

Evaluation of surgery risk factor associated to antithrombotic therapy in patients who underwent colorectal surgery



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BACKGROUND: *Use of antiplatelet therapy in western people is common. The risk of bleeding related to surgical procedure or invasive procedure is higher. We want to analyse the correlation between colorectal surgery, antiplatelet therapy and postoperative surgical complications.*

METHODS: *We categorized: 176 cases treated for colorectal cancer and we recorded the following data: type of surgery, body mass index (BMI), haemoglobin value (Hb); preoperative prothrombin time (PT) and blood transfusions pre and postoperative and during surgery. The analysis focused on two groups: patients who received antiplatelet therapy (AT - antiplatelet therapy) and patients who didn't receive this therapy (NAT - not antiplatelet therapy).*

RESULTS: *In the group of patients who underwent right hemicolectomy, haemoglobin values were lower in patients who received antithrombotic therapy than in patients who didn't receive this therapy with a statistical significance ($p < 0,05$); the same datum resulted in patients who underwent left hemicolectomy. Normal weight patients that received antiplatelet therapy had lower values of haemoglobin without statistical significance (p value not significant). Overweight patients who underwent therapy with antiplatelet agents had lesser Hb value than group that didn't performed this therapy ($p < 0,05$). Patients who received AT showed a bigger percentage of blood transfusions regardless of type of surgery than the second group with statistical significance. Normal weight patients showed a different incidence of blood transfusions between patients who underwent antiplatelet therapy (50%) and patients who didn't receive this therapy (29%) with statistical significance ($p < 0,05$). Overweight patients didn't present this significant difference. We analyzed the incidence of post-operative complications in normal weight patients and overweight patients and we showed that the incidence of complications, both minor and major, was higher in patients who underwent antiplatelet therapy than in the second group regardless of weight.*

CONCLUSIONS: *Antiplatelet therapy in patients who underwent invasive surgery changes the incidence of some risk factors, such as bleeding, and of post-operative complications. This result underlines the importance of careful handling and preparation in patients receiving antithrombotic agents that have to undergo invasive surgery.*

KEY WORDS: Antithrombotic therapy, Bleeding, Colorectal Surgery, Risk factor

Introduction

Use of antiplatelet therapy in Western countries concerns several million people only in the USA¹. Every year 10%

of patients receiving antithrombotic agents undergo invasive surgery that requires temporary suspension of this therapy^{2,3}. Randomized control trials about this matter are still limited and the percentage of bleeding related to all surgical procedures is not exactly defined yet⁴. In Europe the assessment of the risk of bleeding in patients undergoing surgery or invasive procedures was considered by the Guidelines of the Italian Society of Haemostasis and Thrombosis (SISCT)⁵ and by the Guidelines of British Committee for Standards in Haematology (BCSH)⁶. The decision to suspend

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antiplatelet therapy in a patient that will undergo invasive procedures, such as surgery for colorectal diseases, must be the perfect blend between bleeding risk, related to procedure in case of not suspension, and risk in case of suspension of antithrombotic agents⁴. Patients with cancer have a high peri-procedural thrombotic risk due to a procoagulant activity of the tumour, a hormone therapy, the use of angiogenesis inhibitors, a possible preoperative radiotherapy and the presence of central venous catheters⁷; however these patients present a high risk of bleeding related to antiplatelet therapy, chemotherapy, thrombocytopenia and hemorrhage from tumor tissue⁸. In patients with coronary stent that receive dual antiplatelet therapy the cardiovascular risk must be related to timing of possible surgery within the first year from the beginning of this therapy when mortality risk is high⁹. Without universal risk stratification, invasive procedures with bleeding rate of 1,5 % or made/realized in some specific sites (such as intracranial, intraspinal, intraocular, retroperitoneal, intrathoracic and pericardial space) were considered as high risk treatments¹⁰. In colorectal surgery bleeding is a dreaded complication and it is an important cause of morbidity^{11,12}. Blood transfusions in surgical patients are related to non-infectious aftermaths and they are very expensive for National Health System^{13,14}. In this paper we want to analyse the correlation between colorectal surgery, antiplatelet therapy and post-operative surgical complications; we detected data according to Clavien-Dindo Classification of Surgical Complications¹⁵ based on the therapy used to correct a specific complication. We considered both intraoperative and postoperative complications. In the first group we included bleedings, bowel lesions and injury of genitourinary system. The postoperative complications considered are hemorrhage, anastomotic leakage with abdominal fluid collections, adynamic ileus and infection of surgical incision/laparotomy¹⁶⁻¹⁸. Presence of comorbidities, age, obesity, nutritional status of patient are important independent factors in the assessment of surgical risk.

Material and Methods

We established a dedicated retrospective database to analyze patients submitted to colorectal surgery at OU

General Surgery and Organ Transplantation, University Hospital of Parma, from January 2011 to September 2013 after permission to consult operative register and to collect data by Hospital Health Direction. We retrospectively categorized 176 patients and we recorded the following data: type of surgery, body mass index (BMI). We also collected preoperative haemoglobin value (Hb); preoperative prothrombin time (PT) and blood transfusions pre, postoperative and during surgery. The analysis focused on two groups: patients who received antiplatelet therapy (AT - antiplatelet therapy) and patients who didn't receive this therapy (NAT - not antiplatelet therapy).

STATISTICAL ANALYSIS

We divided post-operative complications in minor and major ones and we analysed post-operative course. Patients with missing data were excluded. The median was used for analysis of data; the statistical difference between two groups was analysed by means of the non parametric Mann-Whitney U test. T test was performed to compare different groups. P - value < 0,05 was considered statistically significant.

Results

Patients were divided in three groups based on type of surgery: patients who underwent right emicolectomy (group 1; 102 cases); patients who underwent left emicolectomy (group 2; 51 cases) and patients who underwent low anterior resection of the rectum or abdominoperineal amputation (group 3; 20 cases). Group three was excluded from the analysis because of a very low number of cases. We also divided patients in other three groups based on BMI: 75 normal weight patients (median of the BMI: 22.86 ± 7.78); 75 overweight patients (median of the BMI: 26.92 ± 1.23) and 23 obese patients (median of the BMI: 32.37 ± 1.83). We removed this third group from the study because of the low number of cases of obesity. Every group considered was divided considering patients who received antithrombotic/antiplatelet therapy (AT) and patients who didn't receive this therapy (NAT). Table I shows the data result-

TABLE I - Correlation between type of surgery, preoperative haemoglobin value and preoperative prothrombin time.

	Hb (g/dL)		PT (sec.)	
	AT	NAT	AT	NAT
Right emicolectomy	11.2 ± 1.6 *	12.5 ± 1.9 *	1.09 ± 0.18	1.02 ± 0.08
Left emicolectomy	11.7 ± 1.7 **	12.9 ± 1.8 **	1.1 ± 0.10	1.01 ± 0.07

Legend: Hb: preoperative hemoglobin value; PT: preoperative prothrombin time; AT: patients who received antiplatelet therapy; NAT: patients who didn't receive this therapy; * p < 0.05; ** p < 0.05.

TABLE II - Correlation between body mass index, preoperative haemoglobin value and preoperative prothrombin time.

	Hb (g/dL)		PT (sec.)	
	AT	NAT	AT	NAT
Normal weight	11,7 ± 1,3	12,3 ± 1,7	1,06 ± 0,08	1,01 ± 0,08
Overweight	11,2 ± 1,9 *	12,8 ± 1,9 *	1,13 ± 0,11	1,01 ± 0,08

Legend: Hb: preoperative hemoglobin value; PT: preoperative prothrombin time; AT: patients who received antithrombotic/antiplatelet therapy; NAT: patients who didn't receive this therapy; * p < 0,05.

TABLE III - Correlation between type of surgery and blood transfusions in two groups analyzed. N: number of patients.

	Patients (N)		Blood transfusions	
	AT	NAT	AT	NAT
Right emicolectomy	27	75	41 %*	19 %*
Left emicolectomy	13	38	38 %**	18 %**

Legend: AT: patients who received antithrombotic/antiplatelet therapy; NAT: patients who didn't receive this therapy; * p < 0,05; ** p < 0,05.

TABLE IV - Correlation between body mass index and blood transfusions. N: number of patients; AT: patients who received antithrombotic/antiplatelet therapy.

	Patients (N)		Blood transfusions	
	AT	NAT	AT	NAT
Normal weight	24	51	50 % * (a)	29 % *(b)
Overweight	19	56	16 % **(a)	16 % **(b)

Legend: NAT: patients who didn't receive this therapy; * p < 0,05; ** p < 0,05; (a) p < 0,05;(b)p<0,05..

ed from the correlation between type of surgery, preoperative hemoglobin (Hb) value and preoperative prothrombin time (PT). In the group of patients who underwent right emicolectomy, haemoglobin values were lower in patients who received antithrombotic therapy than in patients who didn't receive this therapy with a statistical significance (p < 0,05); the same datum resulted in patients who underwent left emicolectomy. No significant differences about type of surgery resulted between two groups analyzed (p value not significant). The correlation between BMI, Hb and PT was also performed (Table II). Normal weight patients that received antiplatelet therapy had lower values of haemoglobin without statistical significance (p value not significant). Overweight patients who underwent therapy with antithrombotic/antiplatelet agents had lesser Hb value than group that didn't performed this therapy (p < 0,05). Table III shows the relationship between type of surgery and blood transfusions. Patients who received AT showed

a bigger percentage of blood transfusions regardless of type of surgery than the second group with statistical significance. We also described the correlation between BMI and blood transfusions (Table IV). Normal weight patients showed a different incidence of blood transfusions between patients who underwent antiplatelet therapy (50%) and patients who didn't receive this therapy (29%) with statistical significance (p < 0,05). Overweight patients didn't present this significant difference. In both two groups analyzed (AT and NAT) normal weight patients showed a bigger incidence of blood transfusions than overweight (p < 0,05). We didn't find any significant differences between post-operative complications, type of surgery (left or right emicolectomy) and AT or NAT (p value not significant); we divided complications in two groups: minor and major ones but we didn't see any significant differences between the groups analyzed (Table V). We analyzed the incidence of post-operative complications in normal weight patients and overweight

TABLE V - Correlation between type of surgery and type of complications in two groups analyzed. N: number of patients.

	Patients (N)		Major complications		Minor complications	
	AT	NAT	AT	NAT	AT	NAT
Right emicolectomy	27	75	15%	5%	19%	12%
Left emicolectomy	13	38	15%	5%	8%	13%

Legend: AT: patients who received antithrombotic/antiplatelet therapy; NAT: patients who didn't receive this therapy.

TABLE VI - Correlation BMI and post-operative complications. N: number of patients; AT: patients who received antithrombotic/antiplatelet therapy.

	Patients (N)		Post-operative complications (minor and major)	
	AT	NAT	AT	NAT
Normal weight	24	51	38% *	12% *
Overweight	19	56	37% **	13% **

Legend: NAT: patients who didn't receive this therapy. * p <.0.05; ** p < 0.05

patients and we showed that the incidence of complications, both minor and major, was higher in patients who underwent antiplatelet therapy than in the second group regardless of weight (Table VI). We didn't find this significant correlation between BMI, AT or NAT, major or minor complications.

Conclusions

Some Authors ¹⁹⁻²² declared that antiplatelet therapy in patients who underwent invasive surgery changes the incidence of some risk factors, such as bleeding, and of post-operative complications. In our paper we reported that haemoglobin value changed according to antiplatelet therapy but we didn't find any significant correlation between Hb, BMI and type of surgery. We observed lower Hb value in patients that underwent right emicolectomy compared to patients that underwent left emicolectomy and we ascribed this result to clinical presentation of right colon cancer. Intra and post-operative blood transfusions were changed from therapy with antithrombotic agents but weren't modified from type of surgery. In literature overweight patients present a higher risk of blood transfusions than normal weight cases ²³⁻²⁷; in this study we singly showed that normal weight patients presented a higher incidence of blood transfusions without any correlation with antiplatelet therapy and type of surgery. The relation between postoperative complications and BMI is connected to the antiplatelet therapy with a significant difference ²⁰⁻²⁴. Antiplatelet therapy defines Hb value and its correlation with blood transfusions and postoperative com-

plications. This result underlines the importance of careful handling and preparation in patients receiving antithrombotic agents that have to undergo invasive surgery.

Riassunto

I trattamenti antiplatelettrici sono comuni nel mondo occidentale ed il rischio di sanguinamento correlato a procedure chirurgiche o comunque invasive è di conseguenza elevato e pertanto abbiamo voluto analizzare la correlazione tra la chirurgia del colon-retto, la terapia antiplatelettrica e le complicanze chirurgiche postoperatorie. Sono stati studiati 176 pazienti operati per tumori del colon-retto considerando i seguenti dati: tipo di intervento chirurgico, l'indice di massa corporea (BMI), il valore dell'emoglobina (Hb); PT preoperatorio e le trasfusioni di sangue pre e post-operatorie e durante lo stesso intervento chirurgico. L'analisi si è concentrata su due gruppi: pazienti sottoposti a trattamento antiplatelettrico (AT: terapia antiaggregante) e pazienti non trattati (NAT: non terapia antiaggregante platelettrica). Nei gruppi di pazienti sottoposti a emicolectomia destra, i valori di emoglobina erano più bassi nei pazienti che hanno ricevuto la terapia antitrombotica rispetto ai pazienti che non hanno ricevuto questa terapia, con una significatività statistica (p <0,05); dati analoghi sono stati osservati nei pazienti sottoposti a emicolectomia sinistra. I pazienti di peso normale trattati con terapia antiaggregante avevano valori più bassi di emoglobina senza significatività statistica (valore di p non significativo).

I pazienti in sovrappeso sottoposti a trattamento antiaggregante hanno presentato valori di Hb inferiori a quelli non trattati ($p < 0,05$).

La percentuale di emotrasfusione è risultata maggiore nei pazienti sottoposti a trattamento antiaggregante (AT) a prescindere dal tipo di intervento chirurgico rispetto al secondo gruppo con significatività statistica.

Tra i pazienti normopeso si è registrata una diversa incidenza di trasfusione di sangue nei pazienti trattati con AT (50%) e quelli non trattati (29%) con un significato statistico ($p < 0,05$), mentre i pazienti in sovrappeso non hanno presentato questa significativa differenza.

È stata analizzata l'incidenza di complicanze post-operatorie in pazienti di peso normale e pazienti in sovrappeso e abbiamo rilevato l'incidenza di complicanze, sia minori che maggiori, è stata più alta nei pazienti sottoposti a terapia antiaggregante rispetto al secondo gruppo indipendentemente dal peso.

In conclusione, la terapia antiaggregante in pazienti sottoposti ad interventi chirurgici invasivi cambia l'incidenza di alcuni fattori di rischio, come il sanguinamento e le complicanze post-operatorie. Questo risultato sottolinea l'importanza di una corretta manipolazione e preparazione nei pazienti trattati con agenti antitrombotici che devono subire un intervento chirurgico invasivo.

References

1. Roger VL, Go AS, Lloyd J, et al: *Heart disease and stroke statistics-2012 update: A report from the American Heart Association*. Circulation, 2012; 125(1):e2-e220.
2. Douketis JD, Spyropoulos AC, Spence FA, et al.: *Perioperative management of antithrombotic therapy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physician Evidence based Clinical practice Guidelines*. Chest, 2012; 141:1077-80.
3. Illuminati G, Ceccanei G, Pacilè MA., et al.: *Dual antiplatelet treatment in patients candidates for abdominal surgery*. Ann Ital Chir, 2013; 84:291-94.
4. Baron TH, Kamath PS, McBane RD, et al.: *Antithrombotic therapy and Invasive Procedures*. N Engl J Med, 2013; 369:1079-80.
5. Cosmi B, Alatri A, Cattaneo M, et al.: *Assessment of the risk of bleeding in patients undergoing surgery or invasive procedures: guidelines of the Italian Society for Haemostasis and Thrombosis (SISST)*. Thromb Res, 2009; 124:e6-e12.
6. Chee YL, Crawford JC, Watson HG, Greaves M: *Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Hematology*. Br J Haematol, 2008; 140:496-504.
7. McBane RD, Wysokinski WE, Daniels PR, et al.: *Periprocedural anticoagulation management of patients with venous thromboembolism*. Arterioscler Thromb Vasc, Biol, 2010; 30:442-48.
8. Lyman Gh and K.NM: *Prevention and treatment of venous thromboembolism among patients with cancer: the American Society of Clinical Oncology Guidelines*. Thromb Res, 2010; 125:120-27.
9. Kleiman LS: *Grabbing the horns of a dilemma: The duration of dual antiplatelet therapy after stent implantation*. Circulation, 2012; 125:1967-970.
10. Eisen GM, Baron TH, Dominitz JA, et al.: *Guideline on the management of anticoagulation and antiplatelet therapy for endoscopic procedures*. Gastrointest Endosc, 2002; 55:775-79.
11. Karkouti K, Dattilo KM: *Perioperative hemostasis and thrombosis*. Can J Anaesth, 2006; 53:1260.
12. Karkouti K, Wijeyesundera DN, Yau TM, et al.: *The independent association of massive blood loss with mortality in cardiac surgery*. Transfusion, 2004; 44:1453.
13. Hendrickson JE, Hillyer CD: *Noninfectious serious hazards of transfusion*. Anesth Analg, 2009; 108:1499.
14. Vincent JL, Baron JF, Reinhart K, et al.: *Anemia and blood transfusion in critically ill patients*. JAMA, 2002; 288:1499-507.
15. Dindo D, Demartines N, Clavien PA: *Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey*. Ann Surg, 2004; 240:205-13.
16. Artinyan A, Nunoo-Mensah JW, Balasubramaniam S, et al.: *Prolonged postoperative ileus definition, risk factors, and predictors after surgery*. World J Surg, 2008; 32:1495-1500.
17. Klotz HP, Candinas D, Platz A, et al.: *Preoperative risk assessment in elective general surgery*. Br J Surg, 1996; 83:1788-791.
18. Longo WE, Virgo KS, Johnson FE, et al.: *Risk factors for morbidity and mortality after colectomy for colon cancer*. Dis Colon Rectum, 2000; 43:83-91.
19. Singla S, Sachdeva R, Uretsky BF: *The risk of Adverse cardiac and Bleeding Events following non cardiac surgery relative to antiplatelet therapy in patients with prior percutaneous coronary intervention*. J Am Coll Cardiol; 2012; 2005-16.
20. Fujikawa T, Tanaka A, Abe T, et al.: *Does antiplatelet therapy affect outcomes of patients receiving abdominal laparoscopic surgery? Lessons from more than 1000 laparoscopic operations in a single tertiary referral hospital*. Am Coll Surg, 2013; 217(6):1044-53.
21. Fujikawa T, Tanaka A, Abe T, et al: *Effect of antiplatelet therapy on patients undergoing gastroenterological surgery. Thromboembolic risks versus bleeding risks during its perioperative withdrawal*. World J Surg, 2015; 39(1):139-49.
22. Baron HT, Kamath PS, Mc Bane RD: *Management of antithrombotic therapy in patients undergoing invasive procedures*. N Engl J Med, 2013; 368:2113-124.
23. Dostalík J, Martinek L, Vaura P, et al: *Laparoscopic colorectal surgery in obese patients*. Obes Surg, 2005; 15(9):1328-331.
24. Pikarsky AJ, Saida Y, Yamaguchi T, et al: *Is obesity a high risk factor for laparoscopic colorectal surgery?* Surg Endosc, 2002; 16(5):855-58.
25. Delaney CP, Pokala N, Senagore AJ, et al.: *Is laparoscopic colectomy applicable to patients with body mass index >30? A case matched comparative study with open colectomy*. Dis Colon Rectum, 2005; 48(5):975-81.
26. Hoer J, Lawong G, Klinge U, Schumpelick U: *Factors influencing the development of incisional hernia. A retrospective study of 2983 laparotomy patients over a period of 10 years*. Chirurg, 2002; 73(5):474-80.
27. Smith RL, Bohl JK, McElearney ST, et al.: *Wound infection after elective colorectal resection*. Ann Surg, 2004; 239(5):599-607.