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Bioinert Properties of a Coronary Stent with Nanostructural Carbon Coating.

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ABSTRACT

The article is dedicated to study of bioinert properties of a coronary stent with nanostructural carbon coating by the up-to-date methods of intravascular visualization. It was evidenced that use of a stent with nanostructural carbon coating results in reduction of the risk of in-stent stenosis by more then 2 times as compared to endoprostheses made of stainless steel without surface modification and does not induce thrombogenesis when standard antiaggregant doses are used.

Keywords: coronary heart disease, coronary arteries stenting, in-stent restenosis, bioinertness, stent biocompatibility.

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INTRODUCTION

At the present time it is difficult to imagine coronary heart disease (CHD) treatment without use of endovascular technologies. Notwithstanding that implementation of the vascular stenting technology advanced ischemic manifestations treatment efficiency it didn't allow to obtain the intended result: incidence of restenosis and in-stent stenosis remains high and makes 27-30% [1-5].

The modern literature states that restenosis is principally caused by a stent itself [6]. Barotrauma of an artery wall occurring at time of implantation initiates an inflammatory process, and metallic base of a stent being a foreign matter supports the inflammation during the whole period of endothelialization thus promoting restenosis. By providing a stent with bioinert properties it is possible to influence on an inflammation process in an artery wall and as a consequence to reduce restenosis probability.

Currently carbon as the most frequent element in the human body is regarded as the most promising bioinert material. Amorphous carbon is used for a coronary stent coating. There are a plenty of works investigating stents with diamond-like coating (this is the exact name which is usually used to describe a group of surfaces containing carbon in two hybrid states (diamond and graphite) - DLC) [7-11]. There results are quite conflictive [12-14]. That's why we consider investigations in this field to be perspective with a view of a possibility to create a DLC with high content of a diamond-like hybrid form of carbon.

Work objective: to investigate bioinert properties of a stent with nanostructural carbon coating by a method of intravascular visualization at time of implantation into the coronary arteries.

MATERIALS AND METHODS

Experimental samples of the coronary balloon stents with nanostructural carbon coating prepared by the Research and Educational Center "Nanostructural materials and alloys" of the Research Institute attached to Belgorod National University, research supervisor - Doctor of Physical and Mathematical Sciences, Professor Kolobov Y. R., and by "Laboratory of ionic-plasma deposition" of the RI attached to Belgorod National University, research supervisor - Doctor of Physical and Mathematical Sciences, Professor Kolpakov A.Y., were a subject of investigation. Yearling sheep with the weight of 45-60 kg were selected as test animals. An experimental group included 54 stents with nanostructural surface modification by carbon with the diameter of 3 mm and the length of 15 mm. A control group consisted of the same number of stainless steel stents of the identical design and dimensions. Experimental implantations were made to the front interventricular artery (FIVA) and the circumflex artery (CA) of the animals' heart. In order to prevent the thrombogenesis reaction 75 mg of clopidogrel were orally administered to the animals with water 3 days before surgery. The stents distribution among the coronary arteries as well as specific features of their implantation is shown in Table 1.

Table 1: Distribution of implanted stents

Implantation parameters	Experimental group	Control group
Location: - (FIVA) - (CA)	 27 27	 27 27
Surgical approach	Transaortic	Transaortic
Anesthesia	Intravenous	Intravenous
Surgery timing, min.	26.3±2.2	26.3±2.2
Implantation pressure, atm	14	14

Remarks: FIVA - the front intraventricular artery; CA - the circumflex artery.

The investigation control points are set to 14, 28 and 180 days after surgery. On these days we performed intravascular ultrasound study (IVUS) in order to determine early (thrombosis) and late (restenosis) stage of lumen loss in the stented segments. After compulsory angiography a coronary guide was introduced into the FIVA distal arterial bed. An IVUS sensor of "IVUS-HRI" apparatus was led trough the guide to the distal part of a guiding catheter after which a software-based calibration was carried out.

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Subsequently the IVUS sensor was guided through the coronary guide beyond the stent implantation zones under X-ray control. Traction of the sensor towards proximal end was carried out by means of "IVUS-HRI" apparatus at a speed of 2 mm per second. Ultrasound study of the stented segments was performed. The sensor was returned completely into the guiding catheter. The guide was withdrawn from the FIVA and introduced into the CA distal bed. The ultrasound sensor was recalibrated and led beyond the stented segments of the circumflex artery. Ultrasound study of the stented segments was performed by means of moving the sensor towards proximal direction at a speed of 2 mm per second.

After that an analysis of the obtained data was fulfilled with the aid of the apparatus. The following parameters were evaluated:

- A degree of the stent endothelialization (percent of in-stent stenosis);
- Absence or presence of intraluminal lesions;
- Absence or presence of dissection.

A degree of the stent endothelialization was determined as a ratio (expressed in percents) of the minimum area of the artery stented segment lumen to the area of circumference enclosed by the stent. The maximum values of the lumen loss for each stented segment and average values for a group were determined. A statistical analysis of the obtained data was performed by means of MS Excel electronic table. The results reliability was verified via the Student's validation criterion.

RESULTS

At the early stages of the experiment (up to 28 days) the results of sonography evidenced neointimal proliferation over the stent surface both in the experimental and the control groups. The thickness of the newly formed intima was even and did not exceed 1% of the artery lumen cross section area. No cases of intima dissection were observed along the stented segment border. A distinction in the thrombogenesis reaction between the experimental and the control groups was discovered at the early stages. Mural thrombi (Fig.1) were found in 6 (11.1%) stented segments of the control group (4 of them at the term of 14 days and 2 of them at the term of 28 days after implantation). No mural thrombi were observed in the experimental group. It worth mentioning that in none of the cases mural thrombogenesis resulted in occlusive thrombosis or distal embolism. At the term of 180 days we didn't find mural thrombosis in any of the examined segments in the both groups.

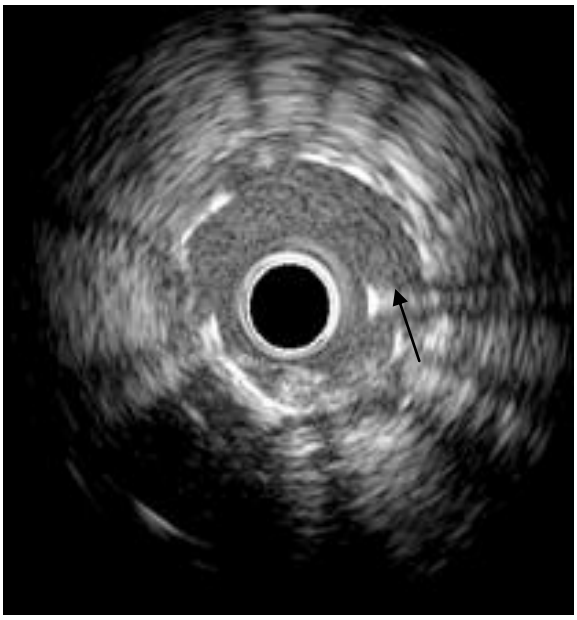

Figure 1: Mural thrombus in the stainless steel stent in the CA

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At the term of 180 days IVUS revealed significant visible changes namely neointimal proliferation over the stent surface both in the experimental and the control groups. However if the control group showed uneven asymmetric neointimal proliferation with the signs of late lumen loss up to one third of the vessel cross section area (Fig. 2), the stented segments of the experimental group exhibited even endothelialization and smooth border of transition to the native artery segment. The maximum lumen loss made up to 14.3% of the cross-section area (Fig. 3).

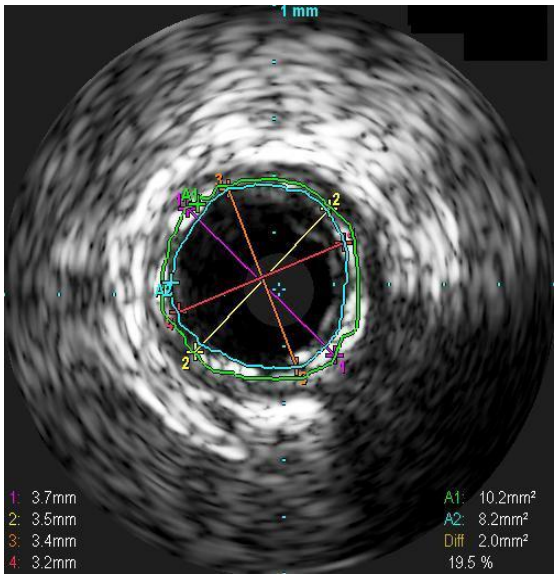

Figure 2. The steel stent in the CA. 19.5% lument loss

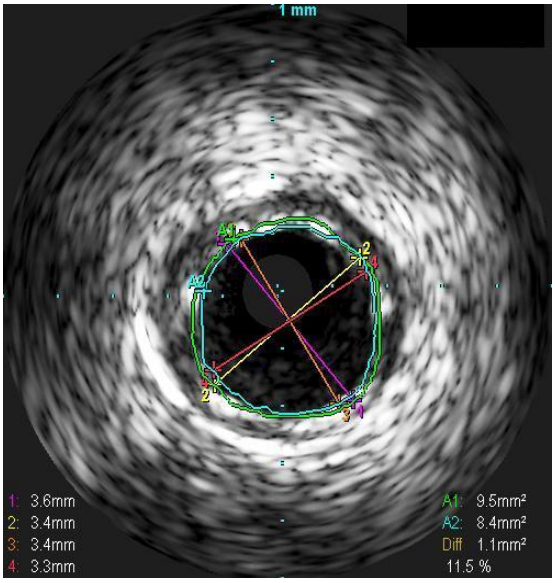

Figure 3: The stent with modified surface in the FIVA. 11.5% lumen loss

Average restenosis values inside the stent were as follows. In the experimental group the late lumen loss in the FIVA made 9.75±1.03%, in the CA 9.2±0.3%. In the control group: in the FIVA 25.1±1.63% and in the CA 22.03±2.7% correspondingly. Average restenosis value for all of the stented segments of the experimental group made 9.5±0.3%, in the control group made 23.6±1.53%. (P<0,01).

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CONCLUSIONS

- Implantation of a stent with nanostructural coating does not prevent natural reparative processes taking place in an artery wall, does not induce thrombotic masses formation given use of the standard doses of antiaggregants.
- The experimental stents with nanostructural coating are positively less affected by in-stent restenosis as compared to the stents without modified surface which evidences higher bioinertness of such stent coating.

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