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## Original Article

# The influence of metabolic syndrome in the outcomes of colorectal cancer patients

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## ABSTRACT

**Aims:** Determine the influence of metabolic syndrome and its different components in the outcomes of colorectal cancer surgery at 30 days.

**Materials and methods:** Prospective study that included all patients submitted to elective colorectal cancer surgery between August 2015 and August 2016 at Hospital de Braga. Clinical and laboratory parameters evaluated pre-operatively were: central obesity, blood pressure, fasting glucose, triglycerides levels and HDL cholesterol levels. Any complications during the first 30-days after surgery were recorded (readmission, reintervention, anastomotic dehiscence, morbimortality).

**Results:** One hundred and thirty-four patients were included. Metabolic syndrome was diagnostic in 40.7% of patients with the ATPIII definition, 67.5% with the AHA definition and 67.0% with the IDF definition. At 30 days after colorectal cancer surgery, 73.1% patients don't have any complication, 15.7% have minor complications (grade I/II of Clavien-Dindo classification), 11.1% have major complications (grade III/IV/V of Clavien-Dindo classification) and 1.5% have died from surgical complications (grade V of Clavien-Dindo classification). The statistic analysis didn't reveal any association between MS, or its different components, and surgical outcomes.

**Conclusion:** This study seems to indicate that metabolic syndrome don't have any influence in surgical outcomes of colorectal cancer surgery.

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## 1. Introduction

The terms “metabolic syndrome” (MS) stand for a cluster of interrelated risk factors of metabolic origin that have been proved to predict a higher risk of atherosclerotic cardiovascular disease as well as type 2 diabetes mellitus expressing, this way, its clinical importance. With a prevalence of approximately 24,6–30,9% in Europe [1] the development of this syndrome appears to be directly related to abdominal obesity and insulin resistance [2].

Since its initial description (approximately 80 years ago) [1] many different definitions have been proposed by several institutions, but they all agree on the same basic components, namely hypertension, dyslipidemia, insulin resistance and central obesity.

The most popular definitions are those from National Cholesterol Education Program – Third Adult Treatment Panel (NCEP-ATPIII), or just ATPIII, from 2001 [3], the International Diabetes Federation (IDF), from 2005 [4], and, finally, the American Heart Association/National Heart Lung and Blood Institute (AHA/NHLBI), from also 2005 [2].

Besides the cardiovascular consequences of the metabolic syndrome, in several cohort studies and meta-analyses, this entity has been proven to increase cancer risk in general [5,6] with major effects on the gastrointestinal tract, namely increasing the risk of non-neoplastic gastrointestinal disorders, precursor lesions and CRC itself [7]. This relationship between metabolic syndrome and the risk of colorectal cancer is at the moment supported by a large number of studies [1,8,9], and this linkage is mainly explained by abdominal obesity and insulin resistance with a multifactorial mechanism of carcinogenesis involving the action of adipokines, inflammatory cytokines, adiponectin, leptin, IGF-1 and others [1].

Colorectal cancer represents an important health issue, as being the third most common cancer in men and the second in women worldwide (10.0% and 9.2% of the total, respectively) [10]. These

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numbers seem to be rising dramatically worldwide due to urbanization, aging, diet changes and lifestyle [11].

At least one study of our knowledge has already proved the deleterious influence of MS on CRC prognosis, with significantly shorter survival and higher recurrence and liver metastasizing rates, implying that MS is an important prognostic factor for CRC [12]. Moreover, this deleterious influence was also proved for the outcomes of CRC surgery at 30 days, showing a higher rate of postoperative complications and a longer hospital stay in patients classified with the AHA/NHLBI definition of MS. Also in this study from 2009, high blood pressure and high triglyceride levels were as well considered important risk factors for severe complications after CRC surgery, but only the presence of the cluster of metabolic abnormalities that constitute MS was proven to be an independent variable in the multivariate analysis, and not each individual component [13].

Concerning the influence of obesity in surgery outcomes, WC proved to be an independent risk factor for the development of parastomal hernia after permanent colostomy [14]. Another study published in 2013 proved that waist-hip-ration (as a measure of central obesity) had a significant influence in negative outcomes after CRC surgery, namely reoperation, medical complications, intraoperative complications and conversion to open approach, being this prediction effect superior to the one verified when measuring BMI and or WC [15]. Obesity was also associated with an increase in anastomotic leakage after rectal cancer resection [16].

Furthermore, a study concerning the financial implications of CRC surgery in obese patients has detected a significant increase in hospital expenses due to a higher rate of severe complications. The major contributors for these costs were wards stay, operations, and intensive care units [17].

The aim of this study is to determine the influence of MS and different components of MS (high fasting glucose, central obesity, high blood pressure, high triglycerides levels and low HDL cholesterol levels) in the outcomes of CRC surgery at 30 days (reintervention, readmission, dehiscence and morbimortality).

## 2. Methods

### 2.1. Study oversight and patients inclusion

This study included all the patients with a confirmed diagnosis of colorectal adenocarcinoma who underwent elective surgery at Hospital de Braga during August 2015 till August 2016. Patients who presented evidence of metastasis before or at surgery, necessity of removal of other organs due to tumor invasion, synchronous tumors or history of other malignant tumors within 5 years, history of familial adenomatous polyposis and hereditary non-polyposis colorectal carcinoma were excluded.

### 2.2. Data collection

At the first moment of evaluation, during pre-operative consultation, data were collected concerning patient's age, gender, history of arterial hypertension, diabetes mellitus, dyslipidemia, prior neoplasms, usual medication (with special concern for hypertension, diabetes, high triglycerides and low HDL cholesterol specific treatments) and family history of neoplasms. On the day prior to their admission to the hospital for surgery, the patients were requested to present themselves at Clinical Academic Center at Hospital de Braga for an anthropometric evaluation, carried out, all times, by the same nurse, which included height, weight and waist circumference measurement, as well as collection of blood samples for evaluation of fasting glucose, HDL cholesterol and triglycerides levels. During a period of 30 days following surgery, data about complications were collected and registered, namely

morbimortality, readmission, reintervention and anastomotic dehiscence. Morbimortality was posteriorly classified according to Clavien-Dindo's classification [18].

### 2.3. Statistical analysis

Statistical analysis was performed using SPSS – Statistical Package for the Social Science Program, version 23.

Descriptive statistics are presented as absolute frequencies (n) and relative (%) for categorical variables, and mean (M) and standard deviation (SD), or median (Mdn) and interquartile ranges, for quantitative variables, depending on whether or not symmetry of the distributions was ensured. The chi-square test was used to identify associations between dichotomous outcomes (morbimortality, dehiscence, reintervention and readmission) and the independent variables. When the maximum assumed 20% of cells with the expected frequency of less than 5 was exceeded, Fisher's test ( $2 \times 2$  tables) was used. The Mann-Whitney test was used to compare the outcome measured on an ordinal scale (Morbimortality according to Clavien-Dindo classification) with the independent variables. Finally, logistic regressions were used to measure the risk of the independent variables on the dichotomous outcomes. The significance level for rejection of  $H_0$  was 5% ( $p < 0.05$ ).

### 2.4. Ethical issues

The present study was approved by the Ethic Committee of Hospital de Braga. The investigators made sure to safeguard the anonymity and confidentiality of all the participants. A written informed consent was obtained from each patient.

## 3. Results

The present study included a sample of 134 patients with CRC diagnoses, with a mean age of 67.91 years old, 82 males and 52 females. 46 (40.7% in 113) of these patients were diagnoses with MS according to the ATPIII definition, 79 (67.5% in 117) according to the AHA definition and 71 (67.0% in 106) according to the IDF definition. These data are shown in Table 1. We were not able to collect the necessary information for these diagnoses in some of the patients (ND in the table), most often by absence of the patient from the appointments with the nurse for measurement of anthropometric parameters and blood samples collection.

**Table 1**  
Sample characterization; ND = No data.

	Statistics
Age M (SD)	67.91 (12.94)
Gender n (%)	
M	82 (61.2%)
F	52 (38.8%)
MS n (%)	
ATPIII Definition	n = 113
No	67 (59.3%)
Yes	46 (40.7%)
ND	21
AHA Definition	n = 117
No	38 (32.5%)
Yes	79 (67.5%)
ND	17
IDF Definition	n = 106
No	35 (33.0%)
Yes	71 (67.0%)
ND	28

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