, 0.94% of the total patients. Four of the patients (23.53% of the appendiceal tumour patients) were found to have benign

appendiceal tumours (adenomas and polyps). Of the remaining 13 patients with appendiceal malignancies, ten patients (58.82%) were diagnosed with appendiceal carcinoid tumours. Of the remaining patients, there were two patients with high-grade appendiceal mucinous neoplasms and one patient with low-grade appendiceal mucinous neoplasm (Table 1).

A total of 415 cases presented with complicated appendicitis, as opposed to 1394 cases of uncomplicated appendicitis. There was no statistically significant difference in the presence of complicated vs uncomplicated appendicitis in patients presenting with appendiceal neoplasms. Of the patients presenting with carcinoid tumours of the appendix, six (60%) presented with localised disease, three patients (30%) with locally advanced disease, and one patient with distant metastasis evident in postoperative staging. Tumour size was less than 1cm in six patients (46.1%), between 1 and 2 cm in three patients (23.07%), between 2 and 5 cm in two patients (15.3%), and more than 5cm in two patients (15.3%) (Table 2). The sum of the patients experienced uneventful postoperative periods and were discharged home without further complications. In seven patients (53.8%), the operation was converted to right-sided hemicolectomy either due to the size of the primary tumour, or the presence of locally advanced disease. Average hospital stay differed between patients diagnosed with appendiceal tumours, vs patients that had either complicated or uncomplicated appendicitis without malignancy (5.7 days vs 3.26 days, $p < 0.05$). Age, gender, and rates of postoperative complications did not differ significantly between the two subgroups.

TABLE 1: Descriptives of appendicectomy patients.

Descriptives	No of Patients
Age	32.6 (15-85)
Gender	
Female	821 (45.38%)
Male	688 (54.6%)
Operative Approach	
Laparoscopic	959 (53.01%)
Open	850 (45.99%)
Appendiceal Tumours (Total)	17 (0.94%)
Benign Appendiceal Lesions	4 (23.53%)
Appendiceal Carcinoid	10 (58.82%)
HAMN	2 (11.7%)
LAMN	1 (5.85%)

TABLE 2: Characteristics of appendiceal tumour patients.

Characteristic	No of Patients
Diameter Size (cm)	
<1	6 (46.1%)
1-2	3 (23.07)
2-5	2 (15.3%)
>5	2 (15.3%)
Conversion rate	7 (53.8%)
Average Hospital Stay (days)	5.7
Disease Stage	
Local	6 (46.1%)
Locally Advanced	3 (23%)
Distal Metastasis	1 (0.05%)

DISCUSSION

The first-ever report of an appendiceal mass attributed to a tumour was published in 1882, with the first case series being published in 1903 [12,13]. Since then, appendiceal tumours remain a largely elusive ailment, with physicians struggling to produce large reports of patient series that would bring about the creation of definitive management guidelines. To complicate matters further, histological subtyping of appendiceal tumours reveals a large number of distinct histological subtypes, often associated with differences in patient prognosis. Perhaps the greatest issue regarding appendiceal neoplasms is that they more often than not become symptomatic at advanced stages, or present as a bout of acute appendicitis, meaning that they leave little room for early diagnosis and management, especially in an elective fashion.

Our results seem to be in line with previous findings of the largest studies on appendiceal tumours. With an incidence rate of less than 2% overall in patients that are incidentally found to be ailed by appendiceal tumours and a small prevalence of males over female patients, our experience further confirms current findings [10–13,17-20]. Appendiceal tumours are usually located at the tip of the appendix, with a diameter of less than 1cm in most cases. Although this was also true in our patient cohort, we did encounter patients with neoplasms larger than 1cm (53.9%). This difference can be attributed to the selective inclusion of patients undergoing emergency appendicectomy with a preoperative diagnosis of acute appendicitis alone, rather than the inclusion of both emergency and elective surgery of neoplasms that is expected to apply to earlier-stage carcinomas [10].

Perhaps the most controversial aspect of appendiceal

malignancies is histological classification. The 2019 update in the WHO classification of appendiceal tumours, brought about several changes that need to be discussed and kept in mind by surgeons treating appendiceal tumours. The term "sessile polyp" was replaced by "sessile lesion", now indicating that a polypoid formation is not necessary to diagnose a sessile lesion of the appendix, a change that could lead to a rise in the incidence of appendiceal neoplasm diagnosis [10,11]. The WHO 2019 classification, also moved closer to the PSOGI classification of mucinous neoplasms of the appendix, which abandoned complex nomenclature, often found to have little to no effect in the effective clinical classification of patients and patient survival outcomes. Tumour grade is now considered the cardinal characteristic, with LAMNs being included as Grade I neoplasms, and HAMNs being Grade 2 (primarily) and Grade 3 tumours [10,11]. It is essential that the surgeon assigned to such cases is familiar with the new nomenclature since it closely correlates with patient management strategies and the referral to the oncologist.

In a 2021 statement, a joint force of the PSOGI and EURACAN committees published what are now the latest clinical-oriented management guidelines for appendiceal tumours based on the latest classification changes. Inclusion of preoperative CEA and CA 19.9 in preoperative evaluation of patients is now strongly recommended after several studies proved that the levels of these biomarkers do not only correlate with the presence of appendiceal malignancy, but also with the survival rates of patients [17-23]. Due to the nature of our study cohort (emergency surgical patients) we did not have the ability to evaluate such biomarkers. Simple polyps that do not exhibit malignant cells can be managed by appendicectomy alone, as was done in our patients as well. Carcinoid tumours of the appendix that consisted the largest subgroup of malignancy patients, require a therapeutic right-sided hemicolectomy if they are larger than 1-2 cm in diameter, mesoappendiceal invasion of more than 3 mm or with high rates of Ki67 indexes [21,22, 24-26]. Macroscopic evidence of peritoneal spread is now considered an indication for either the use of intraoperative HIPEC, or adjuvant chemotherapy. One area of remaining debate is the management of LAMN and HAMN occurrences for which no clear recommendations can be made. Although authors have described the expectant management strategy for LAMN lesions, recurrence rates seem to indicate the need for more radical approaches. As of now, despite the low level of evidence, HAMN lesions are managed aggressively, in a similar fashion to adenocarcinoma. These gaps in knowledge have been the reason for a more radical approach after our intraoperative diagnosis of appendiceal neoplasms, with right-sided hemicolectomies being performed in most patients with gross disease irrespective of histological subtype [24–28].

CONCLUSIONS

Appendiceal tumours are an extremely rare, mostly incidental finding. Despite their rarity, their biological behaviour can vary according to the histological subtype and can manifest as aggressive malignancy. Lack of patient data is the main reason behind gaps in current knowledge regarding their management. Our work presents the 15-year experience of a tertiary center in the management of appendiceal malignancies.

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