Clinical and Pathological Characteristics of Mucinous Colorectal Adenocarcinoma: A Comparative Study

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Received 2015 November 5; Accepted 2015 November 30.

Abstract

Background: Mucinous adenocarcinoma accounts for approximately 5%-15% of all colorectal cancers.

Objectives: The aim of this study was to investigate the clinicopathological characteristics of patients with mucinous colorectal adenocarcinoma.

Patients and Methods: This retrospective study was carried out by reviewing the medical records of 70 mucinous colorectal cancer (MCC) patients who were diagnosed and treated at a tertiary academic hospital between 2005 and 2010. For the comparative analysis, 491 patients with non-mucinous colorectal cancer (NMCC) were included.

Results: Of 561 patients with colorectal adenocarcinoma, 70 patients (12.5%) had the mucinous type. There were 42 (60%) men and 28 (40%) women, with a median age of 55 years old (range 24-81 years) included in the study. We did not find any differences regarding the patients’ mean age (P = 0.408) and male/female ratio (P = 0.700) between the MCC and NMCC; however, there was a predilection for the right colon and sigmoid colon in the MCC, when compared to the NMCC (P = 0.02). In addition, the MCC tended to have a larger tumor size (P = 0.004), higher histological grade (P < 0.001), higher node stage (P < 0.001), higher number of dissected nodes (P = 0.013), higher number of positive nodes (P < 0.001), and a higher rate of perineural invasion (P = 0.013) compared to the NMCC.

Conclusions: This study indicates that most clinicopathological characteristics of MCC are different from those of NMCC. In addition, there was an association between the mucinous subtype and adverse pathological features in the patients with colorectal cancer.

Keywords: Colorectal Cancer, Mucinous Adenocarcinoma, Pathology, Characteristics

1. Background

Colorectal cancer is one of the most prevalent and leading causes of cancer deaths worldwide (1). Adenocarcinomas account for the vast majority of colorectal cancers, and they are further classified by histological grade (2). Mucin production is a common histological feature in colorectal adenocarcinomas; however, abundant mucin production, such as that seen in mucinous adenocarcinoma and signet ring adenocarcinoma, is less frequent. Mucinous adenocarcinoma is an adenocarcinoma in which the cancer cells produce greater than 50% extracellular mucin (3, 4), and this histopathological subtype accounts for approximately 5% to 15% of all colorectal cancers (5-8). Most reports indicate that mucinous adenocarcinomas have a propensity to originate from the right colon. They tend to have a larger tumor size and to present at a more advanced stage (3, 4, 6, 9). However, there is a paucity of literature regarding colorectal mucinous adenocarcinoma in Iran (10).

2. Objectives

This study aimed to compare the clinical and pathological characteristics of 70 colorectal mucinous cancers (MCCs) with 491 non-mucinous cancers (NMCCs).

3. Patients and Methods

This retrospective study was carried out by reviewing and analyzing the medical records of all patients with primary colorectal adenocarcinoma, who were diagnosed and treated at the Namazi hospital between 2005 and 2010. Of the 561 patients with colorectal adenocarcinoma, 70 patients had MCC, while the remaining 491 patients had NMCC. All of the patient and tumor characteristics, including the age at presentation, sex, primary tumor location, tumor size, histological type, tumor grade, primary tumor and node stage, surgical margin status, number of lymph nodes dissected, number of involved lymph nodes, lymphatic vascular invasion, and perineural invasion, were extracted from the patients’ files. Tumor staging was performed using the seventh edition of the American joint committee on cancer (AJCC) tumor, node, and metastases (TNM) staging system (11).
this study, we performed a comparative analysis between the MCC and NMCC in terms of the distribution of the clinical and pathological features.

3.1. Statistics

The statistical analyses were carried out using IBM SPSS Statistics version 19.0 (IBM Co. Armonk, NY, USA). The chi-square, Fisher's exact, and Mann-Whitney tests were used for comparing the categorical clinicopathological characteristics as appropriate. In addition, the student t-test was used for comparing the continuous variables, such as the age, tumor size, number of lymph nodes dissected, and number of involved lymph nodes. All of the statistical tests were two-sided, and P values of less than 0.05 were considered to be statistically significant.

4. Results

In the MCC group, there were 42 men and 28 women, with a median age of 55 years old (range 24 - 81 years). In the NMCC group, there were 281 men and 210 women, with a median age of 56 years old (range 18 - 88 years). There were no differences with regard to the patients' mean ages [54.4 (± 15) vs. 55.9 (± 13.4) (P = 0.408)] and male/female ratios [1.5 vs. 1.3 (P = 0.700)] between the MCC and NMCC groups. Table 1 represents a comparison of the clinicopathological characteristics between the 70 patients with MCC and 491 patients with NMCC. Accordingly, there was a predilection for the right colon and sigmoid colon in the MCC, when compared to the NMCC (P = 0.012).

| Table 1. Clinicopathological Characteristics of 70 Patients With Mucinous Colorectal Adenocarcinoma, and 491 Patients With Non-Mucinous Colorectal Adenocarcinoma* |
|---|---|---|---|
| Characteristics | MCC | NMCC | P Value |
| Patient number | 70 (12.5) | 491 (87.5) | 0.700 |
| Gender | | | |
| Male | 42 (60) | 281 (57) | |
| Female | 28 (40) | 210 (43) | |
| Age* | 54.4 (15) | 55.9 (13.4) | 0.408 |
| Primary site | | | 0.012 |
| Right and transverse colon | 22 (31) | 87 (18) | |
| Left colon | 6 (9) | 46 (9) | |
| Sigmoid colon | 18 (26) | 99 (20) | |
| Rectum | 24 (34) | 259 (53) | |
| Tumor size, cm* | 5.4 (1.8) | 4.7 (2.3) | 0.004 |
| Tumor grade | | | <0.001 |
| Grade I | 35 (50) | 336 (68) | |
| Grade II | 23 (33) | 132 (27) | |
| Grade III | 12 (17) | 23 (5) | |
| Pathological tumor stage | | | 0.975 |
| T1 | 1 (1.5) | 6 (1) | |
| T2 | 15 (21.5) | 96 (19.5) | |
| T3 | 52 (74) | 372 (76) | |
| T4 | 2 (3) | 17 (3.5) | |
| Pathological node stage | | | <0.001 |
| N0 | 40 (59) | 299 (63.5) | |
| N1 | 8 (12) | 12 (24) | |
| N2 | 20 (29) | 59 (12.5) | |
| Surgical margin status | | | 0.779 |
| Free | 64 (94) | 460 (95) | |
| Involved | 5 (6) | 26 (5) | |
| Number of dissected nodes* | 8.6 (7.4) | 11.2 (10.4) | 0.013 |
| Number of positive nodes* | 1.2 (2.4) | 2.9 (6.2) | <0.001 |
| AJCC Stage | | | 0.805 |
| I | 13 (19) | 83 (17) | |
| II | 28 (40) | 219 (46) | |
| III | 24 (35) | 157 (33) | |
| IV | 4 (6) | 19 (4) | |
| Lymphatic vascular invasion | | | 0.668 |
| Present | 46 (67) | 308 (63.5) | |
| Absent | 23 (33) | 177 (36.5) | |
| Perineural invasion | | | 0.048 |
| Present | 42 (61) | 353 (73) | |
| Absent | 27 (39) | 133 (27) | |

Abbreviations: AJCC, American joint committee on cancer; MCC, mucinous colorectal cancer; NMCC, non-mucinous colorectal cancer.

*aValues are expressed as No. (%) unless otherwise indicated.

*bValues are expressed as mean (SD).
In addition, the MCC tended to have a larger tumor size ($P = 0.004$), higher histological grade ($P = 0.001$), higher node stage ($P = 0.001$), higher number of dissected nodes ($P = 0.03$), higher number of positive nodes ($P = 0.001$), and higher rate of perineural invasion ($P = 0.03$) when compared to the NMCC. However, we did not find a statistical difference in terms of the surgical margin status, pathological tumor stage (T-stage), AJCC stage, and the presence of lymphatic vascular invasion between the MCC and NMCC.

5. Discussion

Mucinous adenocarcinoma is a distinct histological subtype of colorectal cancer. This pathological entity has been widely investigated in the literature; however, there is very limited research regarding the status of patients with MCC in Iran (10). In the current study, we found that most of the clinicopathological characteristics of those patients with MCC are different from those with NMCC. In one study, Safaee et al. (10) evaluated the clinicopathological characteristics and survival rates of patients with MMC colorectal cancer between 2002 and 2008. They found 1283 patients with colorectal cancer, of which 110 (8.6%) had MCC. The median age at presentation was 50 years, and the right colon was the dominant location for the MCC; however, they did not perform a comparative analysis between the patients with MCC and those with NMCC. In the present study, the median age of the patients with MCC was 55 years old, and we found a higher rate of right colon involvement when compared to NMCC, which is similar to the findings of Safaee et al. (10).

In a similar report, Song et al. conducted a study on 144 (7%) patients with MCC and 1837 patients with NMCC diagnosed between 1994 and 2007. They determined that MCC tends to occur in younger patients, have a large tumor size, and present at a higher nodal and tumor stage (8).

In a recent study, Jimi et al. compared the clinicopathological features of 23 patients with MCC to 403 patients with NMCC. They found statistically different features of the primary tumor location, primary tumor stage (T-stage), peritoneal dissemination, distant metastasis, AJCC TNM stage, and maximum tumor size between the MCC and NMCC (12). Their findings regarding the higher rate of right colon involvement and larger tumor size in the MCC (compared to the NMCC) were consistent with our study results. In a large, institutional-based cohort with a long-term follow-up study, Park et al. investigated a prognostic comparison between MCC and NMCC. They found that MCCs tend to have a larger tumor size, higher preoperative carcinoembryonic antigen (CEA), higher pathological T-stage, more right-sided colon locations, and more common high frequency microsatellite instability (13). Some of their findings, such as the larger tumor size and more right-sided colon locations, were in agreement with our study results.

Maeda et al. investigated the significance of the mucinous component in the histopathological classification of colon cancer. They evaluated 1038 tumors, of which 877 (84%) were NMCCs, 123 (12%) with (1%) mucin components, and 38 (4%) were MCCs. They found a larger tumor size and a higher proportion of right-sided tumors in the MCCs when compared to the NMCCs (14). These findings were comparable with our results. In another study, Numata et al. described the clinicopathological features of mucinous adenocarcinoma in Japan. They compared the clinicopathological features of 144 patients with mucinous and 2673 with non-mucinous adenocarcinomas, and found that the patients with MCCs had larger primary tumors, higher pathological T-stages, higher preoperative CEA serum levels, higher rates of nodal and distant metastases, and more metastatic sites (15).

Mekenkamp et al. conducted a study assessing the prognostic impact of mucinous histology in 1010 patients with metastatic colorectal cancer. They found that 99 patients (10%) with MCC were older, with a larger primary tumor size and higher T-stage, compared to the 911 patients with NMCC (9). In one large study, Hyngstrom et al. evaluated the clinical features among patients with mucinous histologies of colorectal adenocarcinoma using data from the national cancer data base (NCDB), including 244794 patients aged 18 - 90 years old with colorectal adenocarcinoma. Of which, 25546 patients (10%) had MCC, which was more frequently right-sided, and associated with a higher stage (6). Moreover, in a population-based study, Du et al. investigated the incidence and survival of MCC patients in Singapore. A total of 627 (4%) of 15762 patients had MCC, and the authors found that the MCC rate was higher in the younger age groups, advanced stages of the disease, and the right colon (16). Verhulst et al. in a systematic review and meta-analysis, reviewed 44 studies including 222256 patients with colorectal cancer. They found that MCC originates more often from the right colon, and is less frequent in male patients. Moreover, the authors did not find a statistical difference in the proportion of stage IV patients at presentation between MCC and NMCC (5). In general, reports from Asian countries have shown a lower incidence of MCC when compared to Western countries. No association was found between the patients’ age and gender predilection in most of the studies. However, most of the reports showed a larger tumor size, higher proportion of right-sided tumors, and advanced disease stage in MCC, compared to NMCC (7, 8, 16).

This study indicates that most clinicopathological characteristics of MCC are different from those of NMCC, and that there is an association between the mucinous subtype and adverse pathological features in patients with colorectal cancer.

Footnotes

Authors’ Contribution: Sare Hosseini: involved in the design, literature review, data collection, writing and revising the manuscript, and approval of the final version; Shadi Zohourinia: involved in the conception, design, lit-
literature review, writing the manuscript, and approval of the final version; Mohammad Zare-Bandamiri: involved in the conception, design, literature review, writing the manuscript, and approval of the final version; Maral Mokhtari: involved in the conception, design, literature review, writing the manuscript, and approval of the final version; Soudabeh Pourhashemi: involved in the conception, design, literature review, writing the manuscript, and approval of the final version; Massood Hosseinzadeh: involved in the conception, design, literature review, writing the manuscript, and approval of the final version; Mohammad Mohammadianpanah: involved in the concept, design, data collection, literature review, writing and revising the manuscript, and approval of the final version.

Funding/Support: This study was supported by the colorectal research center at Shiraz University of Medical Sciences.

References

1. Edwards BK, Noone A, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, et al. Annual Report to the Nation on the status of cancer, 1975–2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. Cancer. 2014;120(9):1290–314. [PubMed: 24343177]

2. Hosseini S, Moaddabshoar L, Hemati S, Mohammadianpanah M. An Overview of Clinical and Pathological Characteristics and Survival Rate of Colorectal Cancer in Iran. Ann colorectal res. 2014;2(1):e7264. doi: 10.37795/acr-7264.

3. Deburne H, Ceelen W. Mucinous differentiation in colorectal cancer: molecular, histological and clinical aspects. Acta Chir Belg. 2013;113(6):385–90. [PubMed: 24494463]

4. Perez-Villamil B, Romero-Lopez A, Hernandez-Prieto S, Lopez-Campos G, Calles A, Lopez-Arienjo A, et al. Colon cancer molecular subtypes identified by expression profiling and associated to stroma, mucinous type and different clinical behavior. BMC Cancer. 2012;12:260. doi: 10.1186/1471-2407-12-260. [PubMed: 22725270]

5. Verhulst J, Ferdinandle I, Demetter P, Ceelen W. Mucinous subtype as prognostic factor in colorectal cancer: a systematic review and meta-analysis. J Clin Pathol. 2012;65(5):381–8. doi: 10.1136/jclinpath-2011-200340. [PubMed: 22259177]

6. Hyngstrom JR, Hu CY, Xing Y, You TN, Feig BW, Skibber JM, et al. Clinicopathology and outcomes for mucinous and signet ring colorectal adenocarcinoma: analysis from the National Cancer Data Base. Ann Surg Oncol. 2012;19(9):2844–21. doi: 10.1245/s10434-012-2321-7. [PubMed: 22476818]

7. Jivapaisarnpong P, Boonthongtho K. Clinicopathological characteristics of mucinous and non-mucinous adenocarcinoma in the colon and rectum in Rajavithi Hospital, Thailand. J Med Assoc Thailand. 2011;94:541–5.

8. Song W, Wu SJ, He YL, Cai SR, Zhang CH, Zhang XH, et al. Clinicopathologic features and survival of patients with colorectal mucinous, signet-ring cell or non-mucinous adenocarcinoma: experience at an institution in southern China. Chin Med J (Engl). 2009;122(1):3486–8. [PubMed: 19779934]

9. Mekenkamp LJ, Heestereek KJ, Koopman M, Tol J, Teerenstra S, Venderbosch S, et al. Mucinous adenocarcinomas: poor prognosis in metastatic colorectal cancer. Eur J Cancer. 2012;48(4):501–9. doi: 10.1016/j.ejca.2011.12.004. [PubMed: 22226571]

10. Salae M, Moghimi-Delkordi B, Fatemi SR, Ghiasi S, Nemati-Malek F, Zali MR. Characteristics of colorectal mucinous adenocarcinoma in Iran. Asian Pac J Cancer Prev. 2010;11(5):1375–9. [PubMed: 2198295]

11. Frederick LG, David LP, Irvin DF, April GF, Charles MB, Daniel GH, et al. Colon and Rectum. In: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. American Joint Committee on Cancer. AJCC Cancer Staging Manual. 7th ed. New York: Springer; 2010. p. 143.

12. Jimi S, Hotokezaka M, Ikeda T, Uchiyama S, Hidaka H, Maehara N, et al. Clinicopathological features, postoperative survival and prognostic variables for cancer-related survival in patients with mucinous colorectal carcinoma. Surg Today. 2015;45(3):329–34. doi: 10.1007/s10595-014-0943-z. [PubMed: 24989628]

13. Park JS, Huh JW, Park YA, Che YB, Yun SH, Kim HC, et al. Prognostic comparison between mucinous and nonmucinous adenocarcinoma in colorectal cancer. Medicine (Baltimore). 2015;94(15):e658. doi: 10.1097/MD.0000000000000658. [PubMed: 25881840]

14. Maeda Y, Sadahiro S, Suzuki T, Haruki Y, Nakamura N. Significance of mucinous component in the histopathological classification of colon cancer. Surg Today. 2015. doi: 10.1007/s10595-015-9550-2.

15. Numata M, Shiozawa M, Watanabe T, Tamagawa H, Yamamoto N, Morigasa S, et al. The clinicopathological features of colorectal mucinous adenocarcinoma and a therapeutic strategy for the disease. World J Surg Oncol. 2012;10:109. doi: 10.1186/1477-7819-10-109. [PubMed: 22705376]

16. Wu W, Mah JT, Lee J, Sankila R, Sankaranarayanan R, Chia KS. Incidence and survival of mucinous adenocarcinoma of the colon-rectum: a population-based study from an Asian country. Dis Colon Rectum. 2004;47(1):78–85. doi: 10.1007/s10350-003-0014-9. [PubMed: 1479155]