Impact of the Content of Collagens I and III and Their Ratio in Cancer Patients for the Formation of Postoperative Ventral Hernia

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Comparative morphological analysis of collagens I and III content in the connective tissue in various groups of surgical patients, including tumor patients with ventral hernias, was carried out. The total content of collagen and collagen I/III ratio were the highest in cancer patients in comparison with non-tumor patients with hernias and with patients without hernias or tumors. Hence, factors not associated with collagen synthesis predominate in the pathogenesis of hernia formation in patients operated for malignant tumors.

Key Words: *collagen; postoperative ventral hernia; malignant tumor*

Surgical treatment of malignant tumors of abdominal organs is usually realized through the median access, but 2-25% patients develop postoperative ventral hernias (POVH) after laparotomy [3]. The incidence of POVH increased at least 9-fold over the recent decade [1,6]. The incidence of POVH relapses after autoplasty and prosthetic plastic repair remains high (14.0-54.8% [5]). Chemo- and radiotherapy have a negative impact on intact tissues [4], including the effects of these therapies on tissue reparation.

It is hypothesized that disorders in collagen metabolism and connective tissue diseases contribute to the formation of hernias and their relapses after plastic repair.

Collagens are the main components of the extracellular matrix. They form a complex system consisting of 19 collagens, glycoproteins, and proteoglycanes [8]. The level of fine collagen III increases in the granulation tissue during wound healing. This collagen later transforms into a thicker highly cross-linked collagen I. The fibrils produced from collagen III are significantly thinner than the fibrils produced by true collagen I [7]. Accumulation of collagen III impairs the strength of the connective tissue and can promote POVH formation [2].

We studied the content of collagens I and III and their ratio and the contribution thereof into hernia formation in tumor patients.

MATERIALS AND METHODS

The study was carried out in 67 patients (26 men and 41 women aged 42-73 years, mean age 56.4±5.3 years). The patients were divided into 3 groups. Group 1 (n=22) consisted of patients previously operated for gastric, rectal, uterine, and ovarian malignant tumors. All these patients had POVH, for which they were operated later. Group 2 (n=25) included patients operated for primary inguinal and femoral hernias. Group 3 (n=20; control) consisted of patients without POVH who were operated for gastric ulcers, appendicitis, cholecystitis, acute ileus, and varicocele.

Biopsy of the anterior abdominal wall aponeurosis was carried out in all patients during the latest intervention in order to measure the ratio of collagens I and III in the connective tissue. Paraffin sections were stained by Sirius Red (Polysciences Inc.) and examined under Nikon Eclipse E200 microscope in polarized light at ×200. Three visual fields were selected

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at random in each preparation and photographed. Red fields in the photographs corresponded to collagen I, green ones to collagen III; microstructures stained differently (black) were regarded as "not collagen". The absolute content of each collagen was estimated by red or green pixels. The content of each collagen was estimated as the mean for 3 photographs.

The summary contribution of both collagens into the structure of the connective tissue was evaluated as the ratio of the mean sum of red and green pixels to the mean number of pixels of the photograph.

All histological studies and expert evaluation of the correspondence of the edited digital photos to the actual microscopic picture were carried out by the same morphologist.

All studied variables had no normal distribution, and hence, were evaluated using nonparametric tests and the appropriate descriptive statistics.

RESULTS

The median of ratio of two collagens was maximum in group 1 and minimum in group 2 (Table 1). The differences between the groups were significant (Kruskal–Wallis test, p=0.0022). Paired comparison of the groups (Mann–Whitney test) revealed no differences between groups 1 and 3 (p=0.082), highly significant difference between groups 1 and 2 (p=0.0009), and significant difference between groups 2 and 3 (p= 0.049). Hence, the content of collagen III in comparison with collagen I obviously increased only in patients with primary hernias. No disorders in collagen synthesis were detected in group 1 in comparison with the control group.

The total content of collagen in the preparations differed significantly in the groups (p=0.018, Kruskal–Wallis test; Table 2). Paired comparisons (Mann–Whitney test) showed no differences between groups 1 and 2 (p=0.98). Groups 1 and 3 differed highly significantly (p=0.007), groups 2 and 3 differed significantly (p=0.046).

Hence, the total content of collagen and collagen I/collagen III ratio were maximum in group 1 in comparison with groups 2 and 3.

At present, POVH are treated exclusively by surgical methods with a differentiated approach to choice of the method of intervention with consideration for the shape and size of hernia, status of abdominal wall tissues, and general status of the patient. Since the total level of collagen and collagen I/collagen III ratio in tumor patients with POVH did not differ from those in the controls, other pathogenetic mechanisms of hernia formation should be considered. It is obvious that the appearance of POVH in tumor patients depends on the initial status (anemia, hypoproteinemia, cancer exhaustion) and special oncological treatment (chemo- and radiotherapy), which inhibit reparation. This can serve as an argument in favor of preventive use of autoplastic or prosthetic technologies for prevention of POVH in cancer patients.

REFERENCES

1. G. I. Veronskii and V. A. Zotov, *Vestn. Khir.*, No. 5, 92-97 (2000).
2. A. A. Gostevskoi, *Ibid.*, No. 6, 93-95 (2007).
3. V. V. Grubnik, A. A. Losev, N. R. Bayazitov, and R. S. Parfentyev, *Modern Methods for Abdominal Hernia Treatment* [in

TABLE 1. Collagen I/Collagen III Ratio in the Connective Tissue

Group	Minimum value	Maximum value	Lower quartile	Median	Upper quartile
1	0.360	7.211	1.516	2.646	4.627
2	0.110	6.297	0.559	0.880	1.471
3	0.285	11.811	0.889	1.505	2.938
Total	0.110	11.811	0.780	1.495	2.905

TABLE 2. Relative Content of Total Collagen in the Preparation

Group	Minimum value	Maximum value	Lower quartile	Median	Upper quartile
1	0.182	0.478	0.299	0.378	0.443
2	0.081	0.647	0.273	0.314	0.439
3	0.115	0.498	0.213	0.255	0.345
Total	0.081	0.647	0.243	0.318	0.424

Russian], Kiev (2001).
4. N. O. Milovanov and B. L. Shilov, *Plastic Repair of Radiation Injuries* [in Russian], Moscow (1998).
5. A. D. Timoshin, A. V. Yurasov, and A. L. Shestakov, *Surgical Treatment of Inguinal and Postoperative Abdominal Hernias* [in Russian], Moscow (2003).
6. K. D. Toskin, V. V. Zhebrovskii, Altraide Godstaim, and E. P. Oturin, *Klin. Khir.*, No. 2, 9-10 (1993).
7. A. M. Romanic, E. Adachi, K. E. Kadler, *et al.*, *J. Biol. Chem.*, **266**, No. 19, 12,703-12,709 (1991).
8. D. J. Tilstra and P. H. Byers, *Annu. Rev. Med.*, **45**, 149-163 (1994).