



In elderly population prophylactic anticoagulation favors early detection of digestive track cancers: an observational study in eastern Poland

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The launch of non-VKA oral anticoagulants (NOACs) caused revolution in thrombosis prevention, which was mainly due to their safety and simplicity in treatment when compared to vitamin K antagonists (VKA). Clinical observations indicate that despite the benefits of NOACs, many patients still use VKA even if they cannot cope with dose modifications and often do not control INR.

In the Department of Internal Diseases of Medical University of Lublin (Poland) the large group of hospitalised patients are the elderly with atrial fibrillation on the prophylactic antithrombotic therapy. Some of them have coexisting anemia and undergo extended diagnostics, which in the past had repeatedly resulted in the detection of gastrointestinal (GI) tumors at a very early stage that enabled an effective surgical treatment.

The objectives of the presented study were: (1) compare the frequency of GI tumors detection among the elderly patients (defined as ≥ 75 years of age) treated with oral anticoagulants and their peers in entire population of the Lublin region (western Poland); and (2) determine if in the examined group of elderly patients there was a difference in the predisposition to bleeding depending on the used therapy-VKA, NOAC and low molecular weight heparin (LMWH).

Data presented in the study were collected prospectively for twelve months, from May 2017 to April 2018. The qualification conditions were an admission to the clinic due to anemia of the unknown reason and ongoing prophylactic antithrombotic therapy, mostly due to atrial fibrillation. The drugs used for this reason included: VKA-acenocoumarol and warfarin, NOAC-rivaroxaban, apixaban and dabigatran and LMWH in the form of enoxaparin. The therapy of some of the patients was modified during hospital stay, but the analysis included treatment applied before the admission to the clinic.

Moreover, the additionally collected data encompassed: epidemiological data (age, sex), red blood cell parameters (Hb, RBC, MCV, and Ret), CHA2DS2-VASc and HAS-BLED scores and the information about the finally diagnosed cause of anemia. Following the definition of World Health Organization, anemia was defined as haemoglobin concentration below 12 g/dL for women and below 13 g/dL for men.

The epidemiological data about the population of the Lublin region was taken from publicly available data from the regional cancer registry.^[1,2] GI tumors were defined according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems as codes C15–C21, which encompasses digestive tract from esophagus to anus. Statistical analysis was performed using Student's *t* test. Value $P < 0.1$ was considered statistically significant. The study was accepted by the Bioethical Committee of the Medical University of Lublin (No. KE-0254/188/2018).

Eventually, the study involved 150 patients, 87 women and 63 men. The number of 86 (57.3%) respondents was qualified as the elderly. Anemia was found in 75 patients (50%) and in 9 patients (6%) was caused by GI cancer. In the subgroup of the elderly GI cancer was diagnosed in seven cases and all of these neoplasms were colorectal cancers (CRC) (8.1%). Nevertheless, probably in three consecutive patients in this subgroup, anemia was also a result of developing cancer, but these patients did not agree or were disqualified from an endoscopic examination because of poor performance status. The median values of the CHA2DS2-VASc and HAS-BLED scales were alike in the patients with and without anemia, therefore they were not further analysed. A detailed analysis comparing anaemic patients with the entire study group and the elderly patients with anemia with all aged patients is presented in Table 1. More than half (58.7%) of all patients were treated with NOAC, 26% of patients used VKA and 15.3% were treated with LMWH. Similar statistics apply to

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Table 1. Characteristics of patients with anemia vs. all patients and elderly patients with anemia vs. all elderly patients.

Variables	Patients with anemia/All patients	Elderly patients with anemia/All elderly patients
Total	75/150 (50%)	45/86 (52.3%)
Confirmed cancer-related anemia	9/150 (6%)	7/86 (8.1%)
Female	38/87 (43.7%)	23/54 (42.6%)
Male	37/63 (58.7%)	22/32 (68.7%)
Mean age, yrs	78/76	83/88
Mean haemoglobin level, g/dL	10.4/12.25	10.1/12.1
Mean CHA ₂ D ₂ VASc, score	4/4	5/5
Mean HAS-BLED, score	2/2	2/2

elderly patients. Regardless of the age group, anemia was most common in patients treated with NOAC. 70% of elderly patients with cancer used NOAC. The exact data concerning antithrombotic therapy is presented in Table 2.

The most current available data from regional cancer registry shows that in the year 2010, 102127 women and 50582 men aged ≥ 75 years were registered as inhabitants of the Lublin region (eastern Poland). It seems that in a given year, there were 1003 new diagnoses of neoplastic diseases, with 180 GI tumors in women aged ≥ 75 years old. It represented respectively 1% and 0.17% of the population of all women from the region in this age group.^[1] In men, 1171 new cancers were diagnosed, including 193 GI cancers, which was respectively 2.3% and 0.38% of all men ≥ 75 years of age.^[2] In our study, the data were derived from full 12 months; therefore they might be compared with presented general data. Our statistic showed that 8.1% of the elderly patients were diagnosed with GI cancer and this value would probably increase to 11.6% if three more patients had continued diagnosis. The frequency of GI cancer incidence between our subgroup of aged patients and the compared general popu-

lation of the elderly from Lublin region showed statistical significance at 10% for both sexes ($P \leq 0.1$) (Table 3).

Patients aged over 85 years with GI tumors, especially with CRC are increasing in number. It seems that approximately 60% of CRC are diagnosed in patients over 70 years of age and 43% over 75 years of age.^[3] The advanced age alone is not a contraindication for radical treatment, especially in the cases when cancers are at early stages. The authors of the British study have analyzed the results of CRC treatment in senior patients and showed that curative surgery and any other treatment significantly prolongs life in comparison to best supportive care (41.6 months; 27.3 months vs. 9.3 months, consecutively).^[4] These results indicate that, in the perspective of prolonged life expectancy, seniors should be screened and treated. The reality is that in this phase of the life cycle, treatment of any cancer is often suboptimal.

The disproportion in the frequency of cancer incidence in patients ≥ 75 years of age in our study to the general population of our region might suggest that the use of anticoagulant therapy promotes the early diagnosis of cancer by hastening the exposure of anemia. This process has been previously described

Table 2. Anticoagulant therapy profiles in divided subgroups of patients.

Anticoagulant therapy	All patients	All patients with anemia	All aged patients	Aged patients with anemia	Aged patients with cancer-related anemia
VKA	39 (26%)	18 (24%)	23 (26.7%)	13 (28.9%)	2 (29.6%)
NOAC	88 (58.7%)	40 (53.3%)	48 (55.9%)	21 (46.7%)	5 (71.4%)
LMWH	23 (15.3%)	17 (22.7%)	15 (17.4%)	11 (24.4%)	0 (0%)
Total	150 (100%)	75 (100%)	86 (100%)	45 (100%)	7 (100%)

The percentages in brackets (%) refer to the total number of patients in the consecutive subgroups. The used term 'aged patients' is, as in the main text, defined as ≥ 75 years of age. LMWH: low molecular weight heparin; NOAC: non-VKA oral anticoagulants; VKA: vitamin K antagonists.

Table 3. Statistical comparison of the aged patients covered by the presented 12 month long study with the general population of people over 75 years in the Lublin region (eastern Poland) in the year 2010.

	People aged over 75 years old	People with newly diagnosed GI cancer	Statistical significance of comparing our patient with the general population, <i>P</i>
Our patients	86	7	
General population, males	50582	193	$P = 0.1^*$
General population, females	102127	180	$P = 0.03^*$

*Statistical significance was considered as $P \leq 0.1$. GI: gastrointestinal.

in the literature as “anticoagulation GI stress-test”.^[5] Such early detection of cancer during prophylactic anticoagulation is a beneficial coincidence. Especially when the problem is right-sided colon cancer which gives late symptoms and is easy to be missed at the early stages. Right-sided colon cancer is almost two times more common with patients over 70 years.^[6]

In our study, the most frequently anemia was the complication of NOACs, both in all studied patients as well as a distinguished subgroup of the elderly patients. This observation is consistent with literature data showing that NOAC more often than VKA cause GI bleeding, which results in unmasking pre-existing malignancies.^[7,8] Anticoagulant-related GI bleeding occurs most often within the first month of the therapy.^[5]

In conclusion, there is a significant disproportion in the frequency of the GI cancer incidence between the studied subgroup of senior patients with anticoagulation-related anemia and their peers in the general population. Tumor-related GI bleeding is mostly the complication of NOACs therapy.

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