RESEARCH ARTICLE

The Prevalence of Malignant Tumors of the Appendix in Patients with a History of Appendectomy and its Association with Demographic and Laboratory Variables

Behnam Reza Makhsosi[1], Fatemeh Darabi[2], Tara Mazaheri[3], Mansour Rezaei[4], Zohair Mazaheri[5], Alireza Rohban[6]

Received on: 01 August 2021; *Accepted on*: 06 September 2022; *Published on*: 07 December 2022

Abstract

Aim: Appendicitis is one of the major causes of acute abdominal pain and one of the most common reasons for emergency surgery. Studies have shown that those that have undergone appendectomy are more likely to develop malignant tumors of the appendix. The present study investigates the prevalence of the appendix's malignant tumors in patients with a history of appendectomy and its association with demographic and laboratory variables.

Materials and methods: This study is descriptive, in which 4940 patients with a history of appendectomy between 2011 and 2018 in Imam Reza Hospital, Kermanshah, Iran, have been studied. Initially, the patients' medical files were investigated, and the necessary demographic and laboratory information were extracted. Then, the data were analyzed by descriptive statistics, including mean and variance for quantitative variables and frequency/percentage plus two-dimensional contingency tables for qualitative variables by SPSS 21.

Results: The mean age of the patients with appendectomy was 25.50 years, and the prevalence of malignant tumors of the appendix in patients was 0.5%. Overall, 41 cases (0.8%) showed positive pathology regarding the existence of a tumor in the appendix; among them, 26 cases (0.5%) had malignant types, while 15 cases (0.3%) showed benign types. Out of the 26 cases with the appendix's malignant tumors, 14 were male (53.8%), and 12 were female (46.2%). The majority of malignant tumors of the appendix were observed in those above 50 years of age. Among the malignant tumors, 9 (34.61%) were adenocarcinoma mucinous, 6 (23.07%) were carcinoid, 5 (19.23%) were adenocarcinoma, 5 (19.23%) were malignant mucocele, and 1 (3.84%) was cystadenoma. The relationship between the number of white blood cells (WBC) and the appendix's malignant tumors was significant; the WBC count was significantly lower in those with malignant tumors compared to others. In addition, the relationship between age and the existence of malignant tumors was significant ($p = 0.025$); older individuals were significantly more likely to develop malignant tumors of the appendix compared with younger individuals. The study results did not show any significant relationship between gender and the presence of malignant tumors of the appendix ($p = 0.340$).

Conclusion: Concerning the local invasion and distant metastasis of some appendix tumors, follow-up of pathology reports by the patient (especially older ones) as well as the physician plus post-appendectomy checkup within short and regular time intervals and, if required, follow-up treatment is essential.

Keywords: Appendicitis, Appendectomy, Iran, Tumors.

World Journal of Laparoscopic Surgery (2022): 10.5005/jp-journals-10033-1530

Introduction

The appendix is an essential organ of the gut-associated lymphoid tissue system, whose physiological function is mostly unknown.[1] Some hypotheses suggest that the appendix plays a vital role in training, developing, and maturing the immune system.[2] When the appendix suffers infection and inflammation, appendicitis occurs, which is one of the most common acute abdominal diseases requiring surgery.[3] The risk of mortality in acute appendicitis has been reported 7–8%.[4] In the United States, around 77,000 people develop appendicitis every year, incurring 680 million dollars to the government.[5] The incidence of appendicitis throughout the lifetime is 8.6% and 6.7% for men and women, respectively.[6] The prevalence of appendicitis differs across various populations, regions, and ages.[7] Although lymphoid hyperplasia and fecalith are the most common factors underlying acute appendicitis, other factors have also been identified, including pinworms and tumors as the etiological factors.[8] Despite antibiotic treatment, laparoscopy appendectomy is established as a standard treatment for acute appendicitis.[9,10]

Appendix cancer is very rare,[11,12] yet less than 1% of those experiencing appendectomy have the chance of developing

[1]Department of General Surgery, School of Medicine, Kermanshah University of Medical Sciences; Imam Reza Hospital, Kermanshah, Iran

[2]Department of Public Health, Asadabad School of Medical Sciences, Asadabad, Iran

[3,5]Department of General Surgery, Kermanshah University of Medical Sciences, Kermanshah, Iran

[4]Department of Biostatistics and Epidemiology, School of Health, Social Development and Health Promotion Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

[6]Department of Rehabilitation Management, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran

Corresponding Author: Tara Mazaheri, Department of General Surgery, Kermanshah University of Medical Sciences, Kermanshah, Iran, Phone: +98 9188871487, e-mail: Tara.mazaheri.tm@gmail.com

How to cite this article: Makhsosi BR, Darabi F, Mazaheri T, *et al*. The Prevalence of Malignant Tumors of the Appendix in Patients with a History of Appendectomy and its Association with Demographic and Laboratory Variables. World J Lap Surg 2022;15(3):235–238.

Source of support: Nil

Conflict of interest: None

appendix cancer on average.[13] Pathologically, appendix tumors are diverse, and it seems that the risk of developing various neoplasms of the appendix (except for malignant carcinoid, which involves women three times more than men) is the same for both males and females.[14] Carcinoid is the most common appendix tumor, while adenocarcinoma, lymphosarcoma, paraganglioma, and granular-cellular tumors account for only 10–20% of appendix tumors.[15] Most carcinoid tumors are asymptomatic, and on average, it usually takes 9 years to diagnose the tumor from the time of early symptoms.[16] When the tumor is located on the appendix base, it blocks the hole, whereby the patients manifest symptoms similar to those of appendicitis.[17] The present study aims to examine the prevalence of malignant tumors of the appendix and determine its association with demographic and laboratory variables in 4940 patients who have undergone appendectomy in Imam Reza Hospital in Kermanshah, Iran.

Materials and Methods

The present study is descriptive cross-sectional, with the study population consisting of all patients who had undergone appendectomy in 2011–2018 in Imam Reza Hospital in Kermanshah, Iran. The exclusion criteria included lack of pathology tests in the file, incomplete information, suffering cancers before appendectomy, metastasis to appendix before appendectomy, taking chemotherapeutic and corticosteroid drugs, radiotherapy, and use of other immunosuppressive drugs in patients with acquired immune deficiency syndrome (AIDS). From 6086 medical files of patients undergoing an appendectomy, 1146 were excluded, and eventually, 4940 files were examined. The required information, including age, gender, type of tumor, and laboratory information, was collected from these files.

Data Analysis

The Kolmogorov–Smirnov test was used to check the normality of data distribution. The data were analyzed using descriptive statistics, including mean and variance for quantitative variables and frequency/percentage plus two-dimensional contingency tables for qualitative variables by SPSS 21. The *p*-value was considered statistically significant if $p \leq 0.05$.

Results

The results indicated that most patients who had undergone appendectomy in the mentioned hospital were male (n = 3017, 61%), and the rest were female (n = 1923, 39%). The mean age of the studied patients was 25.50 ± 15.16 years. The youngest patient was a one-day-old neonate, while the oldest patient had 94 years of age. Out of all patients undergoing an appendectomy, 41 (0.8%) showed positive pathology regarding tumor in the appendix; out of them, 26 (0.5%) had malignant, while 15 (0.3%) showed benign types. Among the malignant tumors, 9 (34.61%) were adenocarcinoma mucinous, 6 (23.07%) were carcinoid, 5 (19.23%) were adenocarcinoma, 5 (19.23%) were malignant mucocele, and 1 (3.84%) was cystadenoma. Among the benign tumors, 9 (60%) were follicular hyperplasia, 3 (20%) were lymphoid hyperplasia, 1 (6.6%) was mucinous cystadenoma, 1 (6.6%) was sinus histiocytosis, and 1 (6.6%) was follicular lymphoid hyperplasia. The frequency distribution of different types of malignant and benign tumors of the appendix is presented in Table 1.

Out of the 26 cases with the appendix's malignant tumors, 14 (53.8%) were male, and 12 (46.2%) were female. The results found no significant relationship between gender and the presence of the appendix's malignant tumors (p = 0.340). The majority of cancerous cases were observed in those above 50 years of age. In addition, the relationship between age and the existence of malignant tumors was significant (p = 0.025); older individuals were significantly more likely to develop malignant tumors of the appendix compared to younger individuals (Fig. 1). The mean WBC count in those with appendectomy was 12.34 ± 4.184 Tho/µL. White blood cell count equal to and larger than 12 Tho/µL was considered positive (57.2% of cases), and below this value was regarded as negative (42.8% of cases). The relationship between the number of WBC and the appendix's malignant tumors was significant; the WBC count was significantly lower in those with malignant tumors compared to others (Fig. 2). The mean erythrocyte sedimentation rate (ESR) in

Ethics approval: Ethical approval (code: IR. KUMS. REC.1398.185) was granted from the Kermanshah University of Medical Sciences Ethics Committee.

Table 1: The frequency distribution of appendix tumors in patients undergoing appendectomy (n = 41)

Type of tumor	*Frequency*	*Percentage*
Malignant tumors		
Adenocarcinoma mucinous	9	34.61
Carcinoid	6	23.08
Adenocarcinoma	5	19.23
Mucocele	5	19.23
Cystadenoma	1	3.85
Total	26	100
Benign tumors		
Follicular hyperplasia	9	60
Lymphoid hyperplasia	3	20
Mucinous cystadenoma	1	6.7
Sinus histiocytosis	1	6.7
Follicular lymphoid hyperplasia	1	6.7
Total	15	100

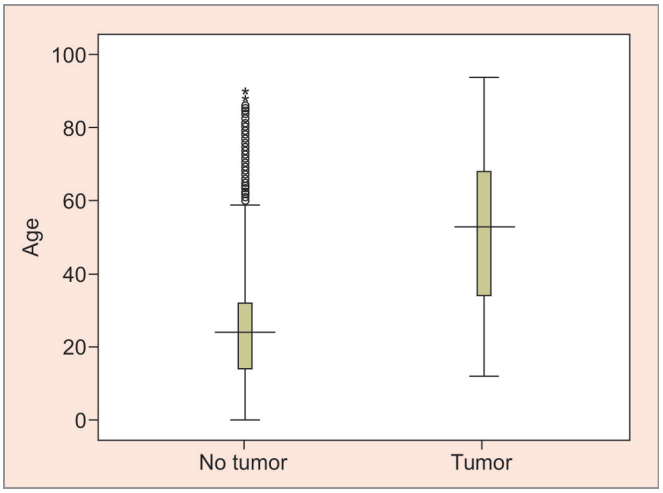

Fig. 1: Age comparison between the groups showing malignant tumors and no tumor (n = 4940)

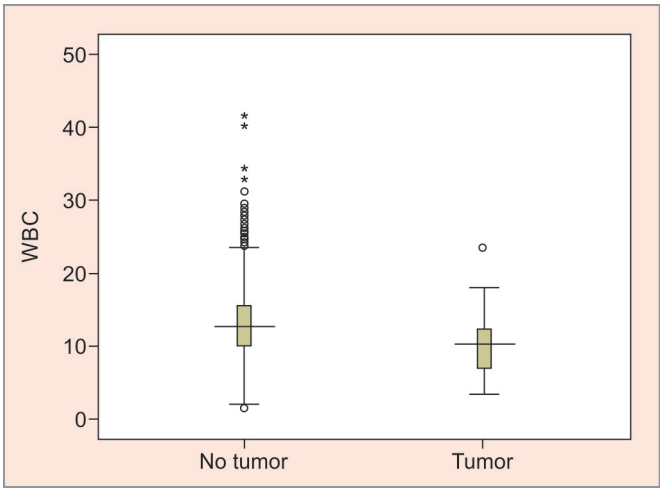

Fig. 2: Comparison of the WBC count in those with malignant tumors and no tumor ($n = 4940$)

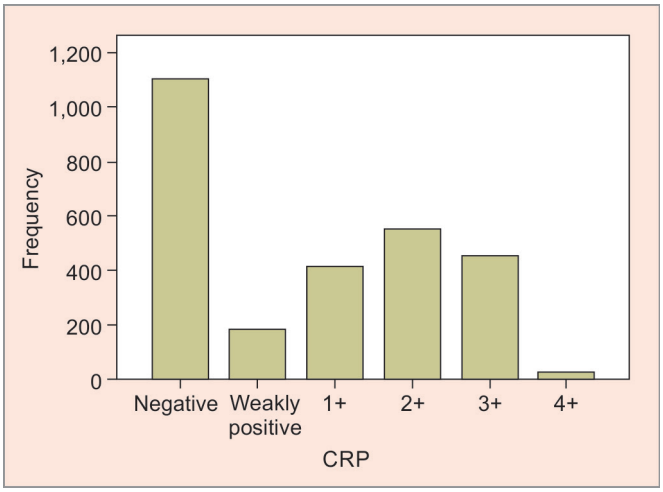

Fig. 3: CRP values in the studied population ($n = 4940$)

the studied population was 25.04 ± 23.98 mm/h. No significant relationship was observed between ESR and the presence of malignant tumors of the appendix. Moreover, the C-reactive protein (CRP) test results showed 40.4% negative and 59.6% positive cases. No significant relationship was observed between CRP level and the presence of the appendix's malignant tumors (Fig. 3).

Discussion

This study investigated the prevalence of the appendix's malignant tumors and determined the possible relationship between these tumors and demographic and laboratory variables in 4940 patients with a history of appendectomy in Imam Reza Hospital, Kermanshah. The results showed that the prevalence of the appendix's malignant tumors in those who had undergone appendectomy was 0.5%. Here, 61% of patients were male. In this regard, other studies have also shown a higher prevalence of appendectomy among men.[18] In the present research, the primary type of malignant tumor was mucinous adenocarcinoma (34.61%), followed by carcinoid tumor (23.07%). The prevalence of carcinoid tumors in this study across the entire population was 0.0012%. This value is slightly lower than the value obtained in the study by Chinifroush et al. in Iran (0.0019%),[19] Vessal et al. in Iran (0.0024%),[20] Guraya et al. in Saudi Arabia (0.0058%),[21] and Tchana-Sato et al. in Belgium (0.0040%).[13] In a study performed by Ahmadi Nejad et al. in Lorestan province, Iran, the prevalence of the appendix's carcinoid tumors in those with a history of an appendectomy was reported at 0.17%.[22] Although the prevalence of carcinoid tumors in the general population of the United States has been estimated to be 1–2 per 100,000 people,[23] it seems that the actual prevalence might be higher. Note that the incidence of carcinoid tumors is often asymptomatic and can often remain so for years.[24] Based on the obtained results, although no significant relationship was found between gender and the presence of malignant tumors of the appendix, the frequency of malignant tumors was higher in men. Unlike the results obtained from the present study, other investigations have shown a higher incidence of the appendix's malignant tumors in women.[19,23,25] In our study, a significant relationship was observed between presence of malignant tumors of the appendix and age, with older individuals showing larger numbers of malignant tumors. C-reactive protein assessment in the patients showed 40.4% negative and 59.6% positive cases. No significant relationship was found between CRP level and presence of malignant tumors of appendix. C-reactive protein is an acute phase reactant synthesized by the liver in response to infection. The serum levels of this protein begin to rise 6–12 h after initiation of tissue inflammation. C-reactive protein assessment is often done easily and rapidly in laboratories, with studies showing that CRP level can confirm appendicitis with high accuracy.[26,27]

Conclusion

Since the diagnosis of malignant tumors of the appendix may not be made easily, noting some variables, including advanced age and high WBC count in the laboratory test, can help diagnose malignant tumors. Moreover, given the malignancy as well as local invasion and distant metastasis of some appendix tumors, follow-up of the pathology report by the patient (especially older individuals) as well as physician and during checkup following appendectomy within short and regular intervals and if required follow-up treatment is essential.

Acknowledgments

The proposal of this research has been approved by the Research Deputy of Kermanshah University of Medical Sciences with the code of 980527. The authors highly appreciate those who cooperated with us in this research, as well as the general surgeons of Imam Reza Hospital in Kermanshah.

Orcid

Mansour Rezaei https://orcid.org/0000-0002-6446-7289

References

1. Kooij I, Sahami S, Meijer S, et al. The immunology of the vermiform appendix: a review of the literature. Clin Exp Immunol 2016;186(1):1–9. DOI: 10.1111/cei.12821.
2. Gebbers JO, Laissue JA. Bacterial translocation in the normal human appendix parallels the development of the local immune system. Ann N Y Acad Sci 2004;1029:337–343. DOI: 10.1196/annals.1309.015.
3. van Rossem CC, Bolmers MDM, Schreinemacher MHF, et al. Diagnosing acute appendicitis: surgery or imaging? Colorectal Dis 2016;18(12):1129–1132. DOI: 10.1111/codi.13470.

4. Georgiou R, Eaton S, Stanton MP, et al. Efficacy and safety of nonoperative treatment for acute appendicitis: a meta-analysis. Pediatrics 2017;139(3):e20163003. DOI: 10.1542/peds.2016-3003.
5. Guthery SL, Hutchings C, Dean JM, et al. National estimates of hospital utilization by children with gastrointestinal disorders: analysis of the 1997 kids' inpatient database. J Pediatr 2004;144(5):589–594. DOI: 10.1016/j.jpeds.2004.02.029.
6. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg 2002;137(7):799–804. DOI: 10.1001/archsurg.137.7.799.
7. Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 1990;132(5):910–925. DOI: 10.1093/oxfordjournals.aje.a115734.
8. Alemayehu H, Snyder CL, Peter SDS, et al. Incidence and outcomes of unexpected pathology findings after appendectomy. J Pediatr Surg 2014;49(9):1390–1393. DOI: 10.1016/j.jpedsurg.2014.01.005.
9. Harnoss JC, Zelienka I, Probst P, et al. Antibiotics versus surgical therapy for uncomplicated appendicitis: systematic review and meta-analysis of controlled trials (PROSPERO 2015: CRD42015016882). Ann Surg 2017;265(5):889–900. DOI: 10.1097/SLA.0000000000002039.
10. Montravers P, Dupont H, Leone M, et al. Guidelines for management of intra-abdominal infections. Anaesth Crit Care Pain Med 2015;34(2):117–130. DOI: 10.1016/j.accpm.2015.03.005.
11. Karanikas M, Kofina K, Markou M, et al. Acute appendicitis as the first presentation of appendiceal metastasis of gastric cancer—report of a rare case. J Surg Case Rep 2018;2018(8):rjy208. DOI: 10.1093/jscr/rjy208.
12. Kelly KJ. Management of appendix cancer. Clin Colon Rectal Surg 2015;28(4):247–255. DOI: 10.1055/s-0035-1564433.
13. Tchana-Sato V, Detry O, Polus M, et al. Carcinoid tumor of the appendix: a consecutive series from 1237 appendectomies. World J Gastroenterol 2006;12(41):6699–6701. DOI: 10.3748/wjg.v12.i41.6699.
14. Deshmukh S, Verde F, Johnson PT, et al. Anatomical variants and pathologies of the vermix. Emerg Radiol 2014;21(5):543–552. DOI: 10.1007/s10140-014-1206-4.
15. Ruoff C, Hanna L, Zhi W, et al. Cancers of the appendix: Review of the literatures. ISRN Oncol 2011;2011:728579. DOI: 10.5402/2011/728579.
16. Horton KM, Kamel I, Hofmann L, et al. Carcinoid tumors of the small bowel: A multitechnique imaging approach. Am J Roentgenol 2004;182(3):559–567. DOI: 10.2214/ajr.182.3.1820559.
17. McCusker ME, Coté TR, Clegg LX, et al. Primary malignant neoplasms of the appendix: A population-based study from the surveillance, epidemiology and end-results program, 1973–1998. Cancer 2002;94(12):3307–3312. DOI: 10.1002/cncr.10589.
18. Khan SA, Khokhar HA, Nasr A, et al. Incidence of right-sided colonic tumors (non-appendiceal) in patient's ≥40 years of age presenting with features of acute appendicitis. Int J Surg 2013;11(4):301–304. DOI: 10.1016/j.ijsu.2013.02.004.
19. Chinifroush M, Mohajeri S, Shirinzadeh B. The prevalence of appendix carcinoid in appendectomized patients Fatemi Hospital in Ardabil. J Ardabil Univ Med Sci 2008;8(3):241–245.
20. Vessal P, Ahmadian Moghaddam H, Vahidi S. Prevalence of carcinoid tumor in appendectomy specimens in hospitals affiliated to Shaheed Beheshti University of Medical Sciences. Iran J Endocrinol Metab 2000;2(3):197–202.
21. Guraya SY, Khairy GA, Ghallab A, et al. Carcinoid tumors of the appendix. Our experience in a university hospital. Saudi Med J 2005;26(3):434–437. PMID: 15806214.
22. Ahmadi Nejad M, Saki M, Azizi M. Study of frequency and Prognosis of appendix carcinoid tumor in appendoctomies done in Shohada hospital in Khorramabad. Yafteh 2010;11(4):5–10.
23. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. Cancer 1997;79(4):813–829. DOI: 10.1002/(sici)1097-0142(19970215)79:4<813::aid-cncr19>3.0.co;2-2.
24. Kulke MH, Mayer RJ. Carcinoid tumors. N Engl J Med 1999;340(11):858–868. DOI: 10.1056/NEJM199903183401107.
25. Sandor A, Modlin IM. A retrospective analysis of 1570 appendiceal carcinoids. Am J Gastroenterol 1998;93(3):422–428. DOI: 10.1111/j.1572-0241.1998.00422.x.
26. Birchley D. Patients with clinical acute appendicitis should have pre-operative full blood count and C-reactive protein assays. Ann R Coll Surg Engl 2006;88(1):27–32. DOI: 10.1308/003588406X83041.
27. Kessler N, Cyteval C, Gallix Bt, et al. Appendicitis: evaluation of sensitivity, specificity, and predictive values of US, Doppler US, and laboratory findings. Radiology 2004;230(2):472–478. DOI: 10.1148/radiol.2302021520.