Practical Application of the Systematizing Wording of Multifocal Lesions of the Gastrointestinal Mucosa Induced by Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Antithrombotic Drugs (ATDs) ("Moscow Formula")

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Abstract

The authors present a unique model of the unified diagnostic decision-support system in the form of alphanumeric characters, which has been developed based on the digestive endoscopy data and is used to interpret the digestive tract lesions resulting from NSAIDs and ATDs treatment (Moscow Classification).

Keywords: *Moscow Formula; Digestive Endoscopy; Digestive Bleedings; Nonsteroidal Anti-Inflammatory Drugs; Antithrombotic Therapy; Drug-Induced Gastrointestinal Injuries*

Abbreviations

AC: Anticoagulants; ATDs: Antithrombotic Drugs; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; ADRs: Adverse Drug Reactions; GSSR: Gastroenterology Scientific Society of Russia; RSSIM: Russian Scientific Society of Internal Medicine; CVDs: Cardiovascular Diseases; E: Esophagus; G: Gaster; D: Duodenum; I: Intestine; C: Colon

Introduction

Issue relevance

Cardiovascular diseases (CVDs) remain the most urgent health challenges in most countries worldwide, including Russia, despite significant progress in CVD diagnosis and management made over the past decades. Experts of the World Health Organization predict further growth in cardiovascular morbidity and mortality both in developed and developing countries, resulting from population aging and lifestyle peculiarities.

CVDs are the leading cause of mortality in the Russian Federation (with a 57% contribution to the overall mortality rate). According to the official statistics, about 40% of people in Russia die at the prime working age (25 - 64 years). The rate of mortality caused by coronary heart disease in men of working age is 10 times higher in Russia than in France; the corresponding rate for cerebral stroke mortality is 6 times higher in Russia than in France.

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As a result, a vast number of oral anticoagulants (ACs) are prescribed every day. In the USA, this number is more than 35 million prescriptions a year. At the same time, uncontrolled use of NSAIDs is still common, which is promoted by widespread advertising of this group of drugs in the mass media.

Studies of frequency and structure of adverse drug reactions (ADRs), especially bleedings, during treatment with ACs + NSAIDs necessitate the development of new approaches to therapy individualization, which will help to improve its efficacy and safety as compared to the spontaneous decision-making method [8,9].

Currently, the annual rate of AC-induced major bleedings is 0.2 - 5.2%, whereas the corresponding rate of fatal bleedings varies from 0.07 to 0.7%.

Still, according to the up-to-date concepts, high-quality diagnosis and treatment can only be provided if the methods that are based on internationally established evidence and guidelines are used [1,10].

In 2016 - 2017, an international working group, including representatives of 9 countries and chaired by Prof. Richard Hunt (McMaster University, Canada), developed and adopted the International Consensus on Guiding Recommendations for Management of Patients with Nonsteroidal Anti-inflammatory Drugs Induced Gastropathy - ICON-G [2].

As per the group's decision, each member country had the right to adjust the established guidelines at the national level; based on this, experts of the Gastroenterology Scientific Society of Russia (GSSR) and the Russian Scientific Society of Internal Medicine (RSSIM) developed and approved the Guidelines for Prevention and Treatment of Esophago-Gastro-Estero-Colopathy Induced by Nonsteroidal Anti-Inflammatory Drugs (XIII National Congress on Internal Medicine, 2017) [3,4], similarly to the International Consensus ICON-G, abbreviated as ICON-II NSAID.

When designing and developing the Guidelines, it was considered necessary to standardize the terminology used to describe lesions of the digestive tract mucosa, using alphanumeric symbols [11].

Thus, the Systematizing Classification of Multifocal Lesions of The Gastrointestinal Mucosa Induced by Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Antithrombotic Drugs (ATDs) (Moscow Classification), was created. It was approved at the 14th National Congress on Internal Medicine in 2018 [6,7].

The new COVID-19 coronavirus infection pandemic declared by the WHO on March 11, 2020, has radically changed medicine worldwide.

Antithrombotic therapy and AC and NSAID treatment during the disease, in particular, have become essential to life.

Meanwhile, the interaction of the drugs for the novel coronavirus infection and the drugs for chronic diseases, patient isolation due to lockdown measures, and occasional loss of the so-called "golden hour" have made fast and reasonable point-of-care decision-making a daily necessity [3,11].

Due to this, the application of the developed classification is as relevant as ever.

Materials and Methods

The authors present a unique model of the unified diagnostic decision-support system in the form of alphanumeric characters, which has been developed based on the digestive endoscopy data and is used to interpret the digestive tract lesions resulting from NSAIDs and ATDs treatment.

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In practice, we suggest step-by-step application of the classification scale which provides a full understanding of the localization and degree of a drug-induced injury of the digestive tract and allows for making a grounded decision on further management strategy. For the reader's convenience, below we provide the alphanumeric symbols used in the Moscow Classification to denote endoscopic visual patterns of gastrointestinal mucosal lesions as well as the atlas illustrating the symbols used.

**Alphanumeric symbols used in the Moscow classification**

General scale

Symbols for the parts of the gastrointestinal tract (type-Roman, italic, upper-case, bold):

- *E (Esophagus)*
- *G (Gaster)*
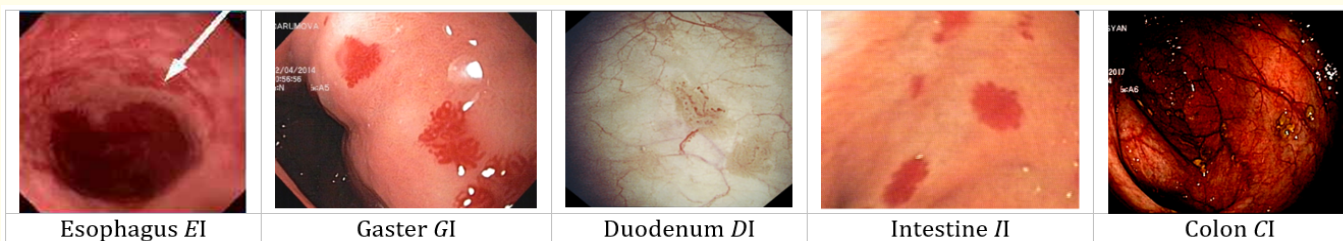- *D (Duodenum)*
- *I (Intestine)*
- *C (Colon)*

Numerical symbols for the visual endoscopic evaluation of the lesion detected (Roman numerals, non-bold-face type, symbols 0, or I, or II, or III, or?)

0 - No changes, no bleeding signs healthy mucous membrane (Figure 1).

| Esophagus *E*0 | Gaster *G*0 | Duodenum *D*0 | Intestine *I*0 | Colon *C*0 |
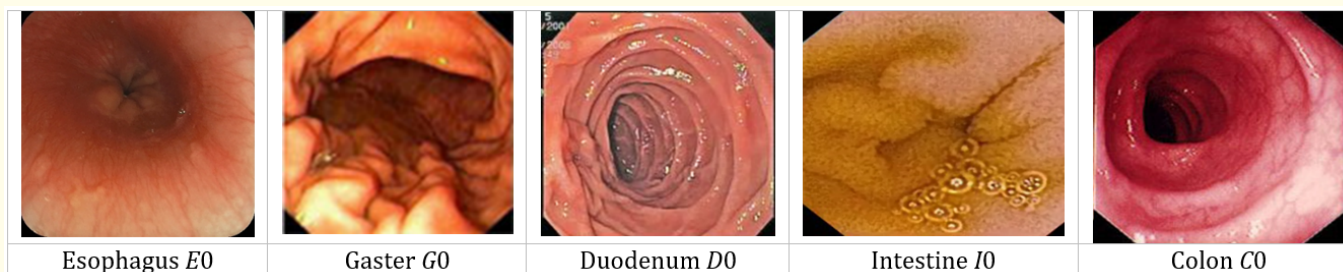
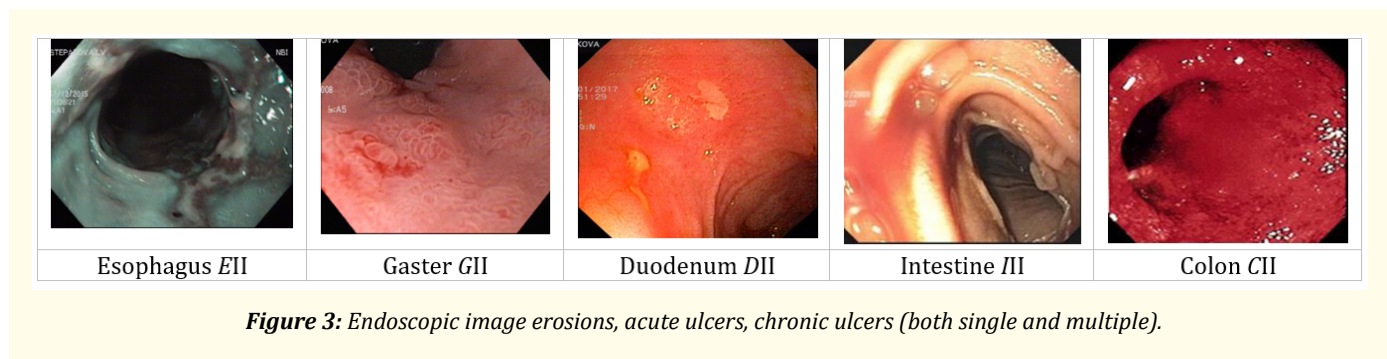*Figure 1: Endoscopic image No changes or signs of bleeding.*

Non-erosive changes ("reddened lesions") (Figure 2): Mucous membrane hyperemia, focal and diffuse hemorrhagic lesions, and multiple bright cherry-red angiodysplasia sites of irregular round or oval shape are detected, which do not rise above the adjacent mucosa of 2 - 5 mm in size and grow pale when instrumentally palpated. No fresh blood leakage is detected.
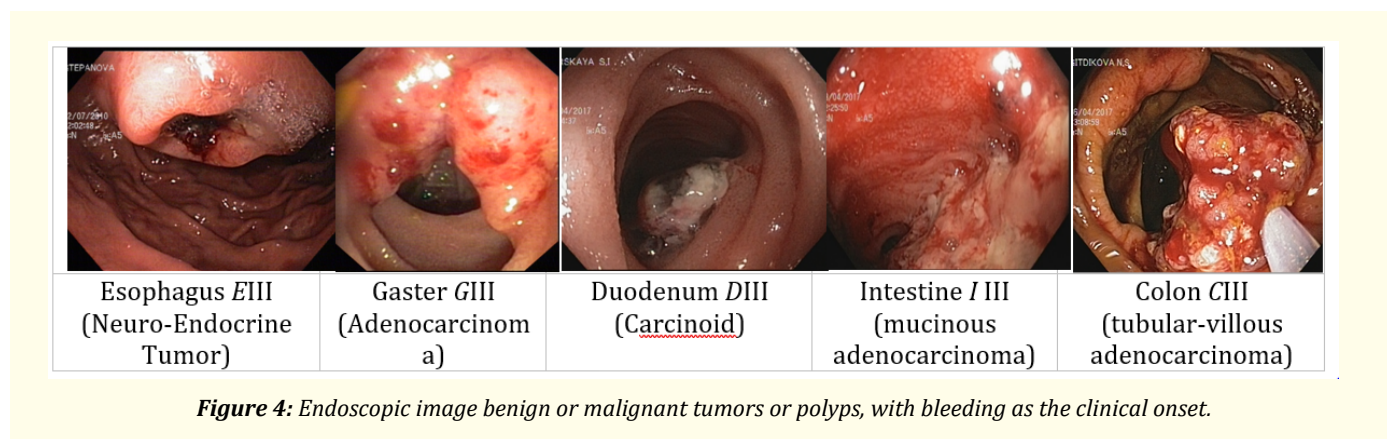

| Esophagus *E*I | Gaster *G*I | Duodenum *D*I | Intestine *I*I | Colon *C*I |

Figure 2:Endoscopic image Non-erosive changes ("reddened lesions").

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In the narrow spectrum mode (NBI-, FICE, i-scan), either enlarged non-tortuous vessels or punctate submucosal hemorrhages in the form of tiny red 1 cm spots are detected.

Erosions, acute ulcers, chronic ulcers (both single and multiple) are detected (Figure 3).

| Esophagus *E*II | Gaster *G*II | Duodenum *D*II | Intestine *I*II | Colon *C*II |

Figure 3: Endoscopic image erosions, acute ulcers, chronic ulcers (both single and multiple).

Benign or malignant tumors or polyps are detected, with NSAID- or ATD-induced bleeding as the clinical onset (Figure 4).

| Esophagus *E*III (Neuro-Endocrine Tumor) | Gaster *G*III (Adenocarcinoma) | Duodenum *D*III (Carcinoid) | Intestine *I* III (mucinous adenocarcinoma) | Colon *C*III (tubular-villous adenocarcinoma) |

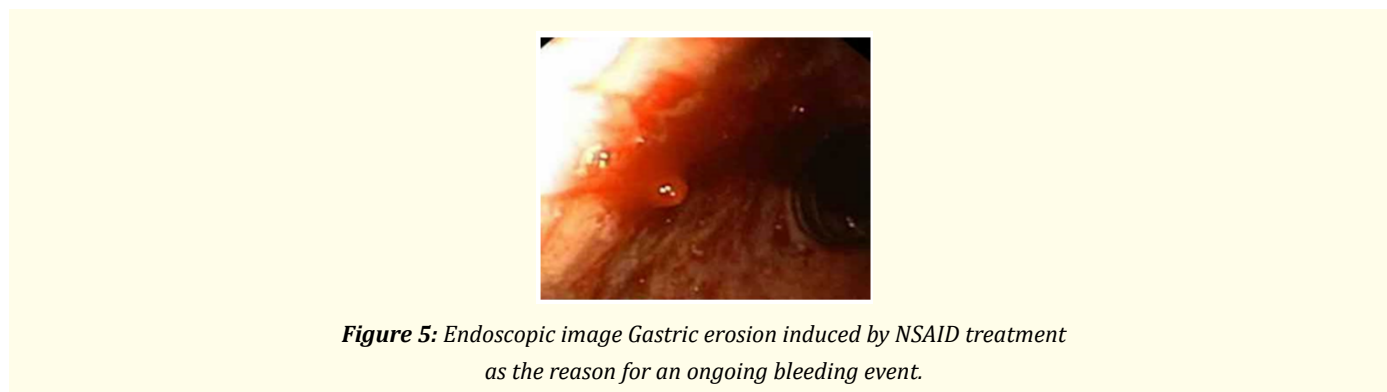*Figure 4:* Endoscopic image benign or malignant tumors or polyps, with bleeding as the clinical onset.

"?" stands for the unknown situation, when the GIT part was not examined for any reason.
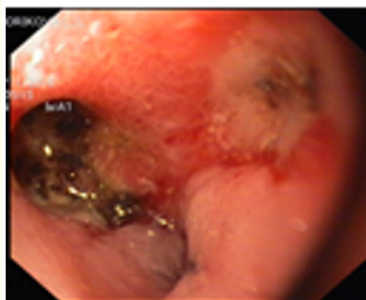
Alphabetic characters (non-bold, upper-case Latin letters a and b) for endoscopic evaluation of the bleeding in the lesion detected

(Based on the Forrest classification, used in the international practice to assess gastric and duodenal ulcer bleedings)

Ongoing (Figure 5).

Figure 5: Endoscopic image Gastric erosion induced by NSAID treatment
as the reason for an ongoing bleeding event.

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Past (Figure 6).

Figure 6: Endoscopic image. Contra-lateral prepyloric ulcers induced by NSAID treatment as the reason for a past bleeding event.

Below are examples of the formulas of the Moscow Classification general scale in the form of alphanumeric characters together with the endoscopic atlas.

Healthy mucous membrane along the entire gastrointestinal tract

*E*0 *G*0 *D*0 *I*0 *C*0 (Figure 1).

Lesions

*E*0 *G*0 *D*I *I*? *C*IIIb - No changes in the esophagus or gaster; non-erosive changes ("reddened lesions") in the duodenum; the intestine was not examined; a colon tumor was detected showing signs of a past bleeding event (Figure 7).

Figure 7: Endoscopic image conclusion: A colon tumor caused by a past bleeding event that has resolved by the time of presentation.

*E*IIb *G*I *D*0 *I*0 *C*0 - Gastric erosions and ulcers showing signs of a past bleeding event; non-erosive changes ("reddened lesions") in the gaster; no changes in the duodenum, intestine, or colon (Figure 8).

Figure 8: Endoscopic image conclusion: Esophageal erosions and ulcers caused by a past bleeding event that has resolved by the time of presentation.

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Results and Discussion

The following clinical case study illustrates the results of the Moscow Formula application:

- A 69-year-old outpatient male diagnosed with hypertension, tachysystolic form of atrial fibrillation, and osteoarthritis of the major lower limb joints and receiving beta-blockers, slow calcium channel antagonists, gastro-resistant aspirin, clopidogrel, and celecoxib. Several days prior to visiting a doctor, the man noted developing nausea, heaviness in the upper abdomen, and black loose stool (twice). At examination: BP = 138/76 mmHg; HR = 84 bpm, arrhythmia; electrocardiography (ECG): tachysystolic form of atrial fibrillation, signs of the left ventricular hypertrophy; Hb = 95 g/L; positive fecal occult blood test; positive fecal Hp serology.

- After esophagogastroduodenoscopy and colonoscopy, the following conclusion was made, based on the Moscow Formula**: *E*0 *G*IIb *D*I *I*? *C*0** (intact esophagus and colon; completed bleeding caused by gastric erosions and ulcers; non-erosive changes ("reddened lesions") of the duodenal mucosa; the jejunum and ileum were not examined).

Conclusion: Gastric erosions and ulcers caused by a past bleeding event

It was decided to examine the intestine, to prescribe such proton pump inhibitors as rabeprazole or pantoprazole (optional), to add rebamipide (cytoprotective agent) [6], and to replace celecoxib with another selective COX-2 inhibitor, which should be used only at the maximum severity of pain syndrome (as assessed by the Visual Analog Scale).

Conclusion

The unique model of the unified diagnostic decision-support system in the form of alphanumeric characters, which has been developed based on the digestive endoscopy data and is used to interpret the digestive tract lesions, such as NSAID- and ATD-induced complications, allows a clinician to make a fast and reasonable point-of-care decision on further management strategy.

Conflict of Interest

The authors declare no conflict of interest.

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