Diverticular disease and colon cancer: a real association between the two diseases?

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BACKGROUND: *During the last century the incidence of diverticular disease (DD), as well as the prevalence of colonic adenocarcinoma (ADK), recorded a marked increase in Western populations. In literature has been reported a higher incidence of sigmoid colon carcinoma associated with diverticular disease suggesting a possible sharing of risk factors and pathogens between these two pathologies.*
MATERIALS AND METHODS: *We prospectively examined 165 patients undergoing left colonic resection from May 2010 to December 2012 at the operating unit of General Surgery and Organ Transplantation of University Hospital of Parma , dividing them into three groups: affected by left colon cancer (120 cases), affected by complicated diverticular disease (29 cases) and affected by both diseases (16 cases). In this last group the indication for surgery has always been oncology based. All cases have been subjected to a 6 months minimum follow-up.*
RESULTS: *The average age of patients operated for colonic ADK was 69.91 years. The average age of patients operated for ADK and concomitant DD, compared to that of patients treated for single DD, was statistically higher (73.8 ± 6.89 VS 60.9 ± 13.5, p = 0.004). It was found instead a higher diverticular inflammation degree in patients treated for DD compared with those treated for ADK associated with DD. No patient with ADK associated with DD showed hepatic metastases, whereas among patients with just ADK, peritoneal carcinomatosis was recorded in 2.6% of cases and liver metastases, always synchronous, in 11 .5%. The lymph nodes positivity instead, has presented a prevalence of 33.5% in patients with ADK and of 7% in patients with associated DD.*
CONCLUSION*: In our study and its comparison with literature we found in synthesis multiple clinical evidences of a possible association between the two diseases. The role played by DD would lead to an early diagnosis of colonic ADK. It remains to be analyzed however the possible etiopathogenetic correlation over time between the two clinical entities, which actually still remains maybe under random association.*

KEY WORD: Colectomy, Colon cancer, Diverticular disease, Early diagnosis, Laparoscopy

Introduction

During the last century the prevalence of diverticulosis has remarkably increased and it represents nowadays an important weight for the healthcare system of industrialized western nations [1-3]. It is estimated that, in Westernized countries, approximately 60% of subjects over the age of 60 will develop colonic diverticula. Diverticulosis presents age-related incidence. Indeed, postmortem studies, allow to reveal how this condition is rare before the age of 40, while it is estimated that approximately 65% of patients over 80 years is suffering from colonic diverticula [4]. The geographical distribution reveals, moreover, that this high prevalence is seen especially in people from North America, Europe and

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Australia, while studies on Asian populations have significantly lower values, with a prevalence from 4.5% to 15% [5]. More often, in these populations, diverticula are highlighted in the right colon, unlike peoples of Western countries that present right isolated diverticulosis in just 2.5% of cases, and involvement of the left colon, more or less extended, in the remaining [6]. A greater importance from clinical point of view is covered by the data showing that approximately 5% of individuals (up to 25% of other authors) with diverticulosis, during the course of their life, can present complications brought by the pathology itself [7]. Diverticular disease, with a mortality rate of 2.5 /100000/year, is at fifth place for importance in terms of direct and indirect costs for health system among gastrointestinal diseases in Western countries.[7] Regarding colorectal cancer (CRC), it is well known how this is considered to be third for frequency and second as cause of cancer death (following lung cancer) among all men tumors. In Western countries, the incidence of colonic carcinoma follows the same age-related trend already seen for diverticular disease, with an incidence of approximately 13/100000/year in subjects aged less than 40 years and 40/100000/year in people over 80 years. Colon cancer prevalence also appears to be 6% in western industrialized countries, while in Asian countries are found 10 times lower values showing a characteristic geographical distribution [1]. It is also important to highlight how cancer and diverticulosis prevalence, in Asian people, increases in the event that the country of origin is abandoned to settle permanently in a Western country, indicating a probable role played by diet and lifestyle in pathogenesis of both diseases in study [5,9,10]. Following this hypothesis, the difference in incidence from region to region seen in our country, could be explained by the increased consumption of foods high in fiber and low in fat, found in southern areas; this difference however, given the progressive approval of diet, will probably be flattened with time [10]. Finally, over the past thirty years, in U.S. and European case studies, it has been found a progressive increase in the incidence of proximal colon cancer, higher than the one in distal colon. This trend in anatomical distribution of colorectal cancer can only be partially explained by the increase in diagnostic and therapeutic capabilities of distal colon treatment, actually marking a real shift in the tumor localization, probably due to the development of different pathogenetic factors such as population aging [11-13]. The increased incidence of diverticulosis in industrialized countries suggests an important role of lifestyle and environmental factors in its pathogenesis. A huge number of studies have attempted indeed to demonstrate that a diet with low fiber intake may be related to the genesis of diverticulitis and diverticular disease. Meanwhile an important cohort study carried out on 47.000 subjects, stratified by age, physical activity and total fat intake, confirmed the inverse relationship between high-fiber diet and risk of diverticular disease [13].The protective effect of fibers would be explained by the role they play in the formation of size increased faecal masses that would induce a greater colic dilatation and a higher frequency of contraction, with a less efficient segmentation, and therefore a lower tendency to the herniation of the wall. There are, however, many studies who criticize this theory and that look to the fibers not as a protective agent for diverticular disease, but rather as a simple treatment of constipation which, in most cases, accompanies this pathology [14]. Similarly, among generic risk factors associated with colon cancer, in addition to age, sex and racial factors, we find elements correlated to the dietary habits of the subject. Obesity, as an independent factor, induces a risk of developing CRC approximately 1.5 times higher compared to normal weight population identified by BMI, showing a stronger relationship in men [16]. The role played by physical activity and intake of fiber helps to support what has already been said about the importance of lifestyle as a risk factor. In particular in some studies it has been found a relative risk of incidence of 24% less for those who exercise regularly compared to sedentary subjects [16]. It has therefore been suggested that, in general, a diet low in red meat, animal fats and cholesterol, and high in fiber, combined with regular physical activity could be protective for CRC [18-20]. Important link between the two diseases appears to be the correlation between CRC and inflammatory bowel diseases, in particular with ulcerative colitis (UC), and to a lesser extent with Chron's disease. The risk of CRC in UC depends on the duration and extent of the disease; in comparative studies stratified by age it is evident that the risk begins to grow about 8-10 years after the onset of symptoms. Proof of this trend is given by the cumulative incidence of CRC that is approximately of 5-10% after 20 years and grows to 12-20% after 30 years of disease [21]. A case-control study found a significant relationship between degree of inflammation histologically demonstrated and risk of CRC [21,22]. There is few knowledge regarding the pathogenesis of colon cancer in chronic inflammatory diseases, although some evidence suggests a pathogenesis different from that of the common sporadic cancer. Among factors supporting a different evolutionary pathway we find the average age of development of this tumor, which precedes about 10 years that of sporadic cancer, and dysplastic foci, which can also be found far from the tumor, in contrast to what commonly occurs in CRC [23]. The particular interest in this pathogenetic model is motivated by the similarities that are found with the possible correlation between diverticular disease and colon cancer. Early as 2007, a French study correlated CRC, UC and diverticulitis showing how, in all these pathologies, an anomaly was present in the expression of the gene responsible for gastric mucin production (M1/MUC5AC), detectable immunochemically, which replaced the gene physiologically expressed in colonic mucosa (MUC2) [24]. Recently, in 2011, it has been

demonstrated that the lymphoplasmic infiltrate colonizing the colonic mucosa of patients with diverticulitis and of patients with ulcerative colitis, is characterized in both cases for the presence of Th2 and Th17 lymphocytes. Besides the sharing of secretion of these cytokines, in both diseases was demonstrated a deficiency in Th1 lymphocytes responsible for the secretion of IFN-γ, normally involved in the interruption of dysplastic processes onset [25].

Materials and Methods

We analyzed the data relating to 165 patients, 89 females and 76 males, aged between 31 and 92 years, operated of left colonic resection from May 2011 to December 2012 by the Division of Chirurgia generale e trapianti d'Organo of Parma Hospital. The patients have undergone intervention for colonic adenocarcinoma in 136 cases and for complicated diverticular disease in the remaining 29 cases. By the analysis of the 136 patients operated for adenocarcinoma we identified in 16 cases (11.8%) the concomitant presence of diverticular disease. We wanted to study within treated patients the concurrent presence of adenocarcinoma and diverticular disease, analyzing the different incidence according to age, sex, operative time, eventual conduct in emergency and Hinchey stage.

All patients in the analysis were subjected to a preoperative diagnostic protocol which provides: blood tests, electrocardiography, chest X-ray, thoraco-abdominal CT pancolonscopy and / or barium enema in case of already known diverticular disease. We also used ASA classification of anesthesiologic risk.

Obtained data were submitted to statistical examination conducted using Student's t-test, considering as statistically significant p-values <0.05.

Results

The follow-up has been at least of 6 months. Within the group of patients treated with left hemicolectomy for adenocarcinoma confirmed as single colonic disease (120 cases) there was a predominance of females with M: F ratio 54/66 (45% / 55%). The average operative time was 174.5 minutes. In four cases an emergency intervention for left hemicolectomy has been necessary. On 120 patients 34 were operated laparoscopically. We recorded nine cases of conversion to laparotomy surgery. In 3 patients laparoscopic treatment has been interrupted for intrinsic factors related to the patient such as the fixity of meso associated to central obesity, in these cases conversion took place before it was possible to finish the high-time of the intervention thereby making necessary an extended xipho-pubic laparotomy. In 2 cases conversion become necessary to control splenic and inferior mesenteric artery bleeding. In 2 patients the conversion has been motivated by the massive adherences presented as surgical outcome of cholecystectomy, appendectomy and isteroannessectomy in the first subject, while in the second as surgical outcome of aorto-femoral by-pass and nephrectomy due to a clear cell carcinoma. Finally in 1 case the conversion has been necessary for difficulties found during the ureter identification wich is then resulted affected by the neoplastic process, while in the latter case, laparoscopy has been interrupted because of the infiltration of ipsilateral Gerota's fascia. In none of the 4 cases, in which a parietal peritoneum infiltration was attested, it has been necessary the transition to traditional surgery. Among the 120 patients underwent surgery 7 have developed post-operative complications.

Among the group of 29 patients treated with hemicolectomy for diverticular disease we noticed a prevalence of females with a M: F ratio of 11/18 (37.9 / 62.1%) and a mean operative time of 192, 9 minutes. In 9 cases the surgery has been performed in urgency. In 20 patients the approach has been laparoscopic with 5 conversions (Hinchey II) during surgery, while 9 patients out of 29 total, have been directly candidated to traditional surgery. By the analysis of the 9 cases operated in urgency we can record the use of a "open" procedure in 6 cases (4 Hinchey III, 2 Hinchey IV) and of laparoscopic procedure in the remaining 3 (2 Hinchey II, 1 Hinchey III). In 6 cases there were complications. Within the group of patients in wich we recorded the concomitant presence of adenocarcinoma and diverticular disease there was a prevalence of males with ratio M: F 11:5 (68.7 / 31.3%). The average operative time has been 181.7 minutes and no intervention has been con-

Table I - *Analysis of groups on surgical treatment*

Surgical indication	Number of patients	Mean operative time (minutes)	Emergency	Laparotomy	Laparoscopy	Complications
ADK	120	174.5	4 (3.3%)	86 (71.7%)	34 (28.3%)	7 (5.8%)
ADK + DD	16	181.7	0	7 (43.7%)	9 (56.3%)	4(25%)
DD	29	192.9	9 (31%)	9 (31%)	20 (69%)	6 (20.7%)

ADK: adenocarcinoma
DD:Diverticular Disease

ducted in emergency. Out of a total of 16 interventions 9 have been conducted with laparoscopic technique, while the remaining 7 have been performed in laparotomy. In 4 cases we have found the presence of intraoperative complications (Table I).

Statistical Analysis

From the comparison of patients in the three groups we can record how the average age, when suffering from adenocarcinoma of the colon and concomitant presence of diverticular disease, is statistically higher compared to that of the group of patients treated for single diverticular disease (73.8 ± 6.89 VS 60.9 ± 13.5, p = 0.004). It is also found in the data a higher degree of intestinal inflammation in patients with diverticular disease alone compared with subjects with colonic neoplasia associated with diverticular disease (12 Hinchey I, 10 Hinchey II, 5 Hinchey III, 2 Hinchey IV VS 9 Hinchey 0, 7 Hinchey I).
There was no statistically significant difference with regard to the average age between patients with adenocarcinoma and patients with association diverticular disease-adenocarcinoma (69.91 ± 11.8 VS 73.8 ± 6.89, p = 0.81).
In the same groups, adenocarcinoma versus adenocarcinoma and diverticular disease, we did not find any statistically significant difference in the analysis of mean operative times, while the statistical significance is evident in the difference of operative times between patients with adenocarcinoma and patients with single diverticular disease (174.5 ± 7.2 VS 194.9 ± 9.4, p <0.05).
When comparing data from patients with adenocarcinoma and those of patients with adenocarcinoma in association with diverticular disease on the basis of the TNM stage of disease, we observed that:
– No patient with adenocarcinoma and simultaneous diverticular disease presented liver metastases or peritoneal carcinomatosis (M0);
– In patients with adenocarcinoma the prevalence of peritoneal carcinomatosis is 2.6%;
– In patients with adenocarcinoma synchronous liver metastases have a prevalence of 11 .5%;
– In patients with adenocarcinoma the lymph node positivity (N +) has a prevalence of 33.5%, while in patients with concomitant diverticular disease, the prevalence of N + is 7%;
– With regard to the extension of disease we highlight how, in patients with adenocarcinoma, neoplasm is predominantly T3 with a tendency to the concomitant lymph node positivity (stage 2 = 22.6%; stage 3 = 26%), but without hepatic involvement. Differently, among patients with a concomitant diverticular disease, there is a higher prevalence of T3 tumors without lymph node extension (43.3%) (Table II).

TABLE II - *Analysis of groups related to disease stage*

	N+	M+
ADK + DD	7%	0
ADK	33.5%	11.5% Liver Metastases 2.6% Peritoneal Carcinosis

ADK:adenocarcinoma
DD:Diverticular disease

Discussion

During last century the prevalence of diverticulosis and colon-rectum cancer has undergone a sharp increase within a segment of population similar for characteristics. In literature in particular it has been repeatedly reported a greater incidence of carcinoma of the sigmoid colon, compared to controls, in patients with diverticula, suggesting the possible sharing of pathogens and risk factors between the two diseases. The association, according to some study data, seems even more important in patients who have experienced at least one episode of diverticulitis. Relying on epidemiological data, distribution, and micro and macroscopic findings recorded, the investigation thus took to investigate a possible causal relationship between these two diseases, relationship that despite the impressive amount of research carried out, is still far from being demonstrated. To support the hypothesis of a causal link between diverticular disease and colon cancer, particularly in the sigma, there is a large group of arguments among which the most easily demonstrable is surely the similarity of the two diseases in their distribution. Both diseases occur particularly in Western countries, most often in people over the age of sixty years and appear rare in the East, in Africa and in subjects under the age of forty. Diverticular disease occurs preferentially in the descending colon and sigmoid colon, whereas diverticula of the right colon are mainly prerogative of eastern populations. These same sites are those historically most affected by CRC, although we are nowadays witnessing a shift that brought this tumor to be located more frequently in right colon. It has been also possible to evaluate how, in both cases, the incidence of disease increases not only in people who move from a country with a low prevalence to a high prevalence one, but also in those who, within the same country, move from a rural to an urban area, highlighting the key role played by environmental factors in the development of these diseases. Due to these findings and to the increased prevalence of both diseases in the last century, diet (high in fat and low in waste) has been called into question as an important factor in the pathogenesis.[1] The slowdown in normal transit of intestinal contents caused by

western diet in fact would induce the formation of diverticula by the increase of colonic intraluminal pressure, while the tumor would be favored by an increase of contact time between possible carcinogens, such as bile salts, and intestinal mucosa. The similarities between these two diseases are also microscopically detectable as alterations of mucosa and extracellular matrix. During the investigations in patients with diverticula it has been demonstrated: the inconstant presence of inflammation (risk factor for CRC), the increase in cell proliferation (also present in adenomas), and the existence of aberrant cryptic foci normally detectable in ulcerative colitis, which is considered a predisposing factor to the onset of cancer. In a recent experimental study the extracellular matrices of nine patients with colon ADK and of nine subjects with diverticulosis were compared using immunohistochemical methods highlighting similarities in these conditions, with a higher level of PAI, TGF-β and CD117 in patients with carcinoma. This study suggests that in diverticulosis profound distortions occur in mucosal structure, presenting similarities with the condition of a real neoplastic mucosa or with circumstances which promote CRC [26]. The same identification of SCAD (Segmental Colitis Associated with Diverticulosis) in itself, of its characteristics and its possible evolution to ulcerative colitis, offers an important input to the hypothesis of diverticulosis no longer seen as a singular disease, but as a possible evolutive condition. In addition to the previously mentioned investigations about the similarities in inflammatory processes of MD SCAD and UC, it seems appropriate to assess the results of two studies that promote the idea of diverticular disease as a possible precancerous condition. The first study focuses his efforts on the immunoenzymatic evaluation (ELISA) of Fecal calprotectin (FC) in stool samples from patients with ulcerative colitis, irritable bowel syndrome (IBS), diverticular disease and SCAD. The FC, which normally increases in the stools of patients with bowel inflammation, was significantly increased only in patients with MD, UC and SCAD, with values comparable in the latter two, highlighting a possible analogy presented by UC and SCAD [27]. The second study, conducted by Tursi et al. in 2006, compares instead the expression of Ki-67 proliferation index in various groups of patients, demonstrating that individuals with asymptomatic diverticulosis present values three times higher compared to healthy individuals, and even that antigen levels in patients with asymptomatic diverticulosis and in patients with UC in remission are very similar. This finding, conclude the authors, indicates that the risk of progression to carcinoma is comparable for UC and diverticulosis [28]. In this case the colon ADK would be thus stimulated and supported by the particular condition of cells from the host tissue suffering from diverticular disease, supporting the ever timely idea, expressed by Paget in 1989, comparing cancer cells to the seed of a plant that "grows only if it falls in congenial soil". The coexistence of colon cancer and diverticular disease has been often observed, in the past, through endoscopy, radiology and postmortem studies, but despite this condition was frequently recorded, the association between the pathologies has been considered accidental until quite recently. Although the first publication on the subject is to be traced back to Morton, who in 1952 published an account of cases he encountered presenting the association of the two conditions, the first major study on this subject (7159 patients involved) was the 1993 study by Stefansson et al. which showed an increase in long-term risk for emergence of left CRC in patients with diverticular disease comparing to the risk in general population [29,30]. Within the same cohort, a 2004 study carried out by the same team reported even higher levels of risk for that portion of patients who had presented at least one episo Over the years other studies, such as the one from Kieff et al. in 2004 and the Italian study performed by Morini et al.[31] in 2002, have attempted to prove the causal link through statistical analysis based on the follow-up of patients with diagnosis of diverticular disease [32,33]. Although data agree in highlighting an increased risk of CRC in patients with diverticular disease, it seems correct to assess the criticisms that have been leveled at these studies. For first is noted as, in analyzing the results, risk of cancer development is actually increased in the first two years of follow-up after diagnosis of diverticulitis, suggesting that the increased incidence may be related only to a greater focus on monitoring patient. This appears clear in the first study of Stefensson in which can be found also an increased risk for other organs cancers. Other criticisms made are related to the possible similarities in the clinical presentation shared between diverticular disease and left colon carcinoma which could then have led to misdiagnosis during data collection [1]. The most important doubt about the validity of asserted hypotesis is cast by the mismatch observed between epidemiological data recorded by endoscopic examination and barium enema, and the most recent data collected instead through the use of CT. An example are the studies by Jin Soon Lee et al. and those made by Granlund et al., implemented by the use of tomography, which shows in fact results that would lead to the demonstration of a random only association between the two diseases, in contrast with previous studies data [34,35]. A 2005 retrospective survey conducted by Krones et al. and based on the study of patients with endoscopic methods and barium enema, showed however the lack of a causal link. The authors explain this result analyzing patients stratification [35]. The lack of stratification (by age and sex) in earlier studies has been then used to re-evaluate the results achieved, which today actually appear too sharp compared to the controversial data reported by recent surveys.

Inside of our series we decided to compare the group of patients suffering from diverticular disease and the group of patients with diverticular disease associated to

adenocarcinoma with patients suffering from colonic adenocarcinoma only (independently from the site). The statistical analysis utilized is similar to that proposed by Kieff in his 2004 study which verified the association between proximal or distal colonic adenocarcinoma and diverticular disease in patients with sigma diverticulosis (extensive distal diverticulosis, EDD), excluding from the groups concerned patients with diverticular disease of the right colon. The author concluded that women with EDD show a statistically higher risk of developing distal colon cancer and that, the presence of left colonic neoplasia in women with EDD, increases the risk of a second tumor in proximal colon [32].

In our study we record the concurrence of left colonic diverticular disease and distal sigma-colon neoplasia highlighting males prevalence (68.7%). None of the patients presented diverticular disease associated with proximal colonic neoplasia neither as first nor as second tumor.

As regards to the distribution our study confirms already known epidemiological data. According to the literature colonic diverticula are present in one third of the population over 45 years and in about two-thirds of that over 85, while colon cancer reaches the maximum frequency between the sixth and seventh decade of life. The comparison between our group of patients with diverticular disease and that of patient with adenocarcinoma of the colon, highlights a statistically significant difference based on age: 60.9 ± 5.13 VS 69.91 ± 11.8. ($p < 0.003$).

In patients with diverticular disease associated with a concomitant adenocarcinoma of the colon we see however an epidemiological shift in the average age toward the typical values of cancer. The average age of this group (73.8 ± 6.89) of patients is almost identical to that of patients with carcinoma in absence of diverticula (69.91 ± 11.8) with no statistically significant differences ($p = 0.81$) while it is much more advanced ($p = 0.004$) compared with the average age of patients with diverticular disease alone (60.9 ± 13.5).

It is also registered as diverticular disease, in association with cancer, is almost always paucysimptomatic with prevalence of patients presenting an Hinchey stage 0 (9/16) and a stage I in the remaining cases (7/16), while in no case we recorded at diagnosis Hinchey stages higher than II. Data therefore agree with those of Kieff study highlighting an association of colon cancer with diverticular disease only in low intestinal inflammation conditions, thus contrasting with the results of Steffenson historical study which saw a stronger association with neoplasia in patients presenting high Hinchey stage.

The pTNM of patients presenting an association of the two diseases is far less advanced than the pTNM recorded in cases of adenocarcinoma as single pathology. In the first group, there was evidence of nodal involvement only in a minority of cases(7% N +) and in no case we detected peritoneal or syncronous liver metastases (100% M0). This data contrasts precisely with that of patients presenting only adenocarcinoma which shows positives lymph nodes (N +) in 33.5%, peritoneal carcinosis in 2.6% and liver metastases in 11.5%. In both tumors we rated a moderately differentiated (G2) grading. These data concerning the less advanced pTNM can be interpreted as consequence of a greater precocity in diagnosis related to mild diverticular disease symptoms, which would bring the patient to medical attention in a shorter time.

If we associate data regarding inflammation and pTNM with those concerning the distribution of the two diseases by age we can suggest an idea for reflection in favor of the hypothesis that sees a causal link between them. Highlighted subclinical inflammation, already assessed as a predisposing factor to the onset of cancer, could trigger mechanisms that would over time lead from chronic inflammation to different degrees of dysplasia and then to real cancer. Even the absence of metastases can be seen as a result of such processes that occur with a slow and gradual evolution, in contrast with more rapid processes such as those classically presented in sporadic colon cancer.

In conclusion, by analyzing diverticular disease in its different evolutions, we recognize the difficulties which arise in finding a real causal link between this and adenocarcinoma, but while waiting for a clear answer on this issue, it seems appropriate to evaluate those which in our view still appear as matter of conflict on the subject. In first place we find correct, because of the waiting attitude adopted after the first episode of acute diverticulitis, the application of a protocol enabling on the one hand, an exclusion diagnosis of a possible concomitant tumor and on the other, the implementation of an endoscopic based follow-up similar to that used for other evolutive diseases such as UC. Since the phlogistic status, which normally accompanies diverticular disease, even when asymptomatic, it may also be indicated the execution of random interdiverticular biopsies during colonoscopic controls. We find necessary to revaluate the data produced in earlier studies in order to develop a population survey actually stratified by age, sex and conditions, which may produce in the future a complete valuation of the possible prognostic progression to malignant transformation, as it has been possible to do for UC. In evaluating the tumoral risk it seems important to identify the real role played by inflammation in diverticulosis and in mechanisms of neoplastic transformation, while defining at same time the possible function that biohumoral monitoring of calprotectin might have in the study of diverticulosis and in the prediction of a shift to dysplasia-neoplasia. Finally we emphasize the importance of diagnostic accuracy in the examination of patients with diverticular disease. In many cases, given the status of phlogosis, it is difficult to perform biopsies to exclude the possible concomitant presence of neoplastic formations, especially in acute conditions. This exam farther exposes patients to the risk of

complications (bleeding, perforation), linked to the particular fragility of the phlogistic colonic wall. We therefore recommend the use of methods that can diagnose preoperatively concomitant neoplastic lesions such as a barium-TC.
In view of this study and of its comparison with literature we find now even more evident the necessity to investigate diverticular disease no longer as an illness in its own right but rather as a clinical picture inside a larger pathological condition in which the diverticulum may play a primary role interesting inflammatory processes and cancer development.

Riassunto

BACKGROUND: Nell'ultimo secolo l'incidenza della malattia diverticolare (MD), così come la prevalenza di adenocarcinoma del colon (ADK), ha registrato nella popolazione occidentale un deciso aumento. In letteratura è stata riportata una maggiore incidenza di carcinoma del sigma associato a malattia diverticolare suggerendo così una possibile condivisione di fattori di rischio e di fattori patogeni tra queste due malattie.
MATERIALI E METODI: Abbiamo esaminato in maniera prospettica 165 pazienti operati di resezione colica sinistra dal maggio 2009 al dicembre 2011 presso l'unità operativa di Clinica Chirurgica e Trapianti d'Organo dell'ospedale di Parma, dividendoli in tre gruppi: affetti da carcinoma del colon sinistro (120 casi), affetti da malattia diverticolare complicata (29 casi) ed affetti da entrambe le patologie (16 casi). In questo ultimo gruppo l'indicazione chirurgica è sempre stata su base oncologica. Tutti i casi sono stati sottoposti a follow-up minimo di 6 mesi.
RISULTATI: L'età media degli operati per ADK del colon è risultata pari a 69.91 anni. L'età media degli operati per ADK e concomitante MD, rispetto a quella dei pazienti trattati per sola MD, è risultata statisticamente maggiore (73.8±6.89 VS 60.9±13.5; p=0.004). Si è riscontrato invece un grado di flogosi diverticolare superiore nei pazienti operati per MD rispetto ai pazienti trattati per ADK associato a MD.
Nessun paziente affetto da ADK associato a MD presentava metastasi epatiche, mentre tra i pazienti con solo ADK si è registrata carcinosi peritoneale nel 2.6% dei casi e metastasi epatiche, sempre sincrone, nell'11.5%. La positività linfonodale ha presentato invece una prevalenza del 33.5% nei pazienti con solo ADK e del 7% nei pazienti con associata malattia diverticolare.
Nei pazienti con solo ADK sono risultati prevalenti i tumori T3 N+ (stadio 2 = 23.6%, stadio 3 = 26%) mentre nel gruppo di pazienti con ADK associato a MD il T3 ha presentato un'alta incidenza (43%), ma con interessamento linfonodale meno frequente.
CONCLUSIONI: Nel nostro studio e nel suo confronto con la letteratura abbiamo riscontrato in sintesi molteplici evidenze cliniche della possibile associazione tra le due patologie. Il ruolo esercitato dalla MD condurrebbe verso una diagnosi precoce di ADK colico. Resta da verificare invece l'eventuale e possibile correlazione etiopatogenetica, nel tempo, tra le due entità morbose, attualmente ancora nell'ambito dell'associazione forse solo casuale.

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