Observational Study

Medicine®

OPEN

Acute complicated diverticulitis is associated with an increased advanced neoplasia diagnosis rate

A retrospective study on 1852 patients

Fadi Abu Baker, MD[a,*], Mohanad Ganayem, MD[b], Amir Mari, MD[c], Randa Taher, MD[b], Mohamad Suki, MD[a], Yael Kopelman, MD[a]

Abstract

Recent reports have documented an unchanged rate of occurrence of colorectal cancer (CRC) and have publicised doubts regarding the benefit of prompt colonoscopy procedures after an episode of acute diverticulitis (AD). These reports mandate further evaluation of colonoscopy yield and timing in this regard. The current study aims to determine whether the rate of advanced colonic neoplasia after AD differs from that of average-risk patients, and to identify risk factors that are associated with their development.

In this retrospective study, we included all patients who had been hospitalized to the surgery ward in the years 2008 to 2016 with radiographically confirmed AD, and had completed colonoscopies within one year of index hospitalization. Patients who were referred for screening colonoscopies during the same years were included as a control group. We compared the rates of diagnosis of CRC and advanced polyps for both groups before and after adjustment for multiple confounders. Moreover, we investigated risk factors that were associated with increased rate of advanced neoplasia diagnosis.

A total of 350 patients were included in the AD group and 1502 patients in the screening colonoscopy control group. The CRC diagnosis rates (1.7% vs 0.3%; $P = .09$) and overall diagnosis rates of advanced neoplasia (12.3% vs 9.6%; $P = .19$) were not significantly different when findings were compared between the AD and control groups, respectively. Cases of complicated diverticulitis, however, were associated with increased risk of advanced neoplasia diagnosis (odds ratio (OR) 3.729, 95% confidence interval (CI) 1.803–7.713; $P = .01$).

The diagnosis rate for advanced neoplasia after AD was not significantly different from that of average-risk populations. A course of complicated AD, however, was a potential risk factor.

Abbreviations: AD = acute diverticulitis, CRC = colorectal cancer.

Keywords: acute diverticulitis, advanced colonic neoplasia, advanced polyp, colorectal cancer, screening colonoscopy

1. Introduction

Diverticular disease of the colon is a common disease that makes a significant contribution to health costs in western and industrialized societies.[1,2] Diverticulitis is the most common complication of diverticulosis and is estimated to develop in approximately 4 to 15 per cent of those who are diagnosed with diverticulosis.[3–6] The incidence of diverticulosis increases with age, as is the case with CRC. Additionally, deficiency of dietary fibre has been suggested to be a factor in the pathogenesis of both disorders. These findings suggest that the risk of development of CRC may be increased among patients who have diverticulitis.[7]

Computed tomography (CT) scans are commonly used to confirm diagnoses of AD and they play a valuable role in the assessment of the disease's severity and the identification of complications.[8]

Despite its high sensitivity and specificity, the reliability of the use of CT to exclude colonic malignancy remains an area of concern, as colonic cancer can mimic the clinical presentation and radiographic features of diverticulitis. For this reason, multiple medical societies have published recommendations regarding the performance of routine colonoscopy to exclude CRC 4 to 6 weeks after an episode of AD.[5–11]

These recommendations, however, are based on expert opinion and limited data,[12–15] and have been challenged lately as recent evidence has suggested that CRC or an alternative diagnosis is much less prevalent than was previously thought.[16–19] Recent

Editor: Simona Gurzu.

The authors received no financial support for the research, authorship, and/or publication of this article.

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

[a] *Department of Gastroenterology and Hepatology, Hillel Yaffe Medical Center, Hadera, Israel, Affiliated to the Technion Faculty of Medicine, Haifa, Israel,* [b] *Department of internal medicine, Hillel Yaffe Medical Center, Hadera, Israel, Affiliated to the Technion Faculty of Medicine, Haifa, Israel,* [c] *Department of Gastroenterology, Nazareth EMMS Hospital, Affiliated with the Faculty of Medicine, Bar Illan University.*

[*] *Correspondence: Fadi Abu Baker, Gastroenterology and Hepatology Institute, Hillel Yaffe MC. Ha-Shalom St, Hadera 38100, Israel (e-mail: fa_fd@hotmail.com).*

How to cite this article: Baker FA, Ganayem M, Mari A, Taher R, Suki M, Kopelman Y. Acute complicated diverticulitis is associated with an increased advanced neoplasia diagnosis rate: a retrospective study on 1852 patients. Medicine 2021;100:5(e24271).

Received: 2 September 2020 / Received in final form: 13 November 2020 / Accepted: 11 December 2020

http://dx.doi.org/10.1097/MD.0000000000024271

studies in this regard have concluded that performance of colonoscopy is unnecessary to exclude malignancy but may be indicated for higher-risk patients who have complicated diverticulitis and CT features or clinical suspicion concerning CRC.[20–27]

Altogether, these data bring into question the clinical utility and cost-effectiveness of the current common practice. More evidence is needed to validate or disprove these widely followed recommendations, and there is a need to improve risk stratification in colonic surveillance after AD and the timing of the performance of colonoscopy after AD, especially in light of the fact that colonoscopy is invasive, burdensome, time-consuming and involves risk.

In our practice these recommendations are followed; patients who have experienced AD are referred routinely for colonoscopy, which occurs within 1 or 2 months after discharge. The current study gathered data regarding the detection rates of CRC and advanced adenoma (AA) at the first-time colonoscopy that had been performed after discharge from a hospital stay that had been due to a CT-proven episode of AD. The aim of the study was to compare these rates with the detection rates that had been found in a control group, which comprised individuals of average risk who had undergone colonoscopy for CRC screening. The second aim was to identify risk factors that were associated with higher incidence of CRC/AA in AD patients.

2. Methods

In this retrospective, single-centre study, we reviewed the electronic reports of consecutive patients who had been admitted with a diagnosis of AD between the years 2008 and 2016 to the surgery ward at Hillel Yaffe Medical Center, which is a university-affiliated hospital in Israel. Patients were included in the study if they had been diagnosed with AD (either uncomplicated or complicated) on clinical grounds, provided that the diagnosis had been confirmed by a CT scan. Patients demographics and disease courses, including hospitalization duration and complications, were documented. Only patients who had undergone follow-up, first-time colonoscopy within 1 year of the index hospitalization were included in the final analysis. Patients were excluded if they were younger than 18 years old; had a prior diagnosis of colon cancer, advanced polyp or inflammatory bowel disease; or if the data set was not complete. For the control group, consecutive patients of average risk who had undergone a screening colonoscopy for CRC during the same years, were included. The primary endpoint was the rate of histologically confirmed CRC, AA and advanced neoplasia (CRC or AA) that was found in both groups before and after adjustment for possible confounders including age, sex and bowel preparation quality. AA was defined as the presence of adenomatos polyps that were larger than 1 cm, more than 25% villous histology, or the presence of high-grade dysplasia. Subgroup analysis was performed to compare the odds of diagnosis of CRC or AA between patients with complicated and uncomplicated diverticulitis and to identify risk factors that were linked with increased diagnosis rates. Complicated AD was defined as any AD case that presented with free perforation, abscesses, fistula formation or obstruction. The study was approved by Hillel Yaffes local Helsinki ethics board, which granted exemption from informed consent in this retrospective study as data collection did not influence medical practice, and patients were receiving standard care without relation to the study.

3. Statistical analysis

Before any statistical processing or analysis was performed, data were visually inspected and checked for outliers. Continuous variables were computed as arithmetic mean and standard deviation, whereas categorical variables were expressed as percentages. Differences between the study and control groups in the quantitative parameters were demonstrated by *t*-test. For categorical parameters, we used Fisher exact tests. A multivariate regression model was generated to assess the odds ratio (OR) of several independent parameters (age, gender, quality preparation, and whether the patient belonged to the control or study groups) on advanced neoplasia diagnosis. We credited a weight to each factor based on its coefficient estimates. $P < .05$ was considered as significant. Analyses were performed by use of the statistical analysis software (SAS Vs 9.4 Copyright (c) 2016 by SAS Institute Inc., Cary, NC, United States).

4. Results

The records and hospitalization reports of 410 patients who had been hospitalized with AD were revised. Sixty patients were excluded as they did not have follow-up colonoscopy reports or they met exclusion criteria. Thus, the data of 350 patients were considered suitable for study and were included in the AD group. Of these patients, 57 (16%) had a complicated disease course that was defined by presence of abscess, perforation, fistula or the need for urgent surgery. The control group comprised 1502 patients who had undergone first-time screening colonoscopies during the same years. Figure 1 outlines the study algorithm and patient recruitment data for both groups. Despite the distinct distribution by age sub-groups, the average age did not differ significantly between the AD and control groups (59.8 ± 13.3 years vs 60.1 ± 6.8 years; $P < .01$, respectively). The study group contained a higher proportion of female patients than did the control group (208 (59%) vs 614 (41%); $P < .01$). In the AD group, follow-up colonoscopies after hospitalization had been performed within 5.4 ± 4.8 weeks (range 1–52 weeks).

Baseline characteristics and endoscopic findings of both groups are shown in Table 1. Diverticulosis to the sigmoid and left colon had been located in more than 90% of patients. This was in good concordance with the location that was described in the CT examinations. During review of colonoscopy reports in both groups, it was found that more patients in the AD group had adequate bowel preparation than in the control group (295 (84%) vs 1109 (74%); $P < .01$).

The CRC diagnosis rates (1.7% vs 0.3%; $P = .09$), AA detection rates (10.6% vs 9.3%; $P = .48$) and overall diagnosis rates of advanced neoplasia (12% vs 9.6%; $P = .19$) were not significantly different between the AD and control groups, respectively (Table 1). This was also evident in multivariate analysis that accounted for age, sex and bowel preparation, as the AD group was not associated with increased overall diagnosis of neoplasia (OR 1.386, 95% CI 0.912–2.1; $P = .126$). In the AD group, the majority of advanced neoplasia (88%) was located distal to the splenic flexure; 49% were identified in the sigmoid or descending colon while 39% were detected within the rectum.

Univariate and multivariate analysis of the data for the AD group to identify risk factors that were associated with an increased advanced neoplasia rate revealed that advanced age (71< vs <50) years (OR 3.156, 95% CI 1.428–6.973) and

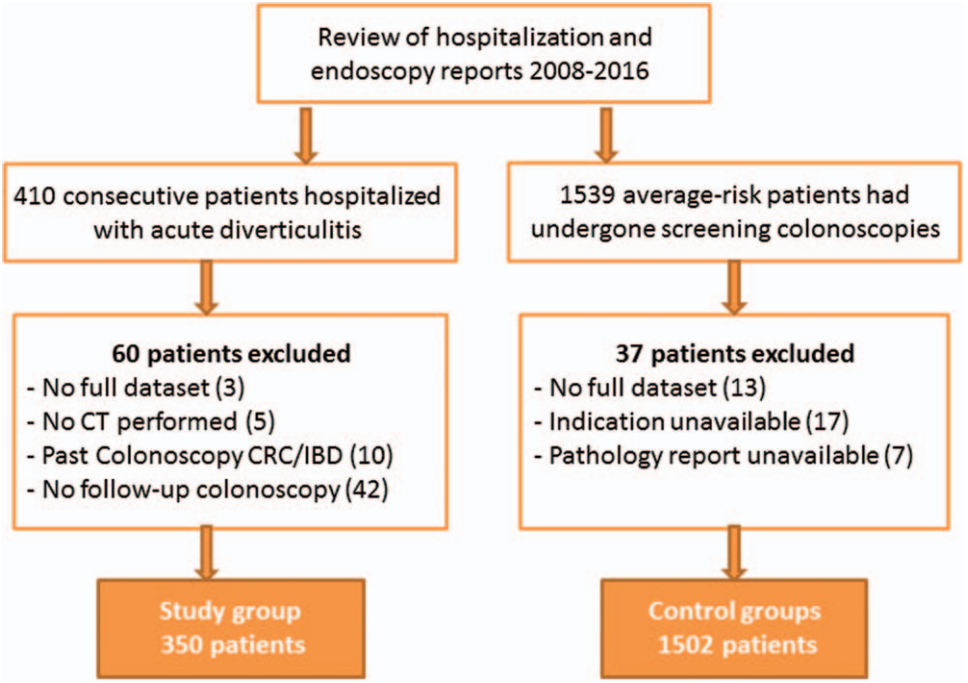

Figure 1. Study algorithm and groups.

Table 1

Baseline characteristics and colonoscopy outcomes.

	Study; n = 350	Control; n = 1502	*P* value
Baseline characteristics			
Age (years)	59.8 ± 13.3	60.1 ± 6.8	*P* = .48
<50	78 (22%)	71 (5%)	
51-70	201 (57%)	1308 (87%)	
>71+	71 (20%)	121 (8%)	
Gender (Male)	142 (41%)	887 (59%)	*P* < .001
Colonoscopy after AD (weeks)	5.4 ± 4.8	N/A	N/A
Colonoscopy outcomes			
Quality of preparation (Adequate)	295 (84%)	1109 (74%)	*P* < .01
Colorectal cancer	6 (1.7%)	5 (0.3%)	*P* = .09
Advanced polyp	36 (10.6%)	139 (9.3%)	*P* = .48
Advanced neoplasia	42 (12%)	144 (9.6%)	*P* = .19

complicated AD presentation (OR 3.729, 95% CI 1.803–7.713; *P* = .01) were associated with increased risk of diagnosis of advanced neoplasia (Table 2).

5. Discussion

The process of changing a widely accepted common practice is long and multi-stepped. The performance of early colonoscopy after any episode of AD is 1 example. Although based on small cohort studies and expert opinions, this practice was supported by several previous guidelines and was implemented widely.[5,9,11] However, the advent of high-resolution CT scanning with improved diagnostic accuracy, along with accumulating reports over recent years that demonstrate overall low risk of malignancy in this setting, has challenged this notion. Now, this situation is overlaid with recent studies that have confirmed that diverticulosis does not confer increased risk of CRC. Taken together, these findings lead to the inference that, in the constellation of diverticular disease, routine and prompt referral for endoscopic evaluation may not be necessary for all patients. Accordingly, the latest American Gastroenterology Association guidelines on the management of AD[28] still advocate the performance of colonoscopy after resolution of AD, but they state that this should be done in appropriate candidates, and conclude that investigation of the yield and timing of colonoscopy after an episode of AD should be a priority for

Table 2

Risk factors for advanced neoplasia diagnosis. A multivariate analysis.

Variable	*P* value	Odds Ratio	95% Confidence interval	
			Upper	Lower
Age (51–70 vs <50 years)	*P* = .106	1.822	0.881	3.771
Age (71< vs 50 years)	*P* < .01	3.156	1.428	6.973
Sex (male)	*P* = .404	1.349	0.667	2.727
Bowel preparation quality (Inadequate)	*P* = .044	0.395	0.160	0.976
Complicated Diverticulitis	*P* < .01	3.729	1.803	7.713

future research. Some innovative recommendations advise that, in patients who have AD that is treated conservatively, early follow-up colonoscopy is not required.[29]

Studies that are performed in different populations may have additional value and referral of AD patients for early routine colonoscopy is widely followed in our practice. Therefore, we designed this study. Our study was unique as it included an average-risk population as a control group and patients with complicated AD as the study group, and we calculated the risk of AA diagnosis in addition to the CRC diagnosis rate with adjustment for possible confounders.

The findings in the current study were similar to those that have been shown in recent studies. We demonstrated that the diagnosis rate of advanced neoplasia in a group of patients who had experienced AD was insignificantly different from that in average-risk populations ((12% vs 9.6%; $P = .19$). A similar retrospective study by Westwood et al,[23] which involved 292 patients, demonstrated that the yield of advanced colonic neoplasia was equivalent to that detected through the screening of average-risk individuals. However, the Westwood study, like a few others, included only uncomplicated AD patients, which may have resulted in a selection bias.

Despite the insignificant difference in our study in terms of CRC diagnosis rate (1.7% vs 0.3%; $P = .09$) between the groups, in numerical terms our findings are similar to those of a recent meta-analysis of 17 observational studies of colonoscopy after AD. This meta-analysis demonstrated that CRC was detected overall in 2.1% of all patients.[30] Taken together, and given that the reported prevalence of CRC in the general population that is detected by screening colonoscopy is between 0.4% and 1.0%, a general recommendation of abstinence from colonoscopy performance in this population seems unreasonable. Rather, a selective approach and matched procedure timing may be of benefit and should be deeply investigated.

It is of note that no synchronous CRCs or other malignancies were reported. This is important, since the presence of CRCs might be associated with other synchronous cancers, such as urological or gynaecological tumors.[31,32] Unfortunately, data on familial gastrointestinal polyposis syndromes were unavailable, as little is known about their occurrence and characteristics in the Israeli population. Although rare, these syndromes are associated with increased prevalence of CRCs and other non-gastrointestinal tumors.[33]

Given the busy schedule of endoscopic departments, it is of paramount importance to enable the allocation of priority to truly high-risk patients, such as those with rectal bleeding or positive faecal occult blood test. Thus, the timing of colonoscopy after AD should be matched to risk and availability of resources. Through the current study, we have demonstrated that complicated AD presentation is associated with increased risk of diagnosis of advanced neoplasia (OR 3.729, 95% CI 1.803–7.713; $P = .01$). Findings that support ours were shown in a recent study by Andrade and colleagues,[34] who reported an increased rate of advanced colonic neoplasia in complicated AD. Factors that were not addressed in our study, such as family history of CRC and conjoining alarm symptoms, may also justify the performance of early endoscopic follow-up. However, further large-scale studies are warranted to identify risk factors and to stratify AD patients accordingly. Risk-related diverticulosis-to-colonoscopy intervals should be determined as well.

Our study was limited as it was of a single-centre and retrospective design. Moreover, the small number of CRC cases may have reduced the power of the study to identify clinically significant differences and decreased our ability to investigate associated risk factors. Several other confounders may have impacted on the CRC and advanced neoplasia diagnosis rates, such as family history of CRC and the occurrence of familial gastrointestinal polyposis syndromes, as discussed earlier. These were not included, as the collection of data regarding family history was incomplete and unreliable.

In conclusion, we demonstrated in our clinic population that the diagnosis rate of advanced neoplasia after AD was insignificantly different from that of an average-risk population. Occurrence of complicated AD, however, may confer a prominently increased risk for its diagnosis and may justify early follow-up colonoscopy. Large-scale prospective studies to define further the impact of such a risk-matched approach are warranted.

Acknowledgment

We would like to express special thanks to Mrs. Ronit Leiba for the statistical consultation and review.

Author contributions

Conceptualization: Fadi Abu Baker, Amir Mari.
Data curation: Fadi Abu Baker, Mohanad Ganayem, Randa Taher, Mohamad Suki.
Formal analysis: Mohanad Ganayem, Randa Taher, Mohamad Suki.
Investigation: Fadi Abu Baker, Amir Mari.
Methodology: Fadi Abu Baker, Amir Mari, Mohamad Suki, Yael Kopelman.
Supervision: Fadi Abu Baker, Amir Mari, Yael Kopelman.
Validation: Amir Mari, Yael Kopelman.
Visualization: Amir Mari, Yael Kopelman.
Writing – original draft: Mohanad Ganayem, Randa Taher, Mohamad Suki.
Writing – review & editing: Fadi Abu Baker, Yael Kopelman.

References

[1] Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. Gastroenterology 2009;136:741–54.
[2] Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. Am J Gastroenterol 2006;101:2128–38.
[3] Parks TG. Natural history of diverticular disease of the colon. Clin Gastroenterol 1975;4:53–69.
[4] Strate LL, Modi R, Cohen E, et al. Diverticular disease as a chronic illness: evolving epidemiologic and clinical insights. Am J Gastroenterol 2012;107:1486–93.
[5] Stollman NH, Raskin JB. Diagnosis and management of diverticular disease of the colon in adults. Ad Hoc Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol 1999;94:3110–21.
[6] Shahedi K, Fuller G, Bolus R, et al. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. Clin Gastroenterol Hepatol 2013;11:1609–13.
[7] Stollman N, Raskin JB. Diverticular disease of the colon. Lancet 2004;363:631–9.
[8] Andeweg CS, Mulder IM, Felt-Bersma RJ, et al. Netherlands society of surgery; working group from netherlands societies of internal medicine, gastroenterologists, radiology, health echnology assessment and dieticians. Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis. Dig Surg 2013;30:278–92.

[9] Jacobs DO. Clinical practice. Diverticulitis. N Engl J Med 2007;357: 2057–66.
[10] Lau KC, Spilsbury K, Farooque Y, et al. Is colonoscopy still mandatory after a CT diagnosis of left-sided diverticulitis: can colorectal cancer be confidently excluded? Dis Colon Rectum 2011;54:1265–70.
[11] Rafferty J, Shellito P, Hyman NH, et al. Practice parameters for sigmoid diverticulitis. Dis Colon Rectum 2006;49:939–44.
[12] Köhler L, Sauerland S, Neugebauer E. Diagnosis and treatment of diverticular disease: results of a consensus development conference. The Scientific Committee of the European Association for Endoscopic Surgery. Surg Endosc 1999;13:430–6.
[13] Balthazar EJ, Megibow A, Schinella RA, et al. Limitations in the CT diagnosis of acute diverticulitis: comparison of CT, contrast enema, and pathologic findings in 16 patients. AJR Am J Roentgenol 1990;154: 281–5.
[14] De Masi E, Bertolotti A, Fegiz GF. The importance of endoscopy in the diagnosis of neoplasms associated with diverticular disease of the colon, and its effect on surgical treatment. Ital J Surg Sci 1984;14:195–9.
[15] Salzman H, Lillie D. Diverticular disease: diagnosis and treatment. Am Fam Physician 2005;72:1229–34.
[16] Agarwal AK, Karanjawala BE, Maykel JA, et al. Routine colonic endoscopic evaluation following resolution of acute diverticulitis: is it necessary? World J Gastroenterol 2014;20:12509–16.
[17] Brar MS, Roxin G, Yaffe PB, et al. Colonoscopy following nonoperative management of uncomplicated diverticulitis may not be warranted. Dis Colon Rectum 2013;56:1259–64.
[18] Choi YH, Koh SJ, Kim JW, et al. Do we need colonoscopy following acute diverticulitis detected on computed tomography to exclude colorectal malignancy? Dig Dis Sci 2014;59:2236–42.
[19] Daniels L, Unlu C, de Wijkerslooth TR, et al. Yield of colonoscopy after recent CT-proven uncomplicated acute diverticulitis: a comparative cohort study. Surg Endosc 2015;29:2605–13.
[20] de Vries HS, Boerma D, Timmer R, et al. Routine colonoscopy is not required in uncomplicated diverticulitis: a systematic review. Surg Endosc 2014;28:2039–47.
[21] Elmi A, Hedgire SS, Pargaonkar V, et al. Is early colonoscopy beneficial in patients with CT-diagnosed diverticulitis? AJR Am J Roentgenol 2013;200:1269–74.
[22] Kim MJ, Woo YS, Kim ER, et al. Is colonoscopy necessary after computed tomography diagnosis of acute diverticulitis? Intest Res 2014;12:221–8.
[23] Schmilovitz-Weiss H, Yalunin E, Boaz M, et al. Does colonoscopy after acute diverticulitis affect its management? A single center experience. J Clin Gastroenterol 2012;46:317–20.
[24] Westwood DA, Eglinton TW, Frizelle FA. Routine colonoscopy following acute uncomplicated diverticulitis. Br J Surg 2011;98:1630–4.
[25] Granlund J, Svensson T, Granath F, et al. Diverticular disease and the risk of colon cancer – a population-based case-control study. Aliment Pharmacol Ther 2011;34:675–81.
[26] Sai VF, Velayos F, Neuhaus J, et al. Colonoscopy after CT diagnosis of diverticulitis to exclude colon cancer: a systematic literature review. Radiology 2012;263:383–90.
[27] Sharma PV, Eglinton T, Hider P, et al. Systematic review and meta analysis of the role of routine colonic evaluation after radiologically confirmed acute diverticulitis. Ann Surg 2014;259:263–72.
[28] Stollman N, Smalley W, Hirano I. AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Management of Acute Diverticulitis. Gastroenterology 2015;149:1944–9.
[29] Sartelli M, Catena F, Ansaloni L, et al. WSES Guidelines for the management of acute left sided colonic diverticulitis in the emergency setting. World J Emerg Surg 2016;11:37.
[30] Rottier SJ, van Dijk ST, van Geloven AAW, et al. Meta-analysis of the role of colonoscopy after an episode of left-sided acute diverticulitis. Br J Surg 2019;106:988.
[31] Tey YQ, Ravi K, Chong CS, et al. Management of locally advanced synchronous colorectal and prostate cancers: a case report. Medicine (Baltimore) 2020;99:e20336.
[32] Căpîlna ME, Rusu SC, Laczko C, et al. Three synchronous primary pelvic cancers–a case report. Eur J Gynaecol Oncol 2015;36:216–8. PMID: 26050365.
[33] Jung I, Gurzu S, Turdean GS. Current status of familial gastrointestinal polyposis syndromes. World J Gastrointest Oncol 2015;7:347–55.
[34] Andrade P, Ribeiro A, Ramalho R, et al. Routine colonoscopy after acute uncomplicated diverticulitis - challenging a putative indication. Dig Surg 2017;34:197–202.