Original paper

# The relationship between diverticula and low-grade mucinous neoplasm of the appendix. Does the diverticulum play a role in the development of periappendicular mucin deposition or pseudomyxoma peritonei?

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Prevalences of diverticulum and low-grade mucinous neoplasm (LGMN) were reported as 0.04-2% and less than 1% in the appendix. In this study, the frequency of diverticulum in LGMN cases, the relationship between diverticula and periappendicular mucin, and the possible role of diverticula in pseudomyxoma peritonei pathogenesis were researched.

Through systematic review and targeted search, 38 LGMN and 96 diverticula were identified, frequencies and relationship between diverticulum and LGMN were analysed.

Diverticulum and LGMN were determined in 4.8% and 1.04%, respectively, of 1922 appendectomy materials specifically grossed by the same pathologist. The prevalence of diverticulum was higher in our study than literature. The difference may be due to detailed macroscopic examination. Diverticulum was detected in 60% of LGMN cases. The rate of diverticulum was found to be significantly higher in LGMNs than non-neoplastic diverticulum ($p < 0.001$). Periappendicular mucin deposition was significantly more frequent in LGMN cases with diverticulum than in other groups ($p < 0.05$). Follow-ups were available in 18 patients; none of them had mucin deposition in the peritoneal cavity.

We detected that periappendicular mucin was highly associated with diverticula in LGMN cases. Periappendicular acellular mucin deposition may not give rise to pseudomyxoma peritonei. We may think that mucin could move out of the appendix through the diverticulum rather than neoplastic spread in some of these cases.

**Key words:** low-grade mucinous neoplasm, appendix, diverticulum.

## Introduction

Mucinous tumours constitute one third of all epithelial tumours of the appendix. However, they are encountered in only 0.3% of appendectomy materials [1]. Because even adenoma-like, well-differentiated, and questionable-invasive tumours in the appendix wall may cause pseudomyxoma peritonei, terminolo-

gy and classification of the mucinous tumours of the appendix is a much-discussed issue. Some authors believe that such tumours represent a ruptured adenoma and dissemination of adenomatous epithelium to the peritoneal cavity, based on their morphological features [2, 3]. Others consider peritoneal dissemination to be evidence of malignancy and accept low-grade mucinous tumours that disseminate as well-differentiated adenocarcinoma [4, 5]. Mucinous tumours of the appendix are grouped into three categories: "adenoma," "low-grade mucinous neoplasm", and "mucinous adenocarcinoma" in the WHO 2010 classification. Tumours limited in mucosa are termed as "adenoma," tumours with pushing invasion in appendiceal wall as "low-grade mucinous neoplasm," and tumours with infiltrative invasion as "mucinous adenocarcinoma" [6]. Diverticulum of the appendix is very rare, with incidence of 0.004-2% [7, 8, 9]. The real incidence could be higher because it might be overlooked in macroscopic examination. Most of the appendiceal diverticula are acquired, and true congenital diverticula are very rare, with an overall incidence of 0.014% [9, 10, 11]. As a consequence of increased intraluminal pressure, acquired diverticula develop through weak points of the muscularis propria, where arteries penetrate, in the form of mucosal herniation. Congenital diverticula also contain muscularis propria in the diverticular wall. Risk of perforation is higher in acquired diverticula than appendicitis due to the absence of muscularis propria [9, 10]. Ruptured diverticulum may cause mucin accumulation on the serosal surface of the appendix mimicking mucinous neoplasms [12, 13]. In spite of having bland cytological features and lack of frank invasion in the appendiceal wall, it is not clear how low-grade mucinous neoplasms (LGMNs) of the appendix could cause pseudomyxoma peritonei. In this study we aimed to determine the frequency of the diverticulum in LGMN cases diagnosed in our clinic, to research the relationship between the diverticulum and mucin pools on serosa and mesoappendix, and to discuss the possible role of the diverticulum in pseudomyxoma peritonei pathogenesis.

## Material and methods

### Case selection

A targeted search for the term "mucinous cystadenoma, mucocele, low-grade mucinous neoplasm" was performed in the author's institutional database and reviewed by two pathologists. From the cases diagnosed before 2011, 18 had adequate macroscopic sampling and met the criteria of LGMN, and were included in the study. 1922 consecutive appendectomy specimens, obtained regardless of the cause, were specifically grossed with emphasis on searching for LGMN and/or diverticula, to determine their frequency, in 2011-2015.

### Classification

The cases were categorised into three groups: LGMN with diverticulum, LGMN without diverticulum, and non-neoplastic diverticulum. The cases were classified according to the following descriptions:

**Diverticulum:** The herniation of appendiceal mucosa through weak points of muscularis propria where arteries penetrate [9] (Fig. 1).

**Low-grade mucinous neoplasm:** Tumours with expansile invasion of the appendiceal wall and lined by neoplastic mucinous epithelium with low to moderate grade cytological atypia [6, 14, 15]. Surface epithelium is usually villous, and sometimes flat or wavy from compression of mucin (Fig. 2). Neoplastic epithelium on fibrotic and hyalinised stroma, rather

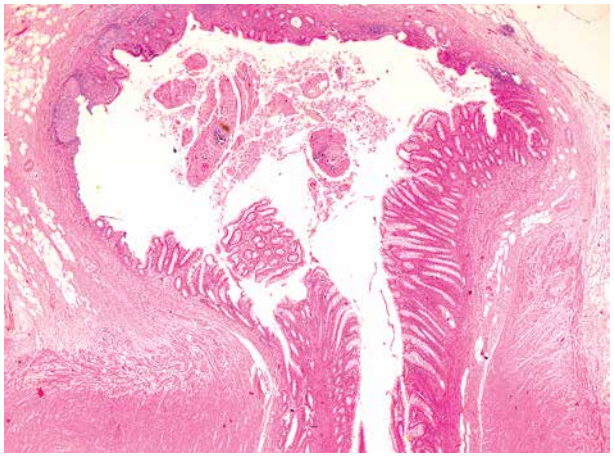

**Fig. 1.** Herniation of appendiceal mucosa through muscularis propria in an intact diverticulum (HE, original magnification 40×)

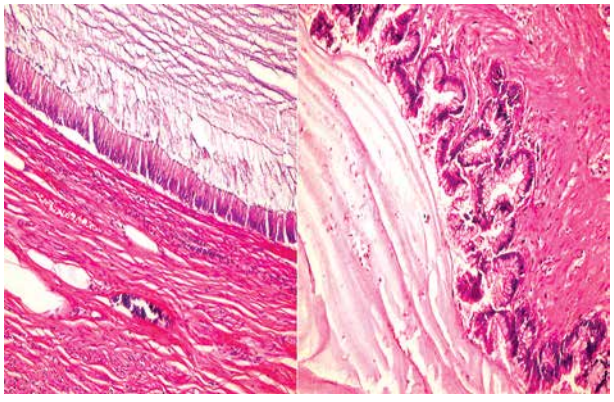

**Fig. 2.** The lining epithelium composed of pseudostratified columnar cells with elongated, hyperchromatic nuclei in low-grade mucinous neoplasm may be flat or undulating due to compression of mucin accumulation (HE, original magnification 200×)

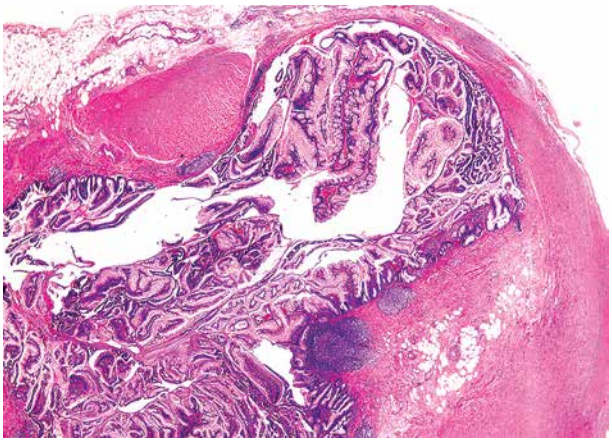

**Fig. 3.** Low-grade mucinous neoplasm involving diverticulum that penetrates between muscle bundles (HE, original magnification 40×)

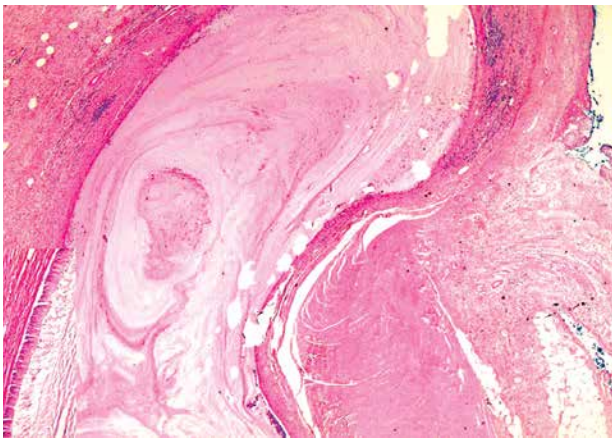

**Fig. 4.** Herniation of intraluminal mucin to mesoappendix through muscularis propria in low-grade mucinous neoplasm. Flattened neoplastic epithelium due to mucin compression in the diverticulum area (HE, original magnification 20×)

than lamina propria and muscularis propria, is an indicator of pushing invasion [14, 15].

**Low-grade mucinous neoplasm with diverticulum:** LGMN with herniated neoplastic epithelium through weak points of muscularis propria where arteries penetrate (Figs. 3, 4).

The three groups were compared in terms of age, sex, size, localisation of the diverticulum, presence of mucin pools on serosa, and/or mesoappendix and calcification.

### Statistical analysis

Mean, standard deviation, minimum and maximum, median, ratio, and frequency values were used for descriptive statistics of data. The Kolmogorov-Smirnov test was used to control distribution of variables. The Tukey test was used to analyse quantitative data, and the ANOVA test was used in sub-analysis. The $\chi^2$ test was used to analyse qualitative data and the Fischer test was used when $\chi^2$ conditions were not met. SPSS 22.0 was used to perform the analyses.

## Results

### Demographics

*Appendiceal low-grade mucinous neoplasm*

Thirty-eight patients were included in the study. Twenty cases were from the specifically sampled group and 18 cases were from the targeted database. Low-grade mucinous neoplasm was observed as 49% in female gender and 51% in male gender. The average age was 51 years. In the cohort that was specifically grossed and investigated for LGMN, the frequency was 1.04% (20/1922).

The number of section (sampling) was 5-22 (average 10), the number of blocks was 3-20 (average eight) in DDMN cases. The appendix was totally sampled in 52% of the cases.

*Appendiceal diverticula*

A total of 96 consecutive diverticulum cases were included in the study. Appendiceal diverticula was seen in 63% of male gender. The average age was 38 years. In the cohort the prevalence was 4.8% (96/1922). The prevalence of diverticulum in 1902 appendectomy materials without LGMN was 5.04% (96/1902). The number of sections was 4-8 (average 5), and the number blocks was 2-4 (average 3) in non-neoplastic diverticulum.

### Comparison of appendiceal low-grade mucinous neoplasm and appendiceal diverticula

In 23 of 38 LGMN cases, diverticulum was detected in the mucinous neoplasm area (60.5%) (Figs. 3, 4, 5, 6). Twelve of 20 LGMN cases (60%), which were specifically sampled cases between 2011 and 2015, were accompanied by diverticulum. Ninety-six diverticula were determined in 1902 cases without LGMN, and the prevalence was 5.04%. There was statistically highly significant difference in terms of presence of diverticulum between LGMN cases and normal appendectomy materials ($p < 0.001$). Table I shows the comparison of two percentage values.

Three appendiceal adenocarcinomas were reported while we were conducting the study. Two of them were mucinous adenocarcinomas and one of them was conventional adenocarcinoma in the setting of Crohn's disease. The entire appendix was infiltrated by tumour in one of the mucinous adenocarcinomas, and diverticulum could not be distinguished. The

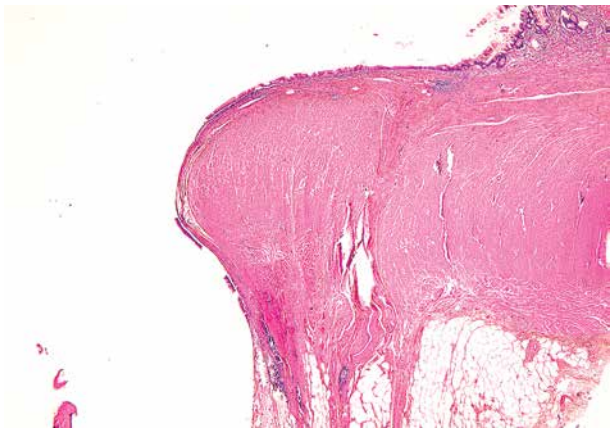

**Fig. 5.** Flattened neoplastic epithelium in low-grade mucinous neoplasm involving the diverticulum area (HE, original magnification 40×)

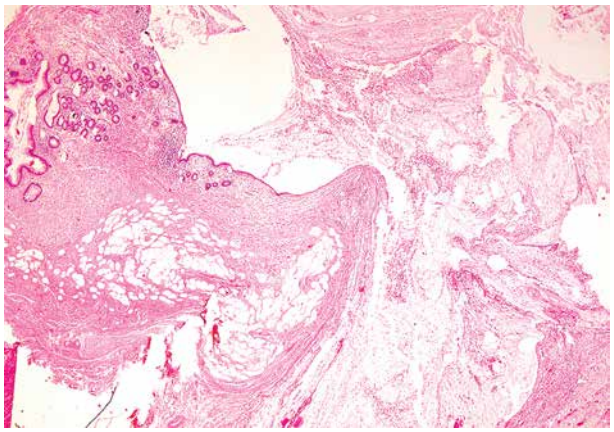

**Fig. 6.** Periappendicular acellular mucin deposition resulting from ruptured diverticulum (HE, original magnification 40×)

**Table I**. Comparison of LGMN and Normal appendectomy in terms of the presence of diverticulum

| Diverticulum | LGMN | | Normal appendectomy | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Present | 12 | 60 | 96 | 5.04 | 0.000 |
| Absent | 8 | 40 | 1806 | 94.96 | |

other mucinous adenocarcinoma, which was a consultation case, did not include diverticula. However, the macroscopic examination was not done by us, so we could not speculate about the presence of diverticula. Diverticulum was not detected in the conventional adenocarcinoma case with Crohn's disease.

The mean age of patients with diverticula was 38.3 ±13.6 years, with LGMN it was 50.8 ± 15.7 years, and with LGMN + diverticulum it was 49.8 ± 19.4 years. In terms of age, there was a statistically significant difference between patients with diverticula and the other two groups, with the diverticula group being younger than the other groups ($p = 0.003$). There was no statistically significant difference in terms of patient age between the LGMN and LGMN + diverticulum groups ($p = 0.977$). No statistically significant difference was found between the three groups in terms of sex distribution ($p = 0.233$).

Macroscopically, the appendix diameter was statistically significantly larger in LGMN and LGMN + diverticulum cases than in non-neoplastic diverticulum cases ($p < 0.001$). The diameter was also statistically significantly larger in the LGMN group than the LGMN + diverticulum group ($p = 0.03$). There was no statistically significant difference in terms of the length of appendix ($p = 0.101$). Table II shows a comparison between the three groups in terms of size, age, sex, localisation, periappendicular mucin deposition, and calcification.

While the diverticulum was located on distal end in all non-neoplastic diverticulum cases, it was located on distal end in 73.9% (n = 17) and on the middle part in 26.1% (n = 6) of LGMN + diverticulum cases. The difference was statistically significantly different ($p < 0.001$). Multiple diverticula were determined in 20.8% (n = 20) of non-neoplastic diverticulum cases, and in 17.4% (n = 4) of mucinous neoplasm with diverticulum cases. However, this difference was not statistically significant ($p > 0.05$).

The tumour was observed through the entire appendix in 53.3% of LGMN cases and 47.8% of LGMN with diverticulum cases. The tumour was located on the distal and middle part of the appendix in other cases. The difference was not statistically significant ($p = 0.740$).

Microscopically acellular mucin pools were detected on the serosal surface of the appendix and/or mesoappendix in 78.3% of the LGMN with diverticulum group, and 33.3% of the LGMN without diverticulum group (Fig. 5, 6, 7). Mucin deposits were detected adjacent to the diverticulum in 13.5% of non-neoplastic diverticula (Fig. 7). Mucin accumulation on serosa and/or mesoappendix was statistically significantly more frequent in LGMN with diverticulum group than other two groups ($p < 0.001$). No statistically significant difference was found between the LGMN and non-neoplastic diverticulum group in terms of mucin accumulation ($p = 0.353$).

Psammomatous calcification was determined in luminal mucin or appendiceal wall in 46.7% of LGMN cases, and 43.5% of LGMN with diverticulum cases (Fig. 8). However, there was no psam-

Table II. Comparison between the three groups

| Parameter | | Non-Neoplastic Diverticulum | | LGMN | | LGMN + Diverticulum | | p |
|---|---|---|---|---|---|---|---|---|
| Age | | 38.3 ±13.6 | | 50.8 ±15.7 | | 49.8 ±19.4 | | 0.003 |
| Size | length (mm) | 63.3 ±18.7 | | 79.3 ±28.2 | | 63.0 ±19.0 | | 0.101 |
| | width (mm) | 11.9 ±4.6 | | 23.6 ±18.8 | | 16.8 ±7.4 | | 0.000 |
| | | n | % | n | % | n | % | |
| Sex | woman | 33 | 34.4 | 7 | 46.7 | 12 | 52.2 | 0.233 |
| | man | 63 | 65.6 | 8 | 53.3 | 11 | 47.8 | |
| Localisation of diverticulum | distal | 96 | 100 | | | 17 | 73.9 | 0.000 |
| | middle | 0 | 0.0 | | | 6 | 26.1 | |
| Localisation of tumour | pan | | | 8 | 53.3 | 11 | 47.8 | 0.740 |
| | distal + middle | | | 7 | 46.7 | 12 | 52.2 | |
| Mucin pools on serosa and/or mesoappendix | present | 13 | 13.5 | 5 | 33.3 | 18 | 78.3 | 0.000 |
| | absent | 83 | 86.5 | 10 | 66.7 | 5 | 21.7 | |
| Psammomatous calcification | present | 0 | 0 | 7 | 46.7 | 10 | 43.5 | 0.000 |
| | absent | 96 | 100 | 8 | 53.3 | 13 | 56.5 | |
| Dystrophic calcification | present | 3 | 3.1 | 2 | 13.3 | 6 | 26.1 | 0.002 |
| | absent | 93 | 96.9 | 13 | 86.7 | 17 | 73.9 | |

momatous calcification in non-neoplastic diverticula. Dystrophic calcification was observed in 3.1% of non-neoplastic diverticulum, 13.3% of LGMN, and 26.1% of LGMN + diverticulum cases. Calcification was statistically significantly less in the diverticulum group than in the LGMN and LGMN + diverticulum groups ($p = 0.002$). There was no statistically significant difference between LGMN and LGMN + diverticulum groups in terms of presence of psammomatous and dystrophic calcification.

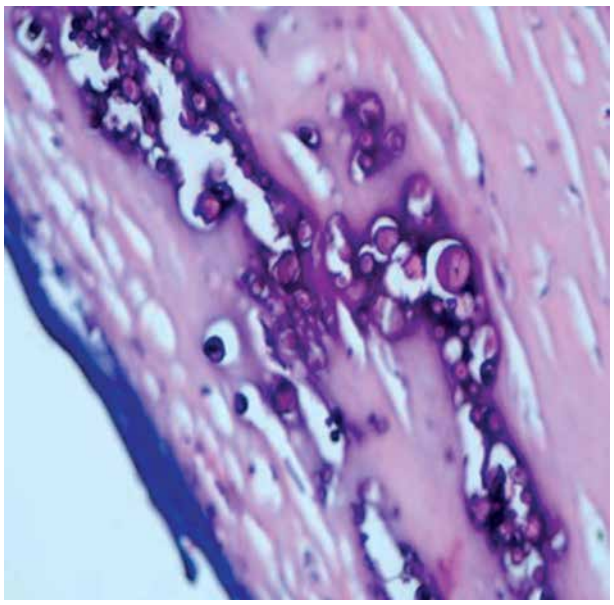

**Fig. 7.** Psammomatous calcification at the appendix wall in low-grade mucinous neoplasm (HE, original magnification 400×)

## Clinical outcome

Follow-up status could be obtained for 18 of total 38 LGMN patients. Follow-up time was between eight months and seven years. One patient died because of non-tumoural cardiac problems. Thirteen of the cases had mucin pools on serosa and/or mesoappendix. Eleven of 13 cases had diverticulum in the LGMN area. None of the patients had clinical complaints and all of them had normal physical examination findings. Every patient had been evaluated by detailed abdominal ultrasonography, some of them by computed tomography and magnetic resonance imaging. No fluid collection or mass formation was detected in periappendicular or intra-abdominal area.

## Discussion

The size of most appendiceal diverticula are less than 0.5 cm. Therefore, they can easily be overlooked during macroscopic examination [16]. Their prevalence is reported between 0.004% and 2% in the literature, and they are mostly seen in men [9]. In our study, the prevalence of diverticulum was found to be higher than rates reported in the literature (4.8%). The difference may be due to macroscopic samplings, which were done in more detail by only one pathologist in the meantime. 65% of non-neoplastic

diverticulum cases in our series were men, which is compatible with the literature. The large majority of diverticula were multiple and seen in 1/3 distal part of the appendix [9, 17]. All non-neoplastic diverticulum cases and 73.9% of mucinous neoplasms were located in the distal end of the appendix in our series. 20.8% of non-neoplastic diverticulum cases and 17.4% of mucinous neoplasms with diverticulum had multiple diverticula.

Acquired pseudo-diverticula, which constitute the majority of the appendiceal diverticula, develop through weak points of the muscularis propria, where arteries penetrate, in the form of mucosal herniation. Increased intraluminal pressure, which occurs as a result of fecalitis, proximally located tumours, and accumulated luminal mucus, plays a part in the formation of the diverticulum. Perforation of a pseudo-diverticulum is frequent because of the absence of a muscular layer [9, 18, 19]. Diverticula accompanying epithelial neoplasms were reported in the literature. In the series by Medlicott and Urbanski a primary appendiceal neoplasm was detected in 30% of acquired diverticulum cases, which were all non-mucinous neoplasms [18]. There are few studies regarding the association of diverticulum with LGMNs. Dupre *et al*. determined 23 diverticula in 1361 appendectomy materials, and 11 of these were accompanied by primary appendiceal neoplasms. Three of eight LGMN cases were accompanied by diverticulum in this study. They suggested that diverticula may give a clue about underlying neoplasms [16]. In the study by Lamps *et al*. diverticula were determined in 8 of 19 LGMNs (42%) [20]. We detected accompanying diverticula in 23 of 38 LGMN cases (60.5%). The difference may be due to our abounding number of cases and detailed macroscopic examination. Diverticula were lined by neoplastic epithelium in all cases. One of the reasons for this co-existence may be the increase of intraluminal pressure caused by mucin production that thinned the muscularis propria and made the mucinous epithelium prolapse through weak points where vessels penetrate. The other possible cause is LGMN development in pre-existing diverticulum. In our study, serosal and/or mesoappendiceal mucin pools were detected in 78.3% of cases with diverticula and in 33.3% of LGMNs without diverticulum, and this difference was statistically significant. Detecting mucin accumulation on mesoappendix in LGMN cases with diverticulum more frequently made us think that diverticula may play a part in the pathogenesis of periappendicular mucin deposition and pseudomyxoma peritonei. Rupture of a diverticulum may cause mucin leak into intraabdominal space. There are very few reports studying the relationship between rupture of the diverticula in LGMNs and pseudomyxoma peritonei. In the study of Lamps *et al.* acellular mucin accumulation was detected around inflamed, perforated diverticulum in the wall of the appendix in three out of eight LGMN cases. However, no accumulation of mucin was seen on serosal surface or mesoappendix [20]. Mucin accumulation was determined on appendix, gallbladder, omentum, and serosal surface of bowels with ruptured diverticulum during appendectomy in only one out of eight cases [20]. In our 13 cases, which had mucin accumulation on mesoappendix, and were followed-up between eight months and seven years, pseudomyxoma peritonei did not develop. Eleven of 13 cases were LGMN cases with diverticulum. In the study by Pai *et al*. with 116 cases of appendiceal mucinous neoplasm, mucinous neoplasms were categorized into four groups: LGMN limited to appendix, LGMN with acellular extra-appendiceal mucin, LGMN with extra-appendiceal neoplastic epithelium, and mucinous adenocarcinoma [21]. Mucin accumulation containing neoplastic epithelium on the bladder and the serosal surface of the descending colon was detected in only 1 out of 14 LGMN cases with acellular periappendicular mucin (7%), 45 months after diagnosis. However, the case was a consultation case. The entire appendix could not be evaluated and the surgical margin status was not known, so it was not possible to be sure that the periappendicular mucin was acellular. The other cases with periappendicular acellular mucin did not recur. Diverticulum was detected in 16% of cases in this group and in 14% of cases in the LGMN with extra-appendiceal neoplastic epithelium group. However, it was not stated if mucin accumulation was due to rupture of the diverticulum. Four of 27 cases with periappendicular neoplastic epithelium had mucin accumulation in the right lower quadrant, and 23 of them had in other abdominal regions at the time of the diagnosis. In three out of four cases with localised mucin accumulation, diffuse abdominal disease developed at the follow-up. The five-year and 10-year survival rates of the patients in this group were reported as 79% and 46%, respectively [21]. Our study and all previous reports on LGMN and diverticula are summarised in Table III. Yantis *et al*. researched the prognostic importance of right lower quadrant limited mucin accumulation with their study involving 65 appendiceal neoplasm cases [22]. As extra-appendiceal mucin accumulation was acellular in 50 cases (77%), periappendicular mucin contained mucinous epithelium in small quantities with low-grade cytological features in 15 patients (23%). After a mean follow-up of 52 months, 96% of patients with acellular mucin were without disease, and diffuse peritoneal disease developed in 33% of patients with neoplastic epithelium. One patient died of the disease. In two patients with acellular mucin and also with disseminated peritoneal disease, the entire appendix could not be evaluated histologically [22]. Similar to

**Table III.** Comparison of the reports on LGMN and diverticula

| | Lamps *et al.* [20] | Pai *et al.* [21] | Dupre *et al.* [16] | Pasaoglu *et al.* |
|---|---|---|---|---|
| Number of cases LGMN | 19 | 101 | 8 | 38 |
| Number of cases LGMN with diverticulum | 8 (41.2%) | 12 (11.9%) | 3 (37.5%) | 23 (60.5%) |
| Number of cases with periappendicular acellular mucin | 0 | 28 | not reported | 23 |
| Number of cases with periappendicular cellular mucin | 1 | 44 | not reported | 0 |
| Number of cases with periappendicular mucin in LGMN with diverticulum | 1 | 11 (91%) | not reported | 18 (78.3%) |
| Number of cases with periappendicular mucin in LGMN without diverticulum | 0 | 63 (70%) | not reported | 5 (33.3%) |
| Number of cases PMP | 1 | 42 | not reported | 0 |

*PMP – Pseudomyxoma peritonei*

our research, in many of the cases in the literature, when the periappendicular mucin was acellular, pseudomyxoma peritonei did not develop. The results of the studies indicate that it carries great importance to sample and examine carefully the entire appendix with serial sections and if necessary with immunohistochemical stains in LGMNs in terms of having periappendicular mucinous epithelium to designate the prognosis of the patients.

In our study, the co-existence of the diverticulum with most of the cases with acellular periappendicular mucin accumulation (78.3%) raised doubts that periappendicular mucin accumulation resulting from rupture of the diverticulum may be associated with better prognosis than mucin accumulation related to expansive invasion. However, the number of cases that were followed-up are few and the follow-up periods are short. In the study by Lamps *et al*., rupture of the diverticulum was correlated with pseudomyxoma peritonei in only one case [20]. No comment was made about the relationship between rupture of the diverticulum and periappendicular mucin without epithelium in other studies. We could not compare the cellular and acellular mucin accumulation with diverticulum due to having acellular mucin in all cases. On the other hand, diverticular involvement of adenomatous epithelium may confuse with expansive invasion, namely with LGMN, as epithelium in adenoma and LGMN is exactly the same. Some authors even interpreted low grade tumours causing pseudomyxoma peritonei as ruptured adenoma and peritoneal dissemination of adenomatous epithelium based on their morphological features [2, 3]. In adenomas, epithelium is surrounded by lamina propria, and the muscularis mucosa is intact. In LGMNs, muscularis mucosa is not observed and neoplastic epithelium is on fibrous stroma [14, 15]. Lamina propria may not be distinguished due to compression on diverticular area, even muscularis mucosa may not be recognised. Extra-diverticular histological features of the lesion may be helpful in differential diagnosis. Diverticula should not be evaluated as expansive invasion. If the mucin produced by the tumour leaks into the peritoneal cavity, the behaviour is determined by the nature of the tumour. We can only claim that rather than neoplastic dissemination, in some of these cases, mucin disseminates out of the appendix via diverticula.

Another point to be emphasised in our study is the accompanying psammomatous calcification with 44.7% of LGMNs. Because dystrophic calcification co-exists either with non-neoplastic diverticula or neoplasms, psammomatous calcification is observed only in neoplastic group. Soft tissue mass with curvilinear calcifications in the right lower quadrant detected with abdominal radiographs is a significant finding with regard to LGMN diagnosis [1, 23, 24]. In LGMNs, calcifications in the wall may be confirmed histopathologically. When the calcification is diffuse, then it is termed as a "porcelain appendix" [1]. However, no article was found evaluating the type of calcification in LGMNs in the literature. In routine histopathological examination of appendectomy materials, the relationship between psammomatous calcification and neoplasms may be kept in mind. Adequate sampling and careful microscopic examination should be done.

In conclusion, we found that the true prevalence of diverticulum is more common than that reported in the literature (4.8%). Diverticulum can be overlooked in routine practice but can be detected more frequently with detailed macroscopic examination. It is much more common in cases with LGMN. Furthermore, we detected that periappendicular mucin was highly associated with diverticula in LGMN cases. The importance of periappendicular mucin in the aetiology of pseudomyxoma peritonei was revealed in various studies. However, pseudomyxoma peritonei was not detected in company with periappendicular

acellular mucin in many cases, as in our study. It could be argued that mucin could move out of the wall of the appendix through the diverticulum rather than disseminating by means of neoplastic spread in some of these cases. Studies with a large number of cases that are followed-up for a long time are needed to reveal the relationship between diverticula, periappendicular mucin, and pseudomyxoma peritonei.

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*The authors declare no conflict of interest.*

## References


1. Lam-Himlin D, Montgomery E, Torbenson M. Nonneoplastic and neoplastic disorders of the appendix. In: Gastrointestinal and Liver Pathology. Iacobuzio-Donahue CA, Montgomery E (eds.). 2nd ed. Elsevier, Philadelphia 2012; 257-296.
2. Qizilbash AH. Mucoceles of the appendix. Their relationship to hyperplastic polyps, mucinous cystadenomas, and cystadenocarcinomas. Arch Pathol Lab Med 1975; 99: 750-755.
3. Ronnet BM, Kurman RJ, Zahn CM, et al. Pseudomyxoma peritonei in women: a clinicopathologic analysis of 30 cases with emphasis on site of origin, prognosis, and relationship to ovarian mucinous tumors of low malignant potential. Hum Pathol 1995; 26: 509-524.
4. Carr NJ, Sobin LH. Unusual tumors of the appendix and pseudomyxoma peritonei. Semin Diagn Pathol 1996; 13: 314-325.
5. Edge SB, Byrd DR, Compton CC, et al. (eds.). AJCC Cancer Staging Manual. (Appendix) Springer, New York, 2010; 133-141.
6. Carr NJ, Sobin LH. Adenocarcinoma of the appendix. In: WHO Classification of Tumors of the Digestive System. Bosman FT, Carneiro F, Hruban RH, N.D. Theise (eds.), 4th ed. WHO press, Lyon 2010; 122-125.
7. Käser SA, Willi N, Maurer CA. Prevalence and clinical implications of diverticulosis of the vermiform appendix. J Int Med Res 2013; 41: 1350-1356.
8. Marudanayagam R, Williams GT, Rees BI. Review of the pathologic results of 2660 appendectomy specimens. J Gastroenterol 2006; 41: 745-749.
9. Abdullgaffar B. Diverticulosis and diverticulitis of the appendix. Int J S Pathol 2009; 17: 231-237.
10. Wetzig NR. Diverticulosis of the vermiform appendix. Med J Aust 1986; 145: 464-465.
11. Everts-Suare EA, Noteboom B. Congenital diverticula of the appendix: review of the world's literature and report of a case. Penn Med J 1961; 64: 1454-1458.
12. Hsu M, Young RH, Misdraji J. Ruptured appendiceal diverticula mimicking low-grade appendiceal mucinous neoplasms. Am J Surg Pathol 2009; 33: 1515-1521.
13. Panarelli NC, Yantiss RK. Mucinous neoplasms of the appendix and peritoneum. Arch Pathol Lab Med 2011; 135: 1261-1268.
14. Misdraji J. Mucinous epithelial neoplasms of the appendix and pseudomyxoma peritonei. Mod Pathol 2015; 28 Suppl 1: 67-79.
15. Misdraji J. Epithelial neoplasms of the Appendix In: Odze RD, Goldblum JR, editors. Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas. 2nd ed. Philadelphia, 2015: 779-801.
16. Dupre MP, Jadavji I, Matshes E, et al. Diverticular disease of the vermiform appendix: a diagnostic clue to underlying appendiceal neoplasm. Hum Pathol 2008; 39: 1823-1826.
17. Place RJ, Simmang CL, Huber PJ Jr. Appendiceal diverticulitis. South Med J 2000; 93: 76-79.
18. Medlicott SAC, Urbanski SJ. Acquired diverticulosis of the vermiform appendix. A disease of multiple etiologies. Int J Surg Pathol; 6: 23-26.
19. Lipton S, Estrin J, Glasser I. Diverticular disease of the appendix. Surg Gynecol Obstet 1986; 168: 13-16.
20. Lamps LW, Gray GF, Dilday BR, et al. The coexistence of low-grade mucinous neoplasms of the appendix and appendiceal diverticula: A possible role in the pathogenesis of pseudomyxoma peritonei. Mod Pathol 2000; 13: 495-501.
21. Pai RK, Beck AH, Norton JA, et al. Appendiceal mucinous neoplasms. Clinicopathologic study of 116 cases with analysis of factors predicting recurrence. Am J Surg Pathol 2009; 33: 1425-1439.
22. Yantiss RK, Shia J, Klimstra DS, et al. Prognostic siginificance of localized extra-appendiceal mucin deposition in appendiceal mucinous neoplasms. Am J Surg Pathol 2009; 33: 248-255.
23. Kim SH, Lim HK, Lee WJ, et al. Mucocele of the appendix: ultrasonographic and CT findings. Abdom Imaging 1998; 23: 292-296.
24. Wakui N, Fujita M, Yamauchi Y, et al. Mucinous cystadenocarcinoma of the appendix in which contrast-enhanced ultrasonography was useful for assessing blood flow in a focal nodular lesion in the tumor cavity: A case report. Exp Ther Med 2013; 6: 3-8


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