Hypertension and chronic kidney disease is highly prevalent in elderly patients with colorectal cancer undergoing primary surgery

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Abstract

Background. Colorectal cancer (CRC) is a common and lethal disease. Hypertension is the most commonly reported comorbidity among cancer patients. Data on its incidence and prevalence is very scarce.

Objectives. The aim of the study was to evaluate the prevalence of hypertension and chronic kidney disease (CKD) in a cohort of 100 consecutive patients with CRC undergoing primary surgical treatment.

Material and methods. The pilot study included 100 consecutive patients with CRC undergoing primary surgery with curative intent within 1 year in the Department of Oncological Surgery in Białystok, Poland. No neoadjuvant therapy was administered before the surgery.

Results. The prevalence of hypertension was 62% among the patients studied. Sixty-five percent of the patients were older than 65 years and hypertension was present in 78% of these elderly patients. The prevalence of CKD was 15%, while that of diabetes was 23%. All CKD patients were older than 65 years of age. The hypertensive patients were more likely to be older and anemic with higher serum fibrinogen, which reflects a general inflammatory state. Elderly hypertensive patients had significantly higher creatinine levels, lower estimated glomerular filtration rate (eGFR) levels ($p < 0.001$) and lower platelet counts.

Conclusions. It is of the utmost importance for oncology patients to have any hypertension diagnosed and treated appropriately in order to prevent complications so they may continue their therapy with the least interruption or discontinuation of treatment and to ensure the best possible outcomes.

Key words: surgery, colorectal cancer, hypertension, chronic kidney disease, elderly

Cite as

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Introduction

Colorectal cancer (CRC) is a common and lethal disease, the 3rd most commonly diagnosed cancer in males and the 2nd most common in females, though the incidence varies markedly.¹ Surgery is the only curative modality for localized colon cancer. For patients who have undergone potentially curative resection of a colon cancer, the goal of postoperative (adjuvant) chemotherapy is to eradicate micrometastases, thereby reducing the likelihood of disease recurrence and increasing the chances of recovery.² Chemotherapy carries a risk of significant toxicities, including emesis, diarrhea, febrile neutropenia, and cardiotoxicity. The frequency and severity of these side effects vary according to the specific drugs used and to the mode of administration. Hypertension is the most commonly reported comorbidity in cancer patients, with a rising incidence that is in line with the aging population of the developed world.¹ In addition, it is also the most common comorbidity reported in cancer registries.¹ However, detailed data on its incidence and prevalence is very scarce. Chemotherapy is a cardiovascular risk factor, particularly when combined with radiotherapy, which is responsible for increasing the incidence of cardiovascular events.³ The aim of this study was to evaluate the prevalence of hypertension and chronic kidney disease (CKD) in a cohort of patients with CRC undergoing primary surgical treatment with curative intent.

Patients and methods

The pilot study included 100 consecutive patients with CRC undergoing primary surgery with curative intent within 1 year in the Department of Oncological Surgery in Białystok, Poland. No neoadjuvant therapy was administered before the surgery. The analyzed data came from the demographic, clinical and laboratory parameters from medical charts. Blood pressure was measured with standard protocols. Hypertension was defined as either a blood pressure of at least 140/90 mm Hg or the use of hypertension medication. Chronic kidney disease was defined according to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines,⁴ with estimated glomerular filtration rate (eGFR) estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.⁵

The study was approved by the appropriate ethics review board. The data were analyzed using STATISTICA v. 13.1 software (StatSoft Inc., Tulsa, USA). The normality of variable distribution was tested using the Shapiro–Wilk W test. Student's t-test was used in statistical analysis to compare differences between groups, with a p-value <0.05 considered statistically significant (when appropriate).

Results

The prevalence of hypertension among all of the patients studied was 62%, but among the elderly patients it was 78%. The mean age of the study population was 67 ±11 years; 65% of the patients were older than 65 years. The prevalence of diabetes was 23%, while the prevalence of CKD was 15%. All CKD patients were older than 65 years of age. The clinical characteristics of the studied patients is shown in Table 1. The hypertensive patients tended to be older and anemic with higher serum fibrinogen, which reflects a general inflammatory state. When we grouped the patients according to age (≤65 years vs >65 years) and presence of hypertension, the elderly hypertensive patients had significantly higher serum creatinine levels (79.56 ±22.1 μmol/L vs 70.72 ±21.22 μmol/L; p < 0.01), lower corresponding eGFR levels according to the CKD-EPI formula (75.5 ±15.97 mL/min/1.72 m² vs 95.72 ±18.00 mL/min/1.72 m²; p < 0.001), higher red blood cell distribution width (RDW) (14.8 ±3.45% vs 13.49 ±2.69%; p < 0.05), and lower platelet counts (248.17 ±106.21 × 10⁹/L vs 299.50 ±140.36 × 10⁹/L; p < 0.05).

Table 1. Clinical and biochemical data of colorectal cancer (CRC) patients with and without hypertension

Parameter	No hypertension (n = 54)	Hypertension (n = 46)
Age [years]	64.51 ±1.62	69.61 ±7.73*
BMI [kg/m ²]	26.98 ±5.51	28.52 ±3.48
Sodium [mmol/L]	139.25 ±2.86	139.54 ±2.72
Potassium [mmol/L]	4.44 ±0.49	4.35 ±0.55
Hematocrit [%]	36.48 ±6.23	39.27 ±5.12*
Hemoglobin [g/L]	117.8 ±27.5	130.4 ±19.1*
Erythrocyte count [×10 ¹² /L]	4.30 ±0.47	4.49 ±0.49*
MCV [fL]	91.32 ±4.91	104.11 ±10.26
MCH [pg]	29.02 ±2.91	27.28 ±4.29*
RDW [%]	11.60 ±6.96	12.18 ±1.33
Leukocyte count [10 ⁹ /L]	7.21 ±3.51	7.41 ±2.54
Platelet count [10 ⁹ /L]	267.11 ±101.88	241.38 ±118.45
Creatinine [μmol/L]	78.68 ±22.10	80.44 ±22.10
Urea [mmol/L]	6.11 ±0.34	5.59 ±1.62
eGFR by CKD-EPI [mL/min/1.72 m ²]	84.59 ±21.23	80.77 ±16.76
APTT [s]	31.78 ±4.17	30.91 ±6.03
INR	1.06 ±0.21	1.05 ±0.25
Fibrinogen [μmol/L]	9.79 ±2.15	10.76 ±2.14*
Glucose [mmol/L]	6.02 ±1.42	6.38 ±1.30
Pulse pressure [mm Hg]	47 ±12	50 ±14
Mean arterial pressure [mm Hg]	97 ±10	104 ±11

BMI – body mass index; MCV – mean corpuscular volume; MCH – mean content of hemoglobin, aptt activated partial thromboplastin time; RDW – red blood cell distribution width; eGFR – estimated glomerular filtration rate; CKD-EPI – Chronic Kidney Disease Epidemiology Collaboration formula; APTT – activated partial thromboplastin time; INR – international normalized ratio. Conversion factors to SI units are as follows: for glucose – 0.0555, for creatinine – 88.4, for hemoglobin – 10, for fibrinogen – 0.0294, and for urea – 0.357; *p < 0.05.

Discussion

In our study, in patients with CRC, the prevalence of hypertension was very high. It was even higher, reaching 78%, in patients older than 65 years. Fraeman et al.⁶ estimated incidence rates of new-onset hypertension in 25,090 adult cancer patients (16% of whom had CRC) and found that crisis-level hypertension (systolic blood pressure >180 mm Hg or diastolic blood pressure >120 mm Hg) was most commonly seen in patients treated for gastric, ovarian, lung, and CRCs. New-onset hypertension was observed during active treatment in about 1/3 of the cancer patients. However, data on the prevalence of hypertension in CRC is very limited. In addition, all of the patients with CKD were over 65 years of age.

In a cohort of patients with CRC in Oman, the prevalence of hypertension was 42% and the prevalence of diabetes was 25%.⁷ Their population was younger (56 years) than ours (mean age: 67 years). In another study on 138 patients with CRC in Malaysia, the prevalence of type 2 diabetes and hypertension was 13% and 34.8%, respectively.⁸ The prevalence of hypertension and type 2 diabetes in relatively young patients (mean age: 53 years) with CRC in Iran was 13.38% and 8.69%, respectively.⁹ It should be stressed that the vast majority of published studies report the effects of CRC treatment and the incidence of adverse events, while data on the prevalence of hypertension and other comorbidities at the time of diagnosis or surgery is lacking. An updated systematic review and comparative meta-analysis by Abdel-Rahman et al.¹⁰ included randomized phase II and phase III trials of patients with solid tumors treated with sunitinib, axitinib, cediranib, or regorafenib describing daily events of hypertension, left ventricular dysfunction, bleeding, or thrombosis. Patients treated with these 4 agents had a significantly increased risk of all-grade hypertension and bleeding.¹¹ However, the data on the prevalence of hypertension before the therapy was not presented. Abdel-Qadir et al.¹¹ evaluated 77 phase III randomized, controlled trials and reported that angiogenesis inhibitors increased the risk of hypertension, arterial thromboembolism, cardiac ischemia, and cardiac dysfunction. Falchook et al.¹² studied patients with advanced solid tumors – including CRC – which were refractory to standard therapy who were treated with a combination of bevacizumab and sorafenib. Two-thirds of the patients experienced adverse events of grade 2 or higher, most commonly hand and foot syndrome ($n = 27$; 24%) and hypertension ($n = 24$; 21%).

The prevalence of CKD was reported to be high in patients with solid tumors,¹³ but the data is also limited. A high prevalence of CKD was reported in 2 other studies as well: ~33% and 27%.^{14,15} In the Belgian Renal Insufficiency and Anticancer Medications study (BIRMA), impaired kidney function, i.e., an estimated Modification Diet in Renal Disease (eMDRD) of <90 mL/min/1.73 m² was reported in 59.5% of CRC cases.¹⁶ In a Korean retrospective

study on 8,223 cancer patients with 1 or more serum creatinine measurements available, the CKD prevalence in CRC patients was 10.2%.¹⁷ This figure is slightly lower than in our study, most likely due to the younger age of the population studied (56 ±14 years vs 67 ±11 years). Moreover, as shown in this study, CKD was associated with an increase in the overall mortality rate of cancer patients (including breast cancer) – approx. 12% – independent of other known risk factors.¹⁷ The possible associations between CKD, hypertension and malignancy were reviewed recently.^{18,19}

Attention should also be paid to the limitations of our study, which consisted of a relatively small sample pooled in just 1 center. The population prevalence of hypertension and CKD was not compared with that of the group of patients with CRC. The fairly homogeneous study group and the lack of a control group might be considered limitations. As we did not perform any follow-up, we cannot indicate any specific benefits coming from paying special attention to the presence and appropriate treatment of any particular comorbidity.

It should be pointed out that large, randomized, controlled trials in general report hypertension as a side effect, but adding the prevalence of elevated blood pressure as a comorbidity would be of great clinical relevance. New-onset or worsening systemic hypertension can be found with numerous chemotherapeutics and is particularly common with antiangiogenic drugs.³ Therefore, the evaluation and treatment of hypertension is a practical starting point for the treatment of cardiotoxicity induced mainly by angiogenic inhibitors. It is of the utmost importance for oncology patients to have any hypertension diagnosed and treated appropriately in order to prevent complications so they may continue their therapy with the least interruption and no discontinuation of treatment and to ensure the best possible outcomes, as patients with early CRC and diabetes or hypertension have a significantly greater risk of cancer recurrence and death after treatment.⁹ In addition, as the prevalence of CKD and hypertension may be further exacerbated by adjuvant therapy, an assessment of kidney function is prerequisite before the introduction of adjuvant treatment.

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