Research Article

Innovative methods of elementosis study in oncourological practice

Tatyana V. Pavlova[1], Vladimir F. Kulikovsky[1], Natalia B. Pilkevich[1], Lyubov A. Pavlova[1], Dmitry V. Bessmertnyy[2], Ivan A. Pavlov[2]

ABSTRACT

Aim: The purpose of this work is to study the content of macronutrients in the tissues with oncourological pathology. **Materials and Methods:** Clinical examination material of 279 people was used in the work, 229 of them were men (82%) and 50 were women (18%). Elemental analysis of oxygen, carbon, calcium, nitrogen, and sulfur was carried out using a detector to record the spectra of characteristic X-ray radiation (EPAX company), which were integrated with "Quanta 600 FEG" scanning electron microscope. **Results:** With prostate cancer, the oxygen content decreased, so during Stage 1, the oxygen content decreased by 36.8% among middle-aged patients, and by 38.6% among elderly patients, Stage 2 – by 32.4% and 28.9%, Stage 3 – by 34.1% and 34.2%, and Stage 4 – by 30.9% and 35.1%. The nitrogen content changed insignificantly, carbon and sulfur decreased. The calcium index among middle-aged patients with Stage 1 prostate cancer increases by 10.6 and by 10.8 times among the elderly, while it is absent among the patients with Stages 2, 3, and 4. The nitrogen content among the patients with renal pathology did not change significantly, but there was a tendency of carbon, calcium, and sulfur increase and oxygen decrease. When they studied the level of macronutrients in bladder cancer, there was a tendency to nitrogen and carbon level increase, and in the groups of Stage 1 and 2 patients, the content of calcium and sulfur increased by 12.5 and 3.8 times, respectively, and oxygen was also reduced. **Conclusions:** We found that all groups demonstrated oxygen content decrease, most pronounced among Stage 2 patients with bladder cancer – 49.5%, which leads to tissue hypoxia in the studied organs. The nitrogen and carbon content varied slightly. The content of calcium and sulfur increases among the patients of all studied groups.

KEY WORDS: Bladder, Kidneys, Oncourology, Prostate, Trace elements

INTRODUCTION

The body of a healthy person has a clear self-regulating system of homeostasis, in which chemical elements play an important role. Their level in the blood and body tissues is subject to certain physiological patterns. Elemental homeostasis is a particular form of the general homeostatic body system, the violation of which affects the body ability to adapt in extreme conditions.[1-3]

The stability of the chemical composition is one of the most important and indispensable conditions for the normal functioning of the body. The kinetics, distribution, and deposition of metal ions are subject to the biochemical regulation of the macroorganism. The change of each of the macro-micronutrients concentration is interconnected. Therefore, both the deficiency of macro- and microelements, as well as their increased concentration, can lead to adverse consequences for human life.[1-3]

In Russia, kidney cancer is the first one in the structure of the urinary tract oncological pathology and accounts for 2.7% of all malignant neoplasms among adults. According to the rate of average annual growth in Russia, this tumor occupies the third place.[4-7]

Due to the constant increase of morbidity and mortality, prostate cancer is one of the urgent problems of oncourology in Russia.[8-10] This pathology is more common among middle-aged and elderly men and takes the 2nd place in the structure of cancer incidence among men, accounting for 14.5%. With age, the risk

Access this article online	
Website: jprsolutions.info	ISSN: 0975-7619

[1]Department of Pathology, Belgorod State National Research University, Belgorod, Russia, [2]Department of Urological, Belgorod Cancer Clinic, Kuibysheva str., 1, 308010, Belgorod, Russian Federation

***Corresponding author:** Tatyana V. Pavlova, Department of Pathology, Belgorod State National Research University, 85, Pobedy St., 308015 Belgorod, Russia. E-mail: pavlova@bsu.edu.ru

Received on: 14-02-2020; Revised on: 21-03-2020; Accepted on: 26-04-2020

of this disease development increases by 3–4% per year.[9] Hence, in 2008, 60 cases of the disease were registered in Russia per 100 thousand people and 162.2 in 2018.[9]

In the structure of oncological morbidity, bladder tumors make up from 2% to 5% of all neoplasms. Every year, 335.8 thousand people become ill with bladder cancer and 132.4 thousand die in the world, that is, one of three dies from this serious disease. Bladder tumors among men occur 3–4 times more often than among women. The increase of patients with bladder cancer in Russia made 8.3%, rising in relative numbers from 8.9 to 9.7 per 100,000 of population. It should be noted that at present, only 45% of patients have an early diagnosis of bladder cancer.[11-12]

Thus, the social significance of this pathology is so great that timely diagnosis of tumors and cancer patient treatment remains an urgent problem of modern oncology.

In this regard, the aim of our study was to study the content of macroelements in the tissues with oncourological pathology.

MATERIALS AND METHODS

The work was based on material received from 2013 to 2018 at the bases of the Belgorod Oncology Center, Belgorod Regional Clinical Hospital of St. Joseph, and the Belgorod Pathological Bureau. The study of the material, analysis, and processing of the obtained results was carried out at the Department of Pathology and at the Belgorod State University, scientific and educational and innovation center "Nanostructured materials and nanotechnologies."

A total of 279 people were studied within the work, of which 229 were men (82%) and 50 were women (18%). Groups were formed according to the age and nosological criteria [Tables 1 and 2].

All subjects did not have chronic forms of diseases in the acute stage as well as severe concomitant somatic pathology. Furthermore, the patients of the control groups did not show complaints of urological nature and did not specifically address the experts of this profile.

For histological examination under light microscopy, samples were excised from various parts of the prostate gland, kidneys, and bladder, which were fixed, embedded in paraffin and sections were prepared on a microtome, followed by their staining with hematoxylin and eosin, then they were studied and photographed using the light microscope "Topic-T" Ceti.

Table 1: Men suffering from prostate diseases

Control	**Men suffering from prostate diseases (*n*=115)**													
			Prostate cancer											
Middle age (40–49 years)	Elderly age (60–83 years)	Benign hyperplasia prostate (Elderly age, 60–77 years)	Middle age *n*=58 (40–49 years)						Elderly age n=42 (61–79 years)					
			I stage ($T_1N_0M_0$)	II stage (T_1-$T_2N_0M_0$)	III stage (T_1-T_3N_1-N_2)	IV stage (T_1-T_3N_1-N_2M_1)	I stage ($T_1N_0M_0$)	II stage (T_1-$T_2N_0M_0$)	III stage (T_1-T_3N_1-N_2)	IV stage (T_1-T_3N_1-N_2M_1)				
n=10	*n*=10	*n*=15	*n*=15	*n*=14	*n*=14	*n*=15	*n*=10	*n*=15	*n*=11	*n*=6				

For scanning electron microscopy, samples were taken without fixation; this made it possible to study them without structural changes in the process of fixation. Macroelement analysis was performed using a detector to record the characteristic X-ray spectra of EPAX company. The detector is integrated with "FE1 Quanta 600 FEG" scanning electron microscope. We have studied the following macronutrients: Calcium, nitrogen, carbon, oxygen, and sulfur.

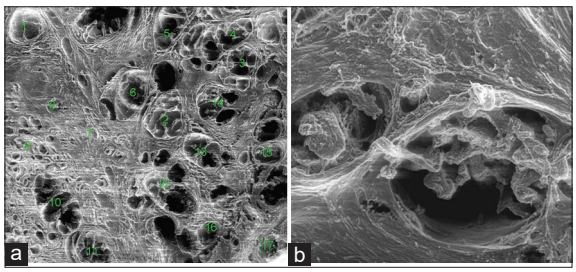

Figure 1: A fragment of the prostate in organ cancer. Stage 2 (T_1-T_2 N_0 M_0). Man, 61 years old. Papillary cancer. 1–17 – Places for the determination of elements (a). Follicular lesions (b) (×1000) fragment of (a) (×100) scanning electron microscopy

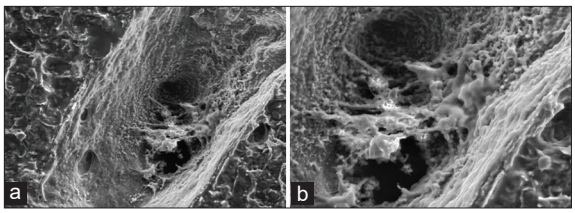

Figure 2: A fragment of the renal medulla in organ cancer. Stage 3 (T_1-T_2-T_3 N_1-N_2 M_0). Man, 64 years old. In the area of oncological damage, there are tumor cells near the tubules and blood vessels and inside them located by clones that are loosely connected to each other. The formation of a tumor embolus inside the vessel. (b) (×1000) Fragment of (a) (×500). Scanning electron microscopy

Statistical analysis of the data was carried out using standard methods of mathematical and statistical processing and the software MS Office Excel and Statistica 6.0.

To identify somatic pathology, diagnostic measures were taken: Collection of complaints and anamnesis with a focused survey on systems and organs, physical examination, as well as laboratory and instrumental methods of the study: General blood test, biochemical general therapeutic blood test, general urinalysis, electrocardiogram registration, study respiratory function, and chest X-ray.

If patients have pathologies of the prostate gland, kidneys, and bladder, a laboratory and instrumental examination was performed to make and clarify the diagnosis: A comprehensive ultrasound examination of the internal organs, lymph nodes, microbiological examination of urine, skeleton bone scintigraphy, and computed tomography, if necessary. The study included the patients with histological verification of the disease.

RESULTS AND DISCUSSION

As the result of the study, it was found that the oxygen content among the control group men was the following: 21.25 ± 1.78% among middle aged, and 20.21 ± 1.87% among the elderly from the total composition of the studied components, decreasing by 23% with benign prostatic hyperplasia (15.53 ± 1.49%). We found that in comparison with the control group, the oxygen content with prostate cancer was significantly reduced. Hence, at Stage 1, it reduced by 36.8% among middle-aged patients, and by 38.6% among elderly, Stage 2 – by 32.4% and 28.9%, Stage

Table 2: Patients with pathology of the kidneys and bladder

Pathology	Age of the patients	Cancer stages	Number of patients
Control (*n*=20)	Middle age (40–49 years)		*n*=10
	Elderly age (60–83 years)		*n*=10
Pathology of the kidneys, bladder (*n*=144)			
Kidney cysts (*n*=22)	Middle age (41–55 years)		*n*=10
	Elderly age (60–78 years)		*n*=12
Kidney cancer (women 40 and men 52) (*n*=92)	Middle age (40–55 years) (*n*=43)	Istage (T_1 N_0 M_0)	*n*=10
		II stage (T_1-T_2 N_0M_0)	*n*=12
		III stage (T_1-T_3 N_1-N_2)	*n*=13
		IV stage (T_1-T_3 N_1-N_2 M_1)	*n*=8
	Elderly age (61–79 years) (*n*=49)	I stage (T_1 N_0 M_0)	*n*=10
		II stage (T_1-T_2 N_0M_0)	*n*=18
		III stage (T_1-T_3 N_1-N_2)	*n*=16
		IV stage (T_1-T_3 N_1- N_2 M_1	*n*=5
Bladder cancer (women 10 and men 20)	Elderly age (60–71 years) (*n*=30)	I stage (T_1 N_0 M_0)	*n*=5
		II stage (T_1-T_2 N_0M_0)	*n*=15
		III stage (T_1-T_3 N_1-N_2)	*n*=6
		IV stage (T_1-T_3 N_1- N_2M_1)	*n*=4

3 – by 34.1% and 34.2%, and Stage 4 – by 30.9% and 35.1% [Table 3].

The nitrogen content among the patients with prostate pathology did not change significantly as compared with the control group, but there was the tendency to carbon and sulfur decrease. The calcium index in the group of middle-aged patients with Stage 1 prostate cancer increases by 10.6 and by 10.8 times among the elderly, and it is absent among the patients with the Stages 2, 3, and 4 [Figure 1].

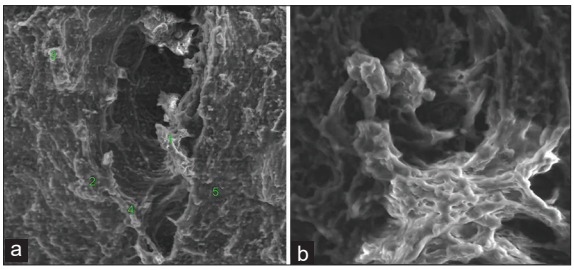

Figure 3: A fragment of the bladder in organ cancer. Stage 3 (T_1-T_2-T_3 N_1N_2 M_0). Man, 69 years old. Clones of tumor cells inside the vessel (1,2,4) with the formation of a tumor embolus (1) and beyond it (3). 1–5 (a) Places of definition of elements. (b) (×2000) Fragment of (a) (×500). Scanning electron microscopy.

When they studied the correlation of macronutrients in the brain layer of the patients with kidney pathology, we found that in comparison with the control group, the oxygen content significantly decreases during Stage 1 kidney cancer – by 25% among middle-aged patients, and by 23.8% among elderly patients, 3 stage – by 15% and 15.7%, and 4 stage – by 14.7% and 15.3%, respectively [Table 4].

The nitrogen content among the patients with renal pathology did not change significantly as compared with the control group, but there was the tendency to carbon, calcium, and sulfur increase [Figure 2].

When they studied the ratio of macronutrients in the cortical layer of the patients with kidney pathology, we found that in comparison with the control group, the oxygen content significantly decreases during Stage 1 kidney cancer among middle-aged patients (by 16%), by 12.7% among elderly patients, and it increases during Stages 3 and 4 [Table 5].

The nitrogen content increases with kidney cysts and during Stage 1 kidney cancer, and during Stages 2 and 4, it decreases 1.6–1.7 times among middle-aged and

Table 3: The ratio of macronutrients in patients with prostate pathology

Ratio of macronutrients (%)			O	N	C	Ca	S
Control	Age	Middle (*n*=10)	21.25±1.78	9.71±1.22	67.97±2.13	0.14±0.01	0.42±0.04
		Elderly (*n*=10)	20.21±1.87	9.91±1.31	68.98±2.14	0.12±0.02	0.45±0.04
Benign hyperplasia prostate	Age	Elderly (*n*=15)	15.53±1.49	10.13±1.27	72.13±1.31	0.10±0.03	0.65±004
Prostate cancer Stage 1 (T_1 N_0M_0)	Age	Middle (*n*=15)	13.42±1.52*	9.08±1.31	73.69±2.41	1.49±0.03	0.71±0.03*
		Elderly (*n*=10)	12.40±1.43*	9.69±1.22	74.88±2.31	1.30±0.05	0.72±0.04*
Prostate cancer Stage 2 (T_1-T_2 N_0M_0)	Age	Middle (*n*=14)	14.36±1,35*	9.08±1.31	71.45±3.11	0	0.85±0.04*
		Elderly (*n*=15)	14.36±1.36*	9.69±1.22	71.56±2.41	0	0.85±0.03*
Prostate cancer Stage 3 (T_1-T_2-T_3 N_1- N_2 M_0)	Age	Middle (*n*=14)	13.99±152*	9.41±143	69.57±1.98	0	0.95±0.01*
		Elderly (*n*=11)	13.29±2.10*	9.50±1.65	70.48±1.65	0	0.90±0.01*
Prostate cancer Stage 4 (T_1-T_2-T_3 N_1-N_2 M_1)	Age	Middle (*n*=15)	14.67±1.56*	9.60±1.32	71.24±2.31	0	0.83±0.03*
		Elderly (*n*=6)	13.10±1.28*	10.09±1.06	73.49±2.51	0	0.93±0.02*

*P<0.05 with respect to the control group

Table 4: The ratio of macronutrients in patients with kidney pathology (cortical layer)

Ratio of macronutrients (%)			O	N	C	Ca	S
Control	Age	Middle (*n*=10)	21.25±1.78	9.71±1.22	67.97±2.13	0.14±0.01	0.42±0.04
		Elderly (*n*=10)	20.21±1.87	9.91±1.31	68.98±2.14	0.12±0.02	0.45±0.04
Kidney cysts	Age	Middle (*n*=10)	20.14±2.03	8.43±1.21	70.28±2.23	0.14±0.05	0.42±0.03
		Elderly (*n*=12)	19.25±1,39	8.59±1.18	71.12±2.51	0.14±0.03	0.40±0.02
Kidney cancer Stage 1 (T_1 N_0M_0)	Age	Middle (*n*=10)	15.83±2.00	13.37±1.92	69.37±2.31	0.38±0.02	0.39±0.03
		Elderly (*n*=10)	15.40±1.52*	12.49±1.31	70.76±2.29	0.40±0.03	0.40±0.04
Kidney cancer Stage 2 (T_1-T_2 N_0M_0)	Age	Middle (*n*=12)	22.91±1.21	9.68±1.42	63.52±1.39	1.15±0.05	1.10±0.05*
		Elderly (*n*=18)	21.81±1.61	9.95±1.29	64.42±1.42	1.25±0.03	1.00±0.03*
Kidney cancer Stage 3 (T_1-T_2-T_3 N_1-N_2 M_0)	Age	Middle (*n*=13)	18.05±1.22*	9.38±1.38	73.05±3.21	0.62±0.05	0.60±0.03*
		Elderly (*n*=16)	17.04±1.25*	9.75±1.65	74.15±2.09	0.52±0.03	0.62±0.04*
Kidney cancer Stage 4 (T_1-T_2-T_3 N_1-N_2 M_1)	Age	Middle (*n*=8)	18.11±1.37*	10.16±1.2	69.67±2.38	0.51±0.05	0.74±0.06*
		Elderly (*n*=5)	17.10±1.3*	11.07±1.33	70.81±3.31	0.54±0.03	0.74±0.07*

*P<0.05 with respect to the control group

Table 5: The ratio of macronutrients in patients with kidney pathology (medulla)

Ratio of macronutrients (%)			O	N	C	Ca	S
Control	Age	Middle (*n*=10)	21.25±1.78	9.71±1.22	67.97±2.13	0.14±0.01	0.42±0.04
		Elderly (*n*=10)	20.21±1.87	9.91±1.31	68.98±2.14	0.12±0.02	0.45±0.04
Kidney cysts	Age	Middle (*n*=10)	18.80±1.99	12.09±1.45	67.76±2.32	0.25±0.04	0.45±0.02
		Elderly (*n*=12)	17.84±1.25	13.41±1.32	66.52±3.36	0.25±0.03	0.42±0.03
Kidney cancer Stage 1 (T_1 N_0M_0)	Age	Middle (*n*=10)	17.82±1.56*	14.41±1.24	66.19±3.12	0.19±0.03	0.39±0.04
		Elderly (*n*=10)	17.63±1.31*	13.32±1.43	67.55±2.46	0.21±0.03	0.40±0.02
Kidney cancer Stage 2 (T_1-T_2 N_0M_0)	Age	Middle (*n*=12)	20.73±1.24*	5.93±1.12	70.98±3.41	0	0.37±0.03
		Elderly (*n*=18)	20.32±1.32*	5.94±1.01	71.40±3.12	0	0.37±0.03
Kidney cancer Stage 3 (T_1-T_2-T_3 N_1-N_2 M_0)	Age	Middle (*n*=13)	24.14±2.01*	4.49±1.14	69.71±2.87	0	0.07±0.03*
		Elderly (*n*=16)	24.01±1.03*	4.53±0.45	70.00±3.31	0	0.04±0.01*
Kidney cancer Stage 4 (T_1-T_2-T_3 N_1-N_2 M_1)	Age	Middle (*n*=8)	23.14±2.05*	5.76±1.23	70.20±2.32	1.17±0.04	1.30±0.14*
		Elderly (*n*=5)	22.30±2.03*	5.81±0.98	71.30±2.98	1.15±0.03	1.10±0.14*

*P<0.05 with respect to the control group

Table 6: The ratio of macronutrients in patients with bladder cancer

Ratio of macronutrients (%)			O	N	C	Ca	S
Control	Age	Middle (*n*=10)	21.25±1.78	9.71±1.22	67.97±2.13	0.14±0.01	0.42±0.04
		Elderly (*n*=10)	20.21±1.87	9.91±1.31	68.98±2.14	0.12±0.02	0.45±0.04
Bladder cancer Stage 1 (T_1 N_0M_0)	Age	Elderly (*n*=5)	15.03±1.41*	13.57±1.68	65.78±1.33	1.75±0.02	1.62±0.04*
Bladder cancer Stage 2 (T_1-T_2 N_0M_0)	Age	Elderly (*n*=15)	10.02±1.08*	13.00±1.07	69.89±2.05	1.75±0.04	1.62±0.08*
Bladder cancer Stage 3 (T_1-T_2-T_3 N_1-N_2 M_0)	Age	Elderly (*n*=6)	19.66±1.71	11.19±1.51	66.80±2.07	0.24±0.03	0.69±0.04*
Bladder cancer Stage 4 (T_1-T_2-T_3 N_1-N_2 M_1)	Age	Elderly (*n*=4)	19.82±1.94	11.22±1.46	66.62±3.04	0.14±0.02	0.69±0.06*

*P<0.05 with respect to the control group

elderly patients, during Stage 3 – 2.1 times in both age groups. There was a tendency toward carbon increase in some groups of patients, as the content of calcium (8.3 and 9.5 times) and sulfur (3 and 2.4 times) increases in the group of patients with Stage 4 kidney cancer.

We found that the oxygen content, in comparison with the control group, in case of bladder cancer of Stages 3–4 does not significantly decrease, and it decreases by 25.6% for Stage 1 and by 49.5% for Stage 2 [Table 6].

With this pathology, the tendency toward an insignificant increase of nitrogen and carbon content was noted in all groups, while in the groups of patients with Stages 1 and 2 of the bladder cancer, the content of calcium and sulfur increased by 12.5 and 3.8 times, respectively [Figure 3].

SUMMARY

Thus, when they studied macronutrients in oncourological pathology, we found that all groups showed oxygen content decrease, most pronounced among the patients with Stage 2 bladder cancer – 49.5%, which leads to tissue hypoxia in the studied organs.

The nitrogen and carbon content varied slightly. Among the patients of all studied groups, the calcium content increases, so, Stage 1 prostate cancer – 10.6–10.8 time increase, kidney cancer – 8.3–9.5 time increase, and bladder cancer – 12.5 time increase. Furthermore, the sulfur content among the patients with kidneys and bladder cancer increased by 2.4 and 3.8 times, respectively.

REFERENCES

1. Chernova DN. Effects of personalized correction of trace element status on human immune function. Trace Elem Med 2018;15:49-51.
2. Kanzhigalina ZK, Kassenova RK, Oradova A. The biological role and importance of trace elements in human life. Bull KazNMU 2013;5:88-90.
3. Pavlova TV, Pilkevich NB, Petrukhin VA, Malyutina ES, Nesterov A, Markovskaya VA, *et al*. New approaches to the study of elementosis in obstetrics. J Int Pharm Res 2019;46:276-80.
4. Zolotukhin OV, Madykin Y, Kochetov MV, Anosova YA. Avdeev AI, Evteev VV. Evaluation of Radiofrequency Ablation Effectiveness During Renal Cell Cancer. Moscow: Materials of the 11th Congress of the Russian Society of Oncourologist; 2016. p. 93.
5. Pavlova TV, Pavlov IA, Pilkevich NB, Chaplygina MA. New approaches in the diagnosis of kidney cancer. Drug Invent Today 2019;12:2094-9.
6. Raaschou-Nielsen O, Pedersen M, Stafoggia M, Weinmayr G, Andersen ZJ, Galassi C, *et al*. Outdoor air pollution and risk for kidney parenchyma cancer in 14 European cohorts. Int J Cancer

2017;140:1528-37.
7. Pavlova TV, Kulikovsky VF, Pavlova LA. Clinical and Experimental Morphology. Moscow, LLC: Medical Information Agency; 2016. p. 256.
8. Alekseev B, Nyushko KM, Krasheninnikov AA, Sergienko SA, Vorobyov NV, Kaprin AD. Trends in the Surgical Treatment of Patients with Prostate Cancer. Moscow: Materials of the 11th Congress of the Russian Society of Oncourologists; 2016. p. 22.
9. Kaprin AD, Starinsky VV, Petrova GV, Herzen PA. The Status of Cancer Care for the Population of Russia in 2018. Russia: The Branch of the Federal State Budgetary Institution "Scientific Medical Research Center for Radiology" of the Ministry of Health of Russia; 2019. p. 236.
10. Buevich NN, Protsenko SA, Nosov AK, Reva SA, Artemyev AS, Berkut MV. The problem of choosing the tactics of managing patients with high and very high risk of prostate cancer: A review of the literature. Oncourology 2019;15:117-24.
11. Khudyashev SA, Kaprin AD. Possibilities of radiation diagnostic method use in staging and determination of bladder cancer treatment tactics. Oncourology 2010;1:12-6.
12. Dugué PA, Bassett JK, Joo JE, Jung CH, Ming Wong E, Moreno-Betancur M, *et al*. DNA methylation-based biological aging and cancer risk and survival: Pooled analysis of seven prospective studies. Int J Cancer 2018;142:1611-9.

Source of support: Nil; Conflicts of interest: None Declared