

# Post-operative peritonitis due to anastomotic dehiscence after colonic resection.

## Multicentric experience, retrospective analysis of risk factors and review of the literature.



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### Post-operative peritonitis due to anastomotic dehiscence after colonic resection. Multicentric experience, retrospective analysis of risk factors and review of the literature

**INTRODUCTION:** *Intraperitoneal sepsis due to anastomotic leakage significantly affects the outcomes of intestinal surgery. The aim of this retrospective review is to examine retrospectively general and local factors involved in anastomotic leakage and their prognostic value.*

**MATERIALS AND METHODS:** *Between April 1998 and April 2008, 367 patients underwent elective (217=59%) or emergency (150=41%) primary colonic resection for benign (77=21%) or malignant (290=79%) disease in our department. We performed the following operations; 124 right colon resections with immediate anastomoses (primary resection), 65 (52.4%) of which were emergency and 59 (47.6%) elective procedures; 171 left colon resections, 73 (42.7%) of which were emergency and 98 (57.3%) elective procedures, and 72 primary rectal resections, 12 (16.7%) of which were emergency and 60 (83.3%) elective procedures. The considered variables were stapled or manual anastomoses, protective stomas and medical comorbidities.*

**RESULTS:** *The perioperative mortality rate was 6.6% for emergency and 3.6% for elective procedures. The leak rate was 8.7% (32/367), 13.3% for emergency and 5.5% for elective procedures. Fistula was observed in 7/124 (5.6%) ileo-colic, 13/171 (7.6%) colo-colic and 12/72 (16.6%) colo-rectal anastomoses, 8 of which were fashioned during emergency surgery. Twenty-one patients with anastomotic dehiscence were treated conservatively (3 underwent reoperation), while 11, with severe dehiscence, in all cases in the left colon, underwent an emergency Hartmann's procedure, with a perioperative mortality rate of 35.7%.*

**CONCLUSIONS:** *In our experience, the site of colonic anastomosis represents the risk factor most strictly related to the anastomotic leak rate, while other technical factors seem weakly associated with leakage. A significantly high percentage of patients (65.6%) with anastomotic fistulas have medical comorbidities.*

**KEY WORDS:** Anastomotic leakage, Colonic anastomoses, Postoperative peritonitis.

### Introduction

In colorectal surgery, especially emergency surgery, sepsis is a frightening complication associated with mortal-

ity and morbidity rates that are still high although they have been greatly reduced during the last few decades, thanks to the improvement of surgical techniques and pre- and postoperative management. The complex interaction among pathogenic agents, the immune system and the infection site determines the extent of sepsis. When the immune system and the defense mechanisms of the peritoneal serosa work efficiently and there is no massive bacterial contamination, circumscribed peritonitis can occur, possibly with abscess formation. However the development of generalized peritonitis triggers the complex physiopathologic process called sepsis.

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The annual incidence of sepsis in the USA is approximately 400.000 cases, with a mortality rate of about 40%. In 30-50% of cases sepsis evolves into multi-organ insufficiency (MOF) with a mortality rate of 50-100%, depending on the number of organs involved. The aim of this retrospective analysis was to investigate the multiple factors which generate serious postoperative peritoneal infections and determine their prognostic value.

## Materials and methods

Between April 1995 and April 2005, 367 patients underwent colon resection for benign or malignant disease in the surgical division V, X, XI of the Policlinic of the Second University of Naples. Two hundred and thirteen (58%) patients were male and 154 (42%) female. Their average age was 67.2 years (range 33 – 88 years). One hundred and fifty (41%) patients had emergency surgery and 217 (59%) elective surgery. 290 patients (79%) were

affected by neoplastic pathology and 77 (21%) by benign pathology: Ninety-two (31,7%) of the neoplastic patients had emergency treatment and 198 (68.3%) had elective treatment. The location of the tumors in the emergency surgery patients was the left colon in 43 (46.7%), the right colon in 37 (40.2%), and the rectum in 12 (13,1%). The location of the tumors in the elective surgery patients was the left colon in 83 (41.9%), the rectum in 60 (30.3%) and the right colon in 55 (27.8%). Fifty-eight of the patients with benign pathology had emergency treatment consisting of 26 resections for intestinal ischemia, 12 for colonic volvulus, 8 for hernias or strangulated incisional hernias, 8 for traumatic and iatrogenic lesions, and 4 for diverticular hemorrhage. Nineteen of the patients with benign disease had elective treatment consisting of, 6 reversals of Hartmann's procedure, 6 recanalizations after traumatic lesions of the colon, 4 resections due to diverticulosis, and 3 segmental colonic resections to remove sessile tubulovillous polyps. Sixty-five (52,4%) out of the 124 anastomoses

TABLE I - *Materials and Methods*

Patients: 367 M:213 (58%)F: 154 (42%) Average Age 67.2 (range 33-88 yy)	Emergency Surgery 150 (41%)	Elective Surgery 217 (59%)
Right colon anastomoses: 124	65 (52,4%) 36 (55.4%): stapler 29 (44.6%): manually	59 (47,6%) 36 (61%): stapler 23 (39%): manually
Left colon anastomoses: 171	73 (42,7%) 52 (71,2%): stapler 21 (28,8%): manually	98 (57,3%) 76 (77,5%): stapler 22 (22,5%): manually
Colorectal anastomoses: 72	12 (16.7%) Mal Tum 12: stapler 12: ileostomy/colostomy.	60 (83.3%) Mal Tum 55 (91.6%): stapler 5 (8.4%): manually 11/60: ileostomy/colostomy
Neoplastic Pathology : 290 (79%)	92 (31%)  Tumor Location Left C: 43 (46.7%) Right C: 37 (40.2) Rectum: 12 (13%)	198 (68.3%)  Tumor Location Left C: 83 (41.9%) Right C:55 (27.7%) Rectum in 60 (30.3%)
Benign Pathology: 77 (21%)	58 resections for: 26: intestinal ischemia; 12: colonic volvulus; 8: hernias or strangulated incisional hernias; 8: traumatic/iatrogenic lesions. 4: diverticular hemorrhage	19: 6 reversals of Hartmann's procedure; 6 recanalizations after traumatic lesions; 4 resections due to diverticulosis; 3 segmental resections for sessile tubulovillous polyps.
Comorbidities: 75/367  (27.2%): blood transfusions ( $\geq 2$ units). (13.3%): malnutrition; (20.44%) diabetic; (11.7%) ischemic cardiomyopathy; (14,1%) chronic obstructive pulmonary disease (COPD)		

constructed after resection of the right colon were fashioned as part of an emergency procedure and 59 (47,6%) as part of an elective procedure. Seventy-three (42,7%) out of the 171 anastomoses constructed after resection of the left colon were fashioned as part of an emergency procedure and 98 (57,3%) as part of an elective procedure. Seventy-two colorectal anastomoses were constructed, all in patients with malignant tumors, 12 (16,7%) in emergency operations and 60 (83,3%) in elective operations. Fifty-five (91,6%) of the latter were fashioned with a stapler and 5 (8,4%) manually, 11 out of 60 with a protective ileostomy/colostomy. In the 12 emergency cases colorectal anastomoses were fashioned with a mechanical stapler followed by construction of a protective ileostomy/colostomy. Out of 124 ileocolic anastomoses, 65 were constructed as part of emergency surgery, 36 (55,4%) with a stapler and 29 (44,6%) manually, whereas 59 were constructed as part of elective surgery, 36 (61%) with a stapler and 23 (39%) manually. Out of 171 colic anastomoses, 73 were constructed as part of emergency surgery, 52 (71,2%), have been carried out with a stapler and 21 (28,8%) manually whereas 98 were constructed as part of elective surgery, 76 (77,5%) with a stapler and 22 (22,5%) manually. As far as comorbidities are concerned, 75/367 patients (20,4%) were diabetic; 52 /367 (14,1%) suffered from chronic obstructive pulmonary disease (COPD), 43/367 (11,7%) from ischemic cardiomyopathy, and 49/367 (13,3%) from malnutrition, as shown by serum levels of albumin < 3g/L. One hun-

dred out of 367 patients (27,2%) received blood transfusions ( $\geq 2$  units) (Table I).

## Results

In patients with anastomotic dehiscence after emergency surgery the perioperative mortality rate was 6.6% (10/150 patients), and in patients anastomotic dehiscence after elective surgery 3.6% (8/217 patients). Taking into consideration only moderate and severe fistulas the rate of anastomotic dehiscence was 8.7% (32/367 patients); 13,3% (20/150 patients) after emergency surgery and 5.5% (12/217 patients) after elective surgery. Dehiscence occurred in 7/124 (5,6%) of ileocolic anastomoses, 13/171 (7,6%) of colics anastomoses and 12/72 (16,6%) of colorectal ones. Twenty-one out of 32 patients with anastomotic dehiscence had one or more associated risk factors (65,6%). Out of the 32 anastomotic dehiscences observed, 21 were treated conservatively with NPT, anti-secretory drugs and ultrasound/CT guided drainage collections. Three of these patients subsequently underwent surgical treatment, due to the failure of the conservative therapy (2 Hartman procedures, 1 ileostomy). The other 11 dehiscences were localized to the remnant left colon, and were managed surgically, due to generalized peritonitis, with Hartmann's procedure. Perioperative mortality in the patients who underwent re-operation was 35,7% (5/14 patients). The cause of these deaths was the toxic-septic state following generalized peritonitis (Table II).

TABLE II - Results

	A/D-Em Surg. *	A/D-El Surg. **	Treatment	Treatment	D/L***	D/L***	D/L***
Perioperative Mortality	6.6% (10/150)	3.6% (8/217)					
A/D : 8,7% (32/367)							
(moderate - severe fistulas)	13,3% (20/150)	5,5% (12/217)	21 conservatively: NPT, anti-secretory drugs, ultrasound/CT guided drainage collections	11 (left colon): surgically, ( <i>generalized peritonitis with Hartmann's procedure</i> )	7/124 (5,6%) ileocolic an.	13/171 (7,6%) colics an.	12/72 (16,6%) colorectal an.
Twenty-one out of 32 patients with anastomotic dehiscence had one or more associated risk factors (65,6%).							

\*anastomotic dehiscence after emergency surgery = A/D-EmS

\*\*anastomotic dehiscence after elective surgery = A/D-EIS

\*\*\*Dehiscence Location = D/L

## Discussion

Anastomotic dehiscence after colorectal surgery is most commonly due to vascular factors and the more distal the anastomosis, the higher the incidence of dehiscence which is 1% after right hemicolectomy, 5% after left hemicolectomy, and reaches 8-10% in low or ultralow colorectal anastomoses. The frequency of this complication increases significantly in emergency colorectal surgery and in particular in surgery for bowel occlusion, (9-13% vs 4% in emergency vs elective surgery), due to visceral distension and, therefore, of a marked lack of homogeneity in the size of the stumps, as well as to a lack of mechanical preparation and the risk of fecal contamination during operation. Among the causes of anastomotic dehiscence both local and general factors can be identified. With regard to the latter, old age does not seem to constitute an important risk, however, according to various studies, an important role is played by certain pathological conditions that occur most frequently in older patients. The incidence of dehiscence triples in patients with COPD (9.5% against 2.9%); in particular, the insufficient alveolar ventilation and the consequent hypoxia and hypercapnia are a great obstacle to the processes of tissue repair. Experimental studies have demonstrated that hypoxia interferes with the hydroxylation of collagen fibrils, resulting in insufficient mechanical resistance<sup>3,4</sup>. Cardiocirculatory insufficiency, worsened by metabolic and electrolyte imbalances and also by the length of the operation, increases the risk of anastomotic dehiscence. The changes in microcirculation and a greater overall susceptibility of the patient to infection associated with diabetes mellitus (DM) favor anastomotic dehiscence. Insulin therapy does not seem to improve the result<sup>3-5</sup>. Other general factors that increase the risk of anastomotic dehiscence are: obesity, protein-calorie malnutrition, acute and massive anemia and blood transfusion, the latter because of the immunosuppressant effect, in particular when more than of two units of blood are transfused in 24 hours and with blood stored for more than 21 days<sup>3-6</sup>. It seems that pre- and post-operative enteral and parenteral nutrition can reverse the changes induced by malnutrition. As far as pharmacological therapy is concerned, the role of corticosteroids remains controversial. Some authors believe it would greatly increase the risk of anastomotic dehiscence (15.4% vs 3%), but others claim the opposite<sup>3-7</sup>. Clinical and experimental studies highlight that short-term administration of corticosteroids in high doses does not interfere with the processes of tissue repair, while the high administration of doses for long periods of time inhibits collagen synthesis and the phenomena of contraction, epithelialization and reshaping of the wound<sup>8-10</sup>. Chemo- and radiotherapy have antiproliferative effects on tumor cells with a high mitotic index and, consequently, also affect the cellular elements involved in the mitotic processes of wound healing. X-rays also affect tissue

trophism, whether neoplastic or not, compromising the microvasculature and inducing fibrotic phenomena<sup>11</sup>. Among the local factors favoring anastomotic dehiscence, closely related to surgical technique, those inherent to the vascularization of the stumps without doubt have a pre-eminent role. Internal blood flow represents the main factor in the recovery of anastomosis and an acute reduction of 10% of the circulating volume due to hemorrhage, significantly increases the risk of dehiscence<sup>12</sup>. Doppler flow meter analysis of the blood flow proximal and distal to colorectal anastomoses has shown a meaningful correlation between dehiscence and reduction of blood flow after vessel separation, (6.2% versus 16%, at the level of the rectal stump; 5.1% versus 12.9%, at the level of the proximal stump). It has been established that the clinical criterion of evaluation of stump oxygenation, i.e. rose color and the absence of pallor and cyanosis, is insufficient to guarantee that an anastomosis will remain intact. It remains to be seen whether routine use of the Doppler flow meter and examination tissue oxygenation can reduce the incidence of anastomotic dehiscence<sup>13</sup>. A precarious blood supply to the intestine before surgery and/or the devascularization of the stumps to be anastomosed in the course of the surgical procedure are definite risk factors for dehiscence. Anaesthesia can also interfere with the perfusion of the rectum, due to sympathetic blockade. In animals the execution of an epidural block increases the blood flow of 22% of the colon and in man some retrospective studies have suggested a reduction of anastomotic dehiscence in the patients subjected to epidural anaesthesia, although recent studies have not confirmed this data<sup>14,15</sup>. Errors in surgical technique are another important cause of anastomotic dehiscence and include: inadequate intestinal preparation, stumps facing the wrong way, hematoma formation near the suture line resulting in inadequate hemostasis, excessive use of the electrical scalpel near the anastomosis, and the presence of neoplastic infiltration of the margins. Tension at the suture line is another common error of surgical technique and a risk factor for rather obvious dehiscence. Stretching of the stumps hinders the repair processes not least because it reduces their vascularization<sup>3</sup>. As far as the method of constructing the anastomosis is concerned, mechanical or manual, a number of studies agree that manual and mechanical sutures are equally effective, if the purse-string suture is correctly placed. The same is valid for the latero-lateral or termino-terminal, or latero-terminal anastomoses<sup>16</sup>. Other errors of technique are, in the mechanical anastomoses, the wrong use of the purse-string in the realization of the tobacco pouch, a stapler not adapted to the diameter of the stumps, by visceral lacerations due to abrupt introduction and/or extraction of the stapler. The use of a stapler in the upper and middle rectum seems to guarantee a better anastomosis than manual suturing. Several studies have shown that for anal anastomoses mechanical suturing is preferable to manual suturing with muco-



sectomy because the suture line is more resistant, execution is simpler, and operative time is reduced<sup>17</sup>. Mechanical anastomoses constructed after anterior resection are associated with an average leak rate of 7-8%, which rises to 10-20% after ultra low anastomoses, even in the hands of experts in colorectal surgery<sup>18</sup>. Actually, it is the center of the anastomoses, rather than the manner in which it is fashioned, which is most closely linked to the occurrence of dehiscence. Colorectal anastomoses are at risk of failure in great part because of the technical difficulties connected with the narrow anatomical space of the pelvis, that makes the preparation of the stumps more complex<sup>19</sup>. Published studies on the use of the drains do not confirm that drains placed adjacent to the anastomosis have an important role in preventing anastomotic dehiscence. Actually, it has been reported that such drains facilitate dehiscence, though at the same time by evacuating blood/fluid collections, they reduce the risk of infected hematoma, which in its turn, is potentially responsible for suture dehiscence. The role of the peritoneal serosa in the healing of the interior of the anastomosis is controversial. It appears unquestionable that the consequences of extraperitoneal dehiscence of an anastomosis are more easily controlled and less serious than those of intraperitoneal dehiscence. The function of the omentum, in particular, would not be to provide a kind of bacteriological barrier, as many people think, but rather to improve the vascularization in the perianastomotic center, above all in the patients with serious arteriosclerosis. Since the consequences of anastomotic dehiscence depend on its clinical severity and different degrees of dehiscence have different prognostic implications, dehiscence is divided into three types, mild, moderate and severe<sup>20</sup>. This attempt at classification is intended to help surgeons decide whether immediate conservative therapy or reoperation is the most appropriate treatment. In cases of colonic fistula with low flow, i.e. < 500 ml/die, that are well drained with signs of mild peritoneal involvement or of localized peritonitis, without systemic infection, conservative treatment is usually adequate. Total parenteral nutrition, associated with the use of antisecretory drugs like octreotide and with aimed antibiotic therapy, generally leads to recovery without the necessity of reoperation. Most authors agree that more serious cases, for example fistula with flow > 500 ml/die, can also be managed conservatively if the patient's clinical condition remains satisfactory and there is an evident reduction in the flow from the drain. In such cases treatment can last for more than the 4-6 weeks usually required for stabilization of the dehiscence. On the contrary, reoperation will be only differed. Conservative treatment is always preceded by ultrasound or CT-guided percutaneous drainage of any fluid collections<sup>21</sup>. In the severe types of dehiscence with localized or diffuse peritonitis and moderate or severe systemic complications, surgical treatment cannot be avoided when conservative treatment is not feasible. The opera-

tions generally performed in these cases are: colostomy with exteriorization of the anastomosis, derivative ileostomy/colostomy, in the cases in which the dehiscence is not complete, or a Hartmann resection. It is essential to perform accurate peritoneal lavage, with aspiration of purulent exudate, removal of the necrotic tissue, opening of abscesses in the peritoneal recesses, abundant irrigation, and drainage of fluid from the peritoneal catheter<sup>22-26</sup>. The internal wall of the anastomoses (mucosal side) is, also in our experience, the risk factor most closely associated with anastomotic dehiscence, whereas other factors of a technical nature, such as the use of mechanical or manual sutures, end-to-end or lateral anastomosis, protective stoma, fibrin glue<sup>27-29</sup>, and drains do not appear to be unequivocally associated with an increase in the dehiscence rate. In a few cases there was no definite association between the general factors considered and the risk of anastomotic dehiscence, but we found an association with systemic disease such as COPD and DM, and with blood transfusions, in a significant percentage (65.6%) of our patients<sup>30-32</sup>. The greater incidence, reported in the literature, of fistulas of ileocolic anastomoses (5.6%) is linked to the prevalence of emergency operations for pathologies of the right colon, in which immediate restoration of intestinal continuity is routine<sup>33-36</sup>. In agreement with the data in the literature, protective stomas proved to be useful in the management of dehiscence of colorectal anastomoses in our patients, but not in its prevention. We fashioned a protective stoma not only in patients with ultralow colorectal anastomoses, but also in some emergency cases when there were doubts about the resistance of the sutures.

## Conclusions

In our experience, the site of colonic anastomosis represents the risk factor most strictly related to the anastomotic leak rate, while other technical factors seem weakly associated with leakage. A significantly high percentage of patients (65.6%) with anastomotic fistulas have medical comorbidities. Old age does not seem to constitute an important risk, but an important role is played by certain pathological conditions that occur most frequently in older patients. The incidence of dehiscence triples in patients with COPD (9,5% against 2.9%). Cardiocirculatory insufficiency, worsened by metabolic and electrolyte imbalances and also by the length of the operation, the susceptibility of the patient to infection associated with diabetes mellitus (DM), chemo- and radiotherapy increase the risk of anastomotic dehiscence. Other general factors that increase the risk of anastomotic dehiscence are: obesity, protein-calorie malnutrition, acute and massive anemia and blood transfusion, X-rays. We can conclude that the preoperative patient's comorbidities assessment plays a role as effective as the

one played by the site of colonic anastomosis in the genesis of anastomotic dehiscence.

### Riassunto

La sepsi peritoneale da deiscenza anastomotica rappresenta ancora oggi una delle principali cause di insuccessi nella chirurgia del colon-retto. Lo scopo di questo studio è di esaminare retrospettivamente una casistica multicentrica costituita da 367 pazienti sottoposti a chirurgia coloretale in dieci anni, analizzando i fattori generali e locali coinvolti nella genesi di deiscenze anastomotiche e considerando il loro specifico valore prognostico. Vengono considerati pazienti trattati chirurgicamente, sia in elezione che in urgenza, sia per patologia benigna che maligna. In questa serie casistica assume rilievo il sito anastomotico, oltre ad altri fattori tecnici ed a patologie mediche associate.

### References

- 1) Milevski WJ, Joehl RJ, Rege RW, Nahrwold DL: *Treatment of anastomotic leakage following low anterior colon resection*. Arch Surg, 1988; 123:968-71.
- 2) Montesani C, De Milito R, Chiappatone S, Narilli P, D'Amato A., Ribotta G: *Critical evaluation of the anastomoses in large bowel surgery: Experience in 533 cases*. Hepato-gastroenterology, 1992; 39:304-8.
- 3) Golub R: *A multivariate analysis of factors contributing to leakage of intestinal anastomoses*. J Am Coll Surg, 1997; 184:364-72.
- 4) Testini M, Scasso S, Lioitola L, et al.: *Comparison of oxidative phosphorylation in the anastomoses of the small and large bowel. An experimental study in the rabbit*. Eur Surg Res, 1998; 30:1-7.
- 5) Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parneix M: *Risk factors for anastomotic leakage after resection of rectal cancer*. Br J Surg, 1998; 85:355-58.
- 6) Mynster T, Nielsen HJ: *The impact of storage time of transfused blood on postoperative infectious complications in rectal cancer surgery. Danish RANX05 Colorectal Cancer Study Group*. Scand J Gastroenterol, 2000 35(2):212-17.
- 7) Jex RK., Van Herden JA., Wolf BG: *Gastrointestinal anastomoses. Factors affecting early complications*. Ann Surg, 1992; 206:138-41.
- 8) Cohen IK, Diegelmann RF, Johnson ML: *Effect of corticosteroids on collagen synthesis*. Surgery, 1977; 82:15.
- 9) Eubanks TR, Greenberg JJ, Dobrin PB, Harford FJ, Gamelli RL: *The effects of different corticosteroids on the healing colon anastomoses and cecum in a rat model*. Am Surg, 1997; 63:266.
- 10) Brown JS, Lee N, Lowe D, Browne RM: *Effect of short-term high dose of steroids on the healing of microvascular anastomoses in a rabbit model. Pilot study*. Br J Maxillofac Surg, 2000; 38:167.
- 11) De Waard JW, Wobbles T, van der Linden CJ, Hendriks T: *Retinol may promote fluorouracil-suppressed healing of experimental intestinal anastomoses*. Arch Surg, 1995; 130:959-65.
- 12) Whitaker BL, Dixon RA, Greatorex G: *Anastomotic failure in relation to blood transfusion and blood loss*. Proc Roy Soc Med, 1970; 63:751.
- 13) Vignali A, Gianotti L, Braga M, Radaelli G, Malvezzi L, Di Carlo V: *Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak*. Dis Colon Rectum, 2000; 43(1):76-82.
- 14) Kato M, Suzuki H, Murakami M, Akama M, Matsukawa S, Hashimoto Y: *Elevated plasma levels of interleukin-6, interleukin-8 and granulocyte colony-stimulating factor during and after major abdominal surgery*. J Clin Anesth, 1997; 9(4):293-98.
- 15) Ryan P, Schweitzer S, Collopy B, Taylor D: *Combined epidural and general anesthesia versus general anesthesia in patients having colon and rectal anastomoses*. Acta Chir Scand Suppl, 1989; 550:146-69; discussion 149-51.
- 16) Secco GB, Fardelli R, Rovida S, et al.: *Studio retrospettivo su 116 casi di anastomosi coloretali, manuali e meccaniche, per cancro del retto*. Chirurgia, 1996; 9:92-98.
- 17) The French Association for Surgical Research, Fingerhut A, Hay JM, Elhadad A, Lacaine F, Flamant Y: *Supraperitoneal colorectal anastomoses: hand-sewn versus circular staples. A controlled clinical trial*. Surgery, 1995; 118(3):479-85.
- 18) Karanjia ND, Corder AP, Bearn P, Heald RJ: *Leakage from stapled low anastomoses after total mesorectal excision for carcinoma of the rectum*. Br J Surg, 1994; 81(8):1224-26.
- 19) Pernacchia A, Viola V, Sarli L, Pietra N: *Deiscenze anastomotiche dopo resezione del colon sinistro e del retto per cancro*. Atti Soc It Chir Roma; 1994. vol.1. Roma: Ediz L. Pozzi, 1994; 59-71.
- 20) Gargiulo A, Benedetti Valentini G, Caserta G, Gargiulo A jr., Manzi F: *Le peritoniti postoperatorie nella chirurgia coloretale*. Atti Soc It Chir 1998, Roma Vol. II. Roma: Ediz L. Pozzi, 1998; 31-38.
- 21) Longo WE, Milson JW, Lavery IC, Church JC, Oakley JR, Fazio VW: *Pelvic abscess after colon and rectal surgery. What is optimal management*. Dis Colon Rectum, 1993; 36:936-41.
- 22) Hirschberg A, Stein M, Adar R: *Reoperation: planned and unplanned*. 1: Surg Clin North Am, 1997; 77(4):897-907.
- 23) Schmidt O, Merkel S, Hohenberger W: *Anastomotic leakage after low rectal stapler anastomosis: Significance of intraoperative anastomotic testing*. Eur J Surg Oncol, 2003; 29(3):239-43.
- 24) Abete M, Ronchetti V, Casano A, Pescio G: *Anastomotic leakage after traditional surgery of the colon and rectum* Minerva Chir, 2003; 58(2):167-74
- 25) Brigand C, Rohr S, Meyer C: *Colorectal stapled anastomosis: results after anterior resection of the rectum for cancer*. Ann Chir, 2004; 129(8):427-32. French.
- 26) Matthiessen P, Hallbook O, Andersson M, Rutegard J, Sjobahl R.: *Risk factors for anastomotic leakage after anterior resection of the rectum*. Colorectal Dis, 2004; 6(6):462-69.
- 27) Ruggiero R, Procaccini E, Gili S, Cremone C, Parmeggiani D, Conzo G, Docimo L, Sparavigna L, Gubitosi A, Docimo, G, Sanguinetti A, Avenia N: *New trends on fibrin glue in seroma after axillary lymphadenectomy for breast cancer*. Giornale di Chirurgia, 2009; 30:305-310.
- 28) Agnifili A, Schietroma M, Carloni A, Mattucci S, Caterino G, Lygidakis NJ, Carlei F: *The value of omentoplasty in protecting colorectal anastomosis from leakage. A prospective randomized study in 126 patients*. Hepatogastroenterology, 2004; 51 (60):1694-697.

- 29) Buie WD, Maclean AR, Attard JA, Brasher PM, Chan AK: *Neoadjuvant chemoradiation increases the risk of pelvic sepsis after radical excision of rectal cancer.* Dis Colon Rectum, 2005; 48 (10): 1868-874.
- 30) Yeh CY, Changchien CR, Wang JY, Chen JS, Chen HH, Chiang JM, Tang R: *Pelvic drainage and other risk factors for leakage after elective anterior resection in rectal cancer patients: A prospective study of 978 patients.* Ann Surg, 2005; 241 (1):9-13.
- 31) Eriksen MT, Wibe A, Norstein J, Haffner J, Wiig JN: *Norwegian Rectal Cancer Group: Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients.* Colorectal Dis, 2005; 7(1):51-57.
- 32) Wong NY, Eu KW: *A defunctioning ileostomy does not prevent clinical anastomotic leak after a low anterior resection: A prospective, comparative study.* Dis Colon Rectum, 2005; 48(11):2076-79.
- 33) Petitti T, Lippolis G, Ferrozzi L: *A serious complication in colorectal surgery: Anastomotic leakage. Our experience.* G Chir, 2005; 26(10):371-74.
- 34) Hsu TC: *Comparison of one-stage resection and anastomosis of acute complete obstruction of left and right colon.* Am J Surg, 2005; 189(4):384-87.
- 35) Hirano Y, Omura K, Tatsuzawa Y, Shimizu J, Kawaura Y, Watanabe G: *Tissue oxygen saturation during colorectal surgery measured by near-infrared spectroscopy: Pilot study to predict anastomotic complications.* World J Surg, 2006; 30(3):457-61.
- 36) Matthiessen P: *Risk factors for anastomotic leakage after anterior resection of the rectum.* Colorectal Dis, 2006; 8(4):366.

