INFLUENCE OF GENETIC, PSYCHOLOGIC AND SOCIO-ANTHROPOLOGICAL FACTORS ON THE POST-OPERATION PAIN INTENSITY IN OPERATIONS OF MEDIUM AND SUBSTANTIAL VOLUME

AUTOREFERAT

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of dissertation work for awarding the scientific degree „PhD“ in specialty „Anaesthesiology and Intensive Care“

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This dissertation work comprises 560 pages and includes figures and tables.

The reference list includes 1100 cited titles, of them are in Cyrillic.

This dissertation work has been discussed and on an extended faculty session of Faculty "Aneasthesiology and Intensive Care", Faculty "Medicine", Medical University (MU) – Pleven city it was directed for public defense.

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The materials for this defense are accessible in Scientific Unit of MU-Pleven city and are published on the web-site of MU-Pleven city - www.mu-pleven.bg.

Note: The tables and figures numbers in the autoreferat do not coincide with the numbers in the dissertation.

CONTENTS:

ABBREVIATIONS USED:

OPRM1 SNP A118G- Single nucleotide polymorphism (SNP), A118G, in the μ-opioid receptor gene

COMT 1947 G>A - Catechol-O-methyltransferase

MDR1 ABCB1 - Multidrug resistance gene

ORID – Opioid induced respiratory depression

VAS - Visual analogue scale for pain

I. INTRODUCTION

The surgical intervention is the most frequent and predictable source of intensive pain. The untreated post operational pain could lead to unwanted psychological and physiologic effects that increase the morbidity and mortality by thus compromising the recovery quality. The total analgesic effect is not unilateral process. It is influenced by numerous genes engaged with the different paths of drug metabolism.

Pursuant the International Association for the Study of Pain it represents unpleasant sensual and emotional condition originated by the action of real or possible damaging effects on the tissues.

That is why its successful management requires the provision of analgesia without undesired side effects. In the anaesthesiology, pharmacogenetics is a science with potential of improving the pain management through predicting the individual response to a particular analgesic before the treatment to begin, and consequently, it could improve the treatment therapeutic course.

II. GOAL AND TASKS:

Goal: Based on the analysis of genetic, psychological and socio-anthropological characteristics of patients subjected to operations with medium and substantial volume (robotic, laparoscopic and conventional ones) in the thorax, abdominal cavity and small pelvis, a managerial algorithm for effective post operational analgesia should be established through opioid analgesics. All this is grounded on the confirmed efficiency of robotic surgery being the only possible conventional surgery alternative for people with genetic polymorphism SNP, OPRM1 118 A>G, COMT 1947 G>A and MDR1 ABCB1.

Tasks:

1. Frequency distribution of patients to be done according:
1.1. Age
1.2. Gender
1.3. Diagnosis
1.4. Applied operative method
1.5. Type of surgical method
1.6. Presence of previous operations
1.7. Number of analgesia per 24 hours
1.8. Presence of accompanying diseases
1.9. Presence of side reactions after the analgesia application
- sickness
- vomiting
- respiratory depression
- cardio-vascular complications

1.20. According to the Visual Analogue Scale (VAS) for pain
1.21. According to the presence of catastrophization
- Rumination
- Magnification
- Helplessness

1.22. According to the Taylor anxiety test
- men

- women

1.23. According to the Beck Depression Inventory

- men
- women

1.24. According to PHQ-9 depression test

- men
- women

1.25. According to COMT 1947 G>A genetic polymorphism (according the alleles AA, AG, GG)

- men
- women

1.26. According to SNP OPRM 118 A>G genetic polymorphism (according the alleles AA, AG, GG)

- men
- women

1.27. According to MDR1 (C3435T) ABCB1 genetic polymorphism (according the alleles CC, CT TT)

- men
- women

1.28. According to the place of residence

- men
- women

1.29. According to the education status

- men
- women

1.30. According family status

- men
- women

1.31. According to the children born

- men
- women

1.32. According to the surgical intervention length (hour, minutes)

1.33. According to the anaesthesia length (hour, minutes)

1.34. According to BMI

1.35. According blood types

1.36. According the hospital type

- state
- private

2. To study the impact of the pre-operational anxiety and depression level (Taylor test and PHQ-9 depression test) as well as the pre- and post-operational depression (Beck Depression Inventory) on the pain intensity post operation (VAS-scale for pain).

3. To assess the frequency of genetic polymorphism SNP OPRM1 118 A>G (according the alleles AA, AG, GG), of genetic polymorphism COMT 1947 G>A (according the alleles AA, AG, GG), as well as of the polymorphism MDR1 (C3435T) ABCB1 (according the allele CC, CT TT), and also their impact on the intensity of post-operation pain (VAS- scale for pain).

4. To survey the inter-relation SNP 118 A>G of OPRM1 gene (according the alleles AA, AG, GG), genetic polymorphism COMT 1947 G>A (according the alleles AA, AG, GG) and the

polymorphism MDR1 (C3435T) ABCB1 (according allele CC, CT TT) and both the pre- and post-operational psychological condition of patients (Taylor anxiety test, Beck Depression Inventory).

5. To estimate the connection between the pre- and post-operational psychological condition of patients (Taylor Test, Beck Depression Inventory and PHQ-9 depression test) with the genetic polymorphism SNP 118 A>G OPRM1 of gene (according the alleles AA, AG, GG), genetic polymorphism COMT 1947 G>A (according the alleles AA, AG, GG) and the polymorphism MDR1 (C3435T) ABCB1 (according alleles CC, CT TT), VAS- pain scale and the **number** of the applied analgesia for 24 hours on **the frequency and the type** of complications (like sickness, vomiting, respiratory depression and cardio-vascular problems) developed due to the applied analgesia.

6. To analyze the relation between the diagnosis, the applied surgical method (open surgery, laparoscopic surgery and robotic surgery), type of surgery (abdominal, thoracal and of the small pelvis) with the different socio-anthropological factors (age, sex, BMI, family status, education, residence address, availability of born kids, length of surgical intervention and anaesthesia) on the pain intensity during the post-operation period(VAS-pain scale) in patients with genetic polymorphisms COMT 1947 G>A, SNP OPRM 118 A>G and MDR1 (C3435T) ABCB1.

7. To find the connection between the three genetic polymorphisms, the pain intensity(VAS-pain test) and the number of analgesia for a period of 24 hours, as well as the presence of previous operations that the patients survived in connection with catastrophizing (Rumination, Magnification and Helplessness) as per patients' sex and surgical method(open surgery, laparoscopic surgery and robotic surgery).

8. To find whether there is connection between the blood group, the three genetic polymorphisms and the intensity of post-operation pain, anxiety and depression.

9. To find the connection between pain existence (VAS-pain scale) and type of hospital where the patients are being treated (state and private).

10. To compare the results achieved with Taylor test, Beck Depression Inventory and PHQ-9 depression test; to find out to what extend these tests are mutually replaceable in their clinic application.

11. To search available prognostic groups or other interrelations.

III. MATERRIAL AND METHODS

STUDIED PATIENTS' QUOTA:

An ambispective, clinical and epidemiological study was carried out comprising 410 patients of UMHAT "Sveta Marina", Pleven city, with 13 different diagnoses covering the period 2018 - 2020. The studied clinical patients quota is with average age 57.52±11.97 comprising the age 27 - 88 yo. From the studied patients 96 (23.4%) are male and 314 (76.6%) female (Fig. 1).

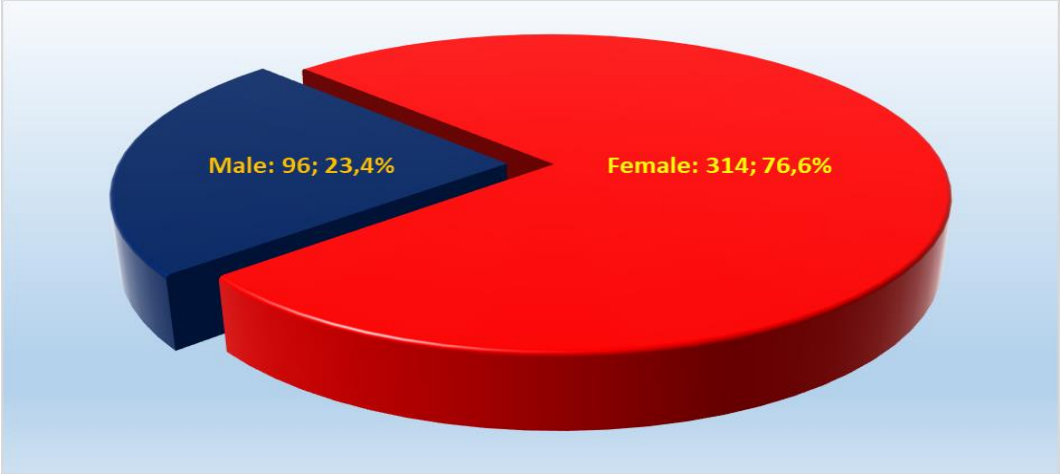


Fig. 1: Frequency distribution of the studied patients' quota according to gender

With male patients the most numerous age group (38) is for 60-69 yo, followed by 29 for 70-79 yo, and the smallest (0) for 20-29 yo. With female patients the most numerous group (96) is for 50-59 yo, followed by 88 for 40-49 yo, and the smallest (3) for 20-29 yo (Fig.2).

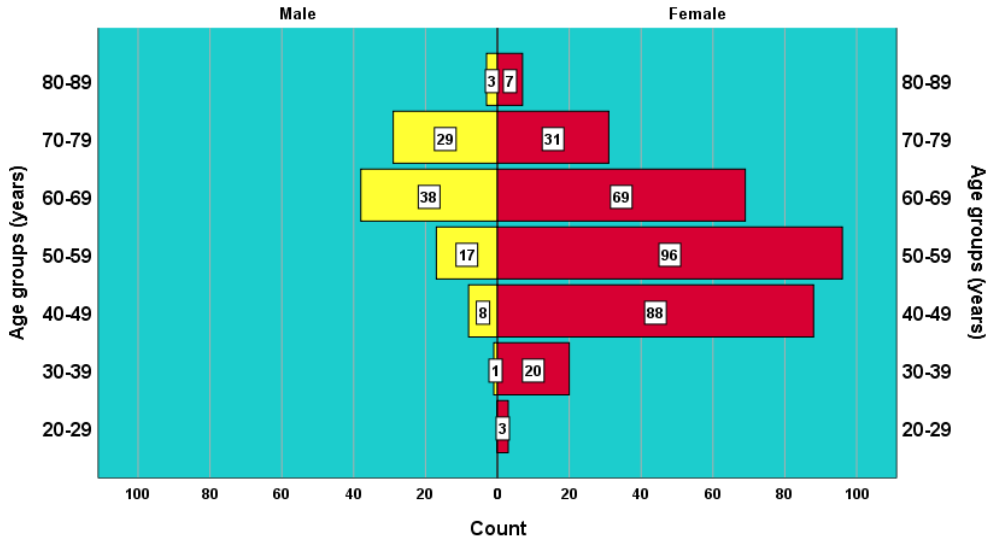


Fig. 2: Distribution of the studied patients according to gender and age.

METHODS:

1. Psychological tests for depression and anxiety:

On the day immediately before the surgical intervention, before the anaesthesia, the patients filled-in the documents for Informed Awareness to participate in this study in compliance with Ethic Commission for Research (ECR) of MU-Pleven, PHQ-9 questionnaire for pre-operative depression, Taylor anxiety test, Beck Depression Inventory, as well as the test for catastrophizing of pain.

The patients filled-in Beck Depression Inventory on the day when the documents were transferred from " Anaesthesiology and Intensive care" Clinic to the respective units.

2. Anaesthetiologic Methods:

All patients received general intubation, inhalation anaesthesia.

Midazolam and Fentanyl were applied for premedication in the habitual premedication dosages.

As introduction anaestetics were used Propofol together with depolarizing muscle relaxant Succinycholine.

The anaesthesia was sustained by Sevoflurane, Tracrium and Fentanyl.

After being extubed the patients received i. m. Morphine and Analgin.

All patients were operated in compliance with the composed schedule. The time needed for anaesthesia and the surgical intervention (in minutes) were reported.

This study did not include:

1. Patients at the age under 18 and above 80.
2. Patients estimated as anaesthesiology risk above III-degree per ASA.

3. Reanimation Methods:

In the Clinic of Anaesthsiology and Intensive Care, the patients were monitored for the main life parameters: В КАИЛ болните бяха мониторирани основните жизнени параметри:

- ✓ Noninvasive arterial blood pressure;
- ✓ Cardiac frequency;
- ✓ ECG;
- ✓ $SpO_{2;}$
- ✓ Diuresis.

The next anaesthesias were rendered when patients mentioned the appearance of pain. It was assessed according to VAS for pain. Indicators as arterial pressure, cardiac frequency and peripheral saturation were reported. The appearance of new symptoms in respiratory, cardio-vascular systems and gastro-intestinal tract were also reported. They were written down in the patient's Questionnaire Card.

Samples of 5 ml venous blood were taken and tested for genetic polymorphisms in the "Molecular Biology" Laboratory at MU-Pleven by the molecular biologists Vladislav Nankov and Tihomir Rashev.

The genetic tests have been financially supported by the following research projects:

1. Project at Research Institute in MU-Pleven city, 2018: "Impact of Some Genetic, Psychological and Socio-Anthropologic Factors on the Intensity of Post-operation Pain in Oncologic Operations of Medium and Substantial Volume in Abdominal Cavity and Small Pelvis".

2. No. 17/2019 - "Relation of Allele Polymorphism C3435T in Gene ABCB1/MDR1with Opioid Sensitivity during the Treatment of Post-operation Pain in Patients who had Robotic, Laparoscopic and Conventional Surgery" - financed by "Research" Fund at MU-Pleven.

4. Method for Polymorphism Genotyping by Allele-Specific Hybridization

5. Statistic Methods

The data have been introduced and processed by IBM statistic packages SPSS Statistics 25.0. and MedCalc Version 19.6.3. As a significance level that rejects the zero hypothesis was accepted $p<0.05$.

The following methods were applied:

IV. RESULTS:

Task 1:

Table 1 demonstrates that:

- The patients with endometrium carcinoma represent the highest percent (21.5%) followed by the patients with cervix uterine carcinoma – 17.3%;
- Patients diagnosed with retroperitoneal tumor, peritonitis, ileus, uterine cervix dysplasia, cholelithiasis, pyloric stenosis, stomach ulcer and uterine sarcoma are the lowest number – one patient only or 0.2%.

Figure 3 demonstrates that:

- Patients who had open surgery represent the highest relative share (59.3%) followed by these who had laparoscopic surgery – 22%.
- Patients who had surgical intervention as robotic surgery represent the smallest group – 77 patients or 18.8%.

The results from Figure 4 demonstrate that:

- Patients who had abdominal surgery are the highest percent (64,9), followed by these who had surgery of the small pelvis– 30,2%;
- The person who had thoracic surgery represent the lowest number - 20 patients or 4,9%.

Table 1: Frequency distribution of patients according their diagnosis

Number of operations	n	Relative share (%)	Sp
Endometrium carcinoma	88	21,5	2,0
Uterine cervix carcinoma	71	17,3	1,9
Uterine leiomyoma	50	12,2	1,6
Ovarian cancer	26	6,3	1,2
Sigma carcinoma	21	5,1	1,1
Prostate gland carcinoma	21	5,1	1,1
Lung carcinoma	18	4,4	1,0
Rectal carcinoma	17	4,1	1,0
Stomach carcinoma	14	3,4	0,9
Hyperplasia of endometrium	14	3,4	0,9
Kidney carcinoma	13	3,2	0,9
Bladder carcinoma	12	2,9	0,8
Ovarian cyst	10	2,4	0,8
Polyp of endometrium	6	1,5	0,6
Carcinoma of colon ascendence	5	1,2	0,5
Uterine prolapse	3	0,7	0,4
Hiatal hernia	3	0,7	0,4
Cecum carcinoma	2	0,5	0,3
Mammal gland carcinoma	2	0,5	0,3
Parametrectomy	2	0,5	0,3
Rectal-vaginal fistula	2	0,5	0,3
Ventral hernia	2	0,5	0,3
Retroperitoneal tumor	1	0,2	0,2
Peritonitis	1	0,2	0,2
Ileus	1	0,2	0,2
Uterine cervix dysplasia	1	0,2	0,2
Cholelithiasis	1	0,2	0,2
Pyloric stenosis	1	0,2	0,2
Stomach ulcer	1	0,2	0,2
Uterine sarcoma	1	0,2	0,2
Total	410	100,0	

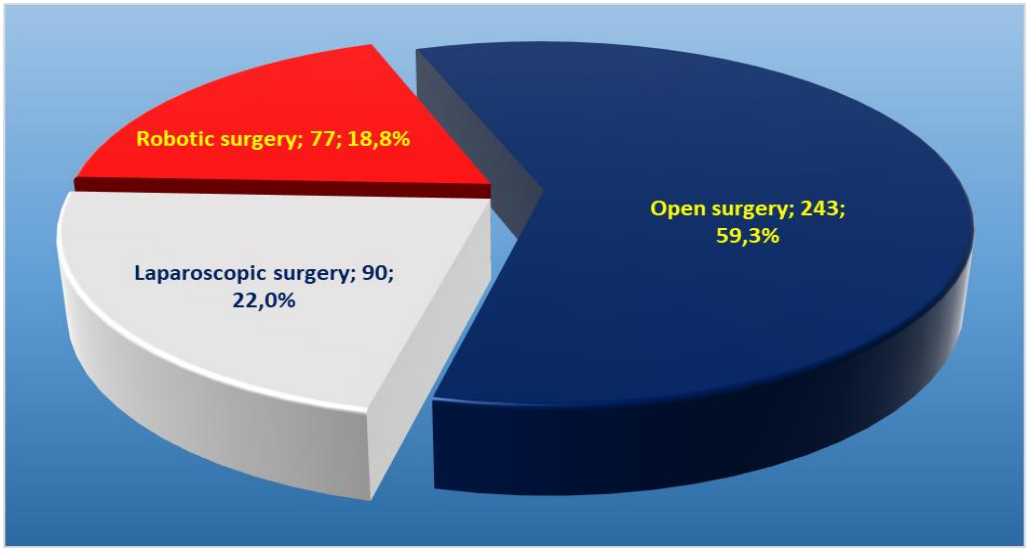


Fig. 3: Frequency distribution of patients according the surgical method applied

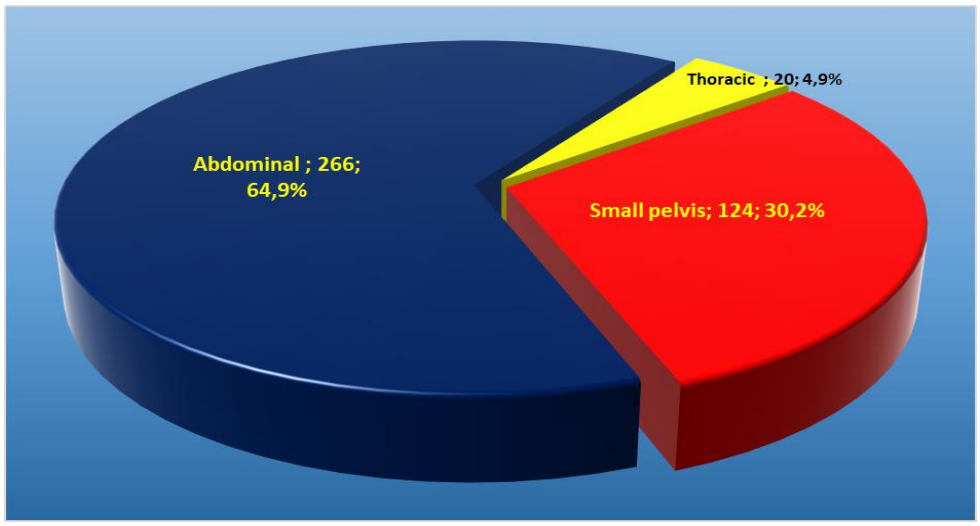


Fig. 4: Frequency distribution of patients according to the the type of surgery

It was stated that patients who had undergone previous surgeries before represent higher percent (68,5%) followed by these without any previous surgical interventions 31,5%, Fig. 5.

Figure 6 demonstrates that patients who had one anesthesia during the post-operation period are the highest number (132 or 32,2%), followed by these who had three times anesthesia – 128 or 31,2%;

It was stated that patients who had NO anesthesia within the first 24 hours represent the lowest number - 28 patients or 6,8%.

The results on Figure 7 demonstrate that 78,3% of the participants in this study have accompanying diseases, while 21,7% of the participants have none.

In connection with the occurrence of side reactions after anesthetics application (Fig.8), we found that:

- Patients who felt sick as anesthetic side effect represent the highest percent (64,4%), followed by these having cardiac-vascular complications - 37,1%;
- Those who developed respiratory depression after the anesthesia applied with Morphine+Analgin represent the lowest number – 75 or 18,3%.

Frequency distribution of patients in compliance with VAS for pain found out that (Fig. 9):

- Patients whose pain is of average intensity represent the highest relative share (38%) , followed by these whose pain is slight or missing at all at motion – 37,3%;
- Patients enduring strong pain are the lowest number – 101 patients or 24,6%.

Results on Fig. 10 demonstrate that according to the parameter “existence of catastrophization”:

- The patients without catastrophization represent the highest percent(54,6%), followed by these whose catastrophization appears as rumination – 24,1%;
- Patients who demonstrated helplessness represent the lowest number – 42 patients or 10,2%.

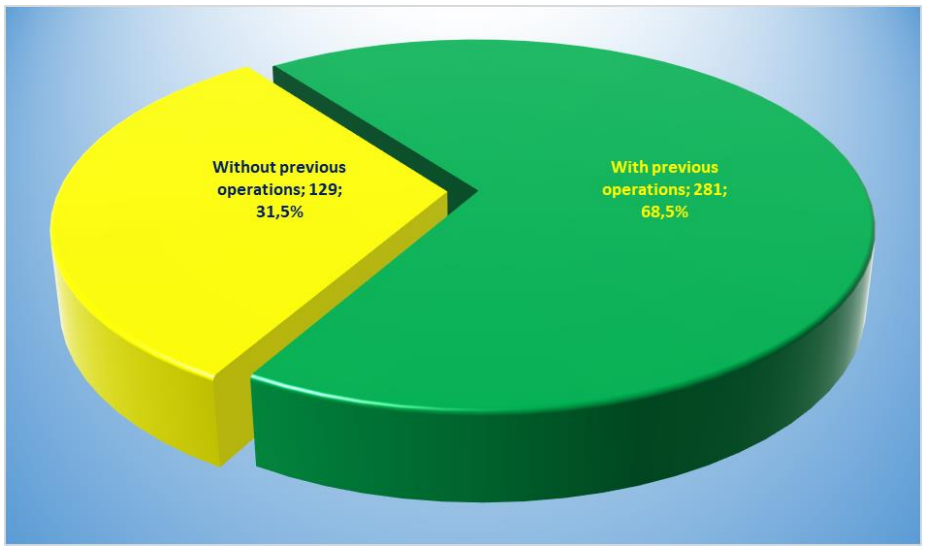


Fig. 5: Frequency distribution of patients according to the existence of previous surgeries

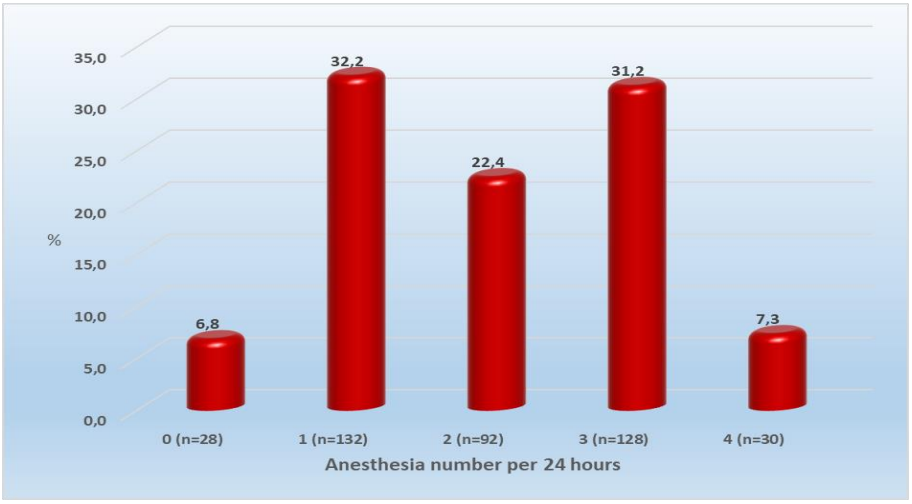


Fig. 6: Frequency distribution of patients according to the number of anesthesia in 24 hours

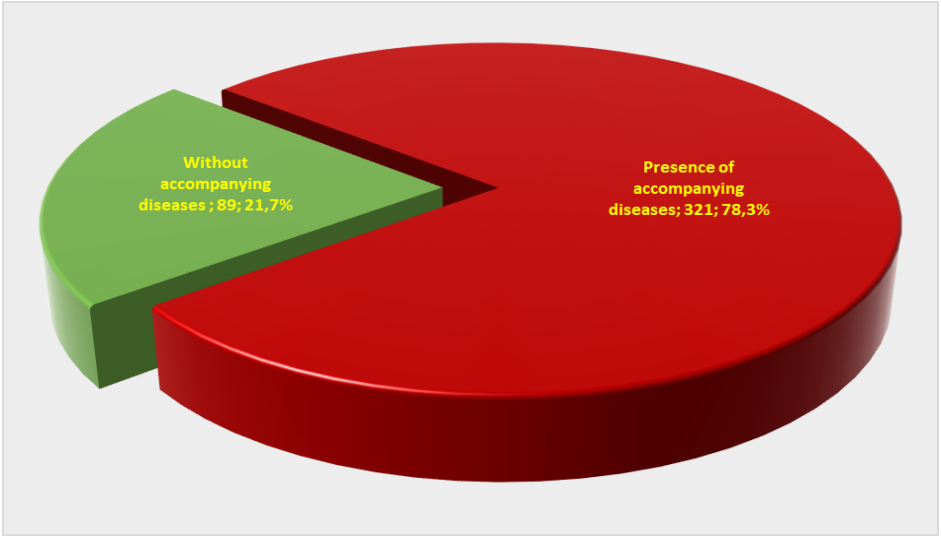


Fig. 7: Frequency distribution of patients according to the presence of accompanying diseases

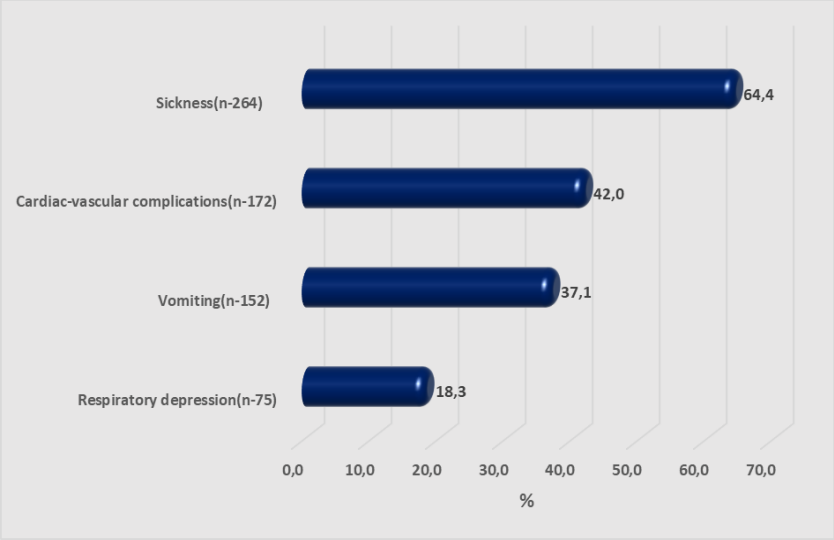


Fig. 8: Frequency distribution of patients according to the presence of side effects after painkillers application

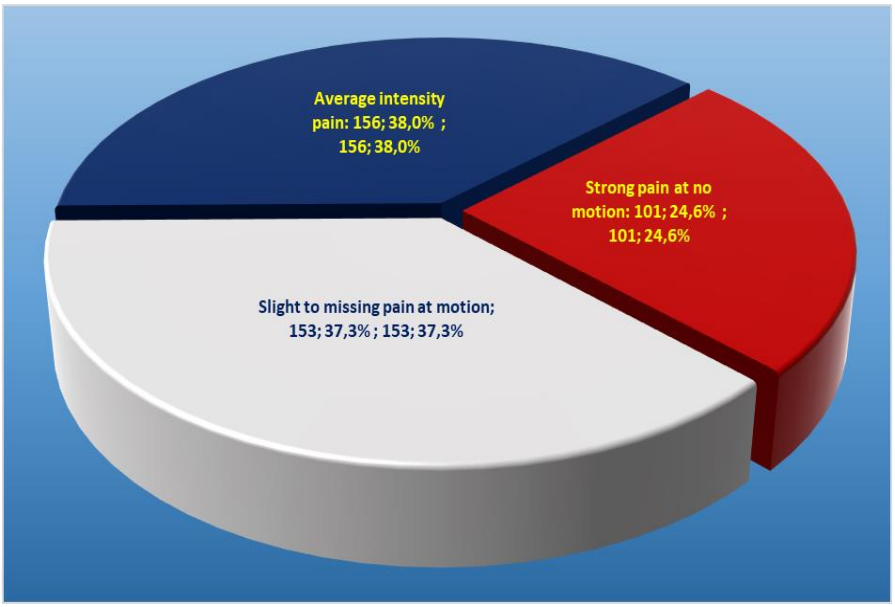


Fig. 9: Frequency distribution of patients according to VAS

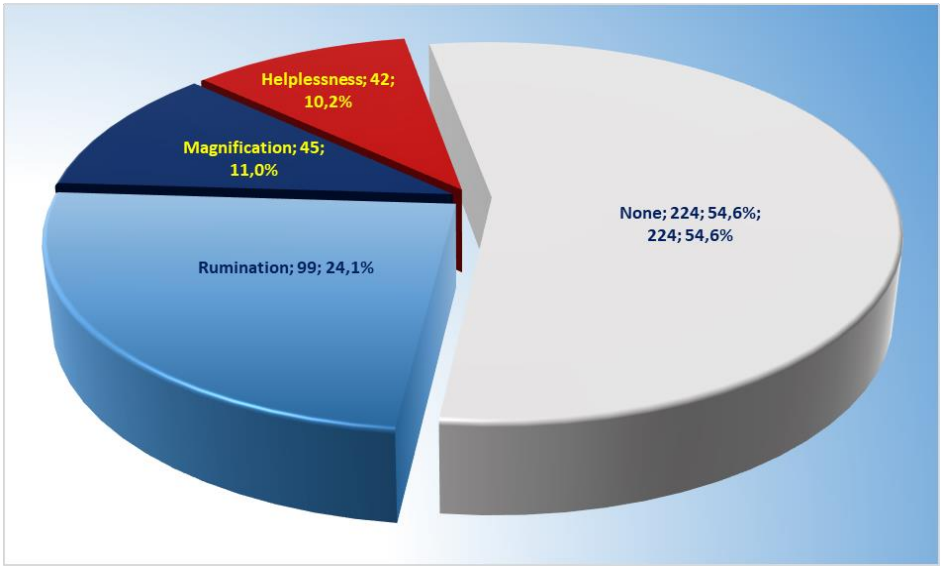


Fig. 10: Frequency distribution of patients according to the presence of catastrophization

- Patients with average anxiety level (6-25 points) represent the highest percent (45,9%), followed by these with low level (0-5 points) – 37,6%. Patients with very high anxiety level (26-50 points) represent the lowest percent (16,6%);
- The relative share of male patients with average anxiety level (55,2%) is significantly higher than the one of female patients (43%). While with the low anxiety level this difference is statistically significant again, but female patients show higher percent (41,4% and 25%, respectively). Statistically reliable difference between both genders is not found on the high anxiety level.

Fig. 12 demonstrates that in compliance with Beck Depression Inventory:

- Patients without depression represent the highest number (39,3%), followed by these with average to severe depression – 20,7%;
- Patients showing extremely severe depression represent the lowest number – 3,9%;
- Statistically reliable difference between both genders was not found in the frequency distribution of Beck Depression Inventory.

The results on Fig. 13 demonstrate that:

- Patients without depression represent the highest number (37,1%), followed by these with average to severe depression – 23,7%;
- Patients with severe depression represent the lowest number – 9,8%;
- Statistically significant difference between both genders was not found in the frequency distribution of PHQ-9 for depression.

From the frequency distribution of patients according to COMT 1947 genetic polymorphism (Fig. 14), it can be seen that:

- Heterozygotes (GA) represent the highest percent (48,3%), followed by GG homozygotes along the normal allele - 26,1%;
- The lowest number are these that are homozygotes along the mutation (AA)– 25,6%;
- Significant difference between male and female patients is not found in the frequency distribution of this type polymorphism.

According to SNP OPRM 118 genetic polymorphism, the frequency distribution of patients demonstrated that (Figure 15)

- Patients with allele AA, i.e. homozygotes along the normal allele, represent the highest relative share (64,9%), followed by AG heterozygotes - 30%;
- GG homozygotes along the mutation represent the lowest number – 5,1%;
- The difference between frequency distribution of this polymorphism is not statistically reliable for both genders.

For the frequency distribution of patients according polymorphism MDR1 can be stated that it is very close to the one of COMT 1947 genetic polymorphism (Figure 16):

- Heterozygotes along allele CT represent the highest percent (51,7%), followed by CC homozygotes along the normal allele - 26,1%;
- The homozygotes along mutation (TT) are the ones with the lowest percent – 22,2%;
- Significant difference in the frequency distribution of this polymorphism is not found between men and women.

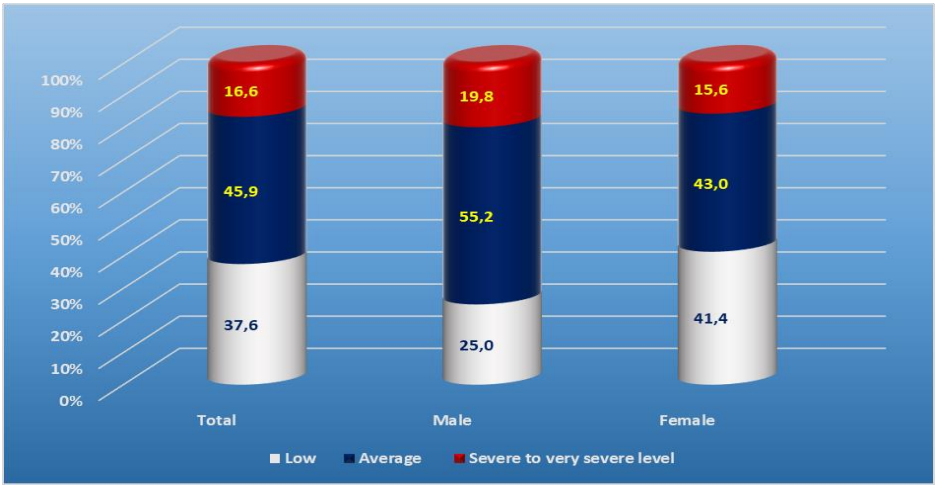


Fig. 11: Frequency distribution of patients in compliance with Taylor Anxiety Test

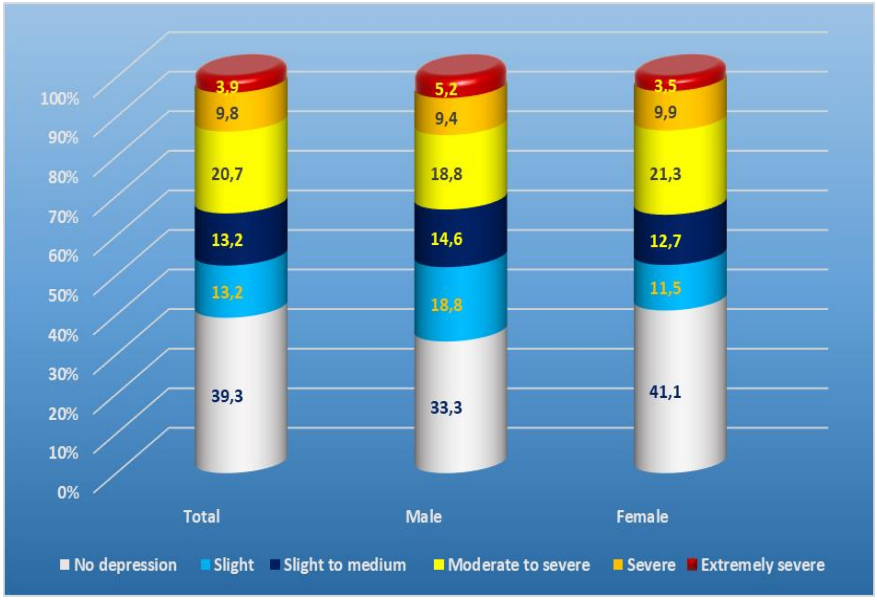


Fig. 12: Frequency distribution of patients in compliance with Beck Depression Inventory

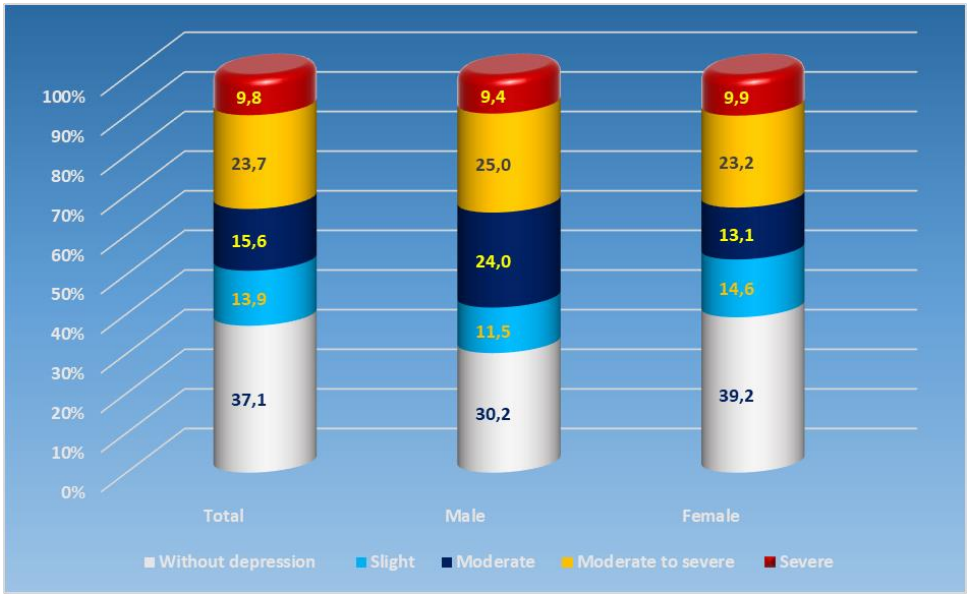


Fig. 13: Frequency distribution of patients in compliance with PHQ-9 depression test

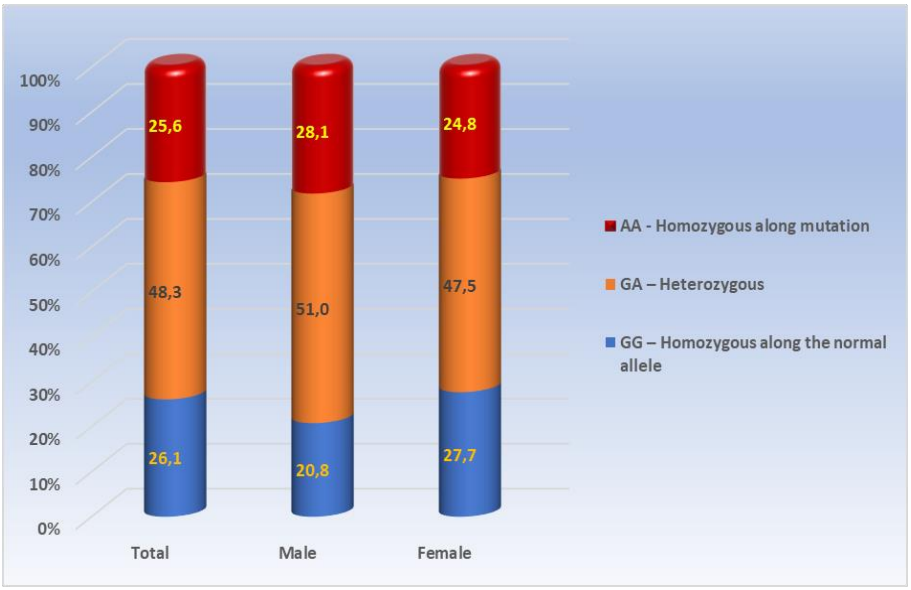


Fig. 14: Frequency distribution of patients according to COMT 1947 genetic polymorphism

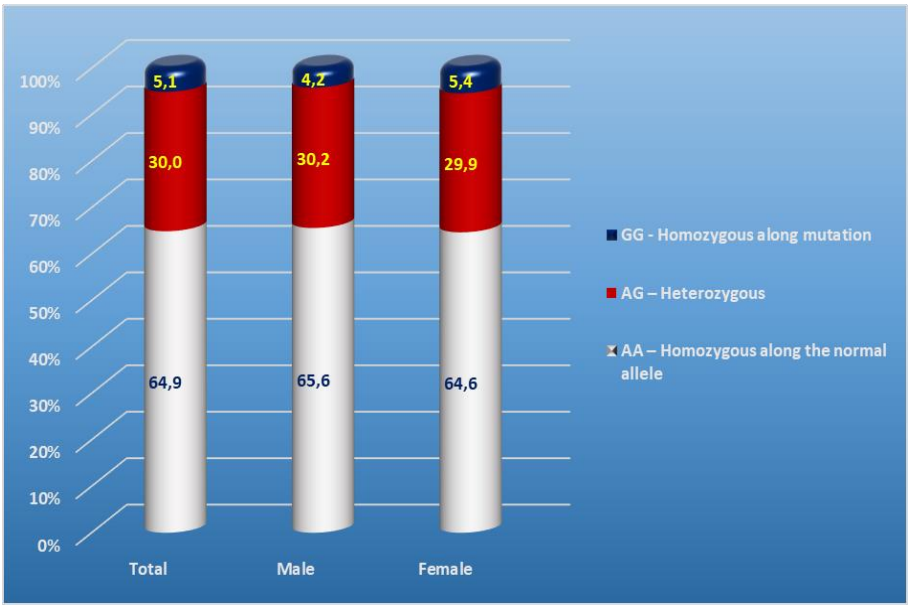


Fig. 15: Frequency distribution of patients according to SNP OPRM1 1947 genetic polymorphism

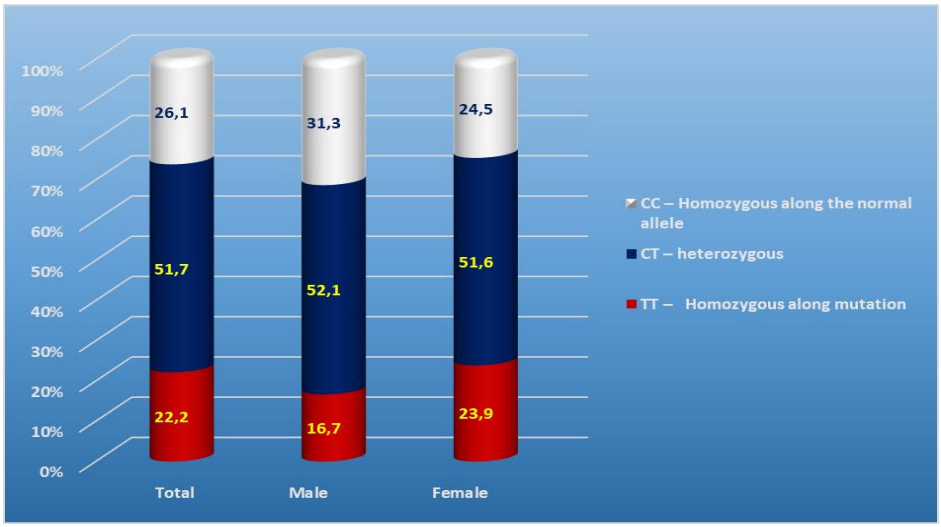


Fig. 16: Frequency distribution of patients according to MDR1 ABCB1 genetic polymorphism

It was stated that patients with urban residence represent higher percent (70.7%), followed by these living in villages – 29,3%, Fig. 17. Statistically significant difference for this parameter is not found between both genders.

The parameter "Education" demonstrated the following results:

- Patients with secondary education represent the highest percent (53,9%), followed by these with masters degree – 26,6%;
- Patients with primary education represent the lowest group– 6,6%. Significant difference between the patients from both genders is found in three education degrees – the number of men with secondary education is significantly higher, the number of women with Bachelor and Masters degree is also higher, Fig. 18.

Results on Fig. 19 demonstrate that according the marital status:

- The married female and male patients represent the highest percent (65,1%), followed by the divorced ones - 14,9%;
- The patients from category "single" represent the lowest number – 6,8%;
- Statistically reliable difference was found between patients of both genders in three of the categories – in category "married" male patients are considerably more, in categories "divorced" and "single" female patients prevail.
- Patients who have children represent higher percent (83,4%), followed by those without children - 16,6%. The significant difference for this parameter between both genders is expressed by higher percent for the women without children and, respectively, considerably higher percent for the men with children (Fig. 20).

The frequency distribution of patients according blood group parameter found the following (Fig. 21):

- Patients with blood type "A" represent the highest relative share (35,6%), followed by the one with zero blood group – 32%;
- Respectively, the patients with blood type „AB" represent the lowest share – 43 patients or 10,5%.

Results on Fig. 22 demonstrate that the ratio private to state health institution is 3:2.

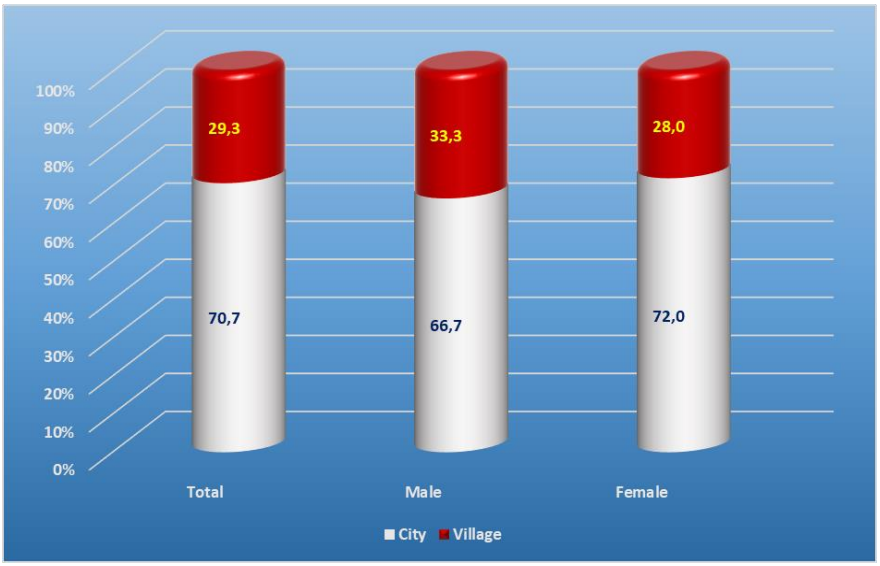


Fig. 17: Frequency distribution of patients according to the place of residence

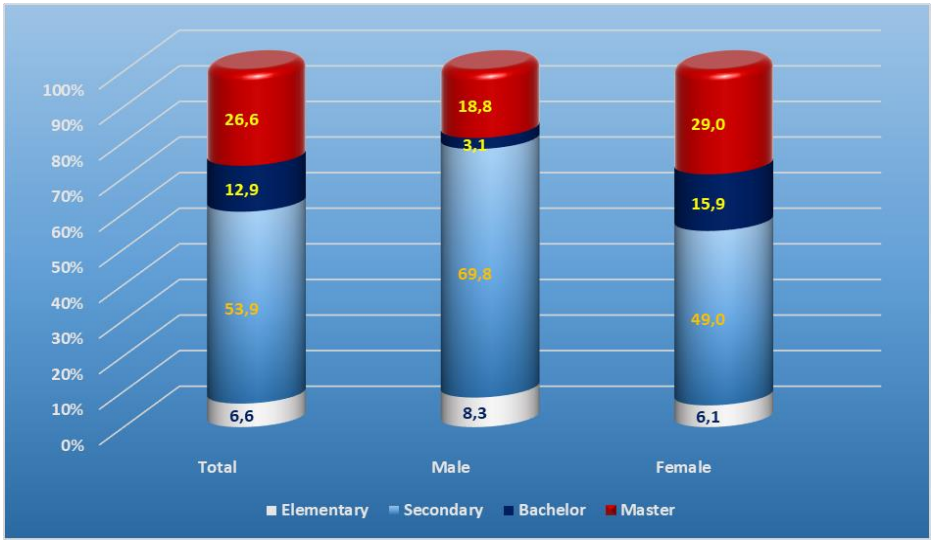


Fig. 18: Frequency distribution of patients according to the education level

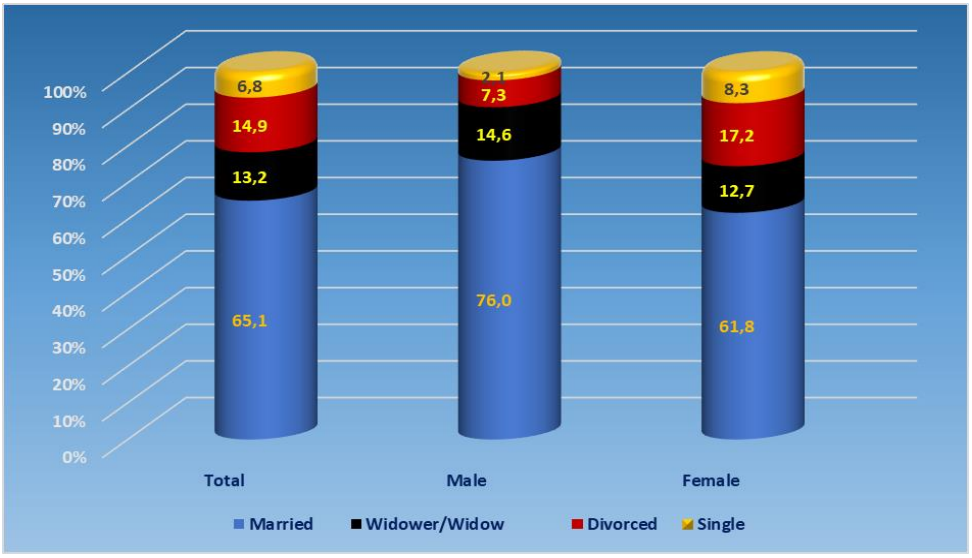


Fig. 19: Frequency distribution of patients according to the marital status

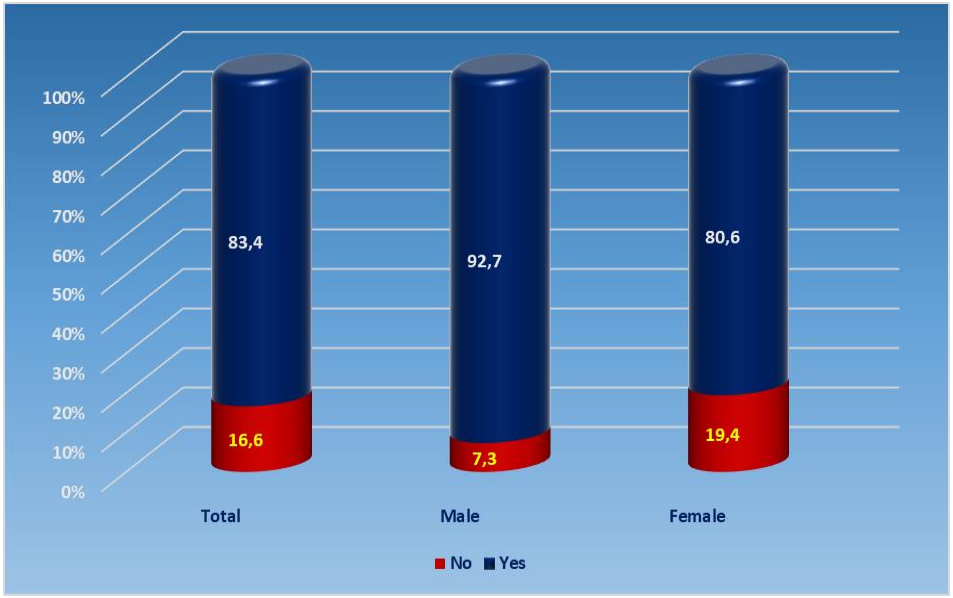


Fig. 20: Frequency distribution of patients according to the children born

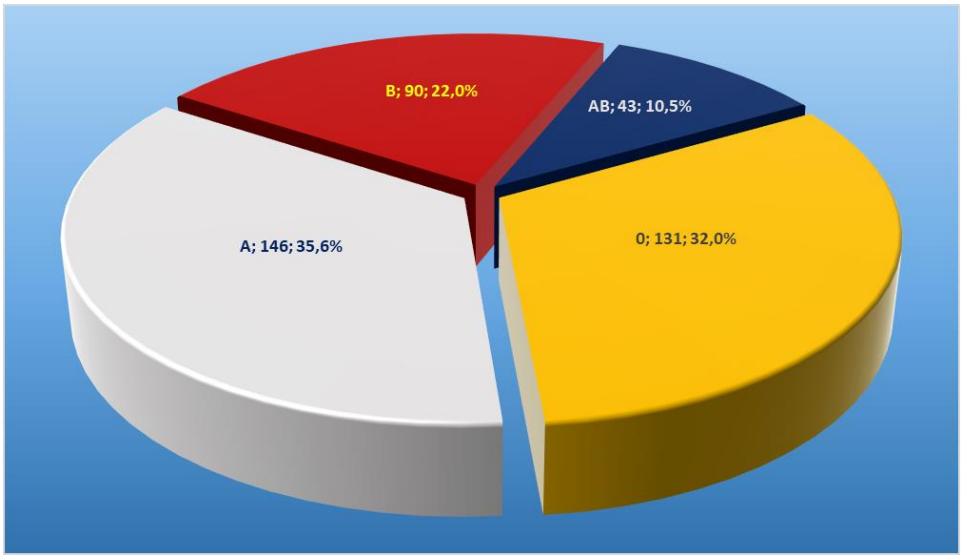


Fig. 21: Frequency distribution of patients according to the blood type

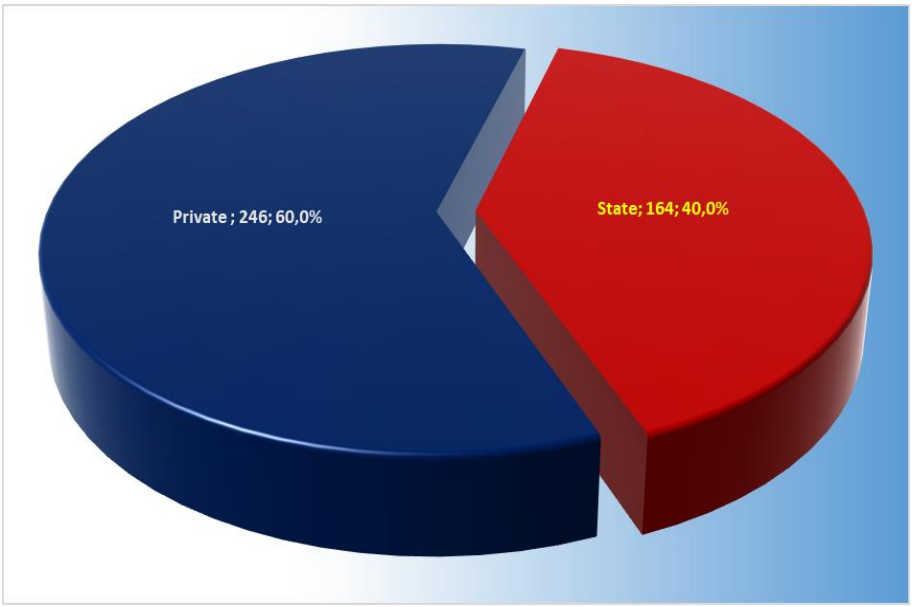
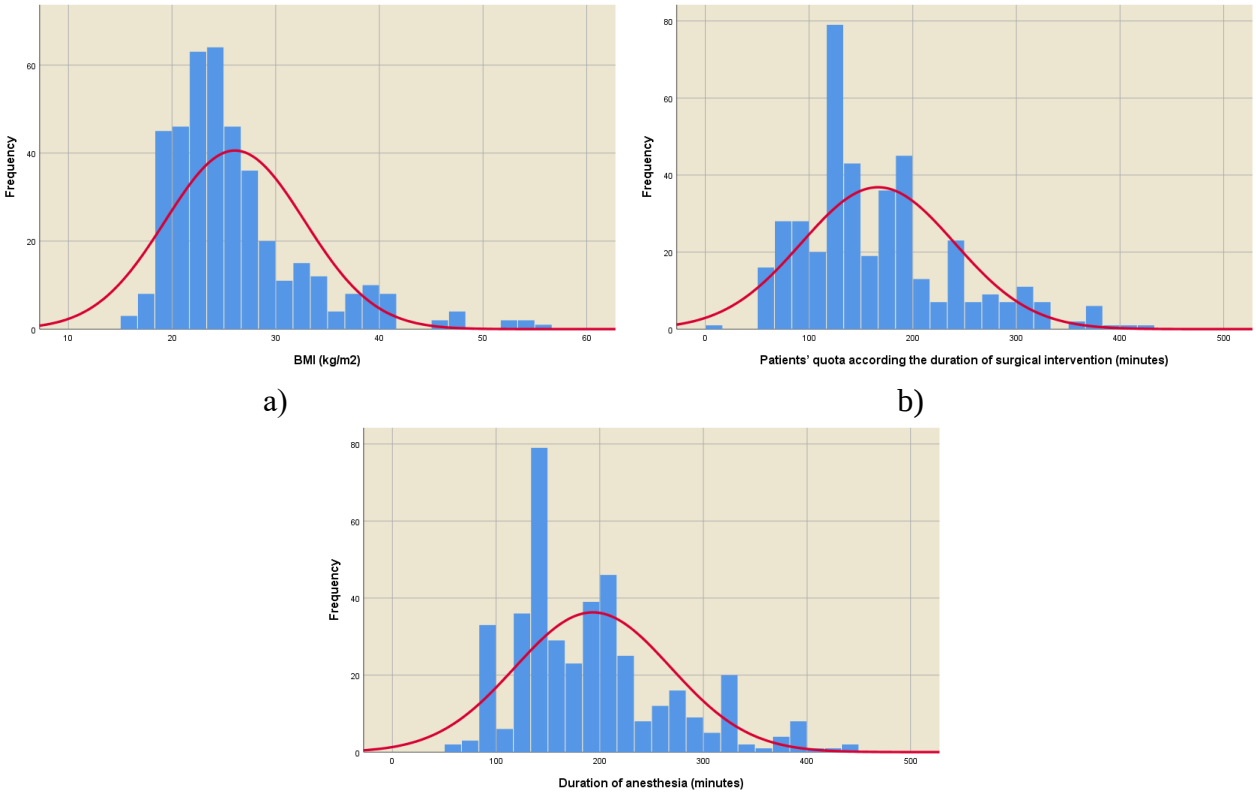


Fig. 22: Frequency distribution of patients according to the type of health institution

The variation analysis of quantitative parameters duration of surgical intervention, anesthesia duration and BMI demonstrated that:

- All three parameters are with frequency distribution that is significantly different from the normal one. The duration of surgical intervention has the highest variation coefficient (44,4%), while BMI has the lowest (25,8%), (Table 2), (Figure 23);
- The patients with normal weight represent the highest percent of all tested (51,2%) according the BMI four-group classification, followed by the overweight patients (25,6%), and the underweight ones (3,7%), (Figure 24).



a) b)

c)

Fig. 23: Frequency distribution of the tested patients' quota according to the of surgery duration, p<0,001 (a); duration of anesthesia, p<0,001 (b); BMI, p<0,001 (c)

Table 2: Variation analysis of the studied quantitative parameters

Parameter	n	Min	Max	$\overline{X}$	SD	Mode	V (%)
Surgery Duration (minutes)	410	10	65	166,48	74,00	120	44,4
Anesthesia Duration (minutes)	410	420	440	193,29	75,13	150	38,9
BMI (kg/m^2)	410	15,24	55,36	26,06	6,72	22	25,8

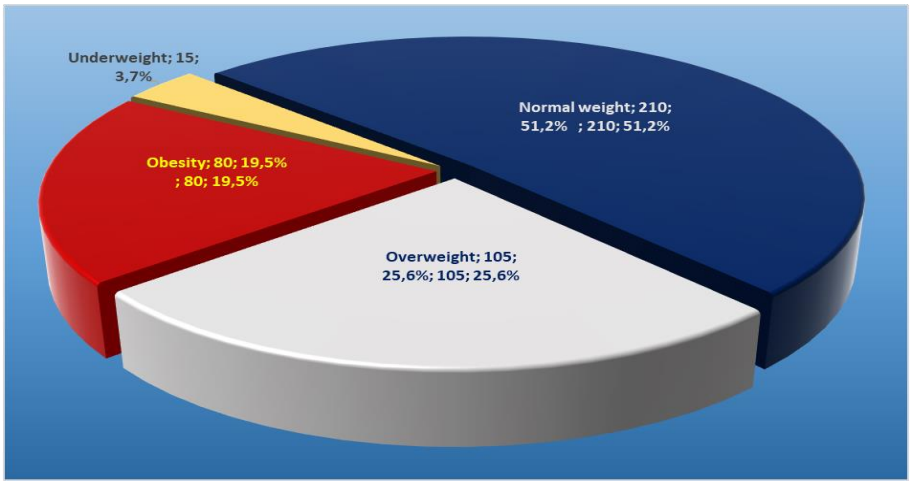


Fig. 24: Frequency distribution of patients according to BMI

Task 2: To study the impact of pre-operation anxiety (Taylor test) and depression levels (Beck's Depression Inventory and PHQ-9 test for depression) on the post-operative pain intensity (VAS for pain).

To study the effect of preoperative anxiety and depression level (Taylor test and PHQ-9 depression test) and pre- and postoperative depression (Beck Depression Inventory) on postoperative pain intensity (measured by VAS) as a first step a correlation analysis was performed to establish that:

- Postoperative pain in compliance with VAS has one-way and strongly expressed correlation with the three tests applied; the difference between the three tests correlation coefficients is statistically void (Table 5);
- Taylor test shows the only statistically significant difference between both genders in the correlation strength with the post-operative pain, for women the coefficient is considerably higher (Table 3):

Table 3: Correlation analysis of the relation between pre-operation anxiety(Taylor test), pre- and post-operative depression (PHQ-9 depression test and Beck Depression Inventory) and the post-operative pain in compliance with VAS

Parameters	Postoperative pain according to VAS			P
	Total	Men	Women	
Taylor test	0,690***a	0,577***a	0,714***a	**0,045**
Beck Depression Inventory	0,670***a	0,634***a	0,698***a	0,329
PHQ-9 depression test	0,650***a	0,600***a	0,670***a	0,320

* - p<0,05, ** - p<0,01, *** - p<0,001

✦ - the identical letters along verticals show lack of significant difference, while the different letters – presence of such difference Taylor test(p<0,05)

The second step was to implement comparative analysis of the pre-operation anxiety and depression levels (Taylor test and PHQ-9 test for depression) and post-operation depression level (Beck's Depression Inventory) for the different intensity levels of post-operation pain (Table 4). The analysis demonstrated significantly higher average values for the three tests applied on the higher postoperative pain according to VAS. This was valid for the whole excerpt, as well as for both genders.

Categorically, the relation between the level of preoperative anxiety and depression and the pain intensity after surgery is shown in Table 5 where it can be seen that:

- The pain with slight intensity represents the highest percent on the low level of Taylor anxiety test, the pain with average intensity – on the average level and the pain with strong intensity – on the high to very high level. Additionally, we have to mention that that maximal percent of patients with severe pain corresponds to the mean anxiety level, not to the high one. This described relation is repeated with males, while with females it is different - the maximal percent of patients enduring severe pain corresponds to the high anxiety level;
- With Beck Depression Inventory the number of categories is considerably higher and the respective postoperative pain reaction in compliance with VAS correlates in quite different mode. In the whole excerpt and separately for both genders, in category " No Depression" the patients with slight pain represent the highest percent and this is statistically reliable. In category "Slight", substantial difference in the relative shares of the three pain levels (mild to missing pain, moderate in intensity and severe) is not found. In "Mild to Moderate" depression category, in the whole excerpt, and especially for women, the pain with mean intensity represents higher relative share (for men, this difference is statistically negligible). In "Moderate to Severe" depression category, in the whole excerpt and for women, the moderate and strong pains are with statistically reliable higher

percents (for men, again there is no significant difference in the frequency distribution of the three pain types – mild to missing pain, moderate and severe one). In “Severe and Extremely Severe” depression category, severe pain is with the highest relative share. Additionally, it has to be mentioned that for the whole excerpt and for women, the maximal relative shares of average and high pain levels correspond to “Moderate to Severe” category. While for men, the average intensity pain represents the highest percent in light depression, and the strong intensity pain - with the categories “Moderate to Severe” and “Severe”.

- With PHQ-9 depression test, the categories are once again more and the respective post-operation pain reaction in compliance with VAS-scale correlates in a different mode. Here also, for the whole extract and separately for both genders, the patients with slight pain statistically represent the highest reliable percent in category “None”. The most frequent reaction in category “None” is pain of average intensity valid for the whole extract, severe pain with male patients and mild pain with female patients. But the difference is statistically reliable only with female patients. The expected relation between the average depression and the pain of average intensity is being found only for the whole extract. With male patients, this depression category has statistically identical distribution of the three types of pain, while with the female patients the average and severe depression categories are significantly more than the slight one. In “Moderate to Severe” depression category, the moderate and severe pains are statistically the most frequent reaction (there is no statistically significant difference in the relative shares). As expected, patients with “Severe Depression” endured severe pain most frequently. In the whole extract and for female patients, moderate and severe pains represent the maximal percents in “Moderate to Severe” depression; while for the male patients this is valid only for the severe pain. In “Moderate” category, moderate pain represents the maximal relative share.

Table 4: Analysis of the impact of preoperative anxiety and depression level (Taylor test and PHQ-9 test for depression) and postoperative depression level (Beck Depression Inventory) on the postoperative pain in compliance with VAS

Extract	Postoperative pain according to VAS	Taylor Test			Beck Depression Inventory			PHQ-9 test for depression		
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
Total	Mild	153	5,88[a]	6,79	153	9,01[a]	5,76	153	4,51[a]	4,33
	Average	156	16,09[b]	8,60	156	18,78[b]	8,24	156	11,51[b]	5,69
	Severe	101	24,75[c]	12,56	101	26,70[c]	11,03	101	15,39[c]	6,23
Men	Mild	17	6,12[a]	4,44	17	6,18[a]	3,19	17	3,00[a]	3,16
	Average	44	13,82[b]	7,92	44	16,27[b]	7,51	44	10,86[b]	5,62
	Severe	35	23,17[c]	13,51	35	24,26[c]	11,53	35	14,31[c]	6,57
Women	Mild	136	5,85[a]	7,03	136	9,36[a]	5,92	136	4,70[a]	4,43
	Average	112	16,98[b]	8,72	112	19,77[b]	8,34	112	11,77[b]	5,72
	Severe	66	25,59[c]	12,05	66	28,00[c]	10,62	66	15,95[c]	6,01

* - identical letters demonstrate lack of significant difference, while the different ones – availability of such difference ($p<0,05$)

Table 5: Analysis of the impact of preoperative anxiety level and pre- and postoperative depression on the post-operative pain in compliance with VAS

Tests	Anxiety and depression levels	Frequency	Total			Male			Female		
			Postoperative pain in compliance with VAS								
			Slight	Average	Severe	Slight	Average	Severe	Slight	Average	Severe
Taylor Test (anxiety)	Low	Number	113	30	11	11	9	4	102	21	7
		%	73,9[a]	19,2[b]	10,9[b]	64,7[a]	20,5[b]	11,4[b]	75,0[a]	18,8[b]	10,6[b]
	Average	Number	37	105	46	6	30	17	31	75	29
		%	24,2[a]	67,3[b]	45,5[c]	35,3[a]	68,2[bc]	48,6[ac]	22,8[a]	67,0[b]	43,9[c]
	High to Extremely high	Number	3	21	44	0	5	14	3	16	30
		%	2,0[a]	13,5[b]	43,6[c]	0,0[a]	11,4[a]	40,0[b]	2,2[a]	14,3[b]	45,5[c]
Beck Depression Inventory	None	Number	118	30	13	16	10	6	102	20	7
		%	77,1[a]	19,2[b]	12,9[b]	94,1[a]	22,7[b]	17,1[b]	75,0[a]	17,9[b]	10,6[b]
	Mild	Number	20	26	8	1	12	5	19	14	3
		%	13,1[a]	16,7[a]	7,9[a]	5,9[a]	27,3[a]	14,3[a]	14,0[a]	12,5[a]	4,5[a]
	Mild to moderate	Number	7	41	6	0	11	3	7	30	3
		%	4,6[a]	26,3[b]	5,9[a]	0,0[a]	25,0[a]	8,6[a]	5,1[a]	26,8[b]	4,5[a]
	Moderate to severe	Number	6	48	31	0	10	8	6	38	23
		%	3,9[a]	30,8[b]	30,7[b]	0,0[a]	22,7[a]	22,9[a]	4,4[a]	33,9[b]	34,8[b]
	Severe	Number	1	11	28	0	1	8	1	10	20
		%	0,7[a]	7,1[b]	27,7[c]	0,0[ac]	2,3[bc]	22,9[bc]	0,7[a]	8,9[b]	30,3[c]
	Extremely severe	Number	1	0	15	0	0	5	1	0	10
		%	0,7[a]	0,0[a]	14,9[c]	0,0[ac]	0,0[bc]	14,3[bc]	0,7[a]	0,0[a]	15,2[b]
PHQ-9 depression test	None	Number	112	29	11	15	9	5	97	20	6
		%	73,2[a]	18,6[b]	10,9[b]	88,2[a]	20,5[b]	14,3[b]	71,3[a]	17,9[b]	9,1[b]
	Mild	Number	24	25	8	0	6	5	24	19	3
		%	15,7[a]	16,0[bc]	7,9[ac]	0,0[a]	13,6[a]	14,3[a]	17,6[a]	17,0[a]	4,5[b]
	Moderate	Number	8	42	14	2	16	5	6	26	9
		%	5,2[a]	26,9[b]	13,9[c]	11,8[a]	36,4[a]	14,3[a]	4,4[a]	23,2[b]	13,6[b]
	Moderate to severe	Number	5	56	36	0	13	11	5	43	25
		%	3,3[a]	35,9[b]	35,6[b]	0,0[a]	29,5[b]	31,4[b]	3,7[a]	38,4[b]	37,9[b]
	Severe	Number	4	4	32	0	0	9	4	4	23
		%	2,6[a]	2,6[a]	31,7[b]	0,0[ac]	0,0[a]	25,7[bc]	2,9[a]	3,6[a]	34,8[b]

* - the identical letters along the horizontal lines show that there is NO significant difference, while the different ones – the presence of such one ($p<0,05$)

Task 3: To estimate the frequency of SNP OPRM1 118 A>G genetic polymorphism (according to the AA, AG, GG alleles), of COMT 1947 G>A genetic polymorphism (according the alleles AA, AG, GG), as well as of the MDR1 (C3435T) ABCB1 polymorphism (according to allele CC, CT TT), and their impact on the postoperative pain intensity (VAS for pain).

- With the tested persons with allele AA of genetic polymorphism SNP OPRM1 (total, male and female patients) the patients who mentioned severe pain in the early post-operation period represent significantly lower percent, while with patients with allele AG those enduring severe pain represent higher percent. With patients with allele GG, the difference in frequency distribution of the three pain levels (slight to missing, with average intensity and severe) is statistically negligible.
- Similar relation type in being monitored also in the genetic polymorphism COMT 1947 (total) – patients homozygous along the normal allele GG demonstrate lower percent of severe pain, while in heterozygous GA the patients enduring severe pain represent considerably higher percent. In patients with GG allele, the difference in frequency distribution of the three pain levels is statistically negligible (total, male and female). In male and female patients separately (allele GG), the ones with severe pain represent considerably lower percent only compared to the percent of persons with average intensity pain.
- In connection with polymorphism MDR1 ABCB1, the statistically significant difference in frequency distribution of the three pain levels is monitored only in patients with allele CC, for the total extract. The severe pain represent significantly higher percent compared to the slight pain, but not compared to the medium one; its relative share is not statistically different compared to the one of the other two levels.

These data are shown in Table 6:

Table 6: Analysis of the impact of SNP OPRM1 genetic polymorphism, COMT 1947 genetic polymorphism, as well as of MDR1 polymorphism on the postoperative pain intensity

Parameters	Alleles	Frequency	Total			Male			Female		
			Postoperative pain in compliance with VAS								
			Slight	Average	Severe	Slight	Average	Severe	Slight	Average	Severe
SNP OPRM1 Genetic polymorphism	AA	Number	110	120	36	14	34	15	96	86	21
		%	71,9[a]	76,9[a]	35,6[b]	82,4[a]	77,3[a]	42,9[b]	70,6[a]	76,8[a]	31,8[b]
	AG	Number	37	30	56	1	10	18	36	20	38
		%	24,2[a]	19,2[a]	55,4[b]	5,9[a]	22,7[a]	51,4[b]	26,5[a]	17,9[a]	57,6[b]
	GG	Number	6	6	9	2	0	2	4	6	7
		%	3,9[a]	3,8[a]	8,9[a]	11,8[a]	0,0[a]	5,7[a]	2,9[a]	5,4[a]	10,6[a]
COMT 1947 Genetic polymorphism	GG	Number	43	51	13	2	16	2	41	35	11
		%	28,1[a]	32,7[a]	12,9[b]	11,8[ac]	36,4[bc]	5,7[a]	30,1[ac]	31,3[a]	16,7[bc]
	GA	Number	74	63	61	8	20	21	66	43	40
		%	48,4[a]	40,4[a]	60,4[b]	47,1[a]	45,5[a]	60,0[a]	48,5[ac]	38,4[a]	60,6[bc]
	AA	Number	36	42	27	7	8	12	29	34	15
		%	23,5[a]	26,9[a]	26,7[a]	41,2[a]	18,2[a]	34,3[a]	21,3[a]	30,4[a]	22,7[a]
MDR1 Polymorphism	TT	Number	38	34	19	3	7	6	35	27	13
		%	24,8[a]	21,8[a]	18,8[a]	17,6[a]	15,9[a]	17,1[a]	25,7[a]	24,1[a]	19,7[a]
	CT	Number	85	81	46	12	24	14	73	57	32
		%	55,6[a]	51,9[a]	45,5[a]	70,6[a]	54,5[a]	40,0[a]	53,7[a]	50,9[a]	48,5[a]
	CC	Number	30	41	36	2	13	15	28	28	21
		%	19,6[a]	26,3[ac]	35,6[bc]	11,8[a]	29,5[a]	42,9[a]	20,6[a]	25,0[a]	31,8[a]

* - the identical letters along the horizontal lines demonstrate the lack of significant difference, while the different ones – the existence of such difference ($p<0,05$)

Task 4: To study the relation SNP 118 A>G of OPRM1 gene (according to alleles AA, AG, GG), the COMT 1947 G>A genetic polymorphism (according to alleles AA, AG, GG) and the polymorphism MDR1 (C3435T) ABCB1 (according to allele CC, CT TT) with the pre-operative and postoperative psychological condition of patients (Taylor anxiety test, Beck Depression Inventory and PHQ-9 depression test).

The analysis of the relation between polymorphism types and pre-operation psychological condition of patients (Taylor anxiety test) demonstrates that (Table 7):

- In the SNP OPRM1 genetic polymorphism (total, men and women), the patients with AA allele demonstrate lower average anxiety value according to Taylor anxiety test compared to patients with the other two alleles, whose average values are not statistically different;

- In the COMT 1947 genetic polymorphism (the whole excerpt), the patients with GG allele demonstrated lower average anxiety value compared to the other two alleles, which average values were also not different statistically. In men, the difference between the three alleles' average values is statistically negligible, while with female patients the average values of these with allele AA is higher compared to the ones of patients with the other two alleles; their average values both with male and female patients are not statistically different;

- In the third genetic polymorphism MDR1ABCB1 (the whole excerpt and for women), patients with the CC allele had a statistically significantly higher mean value than those with the TT allele, and lower than those with the CT allele, whose mean value did not differ statistically from those with the other two alleles. In men, the difference between the mean values of the three alleles is statistically negligible.

Analysis of the relation between polymorphism types and the patients' postoperative psychological condition (Beck Depression Inventory) demonstrates that (Table 8):

- In the SNP OPRM1 genetic polymorphism (total, men and women) the patients with AA allele demonstrate lower average value of depression compared to the ones with the other two alleles, whose mean values are not statistically different;

- The analysis found that in COMT 1947 genetic polymorphism (whole excerpt and women), the patients with GG allele demonstrated statistically reliable lower average value of depression compared to the ones with the other two alleles; male patients had higher average value of GA allele compared to the patients with GG allele, but not compared to the patients with AA allele; their mean value was not statistically different compared to the ones of the other two alleles;

We demonstrated that in MDR1 genetic polymorphism (whole excerpt, men and women) there is no statistically reliable difference between the mean values in compliance with Beck Depression Inventory.

Analysis of the relation between the genetic polymorphism types and the pre-operation psychological condition of patients (PHQ-9 depression test) demonstrated that (Table 9):

- In SNP OPRM1 genetic polymorphism (total, men and women), the patients with allele AA demonstrate lower mean value on PHQ-9 test compared to the ones with the other two alleles; the mean values of these patients were not statistically different;

- In the second genetic polymorphism, COMT 1947 (whole excerpt), the patients with allele GG demonstrated statistically reliable lower value on PHQ-9 test compared to the patients with the other two alleles. The average values of GA and AA alleles are not statistically different. With male patients we noticed that the average values difference for patients with the three alleles is statistically negligible; with female patients, the ones with allele AA demonstrate significantly higher average value compared to the these with the other two alleles; their average values are not statistically different;

- In the third genetic polymorphism, MDR1, (whole excerpt and women) it was found that patients with CC allele demonstrate higher average value compared to these with allele TT, and not compared to these with allele CT, whose average value is not statistically different compared to these ones with the other two alleles. In men, the difference of the average values of the patients with the three allele types is statistically negligible.

As for the different categories, the impact of genetic polymorphism SNP OPRM1, genetic polymorphism COMT 1947, as well as the impact of polymorphism MDR1 on pre-operation psychological condition of patients (Taylor test for anxiety) is demonstrated in the following (Table 10):

- With operated patients with allele AA of genetic polymorphism SNP OPRM1 (total, male and female) the patients with higher anxiety level are lower percent, while patients with allele AG the ones with high anxiety level constitute considerably higher percent. In patients with allele GG (whole excerpt and women) these with high anxiety percent represent considerably higher percent compared to these with low anxiety level; this is not valid for the average anxiety level. Its percent is not statistically different than the one of patients with the other two alleles. In men with allele GG the relative share of average anxiety level is statistically reliable lower compared to the ones of the other two levels that are not statistically different;
- In COMT 1947 genetic polymorphism (total) the with homozygous along the normal GG allele comprise lower percent at higher anxiety level, while it is reverse with patients who are heterozygous GA – patients with high level compared to the average level represent the considerably higher percent. This is not valid for the low level which percent is not statistically different from these of the other two levels. With male and female patients the frequency distribution difference of the three anxiety levels at the three alleles is statistically negligible;
- For polymorphism MDR1, the frequency distribution of three anxiety levels shows NO statistically reliable difference with either alleles, with the whole extract and with both genders. По отношение на полиморфизъм MDR1 статистически значима разлика в честотното разпределение на трите степени на тревожност не се наблюдава при нито един от алелите, в цялата извадка и при двата пол.

Table 7: Analysis of the relation between polymorphism types and the patients' preoperative psychological state (Taylor anxiety test)

Polymorphism type	Alleles	Total			Male			Female		
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
SNP OPRM1	AA	266	12,04[a]	9,78	63	12,19[a]	8,26	203	11,99[a]	10,22
	AG	123	18,47[b]	13,81	29	23,14[b]	12,87	94	17,03[b]	13,83
	GG	21	20,76[b]	13,47	4	21,00	22,61	17	20,71[b]	11,44
COMT 1947	GG	107	11,29[a]	8,86	20	11,80[a]	6,69	87	11,17[a]	9,32
	GA	198	15,21[b]	12,83	49	18,51[a]	13,31	149	14,12[ac]	12,53
	AA	105	16,10[b]	11,75	27	14,07[a]	10,34	78	16,81[bc]	12,19
MDR1	TT	91	12,77[a]	10,20	16	15,88[a]	9,72	75	12,11[a]	10,24
	CT	212	14,08[ac]	12,09	50	15,04[a]	11,16	162	13,79[ac]	12,38
	CC	107	16,47[bc]	12,16	30	17,23[a]	13,49	77	16,17[bc]	11,69

* - the identical letters along the vertical lines demonstrate lack of significant difference, while the different ones- the existence of such difference ($p<0,05$)
** - the groups without statistical representativeness are not included in this analysis

Table 8: Analysis of relation between polymorphism types and the patients' postoperative state (Beck Depression Inventory)

Polymorphism type	Alleles	Total			Male			Female		
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
SNP OPRM1	AA	266	14,94[a]	9,11	63	14,25[a]	8,57	203	15,16[a]	9,28
	AG	123	20,77[b]	12,47	29	23,72[b]	11,49	94	19,86[b]	12,68
	GG	21	22,62[b]	12,31	4	21,00	16,99	17	23,00[b]	11,59
COMT 1947	GG	107	13,95[a]	8,70	20	12,90[a]	7,89	87	14,20[a]	8,90
	GA	198	17,97[b]	11,57	49	19,90[bc]	11,62	149	17,34[b]	11,52
	AA	105	18,60[b]	10,61	27	16,19[ac]	9,87	78	19,44[b]	10,78
MDR1	TT	91	15,91[a]	10,32	16	17,50[a]	10,97	75	15,57[a]	10,22
	CT	212	16,94[a]	10,83	50	16,96[a]	10,72	162	16,94[a]	10,89
	CC	107	18,36[a]	11,03	30	18,07[a]	10,96	77	18,48[a]	11,12

* - the identical letters along the vertical lines demonstrate lack of significant difference, while the different – existence of such difference ($p<0,05$)
** - groups without statistical representativeness are not included in this analysis

Table 9: Analysis of relation between polymorphism types and the patients' preoperative psychological state (PHQ-9 depression test)

Polymorphism type	Alleles	Total			Male			Female		
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	n	$\overline{X}$	SD
SNP OPRM1	AA	266	8,69[a]	6,27	63	9,00[a]	5,97	203	8,60[a]	6,36
	AG	123	11,84[b]	7,46	29	14,38[b]	6,60	94	11,05[b]	7,57
	GG	21	12,95[b]	8,35	4	11,50	12,15	17	13,29[b]	7,67
COMT 1947	GG	107	8,07[a]	5,84	20	8,55[a]	5,77	87	7,95[a]	5,88
	GA	198	10,16[b]	7,30	49	12,08[a]	7,07	149	9,53[a]	7,29
	AA	105	11,10[b]	6,93	27	9,89[a]	6,84	78	11,51[b]	6,95
MDR1	TT	91	8,81[a]	6,72	16	10,00[a]	7,55	75	8,56[a]	6,56
	CT	212	9,81[ac]	6,95	50	10,92[a]	6,65	162	9,47[ac]	7,03
	CC	107	10,82[bc]	6,98	30	10,80[a]	7,00	77	10,83[bc]	7,02

* - the identical letters along the vertical lines demonstrate the lack of significant difference, while the different ones – the existence of such difference ($p<0,05$)

** - groups without statistical representativeness are not included in this analysis.

Table 10: Analysis of the impact of genetic polymorphisms SNP OPRM1 and COMT 1947, polymorphism MDR1 on the patients' preoperative psychological state (Taylor anxiety test)

Parameters	Alleles	Frequency	Total			Male			Female		
			Taylor test for anxiety								
			Low	Medium	High	Low	Medium	High	Low	Medium	High
SNP OPRM1 Genetic polymorphism	AA	Number	112	132	22	18	40	5	94	92	17
		%	72,7[a]	70,2[a]	32,4[b]	75,0[a]	75,5[a]	26,3[b]	72,3[a]	68,1[a]	34,7[b]
	AG	Number	37	47	39	4	13	12	33	34	27
		%	24,0[a]	25,0[a]	57,4[b]	16,7[a]	24,5[a]	63,2[b]	25,4[a]	25,2[a]	55,1[b]
	GG	Number	5	9	7	2	0	2	3	9	5
		%	3,2[a]	4,8[ac]	10,3[bc]	8,3[a]	0,0[b]	10,5[a]	2,3[a]	6,7[ac]	10,2[bc]
COMT 1947 Genetic polymorphism	GG	Number	43	56	8	5	14	1	38	42	7
		%	27,9[a]	29,8[a]	11,8[b]	20,8[a]	26,4[a]	5,3[a]	29,2[a]	31,1[a]	14,3[a]
	GA	Number	78	81	39	11	25	13	67	56	26
		%	50,6[ac]	43,1[a]	57,4[bc]	45,8[a]	47,2[a]	68,4[a]	51,5[a]	41,5[a]	53,1[a]
	AA	Number	33	51	21	8	14	5	25	37	16
		%	21,4[a]	27,1[a]	30,9[a]	33,3[a]	26,4[a]	26,3[a]	19,2[a]	27,4[a]	32,7[a]
MDR1 Polymorphism	TT	Number	37	45	9	4	9	3	33	36	6
		%	24,0[a]	23,9[a]	13,2[a]	16,7[a]	17,0[a]	15,8[a]	25,4[a]	26,7[a]	12,2[a]
	CT	Number	84	89	39	13	26	11	71	63	28
		%	54,5[a]	47,3[a]	57,4[a]	54,2[a]	49,1[a]	57,9[a]	54,6[a]	46,7[a]	57,1[a]
	CC	Number	33	54	20	7	18	5	26	36	15
		%	21,4[a]	28,7[a]	29,4[a]	29,2[a]	34,0[a]	26,3[a]	20,0[a]	26,7[a]	30,6[a]

* - the identical letters along the horizontal lines demonstrate the lack of significant difference, while the different ones – the presence of such difference ($p<0,05$)

Task 5: To assess the relation between the preoperative and postoperative psychological state of patients (Taylor, Beck and PHQ-9 depression test) with the SNP 118 A>G genetic polymorphism of the OPRM1 gene (according to alleles AA, AG, GG), the COMT 1947 G>A genetic polymorphism (according to alleles AA, AG, GG) and the polymorphism MDR1 (C3435T) ABCB1 (according to allele CC, CT TT), the VAS pain score and the number of applied analgesia for 24 hours on the complications' frequency and type resulting from the analgesia applied (nausea, vomiting, respiratory depression and cardiovascular complications).

To assess the relation between the preoperative and postoperative psychological state of patients (Taylor, Beck and PHQ-9 depression test) with the postoperative VAS pain score and the number of anesthetics administered in 24 hours, a correlation analysis was performed as a first step (Table 11), according to which:

• The number of applied anesthesia for 24 hours correlates proportionally and in strength with the results of the three tests and postoperative pain by VAS, the difference between the correlation coefficients with the three tests is statistically negligible, and the correlation coefficient with the postoperative pain by VAS is significantly higher than those of the three tests for the whole sample and for women, and for men only with the Taylor test;

• Statistically significant differences between the two sexes in the correlation strength were found in the Taylor test, Beck Inventory and postoperative pain by VAS, with significantly higher coefficients observed in women;

From Table 11 it is clear that:

• In the case of **SNP OPRM1 genetic polymorphism** (total for the subjects and women), patients with the AA allele had a significantly lower mean value of the number of anesthetics administered in 24 hours compared to the other two alleles, which did not differ statistically in their mean values. In men, the difference between the mean values of the number of analgesics in the AA and AG alleles was statistically insignificant;

• In **the COMT 1947 genetic polymorphism** (whole sample and women) - the difference between the mean values of the number of analgesics in those with the three alleles is statistically insignificant. In men, the mean value of those with the GG allele was significantly lower than in patients with the GA allele but not in men with the AA allele, which did not differ statistically from those with the other two alleles;

• For **MDR1** (whole sample) - patients with the CC allele had a significantly higher mean value than those with the other two alleles, which did not differ statistically. Men and women with the CC allele had higher mean values of 24-hour analgesia than patients with the TT allele, but not those with the CT allele, whose mean values did not differ statistically from those of the other two alleles.

The analysis of the relationship between the patients' preoperative and postoperative psychological state, the postoperative pain according to VAS and the number of applied anesthesia for 24 hours on the occurrence of nausea as a result of the applied anesthesia showed that (Table 12):

• **In the whole sample and in women**, all examined indicators (VAS, pre- and postoperative psychological state, and number of analgesics for 24 hours) have significantly higher average values in patients with nausea;

• **In men**, the mean values of the studied indicators (VAS, pre- and postoperative psychological state, and number of analgesics for 24 hours) are higher in patients who had nausea, but only in the number of anesthetics the difference is statistically significant.

The analysis of the relationship between the preoperative psychological state of patients, postoperative pain on the VAS scale and the number of administered analgesia for 24 hours on the occurrence of vomiting as a result of the applied analgesia showed that (Table 13):

• **In the whole sample and in women**, all studied indicators (VAS, pre- and postoperative psychological condition, and number of analgesics for 24 hours) have significantly higher average values in patients with vomiting;

• **In the men** in the study, the mean values of the studied indicators were higher in the patients who vomited, but the difference was statistically significant only in the postoperative pain according to VAS and the number of analgesia.

The analysis of the relationship between the preoperative psychological state of the patients, the postoperative pain according to the VAS and the number of administered analgesia for 24 hours on the occurrence of respiratory depression as a result of the applied analgesia showed that (Table 14):

• **In the whole sample and women**, all studied indicators have statistically significantly higher average values in patients with respiratory depression;

• **In male patients**, the mean values of the studied indicators are higher in those of them who have experienced respiratory depression, but the differences are not statistically significant.

The analysis of the relationship between the preoperative psychological state of patients, postoperative pain by VAS and the number of applied anesthesia for 24 hours on the occurrence of cardiovascular complications as a result of the applied anesthesia showed that (Table 15) **as in the whole sample, so in both sexes separately**, all studied indicators have significantly higher mean values in patients with cardiovascular complications.

Table 11: Correlation analysis between the patients' preoperative psychological state, the postoperative pain according to VAS and the number of administered analgesia for 24 hours

Indicators	Number of administered analgesia for 24 hours			P
	All	Men	Women	
Taylor test	0,577^{***a}	0,336^{**a}	0,628^{***a}	**0,001**
Beck Inventory	0,554^{***a}	0,415^{***ac}	0,592^{***a}	**0,043**
PHQ-9 depression test	0,546^{***a}	0,423^{***ac}	0,581^{***a}	0,072
Postoperative pain by VAS	0,780^{***b}	0,591^{***bc}	0,800^{***b}	**<0,001**

* - p<0,05, ** - p<0,01, *** - p<0,001

Table 12: Analysis of the relation between the patients' preoperative psychological state, the postoperative pain according to VAS and the number of administered analgesia for 24 hours on the occurrence of nausea as a result of the applied analgesia

Excerpt	Indicator	Nausea						P
		No			Yes			
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	
All	Taylor test	146	9,84	10,61	264	16,95	11,62	**<0,001**
	Beck Depresion Inventory	146	12,67	9,75	264	19,53	10,56	**<0,001**
	PHQ-9 depression test	146	6,92	6,61	264	11,48	6,57	**<0,001**
	Postoperative pain by VAS	146	3,84	2,56	264	6,41	2,12	**<0,001**
	Number of analgesia applied for 24 hours	146	1,31	1,00	264	2,38	0,95	**<0,001**
Men	Taylor test	25	15,20	12,73	71	16,10	11,33	0,552
	Beck Depression Inventory	25	16,20	12,20	71	17,82	10,23	0,252
	PHQ-9 depression test	25	9,80	7,98	71	11,06	6,43	0,380
	Postoperative pain by VAS	25	6,04	2,30	71	6,96	1,94	0,054
	Number of analgesia applied for 24 hours	25	1,96	1,06	71	2,55	0,84	**0,010**
Women	Taylor test	121	8,73	9,82	193	17,26	11,74	**<0,001**
	Beck Depression Inventory	121	11,94	9,06	193	20,16	10,63	**<0,001**
	PHQ-9 depression test	121	6,32	6,16	193	11,63	6,63	**<0,001**
	Postoperative pain by VAS	121	3,39	2,38	193	6,20	2,15	**<0,001**
	Number of analgesia applied for 24 hours	121	1,17	0,94	193	2,32	0,98	**<0,001**

Table 13: Analysis of the relation between the patients' preoperative psychological state, the postoperative pain according to VAS and the number of administered analgesia for 24 hours on the occurrence of vomiting as a result of the applied analgesia

Excerpt	Indicator	Vomiting						P
		No			Yes			
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	
All	Taylor test	258	11,81	10,85	152	18,84	11,97	**<0,001**
	Beck Depression Inventory	258	14,50	9,80	152	21,48	10,97	**<0,001**
	PHQ-9 depression test	258	8,26	6,65	152	12,57	6,56	**<0,001**
	Postoperative pain by VAS	258	4,62	2,45	152	6,97	2,12	**<0,001**
	Number of analgesia applied for 24 hours	258	1,65	1,04	152	2,59	0,92	**<0,001**
Men	Taylor test	47	14,85	10,78	49	16,84	12,46	0,474
	Beck Depression Inventory	47	15,74	10,45	49	18,98	10,87	0,121
	PHQ-9 depression test	47	10,02	7,30	49	11,41	6,38	0,243
	Postoperative pain by VAS	47	6,11	2,15	49	7,31	1,82	**0,005**
	Number of analgesia applied for 24 hours	47	2,09	1,00	49	2,69	0,77	**0,002**
Women	Taylor test	211	11,13	10,77	103	19,79	11,67	**<0,001**
	Beck Depression Inventory	211	14,22	9,66	103	22,67	10,86	**<0,001**
	PHQ-9 depression test	211	7,86	6,45	103	13,12	6,60	**<0,001**
	Postoperative pain by VAS	211	4,29	2,40	103	6,81	2,24	**<0,001**
	Number of analgesia applied for 24 hours	211	1,55	1,03	103	2,54	0,98	**<0,001**

Table 14: Analysis of the relation between the patients' preoperative psychological state, the postoperative pain according to VAS and the number of administered analgesia for 24 hours on the occurrence of respiratory depression as a result of the applied analgesia

Excerpt	Indicator	Respiratory depression						P
		No			Yes			
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	
All	Taylor test	335	13,57	11,89	75	18,17	10,48	**<0,001**
	Beck Depression Inventory	335	16,53	10,84	75	19,59	10,21	**0,011**
	PHQ-9 depression test	335	9,34	6,88	75	12,16	6,72	**0,002**
	Postoperative pain by VAS	335	5,21	2,61	75	6,75	2,12	**<0,001**
	Number of analgesia applied for 24 hours	335	1,90	1,09	75	2,44	1,00	**<0,001**
Men	Taylor test	58	14,52	11,78	38	17,92	11,29	0,072
	Beck Depression Inventory	58	16,86	10,94	38	18,21	10,51	0,439
	PHQ-9 depression test	58	10,00	6,63	38	11,84	7,10	0,213
	Postoperative pain by VAS	58	6,41	2,15	38	7,18	1,86	0,138
	Number of analgesia applied for 24 hours	58	2,34	0,95	38	2,47	0,92	0,560
Women	Taylor test	277	13,38	11,92	37	18,43	9,72	**0,005**
	Beck Depression Inventory	277	16,45	10,84	37	21,00	9,84	**0,011**
	PHQ-9 depression test	277	9,20	6,93	37	12,49	6,39	**0,007**
	Postoperative pain by VAS	277	4,96	2,63	37	6,30	2,30	**0,002**
	Number of analgesia applied for 24 hours	277	1,81	1,10	37	2,41	1,09	**0,002**

Table 15: Analysis of the relation between the patients' preoperative psychological state, the postoperative pain according to VAS and the number of administered analgesia for 24 hours on the occurrence of cardiovascular complications as a result of the applied analgesia

Excerpt	Indicator	Cardiovascular complications						P
		No			Yes			
		n	$\overline{X}$	SD	n	$\overline{X}$	SD	
All	Taylor test	238	10,48	10,08	172	19,85	11,78	**<0,001**
	Beck Depression Inventory	238	13,49	9,63	172	22,06	10,32	**<0,001**
	PHQ-9 depression test	238	7,48	6,43	172	13,13	6,24	**<0,001**
	Postoperative pain by VAS	238	4,44	2,47	172	6,95	1,99	**<0,001**
	Number of analgesia applied for 24 hours	238	1,58	1,02	172	2,58	0,93	**<0,001**
Men	Taylor test	33	9,64	7,11	63	19,13	12,26	**<0,001**
	Beck Depression Inventory	33	10,85	7,82	63	20,83	10,50	**<0,001**
	PHQ-9 depression test	33	6,33	5,57	63	13,03	6,33	**<0,001**
	Postoperative pain by VAS	33	5,24	1,90	63	7,49	1,70	**<0,001**
	Number of analgesia applied for 24 hours	33	1,76	0,83	63	2,73	0,81	**<0,001**
Women	Taylor test	205	10,62	10,49	109	20,28	11,53	**<0,001**
	Beck Depression Inventory	205	13,92	9,84	109	22,77	10,20	**<0,001**
	PHQ-9 depression test	205	7,67	6,55	109	13,19	6,22	**<0,001**
	Postoperative pain by VAS	205	4,31	2,53	109	6,63	2,08	**<0,001**
	Number of analgesia applied for 24 hours	205	1,55	1,04	109	2,50	0,99	**<0,001**

The analysis of the relation between the studied types of genetic polymorphism on the occurrence of nausea and respiratory depression as a result of the anesthesia applied found that (Tables 14 and 17):

• **In the whole sample, men and women**, the difference between the relative proportions of patients with and without the considered complications in all types of isomorphism and alleles is statistically insignificant.

The analysis of the dependence between the studied types of polymorphism on the occurrence of vomiting as a result of the applied anesthesia proved that (Table 16):

• **Only in the group of women, in the SNP OPRM1genetic polymorphism, allele GG** - the difference between the relative proportions of patients with and without vomiting is statistically significant;

• Patients with vomiting have a significantly higher percentage.

The performed analysis of the dependence between the studied types of polymorphism on the occurrence of cardiovascular complications as a result of the anesthesia applied showed that (Table 17):

• **In the whole sample and in the group of men, in the SNP OPRM1genetic polymorphism, alleles AA and AG** the difference between the relative proprtions of patients with and without cardiovascular complications is statistically significant;

• In the case of the AA allele, the patients who do not have the complication in question have a significantly higher percentage than in the case of the AG allele, in whom such a complication occurs.

• In women, the difference between the relative proportions of patients with and without cardiovascular complications in all types of isomorphism and alleles is statistically insignificant.

Table 16: Analysis of the dependence between the studied types of polymorphism on the occurrence of nausea as a result of the anesthesia applied

Excerpt	Polymorphism	Alleles	Nausea				P
			No		Yes		
			n	%	n	%	
All	SNP OPRM1	AA	98	67,1	168	63,6	0,479
		AG	43	29,5	80	30,3	
		GG	5	3,4	16	6,1	
	COMT 1947	GG	40	27,4	67	25,4	0,444
		GA	74	50,7	124	47,0	
		AA	32	21,9	73	27,7	
	MDR1	TT	33	22,6	58	22,0	0,620
		CT	79	54,1	133	50,4	
		CC	34	23,3	73	27,7	
Men	SNP OPRM1	AA	18	72,0	45	63,4	0,439
		AG	6	24,0	23	32,4	0,434
		GG	1	4,0	3	4,2	0,966
	COMT 1947	GG	6	24,0	14	19,7	0,894
		GA	12	48,0	37	52,1	
		AA	7	28,0	20	28,2	
	MDR1	TT	4	16,0	12	16,9	0,835
		CT	12	48,0	38	53,5	
		CC	9	36,0	21	29,6	
Women	SNP OPRM1	AA	80	66,1	123	63,7	0,426
		AG	37	30,6	57	29,5	
		GG	4	3,3	13	6,7	
	COMT 1947	GG	34	28,1	53	27,5	0,370
		GA	62	51,2	87	45,1	
		AA	25	20,7	53	27,5	
	MDR1	TT	29	24,0	46	23,8	0,418
		CT	67	55,4	95	49,2	
		CC	25	20,7	52	26,9	

Table 17: Analysis of the dependence between the studied polymorphism types on the occurrence of vomiting as a result of the anesthesia applied

Excerpt	Polymorphism	Alleles	Vomiting				P
			No		Yes		
			n	%	n	%	
All	SNP OPRM1	AA	175	67,8	91	59,9	0,156
		AG	73	28,3	50	32,9	
		GG	10	3,9	11	7,2	
	COMT 1947	GG	68	26,4	39	25,7	0,623
		GA	128	49,6	70	46,1	
		AA	62	24,0	43	28,3	
	MDR1	TT	61	23,6	30	19,7	0,492
		CT	134	51,9	78	51,3	
		CC	63	24,4	44	28,9	
Men	SNP OPRM1	AA	32	68,1	31	63,3	0,622
		AG	12	25,5	17	34,7	0,329
		GG	3	6,4	1	2,0	0,283
	COMT 1947	GG	11	23,4	9	18,4	0,774
		GA	24	51,1	25	51,0	
		AA	12	25,5	15	30,6	
	MDR1	TT	9	19,1	7	14,3	0,810
		CT	24	51,1	26	53,1	
		CC	14	29,8	16	32,7	
Women	SNP OPRM1	AA	143	67,8	60	58,3	0,099
		AG	61	28,9	33	32,0	0,574
		GG	7	3,3	10	9,7	**0,019**
	COMT 1947	GG	57	27,0	30	29,1	0,635
		GA	104	49,3	45	43,7	
		AA	50	23,7	28	27,2	
	MDR1	TT	52	24,6	23	22,3	0,728
		CT	110	52,1	52	50,5	
		CC	49	23,2	28	27,2	

Table 18: Analysis of the dependence between the studied polymorphism types on the occurrence of respiratory depression as a result of the applied anesthesia

Excerpt	Polymorphism	Alleles	Respiratory depression				P
			No		Yes		
			n	%	n	%	
All	SNP OPRM1	AA	217	64,8	49	65,3	0,886
		AG	100	29,9	23	30,7	
		GG	18	5,4	3	4,0	
	COMT 1947	GG	85	25,4	22	29,3	0,308
		GA	159	47,5	39	52,0	
		AA	91	27,2	14	18,7	
	MDR1	TT	69	20,6	22	29,3	0,158
		CT	180	53,7	32	42,7	
		CC	86	25,7	21	28,0	
Men	SNP OPRM1	AA	39	67,2	24	63,2	0,688
		AG	17	29,3	12	31,6	0,811
		GG	2	3,4	2	5,3	0,650
	COMT 1947	GG	9	15,5	11	28,9	0,273
		GA	31	53,4	18	47,4	
		AA	18	31,0	9	23,7	
	MDR1	TT	6	10,3	10	26,3	0,118
		CT	33	56,9	17	44,7	
		CC	19	32,8	11	28,9	
Women	SNP OPRM1	AA	178	64,3	25	67,6	0,731
		AG	83	30,0	11	29,7	
		GG	16	5,8	1	2,7	
	COMT 1947	GG	76	27,4	11	29,7	0,224
		GA	128	46,2	21	56,8	
		AA	73	26,4	5	13,5	
	MDR1	TT	63	22,7	12	32,4	0,304
		CT	147	53,1	15	40,5	
		CC	67	24,2	10	27,0	

Table 19: Analysis of the dependence between the studied polymorphism types on the occurrence of cardiovascular complications as a result of the applied anesthesia

Excerpt	Polymorphism	Alleles	Cardiovascular complications				P
			No		Yes		
			n	%	n	%	
All	SNP OPRM1	AA	170	71,4	96	55,8	**0,001**
		AG	57	23,9	66	38,4	**0,002**
		GG	11	4,6	10	5,8	0,586
	COMT 1947	GG	63	26,5	44	25,6	
		GA	113	47,5	85	49,4	0,927
		AA	62	26,1	43	25,0	
	MDR1	TT	60	25,2	31	18,0	
		CT	118	49,6	94	54,7	0,224
		CC	60	25,2	47	27,3	
Men	SNP OPRM1	AA	28	84,8	35	55,6	**0,004**
		AG	3	9,1	26	41,3	**0,001**
		GG	2	6,1	2	3,2	0,503
	COMT 1947	GG	8	24,2	12	19,0	
		GA	13	39,4	36	57,1	0,243
		AA	12	36,4	15	23,8	
	MDR1	TT	6	18,2	10	15,9	
		CT	16	48,5	34	54,0	0,876
		CC	11	33,3	19	30,2	
Women	SNP OPRM1	AA	142	69,3	61	56,0	
		AG	54	26,3	40	36,7	0,060
		GG	9	4,4	8	7,3	
	COMT 1947	GG	55	26,8	32	29,4	
		GA	100	48,8	49	45,0	0,806
		AA	50	24,4	28	25,7	
	MDR1	TT	54	26,3	21	19,3	
		CT	102	49,8	60	55,0	0,373
		CC	49	23,9	28	25,7	

Task 6: To analyze the relation between the diagnosis, the surgical method used (open surgery, laparoscopic surgery and robotic surgery), the surgery type (abdominal, thoracic and pelvic) and the various socio-anthropological factors (age, gender, BMI, marital status, education, place of residence, presence of children born, education, duration of surgery and anesthesia) on the strength of the pain experienced in the postoperative period (VAS pain scale) in patients with COMT 1947 G>A, SNP OPRM 118 A>G and MDR1 (C3435T) ABCB1 genetic polymorphisms.

Table 32 shows the range of thedescending average values of postoperative pain according to VAS - the scale for diagnoses with statistical representation. The results show that:

- Patients with sigmoid carcinoma have the highest mean pain on VAS (7.71), followed by those with gastric carcinoma with 7.36 and rectal carcinoma (7.18);
- The lowest mean value on VAS pain scale (2.50) is in patients diagnosed with endometrial hyperplasia;
- The first 9 diagnoses in the range of moderate pain, and the last four - in mild to no pain.

Since the study of the relation between the diagnosis, the polymorphism type and the postoperative pain on VAS requires a breakdown of the three alleles, the analysis included only four diagnoses, in which this breakdown should not lead to loss of statistical representation of the formed subgroups.

From Table 21 it is clear that in all four diagnoses there is no statistically significant relation between the studied polymorphism types and the values of postoperative pain on VAS.

The comparative analysis of the postoperative pain on VAS according to the surgical method used showed that there is a significant tendency to reduce the pain intensity from open to robotic surgery (Table 22).

Table 23 includes another supposed factor in the pain severity - the genetic polymorphism type. The results of the performed statistical comparisons are the following:

- In **open surgery**, there is a statistically significant difference between the mean values of postoperative pain by alleles in all the three polymorphism types. In **SNP OPRM1**, the statistically significantly lower mean value was in patients with the normal allele compared to those with the other two ones, whose mean values did not differ statistically from each other, while in **MDR1** a significantly lower mean value was observed in patients with the TT allele (homozygotes by mutation) compared to those with the other two ones, whose mean values do not differ statistically from each other. In **COMT 1947**, the mean values for the three alleles were statistically significantly different, with the lowest in patients with the GG allele, and the highest one in patients with the GA allele;
- In **laparoscopic surgery** in all the three polymorphism types the VAS mean values difference between those with the corresponding alleles is statistically insignificant;
- In **robotic surgery**, only MDR1 polymorphism shows a statistically significant difference between the postoperative pain mean values. The mean value of patients with TT allele was significantly lower than that of those with the CT allele, but not lower than that of patients with the CC allele, which did not differ statistically from those of the subjects in the study with the other two alleles.

Table 20: Comparative analysis of postoperative pain on VAS - according to the diagnosis

Diagnosis	Postoperative pain on VAS		
	n	$\overline{X}$	SD
Sigma carcinoma	21	7,71[a]	2,00
Stomach carcinoma	14	7,36[ac]	1,74
Rectal carcinoma	17	7,18[ac]	2,04
Lung carcinoma	18	7,06[ac]	1,63
Kidney carcinoma	13	6,69[acd]	2,18
Bladder carcinoma	12	6,17[bce]	1,64
Ovarian carcinoma	26	6,00[bcf]	2,19
Cervical carcinoma	71	5,82[bcg]	2,82
Prostate carcinoma	21	5,43[defgh]	2,13
Uterine leiomyoma	50	4,76[hj]	2,19
Endometrial carcinoma	88	4,39[ij]	2,69
Ovarian cyst	10	3,90[jl]	2,08
Endometrial hyperplasia	14	2,50[kl]	1,16

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only diagnoses with statistical representation participated in the analysis

Table 21: Comparative analysis of postoperative pain on VAS by diagnosis and polymorphism

Poly-morphism	Diagnosis	Alleles	Postoperative pain on VAS		
			n	$\overline{X}$	SD
SNP OPRM1	Cervical carcinoma	AA	50	5,28[a]	2,51
		AG	16	7,13[a]	3,22
		GG	5	7,00	3,32
	Endometrial carcinoma	AA	56	3,68[a]	2,22
		AG	28	5,79[a]	3,13
		GG	4	4,50	1,73
	Ovarian carcinoma	AA	14	5,43[a]	1,70
		AG	10	6,40[a]	2,72
		GG	2	8,00	1,41
	Uterine leiomyoma	AA	33	4,06[a]	1,46
		AG	15	5,73[a]	2,66
		GG	2	9,00	1,41
COMT 1947	Cervical carcinoma	GG	21	5,29[a]	2,65
		GA	29	5,93[a]	2,96
		AA	21	6,19[a]	2,84
	Endometrial carcinoma	GG	30	3,67[a]	2,26
		GA	40	5,08[a]	3,04
		AA	18	4,06[a]	2,21
	Ovarian carcinoma	GG	7	5,57	1,90
		GA	11	6,00[a]	2,86
		AA	8	6,38[a]	1,41
	Uterine leiomyoma	GG	11	4,91[a]	2,47
		GA	29	4,69[a]	2,09
		AA	10	4,80[a]	2,39
MDR1	Cervical carcinoma	TT	15	5,47[a]	2,61
		CT	37	5,81[a]	2,87
		CC	19	6,11[a]	3,00
	Endometrial carcinoma	TT	22	3,95[a]	2,26
		CT	50	4,10[a]	2,62
		CC	16	5,88[b]	3,07
	Ovarian carcinoma	TT	10	4,70[a]	1,57
		CT	9	6,56[a]	2,46
		CC	7	7,14	1,86
	Uterine leiomyoma	TT	10	5,90[a]	2,73
		CT	25	4,48[a]	2,12
		CC	15	4,47[a]	1,77

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only diagnoses with statistical representation after allele breakdown were included in the analysis

Table 22: Comparative analysis of the results of postoperative pain on VAS according to the surgical method used

Surgical method used	Postoperative pain on VAS		
	n	$\overline{X}$	SD
Open surgery	243	7,08[a]	1,80
Laparoscopic surgery	90	4,02[b]	1,75
Robotic surgery	77	2,21[c]	0,85

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

Table 23: Comparative analysis of VAS postoperative pain according to the surgical method used and polymorphism type

Polymorphism type	Surgical method used	Alleles	Postoperative pain on VAS		
			n	$\overline{X}$	SD
SNP OPRM1	Open surgery	AA	147	6,52[a]	1,53
		AG	81	7,91[b]	1,88
		GG	15	8,07[b]	1,79
	Laparoscopic surgery	AA	66	3,82[a]	1,47
		AG	22	4,55[a]	2,32
		GG	2	5,00	2,83
	Robotic surgery	AA	53	2,21[a]	0,88
		AG	20	2,10[a]	0,72
		GG	4	2,75	0,96
COMT 1947	Open surgery	GG	66	6,08[a]	1,82
		GA	113	7,66[b]	1,62
		AA	64	7,08[c]	1,66
	Laparoscopic surgery	GG	14	3,86[a]	1,88
		GA	54	3,91[a]	1,66
		AA	22	4,41[a]	1,89
	Robotic surgery	GG	27	2,41[a]	0,97
		GA	31	2,10[a]	0,79
		AA	19	2,11[a]	0,74
MDR1	Open surgery	TT	53	6,13[a]	1,70
		CT	121	7,15[b]	1,83
		CC	69	7,68[b]	1,54
	Laparoscopic surgery	TT	20	4,60[a]	2,54
		CT	44	3,84[a]	1,51
		CC	26	3,88[a]	1,31

	TT	18	1,89[a]	0,96
Robotic surgery	CT	47	2,30[bc]	0,69
	CC	12	2,33[ac]	1,15

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

The comparative analysis of the postoperative pain on VAS according to the surgery type showed that there is a higher mean value of postoperative pain in patients who underwent thoracic surgery compared to abdominal, but not compared to the small pelvic one, whose average value does not differ statistically from those of the other two types (Table 24).

In **abdominal surgery**, all the three polymorphism types have a statistically significant difference between the mean values of postoperative pain by alleles. In SNP OPRM1 and COMT 1947 the statistically significantly lower mean value was in the normal alleles compared to those of heterozygotes, but not in relation to homozygotes by mutation, whose mean values did not differ statistically from those of the other two types of alleles, while in MDR1 the significantly lower mean value is in the allele TT (homozygotes by mutation) compared to the allele CC (homozygones in the normal allele), but not in relation to the CT allele, whose mean value does not differ statistically from those of the other two types;

- In **thoracic surgery** and in all three types of polymorphism, the data do not have the necessary statistical representativeness to make statistically reliable conclusions;

- In **small pelvic surgery**, SNP OPRM1 genetic polymorphism, the mean of subjects with the AA allele (homozygones for the normal allele) was significantly lower than those with the other two alleles, whose mean values did not differ statistically from each other, while in MDR1 polymorphism the mean values of patients with the CC allele (homozygones for the normal allele) was significantly higher than those with the other two alleles, whose mean values did not differ statistically. In the COMT 1947 genetic polymorphism, the difference between the arithmetic means of the VAS postoperative pain on the three alleles was statistically negligible.

Table 24: Comparative analysis of postoperative pain according to VAS on pain by surgery type

Surgery type	**VAS on pain**		
	n	$\overline{X}$	SD
Abdominal	266	5,34[a]	2,57
Thoracic	20	6,80[bc]	1,88
Small pelvic	124	5,60[ac]	2,68

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

The correlation analysis of the dependence between postoperative pain (according to VAS) and the indicators for age, BMI, surgery duration and anesthesia, in the entire sample in both sexes showed the following results (Table 25):

- Throughout the excerpt and in women, the postoperative pain correlates directly and weakly to the age, and unidirectionally and moderately with the surgery duration and anesthesia. The age correlation is significantly lower than with the other two indicators, which do not differ statistically in their correlation coefficients;

- In men, a statistically significant correlation of pain with the indicators considered in the table is not established.

The correlation analysis of the relation between the VAS postoperative pain and age, BMI, surgery duration and anesthesia, showed that by polymorphism type (Table 27):

- In **SNP OPRM1, in patients with the AA allele**, postoperative pain correlates directly and weakly with age, and unidirectionally and moderately with the surgery duration and anesthesia. In those with the **AG allele,** the correlation is only with the last two indicators (surgery and anesthesia), and in those with the **GG allele** a statistically significant correlation of postoperative pain with the considered indicators was not established. Statistically significant correlation coefficients in subjects with the AA allele were significantly higher than those in patients with the AG allele;

- In **COMT 1947** (**all the three alleles**), the postoperative pain correlates directly and moderately with the surgery duration and anesthesia, and in those with the **GA allele** - unidirectionally and weakly with age. The statistically significant correlation coefficients for the three alleles did not differ significantly from each other;

- In **MDR1, TT and CT alleles**, the postoperative pain correlates directly and moderately with the surgery duration and anesthesia, and in people with the CC allele - unidirectional and weak with the same indicators, and moderately and directly proportionally with age. Statistically the credible correlation coefficients for the CT allele have significantly higher values than those of the CC allele, but not than those of the TT allele, which do not differ statistically from those of the other two alleles.

From Table 28 it is clear that the mean value of postoperative pain in men is significantly stronger than that in women.

The comparative analysis of the postoperative pain (according to VAS) by place of residence showed that the average value of those living in rural areas is higher than that of those living in cities (Table 29).

Table 30 shows that the difference between the mean values of patients with and without children was statistically insignificant.

The results of Table 30 show that:

- Marital status is significantly dependent on the postoperative pain’s magnitude;

- Family patients had a statistically significantly lower mean than those of the other three categories (widow/widower, divorced, single), which did not differ statistically from each other.

The conducted comparative analysis by educational qualification showed that education is not a factor influencing the magnitude of postoperative pain (according to the VAS - scale) (Table 31).

The results of the comparative analysis of the postoperative pain (according to the VAS - scale) by sex and polymorphism show that (Table 32):

- **In men with SNP OPRM1** - postoperative pain of those with the allele AA is less than that of patients with allele AG. **In women**, the postoperative pain of those with the AA allele was statistically significantly less than that of patients with the AG and GG alleles, whose mean values did not differ statistically;

- **COMT 1947, men** - the mean postoperative pain of those with the GG allele was significantly lower than that of patients with the GA allele, but not than that of the AA allele, which did not differ statistically from those of the other two alleles. **In women**, the difference between the mean values of the three alleles is statistically negligible;

- **MDR1, men** - the mean postoperative pain of those with the CC allele was significantly higher than that of patients with the CT allele, but not than that of the TT allele, which did not differ statistically from those of the other two alleles. **In women**, the postoperative pain of those with the CC allele was statistically significantly greater than that of patients with the TT allele, but not that of the CT allele, which did not differ statistically from those of the other two alleles.

The results of the comparative analysis of the postoperative pain (according to VAS) by place of residence and polymorphism show that (Table 33):

- **In patients with SNP OPRM1 genetic polymorphism living in a city** - the values of postoperative pain in those with the AA allele are significantly lower than those in patients with the AG allele, but not than that of those with the GG allele, which did not differ statistically from those of the other two alleles. ***Note: since the frequency distribution of postoperative pain on VAS is statistically significantly different from normal, the analysis was performed by applying the nonparametric Mann-Whitney test, which compares not arithmetic means, but so called middle ranks.*** In **rural** residents, the postoperative pain of those with the AA allele was statistically significantly lower than that of patients with the AG and GG alleles, whose mean values did not differ statistically;

- **COMT 1947, city** - the difference between the mean values of postoperative pain and the three alleles is statistically insignificant. In **rural** residents, the postoperative pain of people with the GG allele was statistically significantly lower than that of patients with the GA and AA alleles, whose mean values did not differ statistically;

- **MDR1, city** - the difference between the mean values of postoperative pain of all the three alleles is statistically insignificant. In **rural** residents, the mean postoperative pain of those with CC allele was significantly higher than that of patients with the other two alleles, which did not differ statistically.

The results of the comparative analysis of postoperative pain (according to VAS) by the presence of children born and polymorphism show that (Table 34):

- **SNP OPRM1 no children born** - the postoperative pain of those with the AA allele is significantly less than that of patients with the AG allele. In **those with children born**, the postoperative pain of those with the AA allele was statistically significantly less than that of patients with the AG and GG alleles, whose mean values did not differ statistically;

- **COMT 1947, no children born** - the mean postoperative pain of patients with the GG allele was significantly lower than that of patients with the AA allele, but not that of patients with the GA allele, which did not differ statistically from those of the GA allele. the other two alleles. In **those with children born**, the mean postoperative pain of patients with the GG allele was significantly lower than that of patients with the GA allele, but not than that of the AA allele, which did not differ statistically from those of the other two alleles;

- **MDR1, no children born** - the difference between the mean values of the three alleles is statistically negligible. In **those with children born**, the postoperative pain of patients with the CC allele was statistically significantly stronger than that of patients with the other two alleles, whose mean values did not differ statistically.

The results of the comparative analysis of the postoperative pain (according to) by marital status and polymorphism show that (Table 35):

- **SNP OPRM1, married** - the postoperative pain of those operated on the AA allele is significantly less than that of patients with the AG allele, but not than that of those with the GG allele, whose mean value did not differ statistically from that of the other two alleles. ***Note: since the frequency distribution of postoperative pain on the VAS scale is statistically significantly different from normal, the analysis is performed by applying the nonparametric Mann-Whitney test, which compares not arithmetic means, but the so called middle ranks***. In a **widow/widower**, the postoperative pain of patients with the AA allele is statistically equal to that of patients with the AG allele, while in a divorced and a single person, it is statistically significantly less;

- **COMT 1947** - in all four categories of marital status no significant difference was found between the mean values of postoperative pain of the three alleles;

- **MDR1, married** - the postoperative pain of those with the CC allele is statistically significantly greater than that of patients with the other two alleles, which do not differ statistically from each other. In the **widow/widower**, the mean postoperative pain of patients with the CC allele was significantly higher than that of patients with the TT allele, but not that of the CT allele, which also did not differ statistically from those of the other two alleles. In the other two categories of marital status, the differences between the mean values of the alleles are statistically insignificant.

The results of the comparative analysis of the postoperative pain (according to the VAS) by educational qualification and polymorphism show that (Table 36):

- **In SNP OPRM1, subjects with primary education and a Bachelor's degree** showed a difference between the mean values of postoperative pain in those with the AA and AG alleles, and this difference was statistically negligible. In patients with **secondary education**, the postoperative pain of subjects with the AA allele was less than that of patients with the AG allele. In a **Master's**

degree, the postoperative pain of those with the AA allele is statistically significantly less than that of the other two alleles, whose mean values did not differ statistically from each other;

- **In COMT 1947 genetic polymorphism, patients with primary education** showed a difference between the mean values of postoperative pain stretches that have the AA and AG alleles. This difference is statistically negligible. In **secondary education**, the postoperative pain of those with the AA allele was significantly lower than that of patients with the AG and GG alleles, who did not differ statistically. In the **Bachelor's and Master's degrees** there is no significant difference between the mean values of postoperative pain in the three alleles;

- **In patients with MDR1 genetic polymorphism, and with primary education and Master's degree** - no statistically significant difference between the mean values of postoperative pain in the three alleles was observed. In those with secondary education, the mean postoperative pain of patients with the CC allele was higher than that of patients with the CT allele, but not higher than that of the TT allele, which did not differ statistically from those of the other two alleles. In the Bachelor's degree, the postoperative pain of the studied patients with the TT allele was statistically significantly lower than that of the patients with the other two alleles, which did not differ statistically from each other.

Table 25: Comparative analysis of postoperative pain according to VAS by surgery type and polymorphism type

Polymorphism type	Surgery type	Alleles	Postoperative pain according to VAS		
			n	$\overline{X}$	SD
SNP OPRM1	Abdominal	AA	168	4,82[a]	2,23
		AG	88	6,26[bc]	2,87
		GG	10	6,10[ac]	2,96
	Thoracic	AA	12	6,33	1,37
		AG	7	7,43	2,57
		GG	1	8,00	.
	Small pelvic	AA	86	5,14[a]	2,38
		AG	28	6,43[b]	3,17
		GG	10	7,30[b]	2,67
COMT 1947	Abdominal	GG	66	4,64[a]	2,12
		GA	135	5,62[bc]	2,73
		AA	65	5,48[ac]	2,56
	Thoracic	GG	5	5,80	1,30
		GA	11	7,27	2,05
		AA	4	6,75	1,89

	Small pelvic	GG	36	5,14[a]	2,67
		GA	52	5,83[a]	2,79
		AA	36	5,75[a]	2,53
MDR1	Abdominal	TT	57	4,86[a]	2,36
		CT	133	5,28[ac]	2,63
		CC	76	5,82[bc]	2,59
	Thoracic	TT	5	6,80	2,28
		CT	9	6,22	1,92
		CC	6	7,67	1,37
	Small pelvic	TT	29	4,83[a]	2,56
		CT	70	5,49[a]	2,70
		CC	25	6,84[b]	2,43

* - the same letters vertically mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

Table 26: Correlation analysis of the relation between postoperative pain and age, BMI, surgery duration and anesthesia, in the entire excerpt in both sexes

Indicators	**Postoperative pain (by VAS)**			P
	Total	Men	Women	
Age (years)	0,179[***a]	-0,012	0,113[*a]	-
BMI (kg/m^2)	-0,073	0,021	-0,084	-
Surgery duration (min)	0,366[***b]	0,113	0,373[***b]	-
Anethesia duration (min)	0,364[***b]	0,113	0,366[***b]	-

* - $p<0,05$, ** - $p<0,01$, *** - $p<0,001$

*- the same letters vertically mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

Table 27: Correlation analysis of the relation between postoperative pain and the indicators for age, BMI, surgery duration and anesthesia, by polymorphism type

Indicators	Postoperative pain (on VAS)								
	SNP OPRM1			COMT 1947			MDR1		
	AA	AG	GG	AA	GA	GG	TT	CT	CC
Age (years)	0,245***	0,114	0,102	0,091	0,287***	0,072	0,133	0,113	0,338***
BMI (kg/m^2)	-0,088	-0,106	-0,176	-0,113	-0,077	-0,080	0,012	-0,121	0,001
Surgery duration (min)	0,462^{***a}	0,253^{**b}	0,166	0,358^{***a}	0,382^{***a}	0,352^{***a}	0,303^{**ac}	0,458^{***bc}	0,230^{*a}
Anethesia duration (min)	0,456^{***a}	0,250^{**b}	0,104	0,363^{***a}	0,380^{***a}	0,346^{***a}	0,300^{**ac}	0,462^{***bc}	0,236^{*a}

* - p<0,05, ** - p<0,01, *** - p<0,001

✦ - the same letters horizontally mean no significant difference, and different ones - the presence of such one (p<0,05)

Table 39: Comparative analysis of postoperative pain (on VAS) in both sexes

Postoperative pain (on VAS)						
Men			Women			**P**
n	$\overline{X}$	SD	n	$\overline{X}$	SD	
96	6,72	2,07	314	5,12	2,62	**<0,001**

Table 40: Comparative analysis of postoperative pain (on VAS) according to the place of residence

Postoperative pain (on VAS)						
City			Rural			**P**
n	$\overline{X}$	SD	n	$\overline{X}$	SD	
290	5,21	2,55	120	6,18	2,57	**0,001**

Table 41: Comparative analysis of postoperative pain (on VAS) according to presence of children born

Postoperative pain (on VAS)						
No			Yes			**P**
n	$\overline{X}$	SD	n	$\overline{X}$	SD	
68	5,75	2,48	342	5,44	2,62	0,416

Table 42: Comparative analysis of postoperative pain (on VAS) according to the mariatl status

Mariatl status	**Postoperative pain (on VAS)**		
	n	$\overline{X}$	SD
Married	267	5,14[a]	2,59
Widow/widower	54	6,22[b]	2,48
Divorced	61	5,92[b]	2,34
Single	28	6,54[b]	2,77

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

Table 43: Comparative analysis of postoperative pain (on VAS) according to the level of education

Education	Postoperative pain (on VAS)		
	n	$\overline{X}$	SD
Primary	27	5,78[a]	2,95
Secondary	221	5,39[a]	2,58
Bachelor	53	5,45[a]	2,80
Master	109	5,65[a]	2,44

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

Table 44: Comparative analysis of postoperative pain (on VAS) according to the gender and polymorphism

Polymorphism	Gender	Alleles	Postoperative pain (on VAS)		
			n	$\overline{X}$	SD
SNP OPRM1	Men	AA	63	6,16[a]	1,72
		AG	29	8,07[b]	1,91
		GG	4	5,75	3,86
	Women	AA	203	4,63[a]	2,30
		AG	94	5,84[b]	2,98
		GG	17	7,00[b]	2,52
COMT 1947	Men	GG	20	5,80[a]	1,20
		GA	49	7,18[bc]	2,18
		AA	27	6,56[ac]	2,17
	Women	GG	87	4,64[a]	2,44
		GA	149	5,30[a]	2,74
		AA	78	5,29[a]	2,56
MDR1	Men	TT	16	6,31[ac]	1,85
		CT	50	6,44[a]	2,22
		CC	30	7,40[bc]	1,77
	Women	TT	75	4,67[a]	2,46
		CT	162	5,06[ac]	2,66
		CC	77	5,68[bc]	2,65

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

Table 45: Comparative analysis of postoperative pain (on VAS) according to the place of residence and polymorphism

Polymorphism	Place of residence	Alleles	Postoperative pain (on VAS)		
			n	$\overline{X}$	SD
SNP OPRM1	City	AA	191	4,70[a]	2,25
		AG	88	6,18[bc]	2,83
		GG	11	6,36[ac]	2,87
	Rural	AA	75	5,73[a]	2,17
		AG	35	6,83[b]	3,12
		GG	10	7,20[b]	2,70
COMT 1947	City	GG	76	4,88[a]	2,26
		GA	138	5,28[a]	2,71
		AA	76	5,42[a]	2,53
	Rural	GG	31	4,81[a]	2,41
		GA	60	6,90[b]	2,44
		AA	29	6,14[b]	2,46
MDR1	City	TT	58	4,90[a]	2,54
		CT	155	5,19[a]	2,63
		CC	77	5,49[a]	2,40
	Rural	TT	33	5,06[a]	2,28
		CT	57	5,93[a]	2,54
		CC	30	7,87[b]	2,10

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

Table 46: Comparative analysis of postoperative pain (on VAS) according to the presence of children born and polymorphism

Polymorphism	Children born	Alleles	Postoperative pain (on VAS)		
			n	$\overline{X}$	SD
SNP OPRM1	No	AA	45	5,13[a]	2,11
		AG	19	6,95[b]	2,59
		GG	4	7,00	3,83
	Yes	AA	221	4,96[a]	2,30
		AG	104	6,26[b]	2,97
		GG	17	6,71[b]	2,59
COMT 1947	No	GG	21	4,90[a]	2,45
		GA	30	5,80[ac]	2,59
		AA	17	6,71[bc]	2,02
	Yes	GG	86	4,85[a]	2,27
		GA	168	5,76[bc]	2,76
		AA	88	5,41[ac]	2,56
MDR1	No	TT	17	5,65[a]	2,32
		CT	31	6,06[a]	2,53
		CC	20	5,35[a]	2,58
	Yes	TT	74	4,80[a]	2,45
		CT	181	5,27[a]	2,63
		CC	87	6,34[b]	2,52

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

Table 47: Comparative analysis of postoperative pain (on VAS) according to the marital status and polymorphism

Poly-morphism	Marital status	Alleles	Postoperative pain (on VAS)		
			n	$\overline{X}$	SD
SNP OPRM1	Married	AA	174	4,67[ac]	2,26
		AG	81	6,00[b]	2,97
		GG	12	6,08[bc]	2,78
	Widow/widower	AA	34	6,00[a]	2,09
		AG	16	6,19[a]	3,25
		GG	4	8,25	1,26
	Divorced	AA	40	5,45[a]	2,19
		AG	17	6,88[b]	2,20
		GG	4	6,50	3,51
	Single	AA	18	5,11[a]	2,25
		AG	9	9,00[b]	1,50
		GG	1	10,00	.
COMT 1947	Married	GG	68	4,57[a]	2,31
		GA	132	5,38[a]	2,77
		AA	67	5,24[a]	2,44
	Widow/widower	GG	15	5,33[a]	2,35
		GA	24	6,75[a]	2,36
		AA	15	6,27[a]	2,69
	Divorced	GG	14	5,64[a]	2,27
		GA	30	6,27[a]	2,41
		AA	17	5,53[a]	2,32
	Single	GG	10	5,00[a]	2,11
		GA	12	6,83[a]	3,07
		AA	6	8,50	1,76
MDR1	Married	TT	55	4,71[a]	2,51
		CT	143	4,98[a]	2,57
		CC	69	5,81[b]	2,60
	Widow/widower	TT	15	4,93[a]	2,49
		CT	27	6,33[ac]	2,42
		CC	12	7,58[bc]	1,88
	Divorced	TT	15	5,40[a]	1,96
		CT	31	6,16[a]	2,42
		CC	15	5,93[a]	2,58
	Single	TT	6	6,17	2,79
		CT	11	6,18[a]	3,31
		CC	11	7,09[a]	2,30

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

Table 48: Comparative analysis of postoperative pain (on VAS) according to the level of education and polymorphism

Poly-morphism	Education	Alleles	Postoperative pain (on VAS)		
			n	$\overline{X}$	SD
SNP OPRM1	Primary	AA	13	5,31[a]	2,66
		AG	11	6,09[a]	3,33
		GG	3	6,67	3,51
	Secondary	AA	151	5,04[a]	2,29
		AG	63	6,16[b]	2,97
		GG	7	6,00	3,51
	Bachelor	AA	35	4,86[a]	2,34
		AG	16	6,19[a]	3,27
		GG	2	10,00	0,00
	Master	AA	67	4,88[a]	2,16
		AG	33	6,94[b]	2,51
		GG	9	6,67[b]	1,87
COMT 1947	Primary	GG	15	4,27[a]	2,40
		GA	8	7,88[b]	2,36
		AA	4	7,25	3,10
	Secondary	GG	50	4,52[a]	2,24
		GA	108	5,67[b]	2,68
		AA	63	5,60[b]	2,55
	Bachelor	GG	12	5,50[a]	3,03
		GA	25	5,56[a]	3,08
		AA	16	5,25[a]	2,29
	Master	GG	30	5,47[a]	1,89
		GA	57	5,75[a]	2,67
		AA	22	5,64[a]	2,56
MDR1	Primary	TT	10	5,00[a]	2,26
		CT	12	5,33[a]	3,26
		CC	5	8,40	2,30
	Secondary	TT	46	5,35[ac]	2,51
		CT	118	5,13[a]	2,53
		CC	57	5,96[bc]	2,69
	Bachelor	TT	18	3,89[a]	2,08
		CT	21	6,10[b]	2,90
		CC	14	6,50[b]	2,77
	Master	TT	17	5,00[a]	2,55
		CT	61	5,66[a]	2,56
		CC	31	6,00[a]	2,10

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - only groups with statistical representation participate in the analysis

Task 7: To look for a relation between the three genetic polymorphisms, the pain strength (VAS pain scale) and the number of analgetics in 24 hours, as well as the presence of previous surgeries experienced by patients with the onset of catastrophization (Rumination, Magnification and Helplessness) by gender and surgical method (open surgery, laparoscopic surgery and robotic surgery).

The presence of previous surgeries did not significantly affect the relation between the three genetic polymorphisms, the postoperative pain severity (according to VAS) and the number of analgesics in 24 hours.

The analysis of the relation between the three genetic polymorphisms, the postoperative pain strength (according to the VAS-pain scale) and the number of analgesics in 24 hours, as well as the gender affiliation show that (Table 50):

- **Men with SNP OPRM1 genetic polymorphism and in all alleles** - no significant difference was found between the number of analgesics in those with different pain strength;

- **In men with COMT 1947 genetic polymorphism** - a statistically significant difference between the number of analgesics in those with moderate or severe pain and mild to no pain is found only in the GA allele. The higher number is in patients experiencing stronger pain;

- **In men with MDR1 genetic polymorphism** - a statistically significant difference between the number of analgesics in those with moderate or severe pain and mild to no pain is found only in the CT allele. The higher mean number is of patients with moderate or severe pain;

From the performend analysis it is clear that:

- **In women with SNP OPRM1 genetic polymorphism and alleles AA and AG** - the average number of analgesics is higher in those who experience more pain;

- **In women with COMT 1947 genetic polymorphism** - a significant difference between the number of analgesics in those who experience moderate or severe pain and mild to no pain is found in **all alleles**. The higher mean number is of those who have stronger pain;

- **In women with MDR1 genetic polymorphism** - a significant difference between the number of analgesics in those with moderate or severe pain and mild to no pain is found in all alleles. The higher mean number is of patients with moderate or severe pain.

The analysis of the relation between the three genetic polymorphisms, the postoperative pain strength (according to VAS) and the number of analgesics in 24 hours with the presence of catastrophization (no rumination either) show that (Table 51):

- **Patients in whom no catastrophization was detected** and who have **SNP OPRM1 genetic polymorphism, AA and AG alleles** - the number of analgesics in those with moderate or severe pain is greater than that of those with mild to no pain ;

- **In COMT 1947 genetic polymorphism with GA allele, where there is no catastrophization** - the number of analgesia in patients with moderate or severe pain is statistically significantly higher than that of those with mild to no pain;

- Patients **in whom we did not detect the presence of catastrophization, and who have a MDR1genetic polymorphism, allele CC** - the number of analgesics in those who have moderate or severe pain is statistically significantly higher than those with mild to no pain;

- Patients with **Rumination, SNP OPRM1** - the available data allow only for the **AG allele** to state statistically reliably that the number of analgesics in those with moderate or severe pain is significantly higher than that of those with mild to no pain;

- Patients with **Rumination, COMT 1947** - the available data suggest a statistically significant number of analgesia in those with moderate or severe pain is significantly higher than that of those with mild to no pain only for the GA and AA alleles;

- It was found that in patients with **Rumination and with MDR1 genetic polymorphism** - the available data allow only for the **CT allele** to claim statistically significantly that the number of analgesics in patients with moderate or severe pain is significantly higher than that of those with mild to missing pain.

In patients who developed a catastrophization with Rumination, the differences in the number of analgesia are significantly less significant compared to those where catastrophization is absent.

The analysis of the relation between the three genetic polymorphisms, the postoperative pain strength (according to VAS) and the number of analgesics in 24 hours, as well as the presence of catastrophization (magnification and helplessness) show that (Table 52):

- Patients with **Magnification and SNP OPRM1 genetic polymorphism** - the available data allow a statistically significant analysis to be performed only for the AA allele, in which no significant difference in the number of analgesia was found in those with mild and moderate or severe pain;

- In patients with **Magnification and COMT 1947 genetic polymorphism** - the available data allow a statistically significant analysis to be performed only for the GA allele, in which the number of analgesia in those with moderate or severe pain is statistically significantly higher than that of those with mild to no pain;

- In patients with **Magnification, MDR1** - the available data allow a statistically significant analysis to be performed only for the CT allele, in which there is no significant difference in the number of analgesics in those with mild and moderate or severe pain;

- In patients with **Helplessness in all types of polymorphism**, **all alleles** it was found that the available data did not allow a statistically reliable analysis.

Summary: In patients with proven catastrophization and with Magnification, differences in the number of analgesia are significantly less significant than those where catastrophization was reported.

The analysis of the relation between the three genetic polymorphisms, the postoperative pain strength (according to VAS) and the number of anesthetics in 24 hours, as well as the surgical method (open surgery) show (Table 53):

- In patients with **SNP OPRM1genetic polymorphism, alleles AA and AG** - the number of analgesics in those who have moderate or severe pain is greater than that of those with mild to no pain;

- In patients with **COMT 1947genetic polymorphism, alleles GG and GA** - the number of analgesia in patients with moderate or severe pain is statistically significantly higher than that of those with mild to no pain, while in the AA allele the difference is not statistically significant;

- In patients with **MDR1genetic polymorphism, , CT and CC alleles** - the number of analgesics in those with moderate or severe pain is statistically significantly higher than in those with mild to no pain, while in the TT allele the difference is statistically insignificant.

The analysis of the relation between the three genetic polymorphisms, the postoperative pain strength (according to VAS) and the number of anesthetics in 24 hours, as well as the surgical method applied (laparoscopic and robotic surgery) cannot be performed due to lack of statistical representation. the formed subgroups (Table 54).

Table 49: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and number of analgetics for the last 24 hours, as well as the presence of previous surgeries

Previous surgeries	Polymorphism	Alleles	Pain strength	Number of analgetics in the last 24 hours			P
				n	$\overline{X}$	SD	
No	SNP OPRM1	AA	Weak to none	83	1,71	0,98	**<0,001**
			Moderate or severe	12	2,83	0,72	
		AG	Weak to none	14	1,71	0,99	**0,012**
			Moderate or severe	15	2,80	1,01	
		GG	Weak to none	3	3,00	0,00	-
			Moderate or severe	2	3,00	1,41	
	COMT 1947	GG	Weak to none	28	1,71	1,01	-
			Moderate or severe	5	2,80	0,84	
		GA	Weak to none	43	1,65	1,02	**<0,001**
			Moderate or severe	17	2,88	0,86	
		AA	Weak to none	29	1,93	0,92	-
			Moderate or severe	7	2,71	1,11	
	MDR1	TT	Weak to none	27	1,48	0,98	-
			Moderate or severe	6	2,33	1,03	
		CT	Weak to none	46	1,74	1,02	**<0,001**
			Moderate or severe	14	3,07	0,73	
		CC	Weak to none	27	2,04	0,90	0,073
			Moderate or severe	9	2,78	0,97	
Yes	SNP OPRM1	AA	Weak to none	147	1,72	1,01	**<0,001**
			Moderate or severe	24	2,79	0,83	
		AG	Weak to none	53	1,51	0,95	**<0,001**
			Moderate or severe	41	3,12	0,78	
		GG	Weak to none	9	1,56	0,88	-
			Moderate or severe	7	3,00	1,00	
	COMT 1947	GG	Weak to none	66	1,68	0,93	**0,004**
			Moderate or severe	8	2,88	0,99	
		GA	Weak to none	94	1,61	1,04	**<0,001**
			Moderate or severe	44	3,07	0,82	
		AA	Weak to none	49	1,73	0,97	**<0,001**
			Moderate or severe	20	2,90	0,79	
	MDR1	TT	Weak to none	45	1,62	1,01	**0,009**
			Moderate or severe	13	2,54	0,97	
		CT	Weak to none	120	1,63	1,00	**<0,001**
			Moderate or severe	32	3,06	0,80	
		CC	Weak to none	44	1,80	0,95	**<0,001**
			Moderate or severe	27	3,15	0,72	

* - subgroups without statistical representation do not participate in the analysis

Table 50: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and the number of analgesics for 24 hours in both sexes

Gender	Poly-morphism	Alleles	Pain strength	Number of analgesics in the last 24 hours			P
				n	$\overline{X}$	SD	
Men	SNP OPRM1	AA	Weak to none	48	2,19	0,91	0,124
			Moderate or severe	15	2,60	0,63	
		AG	Weak to none	11	2,18	0,75	0,061
			Moderate or severe	18	2,89	1,08	
		GG	Weak to none	2	1,50	0,71	-
			Moderate or severe	2	3,50	0,71	
	COMT 1947	GG	Weak to none	18	2,11	0,68	-
			Moderate or severe	2	2,50	0,71	
		GA	Weak to none	28	2,29	0,98	**0,015**
			Moderate or severe	21	2,95	0,97	
		AA	Weak to none	15	2,00	0,93	0,152
			Moderate or severe	12	2,58	0,79	
	MDR1	TT	Weak to none	10	1,90	0,88	-
			Moderate or severe	6	2,33	1,03	
		CT	Weak to none	36	2,11	0,89	**0,006**
			Moderate or severe	14	2,93	0,83	
		CC	Weak to none	15	2,47	0,83	0,233
			Moderate or severe	15	2,87	0,92	
Women	SNP OPRM1	AA	Weak to none	182	1,59	0,98	**<0,001**
			Moderate or severe	21	2,95	0,86	
		AG	Weak to none	56	1,43	0,95	**<0,001**
			Moderate or severe	38	3,11	0,73	
		GG	Weak to none	10	2,00	1,05	**-**
			Moderate or severe	7	2,86	1,07	
	COMT 1947	GG	Weak to none	76	1,59	0,98	**<0,001**
			Moderate or severe	11	2,91	0,94	
		GA	Weak to none	109	1,45	0,98	**<0,001**
			Moderate or severe	40	3,05	0,75	
		AA	Weak to none	63	1,76	0,96	**<0,001**
			Moderate or severe	15	3,07	0,88	
	MDR1	TT	Weak to none	62	1,52	1,00	**0,003**
			Moderate or severe	13	2,54	0,97	
		CT	Weak to none	130	1,53	1,00	**<0,001**
			Moderate or severe	32	3,13	0,75	
		CC	Weak to none	56	1,73	0,90	**<0,001**
			Moderate or severe	21	3,19	0,68	

* - subgroups without statistical representation do not participate in the analysis

Table 51: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and the number of analgetics for 24 hours, as well as the presence of catastrophization (no rumination either).

Catastrophization	Poly-morphism	Alleles	Pain strength	Number of analgetics in the last 24 hours			P
				n	$\overline{X}$	SD	
None	SNP OPRM1	AA	Weak to none	165	1,55	0,98	**<0,001**
			Moderate or severe	9	3,11	0,33	
		AG	Weak to none	35	1,49	1,01	**<0,001**
			Moderate or severe	9	3,11	0,60	
		GG	Weak to none	6	1,83	1,17	-
			Moderate or severe	0	-	-	
	COMT 1947	GG	Weak to none	75	1,68	0,96	-
			Moderate or severe	5	3,00	0,00	
		GA	Weak to none	90	1,47	1,01	**<0,001**
			Moderate or severe	10	3,20	0,63	
		AA	Weak to none	41	1,49	0,98	-
			Moderate or severe	3	3,00	0,00	
	MDR1	TT	Weak to none	46	1,35	0,97	-
			Moderate or severe	3	3,33	0,58	
		CT	Weak to none	117	1,55	1,00	-
			Moderate or severe	7	2,86	0,38	
		CC	Weak to none	43	1,77	0,95	**<0,001**
			Moderate or severe	8	3,25	0,46	
Rumination	SNP OPRM1	AA	Weak to none	45	2,18	0,91	0,056
			Moderate or severe	15	2,73	0,80	
		AG	Weak to none	22	1,55	0,96	**<0,001**
			Moderate or severe	13	3,15	0,99	
		GG	Weak to none	4	1,75	0,96	-
			Moderate or severe	0	-	-	
	COMT 1947	GG	Weak to none	12	1,75	0,97	-
			Moderate or severe	4	3,00	1,41	
		GA	Weak to none	35	1,94	1,06	**0,006**
			Moderate or severe	16	2,88	0,89	
		AA	Weak to none	24	2,08	0,83	**0,023**
			Moderate or severe	8	3,00	0,76	
	MDR1	TT	Weak to none	19	2,00	1,00	-
			Moderate or severe	5	2,20	0,84	
		CT	Weak to none	36	1,81	0,95	**<0,001**
			Moderate or severe	13	3,31	0,75	
		CC	Weak to none	16	2,25	0,93	0,220
			Moderate or severe	10	2,80	0,92	

* - subgroups without statistical representation do not participate in the analysis

Table 52: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and the number of analgetics for 24 hours, as well as the presence of catastrophization (magnification, helplessness)

Catastrophization	Poly-morphism	Alleles	Pain strength	Number of analgetics in the last 24 hours			P
				n	$\overline{X}$	SD	
Magnification	SNP OPRM1	AA	Weak to none	15	2,27	0,96	0,682
			Moderate or severe	9	2,44	1,01	
		AG	Weak to none	7	1,86	0,90	-
			Moderate or severe	10	3,20	0,63	
		GG	Weak to none	2	2,50	0,71	-
			Moderate or severe	2	3,00	1,41	
	COMT 1947	GG	Weak to none	6	1,83	0,98	-
			Moderate or severe	4	2,50	1,00	
		GA	Weak to none	10	2,00	0,94	**0,020**
			Moderate or severe	11	3,09	0,83	
		AA	Weak to none	8	2,63	0,74	-
			Moderate or severe	6	2,67	1,03	
	MDR1	TT	Weak to none	4	2,25	0,50	-
			Moderate or severe	4	2,25	0,96	
		CT	Weak to none	11	2,36	1,03	0,116
			Moderate or severe	11	3,09	0,70	
		CC	Weak to none	9	1,89	0,93	-
			Moderate or severe	6	2,83	1,17	
Helplessness	SNP OPRM1	AA	Weak to none	5	1,40	0,55	-
			Moderate or severe	3	3,33	0,58	
		AG	Weak to none	3	1,67	0,58	-
			Moderate or severe	24	2,88	0,95	
		GG	Weak to none	0	-	-	-
			Moderate or severe	7	3,00	1,00	
	COMT 1947	GG	Weak to none	1	1,00	0,00	-
			Moderate or severe	0	-	-	
		GA	Weak to none	2	1,00	0,00	-
			Moderate or severe	24	3,00	0,88	
		AA	Weak to none	5	1,80	0,45	-
			Moderate or severe	10	2,80	1,03	
	MDR1	TT	Weak to none	3	1,33	0,58	-
			Moderate or severe	7	2,43	1,13	
		CT	Weak to none	2	1,50	0,71	-
			Moderate or severe	15	2,93	0,96	
		CC	Weak to none	3	1,67	0,58	-
			Moderate or severe	12	3,25	0,62	

* - subgroups without statistical representation do not participate in the analysis

Table 53: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and the number of analgetics for 24 hours, as well as the surgical method (open surgery)

Surgical method	Poly-morphism	Alleles	Pain strength		Number of analgetics for the last 24 hours			
					n	$\overline{X}$	SD	
Open surgery	SNP OPRM1	AA	Weak to none	or	112	2,48	0,70	**0,008**
			Moderate severe		35	2,83	0,79	
		AG	Weak to none	or	29	2,34	0,77	**<0,001**
			Moderate severe		52	3,10	0,85	
		GG	Weak to none	or	6	2,50	0,84	-
			Moderate severe		9	3,00	1,00	
	COMT 1947	GG	Weak to none	or	53	2,23	0,75	**0,016**
			Moderate severe		13	2,85	0,90	
		GA	Weak to none	or	55	2,62	0,65	**<0,001**
			Moderate severe		58	3,07	0,81	
		AA	Weak to none	or	39	2,54	0,68	0,067
			Moderate severe		25	2,88	0,88	
	MDR1	TT	Weak to none	or	38	2,26	0,72	0,354
			Moderate severe		15	2,53	1,06	
		CT	Weak to none	or	76	2,46	0,74	**<0,001**
			Moderate severe		45	3,09	0,76	
		CC	Weak to none	or	33	2,67	0,60	**0,012**
			Moderate severe		36	3,06	0,79	

* - subgroups without statistical representation do not participate in the analysis

Table 54: Analysis of the relation between the three genetic polymorphisms, postoperative pain on VAS and the number of analgetics for 24 hours, as well as the surgical method (laparoscopic and robotic surgery)

Surgical method	Poly-morphism	Alleles	Pain strength	Number of analgetics in the last 24 hours			P
				n	$\overline{X}$	SD	
Laparoscopic surgery	SNP OPRM1	AA	Weak to none	65	1,18	0,66	-
			Moderate or severe	1	2,00	0,00	
		AG	Weak to none	18	1,11	0,58	-
			Moderate or severe	4	2,25	0,50	
		GG	Weak to none	2	1,50	0,71	-
			Moderate or severe	0	-	-	
	COMT 1947	GG	Weak to none	14	1,43	0,76	-
			Moderate or severe	0	-	-	
		GA	Weak to none	51	1,12	0,62	-
			Moderate or severe	3	2,00	0,00	
		AA	Weak to none	20	1,15	0,59	-
			Moderate or severe	2	2,50	0,71	
	MDR1	TT	Weak to none	16	0,94	0,57	-
			Moderate or severe	4	2,25	0,50	
		CT	Weak to none	43	1,19	0,66	-
			Moderate or severe	1	2,00	0,00	
		CC	Weak to none	26	1,31	0,62	-
			Moderate or severe	0	-	-	
Robotic surgery	SNP OPRM1	AA	Weak to none	53	0,75	0,48	-
			Moderate or severe	0	-	-	
		AG	Weak to none	20	0,80	0,52	-
			Moderate or severe	0	-	-	
		GG	Weak to none	4	1,25	0,96	-
			Moderate or severe	0	-	-	
	COMT 1947	GG	Weak to none	27	0,78	0,58	-
			Moderate or severe	0	-	-	
		GA	Weak to none	31	0,68	0,48	-
			Moderate or severe	0	-	-	
		AA	Weak to none	19	1,00	0,47	-
			Moderate or severe	0	-	-	
	MDR1	TT	Weak to none	18	0,67	0,59	-
			Moderate or severe	0	-	-	
		CT	Weak to none	47	0,79	0,51	-
			Moderate or severe	0	-	-	
		CC	Weak to none	12	1,00	0,43	-
			Moderate or severe	0	-	-	

* - subgroups without statistical representation do not participate in the analysis

Task 8: To determine whether there is a relation between blood type, the three genetic polymorphisms and the strength of postoperative pain.

From Tables 55-58 it is clear that there is no statistically significant relation between blood type, the three genetic polymorphisms and the postoperative pain strength.

Table 55: Analysis of the relation between blood type affiliation and SNP OPRM1 genetic polymorphism

Excerpt	Glood type	Frequency	SNP OPRM1 Genetic polymorphism		
			AA	AG	GG
All	A	n	93	47	6
		%	35,0[a]	38,2[a]	28,6[a]
	B	n	57	26	7
		%	21,4[a]	21,1[a]	33,3[a]
	AB	n	29	12	2
		%	10,9[a]	9,8[a]	9,5[a]
	0	n	87	38	6
		%	32,7[a]	30,9[a]	28,6[a]
Men	A	n	21	7	1
		%	33,3[a]	24,1[a]	25,0[a]
	B	n	17	7	2
		%	27,0[a]	24,1[a]	50,0[a]
	AB	n	10	3	0
		%	15,9[a]	10,3[a]	0,0[a]
	0	n	15	12	1
		%	23,8[a]	41,4[a]	25,0[a]
Women	A	n	72	40	5
		%	35,5[a]	42,6[a]	29,4[a]
	B	n	40	19	5
		%	19,7[a]	20,2[a]	29,4[a]
	AB	n	19	9	2
		%	9,4[a]	9,6[a]	11,8[a]
	0	n	72	26	5
		%	35,5[a]	27,7[a]	29,4[a]

* - the same letters horizontally mean absence of a significant difference, and different ones - the presence of such one ($p<0,05$)

Table 56: Analysis of the relation between blood type affiliation and COMT 1947 genetic polymorphism

Excerpt	Glood type	Frequency	COMT 1947 Genetic polymorphism		
			GG	GA	AA
All	A	n	39	65	42
		%	36,4[a]	32,8[a]	40,0[a]
	B	n	24	44	22
		%	22,4[a]	22,2[a]	21,0[a]
	AB	n	14	21	8
		%	13,1[a]	10,6[a]	7,6[a]
	0	n	30	68	33
		%	28,0[a]	34,3[a]	31,4[a]
Men	A	n	6	14	9
		%	30,0[a]	28,6[a]	33,3[a]
	B	n	7	12	7
		%	35,0[a]	24,5[a]	25,9[a]
	AB	n	3	6	4
		%	15,0[a]	12,2[a]	14,8[a]
	0	n	4	17	7
		%	20,0[a]	34,7[a]	25,9[a]
Women	A	n	33	51	33
		%	37,9[a]	34,2[a]	42,3[a]
	B	n	17	32	15
		%	19,5[a]	21,5[a]	19,2[a]
	AB	n	11	15	4
		%	12,6[a]	10,1[a]	5,1[a]
	0	n	26	51	26
		%	29,9[a]	34,2[a]	33,3[a]

* - the same letters horizontally mean absence of a significant difference, and different ones - the presence of such one ($p<0,05$)

Table 57: Analysis of the relation between blood type affiliation and MDR1 genetic polymorphism

Excerpt	Glood type	Frequency	MDR1 Polymorphism		
			TT	CT	CC
All	A	n	30	85	31
		%	33,0[a]	40,1[a]	29,0[a]
	B	n	22	43	25
		%	24,2[a]	20,3[a]	23,4[a]
	AB	n	8	24	11
		%	8,8[a]	11,3[a]	10,3[a]
	0	n	31	60	40
		%	34,1[a]	28,3[a]	37,4[a]
Men	A	n	2	20	7
		%	12,5[a]	40,0[a]	23,3[a]
	B	n	7	11	8
		%	43,8[a]	22,0[a]	26,7[a]
	AB	n	2	7	4
		%	12,5[a]	14,0[a]	13,3[a]
	0	n	5	12	11
		%	31,3[a]	24,0[a]	36,7[a]
Women	A	n	28	65	24
		%	37,3[a]	40,1[a]	31,2[a]
	B	n	15	32	17
		%	20,0[a]	19,8[a]	22,1[a]
	AB	n	6	17	7
		%	8,0[a]	10,5[a]	9,1[a]
	0	n	26	48	29
		%	34,7[a]	29,6[a]	37,7[a]

* - the same letters horizontally mean absence of a significant difference, and different ones - the presence of such one ($p<0,05$)

Table 58: Comparative analysis of postoperative pain by blood type

Excerpt	Blood type	Postoperative pain (on VAS)		
		n	$\overline{X}$	SD
All	A	146	5,36[a]	2,61
	B	90	5,49[a]	2,52
	AB	43	6,07[a]	2,79
	0	131	5,46[a]	2,56
Men	A	29	6,66[a]	2,09
	B	26	6,69[a]	2,24
	AB	13	6,85[a]	1,77
	0	28	6,75[a]	2,10
Women	A	117	5,03[a]	2,64
	B	64	5,00[a]	2,48
	AB	30	5,73[a]	3,10
	0	103	5,11[a]	2,57

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

The analysis of the relation between blood type affiliation, the three genetic polymorphisms with the preoperative psychological state of the patients (Taylor's anxiety test) showed that (Table 59):

- Patients with **blood type A, genetic polymorphism SNP OPRM1**, allele **AA** have a significantly lower mean value of anxiety according to Taylor than that with allele AG;
- Patients with **blood type A, COMT 1947 genetic polymorphism** - statistically credible lower mean anxiety had patients with the GG allele than that of the AA allele, while the mean value of the GA allele did not differ statistically from those of the other two alleles;
- In patients with **blood type A and MDR1 polymorphism**, the difference between the mean values for the three alleles was statistically negligible;
- In patients with **blood type B, SNP OPRM1 genetic polymorphism** - the patients with the AA allele have lower mean Taylor anxiety than those with the AG allele;
- In patients with **blood type B, COMT 1947 and MDR1 polymorphisms** - the difference between the mean values of the three alleles is statistically insignificant;
- In patients with **blood type AB, SNP OPRM1, COMT 1947 and MDR1polymorphisms** - the difference between the mean values of the three alleles is statistically insignificant;
- **Blood type 0 and SNP OPRM1 genetic polymorphism** is characterized by a significantly lower mean value of Taylor anxiety in patients with the AA allele than in those with the AG allele;
- We proved that in patients with **blood type 0, COMT 1947 and MDR1 polymorphisms** - the difference between the mean values of the three alleles is statistically insignificant.

Analysis of the relation between blood type affiliation, the three genetic polymorphisms with the patients' postoperative psychological state (Beck Depression Inventory) showed that (Table 60):

- In people with **blood type A, genetic SNP OPRM1 and MDR1 polymorphisms** - the difference between the mean values of patients with the respective alleles is statistically insignificant;

- In **blood type A, COMT 1947 genetic polymorphism** - the patients with the GG allele have statistically significantly lower mean value of depression compared to those with the AA allele, but not than that of those with the GA allele, whose mean value did not differ statistically of those in the other two alleles;
- In **blood type B, SNP OPRM1 genetic polymorphism** - the patients with allele AA have significantly lower mean value according to Beck's depression compared to that with allele AG;
- In **blood type B, COMT 1947 genetic polymorphism** with a statistically credible lower mean value of depression are the patients with the GG allele compared to patients with the AA allele, but not than the patients with the GA allele, whose mean value is not different statistically from those of the other two alleles.

It was found that:

- The subjects with **blood type B and MDR1 polymorphism have a difference** between the mean values of the three alleles, which, however, is statistically insignificant;
- **Blood types AB and 0, SNP OPRM1 genetic polymorphism** - significantly lower mean value of Beck Depression Inventory have the patients with the AA allele compared to those with the AG allele;
- **Blood types AB and 0, COMT 1947 and MDR1 polymorphisms** show the difference between the mean values of the three alleles, which is statistically negligible.

An analysis of the relation between the blood type, the three genetic polymorphisms and the preoperative psychological state of the patients (PHQ-9 depression test) found that (Table 61):

- In patients with **blood types A and B and SNP OPRM1 genetic polymorphism** - the depression average values on the PHQ-9 test in patients with alleles AA and AG do not differ statistically;
- In **blood types A and B and COMT 1947 genetic polymorphism** - statistically credible lower mean value of depression had the patients with the GG allele than those with the AA allele, but not than that of subjects with the GA allele, which does not differ statistically from those with the other two alleles;
- It was proved that in **blood types A and B and MDR1 polymorphism - the difference between the mean** values of the three alleles is statistically insignificant;
- In **blood type AB and SNP OPRM1 genetic polymorphism** - the average values of depression on the PHQ-9 test in patients with alleles AA and AG do not differ statistically;
- In **blood type AB and COMT 1947 genetic polymorphism** - the patients with the GG allele have statistically credible lower mean value of depression than that of those with the GA allele, but not than that of those with the AA allele, which does not differ statistically from those with the other two alleles;
- In **blood type AB and MDR1 polymorphism** - the difference between the mean values of the three alleles is statistically insignificant;
- In **blood type 0 and SNP OPRM1 genetic polymorphism** - the patients with the AA allele have significantly lower mean value on the PHQ-9 test for depression compared to those with the AG allele;
- In **blood type 0 and COMT 1947 and MDR1 polymorphisms** - the difference between the mean values of patients with the three alleles is statistically insignificant.

Table 59: Analysis of the relation between blood type, type of polymorphism and the patients' preoperative psychological state (Taylor's anxiety test)

Blood type	Type of polymorphism	Alleles	Taylor's test		
			n	$\overline{X}$	SD
A	SNP OPRM1	AA	93	12,66[a]	10,64
		AG	47	18,30[b]	13,65
		GG	6	26,67	13,87
	COMT 1947	GG	39	11,08[a]	9,66
		GA	65	15,75[ac]	13,09
		AA	42	17,64[bc]	12,44
	MDR1	TT	30	13,17[a]	11,95
		CT	85	14,86[a]	12,41
		CC	31	17,39[a]	12,16
B	SNP OPRM1	AA	57	11,49[a]	9,30
		AG	26	19,58[b]	14,42
		GG	7	17,71	15,12
	COMT 1947	GG	24	11,13[a]	7,75
		GA	44	15,09[a]	14,29
		AA	22	16,23[a]	10,11
	MDR1	TT	22	13,77[a]	9,55
		CT	43	13,67[a]	12,66
		CC	25	15,88[a]	12,80
AB	SNP OPRM1	AA	29	13,97[a]	11,23
		AG	12	18,00[a]	14,03
		GG	2	20,00	7,07
	COMT 1947	GG	14	11,71[a]	9,33
		GA	21	18,43[a]	13,58
		AA	8	13,75[a]	10,04
	MDR1	TT	8	14,63[a]	10,95
		CT	24	14,67[a]	11,31
		CC	11	17,45[a]	14,42
0	SNP OPRM1	AA	87	11,09[a]	8,57
		AG	38	18,08[b]	14,03
		GG	6	18,67	13,75
	COMT 1947	GG	30	11,50[a]	8,83
		GA	68	13,76[a]	11,34
		AA	33	14,64[a]	12,45
	MDR1	TT	31	11,19[a]	8,82
		CT	60	13,05[a]	11,71
		CC	40	15,85[a]	11,52

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - subgroups without statistical representation do not participate in the analysis

Table 60: Analysis of the relation between blood type, type of polymorphism and the patients' preoperative psychological state (Beck Depression Inventory)

Blood type	Type of polymorphism	Alleles	Beck Depression Inventory		
			n	$\overline{X}$	SD
A	SNP OPRM1	AA	93	15,56[a]	9,85
		AG	47	20,36[a]	13,22
		GG	6	30,33	11,40
	COMT 1947	GG	39	14,15[a]	8,60
		GA	65	18,31[ac]	12,08
		AA	42	20,10[bc]	12,51
	MDR1	TT	30	16,17[a]	11,91
		CT	85	17,56[a]	11,18
		CC	31	19,61[a]	12,28
B	SNP OPRM1	AA	57	15,25[a]	9,57
		AG	26	21,19[b]	11,73
		GG	7	18,71	12,38
	COMT 1947	GG	24	13,67[a]	10,14
		GA	44	17,80[ac]	11,90
		AA	22	20,00[bc]	7,56
	MDR1	TT	22	16,00[a]	9,95
		CT	43	17,05[a]	10,71
		CC	25	18,64[a]	11,47
AB	SNP OPRM1	AA	29	15,17[a]	9,49
		AG	12	24,17[b]	13,92
		GG	2	21,50	2,12
	COMT 1947	GG	14	14,07[a]	8,30
		GA	21	21,52[a]	12,56
		AA	8	15,50[a]	10,64
	MDR1	TT	8	21,50[a]	12,62
		CT	24	17,33[a]	10,66
		CC	11	16,82[a]	12,34
0	SNP OPRM1	AA	87	14,01[a]	7,83
		AG	38	19,92[b]	11,85
		GG	6	19,83	13,73
	COMT 1947	GG	30	13,87[a]	8,20
		GA	68	16,68[a]	10,50
		AA	33	16,52[a]	9,56
	MDR1	TT	31	14,16[a]	8,02
		CT	60	15,83[a]	10,65
		CC	40	17,65[a]	9,60

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - subgroups without statistical representation do not participate in the analysis

Table 61: Analysis of the relation between the blood type, the polymorphism type and the patients' preoperative psychological state (PHQ-9 depression test)

Blood type	Type of polymorphism	Alleles	PHQ-9 depression test		
			n	$\overline{X}$	SD
A	SNP OPRM1	AA	93	9,03[a]	6,46
		AG	47	11,45[a]	7,58
		GG	6	16,00	7,77
	COMT 1947	GG	39	7,95[a]	6,00
		GA	65	10,18[ac]	7,31
		AA	42	11,95[bc]	7,11
	MDR1	TT	30	9,13[a]	7,40
		CT	85	10,19[a]	7,01
		CC	31	10,77[a]	6,91
B	SNP OPRM1	AA	57	8,89[a]	6,28
		AG	26	12,19[a]	7,39
		GG	7	9,57	8,83
	COMT 1947	GG	24	7,79[a]	5,99
		GA	44	9,89[ac]	7,44
		AA	22	12,23[bc]	6,19
	MDR1	TT	22	8,73[a]	6,56
		CT	43	9,72[a]	6,73
		CC	25	11,24[a]	7,51
AB	SNP OPRM1	AA	29	9,28[a]	7,29
		AG	12	13,00[a]	7,21
		GG	2	13,00	2,83
	COMT 1947	GG	14	7,86[a]	6,10
		GA	21	12,57[bc]	7,83
		AA	8	9,63[ac]	6,52
	MDR1	TT	8	11,50[a]	7,46
		CT	24	10,17[a]	7,48
		CC	11	10,45[a]	7,17
0	SNP OPRM1	AA	87	8,00[a]	5,70
		AG	38	11,71[b]	7,69
		GG	6	13,83	9,77
	COMT 1947	GG	30	8,53[a]	5,66
		GA	68	9,57[a]	7,05
		AA	33	9,61[a]	7,22
	MDR1	TT	31	7,87[a]	6,05
		CT	60	9,20[a]	6,94
		CC	40	10,70[a]	6,91

* - the same letters on the verticals mean the absence of a significant difference, and the different ones - the presence of such one ($p<0,05$)

** - subgroups without statistical representation do not participate in the analysis

Task 9: To look for a relation between the experienced pain strength (VAS) and the type of medical institution where the patients were treated (public and private)

The results in Table 62 show that:

- There is no statistically significant relation between the medical institution type where the patients were treated (public or private) and the postoperative pain strength (measured by VAS);
- It can be noted, however, that the difference in men is marginally significant ($p<0.1$), as the higher mean value of the pain is experienced by patients treated (anesthetized) in the state medical institution.

Table 62: Comparative analysis of the postoperative pain strength (VAS) according to the medical institution type

Excerpt	Public			Private			P
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
All	164	5,55	2,83	246	5,45	2,42	0,620
Men	43	7,19	1,92	53	6,34	2,12	***0,052***
Women	121	4,98	2,89	193	5,21	2,45	0,369

Task 10: To determine whether the results of the Taylor test, Beck Depression Inventory, and the PHQ-9 depression test overlap.

A comparison of anxiety scores on Taylor test and Beck Depression Inventory showed that (Table 63):

- In the category "No" depression by Beck Depression Inventory had the highest relative share (88.3%) among patients rated with "Low" level on the Taylor test. With the highest percentages (33.5% and 28.2%) among those rated at the level of "Medium" are those who have "Moderate to severe" and "Mild to moderate" depression, but the percentage (total about 62%) is much lower, i.e. the degree of compliance is lower. Among those rated with anxiety "High" with the largest relative shares are the degrees "Severe" (44.1%), "Moderate to severe" depression (32.4%) and only in third place "Extremely severe" depression with 22.1%, which also indicates a weaker correspondence between the two tests at this level;
- The described ratios of the categories in the considered tests coincide in the group of women, while in men, among those assessed with "average" level of anxiety, the highest relative share is two degrees lower on the Beck Depression Inventory – "Mild" depression. In the other two levels of anxiety, the ratios of the two tests coincided with those of the entire sample and the women.

A comparison of anxiety scores on the Taylor test and the PHQ-9 depression test showed that (Table 64):

- The category "No" depression on the PHQ-9 test has the highest relative share (86.4%) among the patients rated "Low" on the Taylor test. The highest percentages (35.1% and 33.0%) among those rated with "Medium" are those with "Moderate to severe" and "Moderate" depression, but the percentage (total about 68%) is quite lower, i.e. the compliance degree is lower. Among those rated with a "High" level of anxiety with the largest share is the "Severe" degree (52.9%),

followed by “Moderate to severe” depression with (44.1%), which indicates a very good correspondence between both tests at this level;

- The described ratios of the categories in the considered tests coincide with those of the group of women, while for men, between those rated with “Medium” and “High” level of anxiety, the highest relative shares are one degree lower on the scale of PHQ-9 test, respectively “Moderate” and “Moderate to severe” depression. At low levels of anxiety, the ratios of the two tests were approximately the same as those of the entire sample and the women.

A comparison of Beck Depression Inventory and anxiety assessments on the Taylor test showed that (Table 65):

- “No” depression of Beck Inventory is best matched (84.5%) by the “Low” Taylor test. In those who received the grades “Mild”, “Mild to moderate” and “Moderate to severe” depression with the highest percentages (68.5%, 98.1% and 74.1%, respectively) were rated with the level of “Medium”, i.e. the degree of compliance is highest in “Mild to moderate”. Among those rated “Severe” and “Extremely severe” with the highest relative shares (75.0% and 93.8%, respectively) are those rated with “High” anxiety level, i.e. the degree of compliance is highest in “Extremely severe” depression;
- The described ratios of the categories in the considered tests coincide both in the group of women and the group of men.

A comparison of Beck Depression Inventory and the PHQ-9 depression test showed that (Table 66):

- Beck’s “No” depression category best corresponds to the “None” category in the PHQ-9 test (88.8%). For those who received a “Mild” grade of depression with the highest percentage (61.1) was the same grade on the PHQ-9 test, ie. the compliance degree is significantly lower. Among those rated “Mild to moderate” with the highest relative share is the category “Moderate” depression on the PHQ-9 test. In those with “Moderate to severe” and “Severe” Beck depression with the highest percentage (77.6 and 52.5, respectively) is “Moderate to severe” on the PHQ-9 test. In patients with “Extremely severe” depression with a very high relative share (93.8%) were assessed with “Severe” depression on the PHQ-9 test, ie. the degree of compliance is highest in “Extremely severe”;
- The described ratios of the categories in the considered tests completely coincide in the group of men, while for women the difference is that the first two places of Beck’s levels are divided between “Moderate to severe” and “Severe” according to PHQ-9 test.

Conversely, a comparison of the PHQ-9 test and Beck Depression Inventory found that (Table 67):

- Very high correspondence of the degree “No” depression (94.1%) and much lower (57.9%) of the category “Mild” depression. Among those rated with “Moderate” depression on the PHQ-9 test with the highest relative share is the category “Mild to moderate” depression according to Beck, but only by 54.7%. In patients with “Moderate to severe” on the PHQ-9 test with the highest percentage (68%) is “Moderate to severe” according to Beck. The “Severe” depression degree between the two tests was only 45%.
- For men, the coincidence of “Mild” depression degree is significantly better - 81.8%, while for “Severe” it falls to 33.3% due to the fact that here in the first place is the category “Extremely severe” according to Beck;
- For the group of women, the conclusions made for the whole sample are largely valid.

A comparison of the depression levels on the PHQ-9 test and the anxiety scores on the Taylor test showed that (Table 68):

Patients rated “Low” on the Taylor test have the highest relative share (87.5%) in the “No” category on the PHQ-9 test. The next three levels of depression on this test have the highest percentages at the “Medium” level (64.9%, 96.9% and 68.0%, respectively), which means that the largest match is between the “Moderate” categories. and “Medium”. The match between the “Severe” and “High” ratings is 90%;

- The described ratios of the categories in the considered tests coincide to a greater extent in women. In men, the significantly lower percentage (69) of coincidence in the categories “No” and “Low” level of depression, as well as “Moderate to severe” with “Medium” depression degree - 58.3%.

Table 63: Frequency distribution of patients according to Taylor’s test and Beck’s Inventory

Excerpt	Beck Depression Inventory	Frequency	Taylor test (anxiety levels)		
			Low	Medium	High
All	No	n	136	25	0
		%	88,3	13,3	0,0
	Mild	n	17	37	0
		%	11,0	19,7	0,0
	Mild to moderate	n	0	53	1
		%	0,0	28,2	1,5
	Moderate to severe	n	0	63	22
		%	0,0	33,5	32,4
	Severe	n	0	10	30
		%	0,0	5,3	44,1
	Extremely severe	n	1	0	15
		%	0,6	0,0	22,1
Men	No	n	21	11	0
		%	87,5	20,8	0,0
	Mild	n	3	15	0
		%	12,5	28,3	0,0
	Mild to moderate	n	0	14	0
		%	0,0	26,4	0,0
	Moderate to severe	n	0	12	6
		%	0,0	22,6	31,6
	Severe	n	0	1	8
		%	0,0	1,9	42,1
	Extremely severe	n	0	0	5
		%	0,0	0,0	26,3
Women	No	n	115	14	0
		%	88,5	10,4	0,0
	Mild	n	14	22	0
		%	10,8	16,3	0,0
	Mild to moderate	n	0	39	1
		%	0,0	28,9	2,0
	Moderate to severe	n	0	51	16
		%	0,0	37,8	32,7
	Severe	n	0	9	22
		%	0,0	6,7	44,9
	Extremely severe	n	1	0	10
		%	0,8	0,0	20,4

Table 64: Frequency distribution of the patients by Taylor test and PHQ-9 depression test

Excerpt	PHQ-9 depression test	Frequency	Taylor test (anxiety levels)		
			Low	Medium	High
All	No	n	133	19	0
		%	86,4	10,1	0,0
	Mild	n	19	37	1
		%	12,3	19,7	1,5
	Moderate	n	1	62	1
		%	0,6	33,0	1,5
	Moderate to severe	n	1	66	30
		%	0,6	35,1	44,1
	Severe	n	0	4	36
		%	0,0	2,1	52,9
Men	No	n	20	9	0
		%	83,3	17,0	0,0
	Mild	n	4	7	0
		%	16,7	13,2	0,0
	Moderate	n	0	23	0
		%	0,0	43,4	0,0
	Moderate to severe	n	0	14	10
		%	0,0	26,4	52,6
	Severe	n	0	0	9
		%	0,0	0,0	47,4
Women	No	n	113	10	0
		%	86,9	7,4	0,0
	Mild	n	15	30	1
		%	11,5	22,2	2,0
	Moderate	n	1	39	1
		%	0,8	28,9	2,0
	Moderate to severe	n	1	52	20
		%	0,8	38,5	40,8
	Severe	n	0	4	27
		%	0,0	3,0	55,1

Table 65: Frequency distribution of patients according to Beck Depression Inventory and Taylor test

Excerpt	Taylor test (anxiety levels)	Frequency	Beck Depression Inventory					
			No	Mild	Mild to moderate	Moderate to severe	Severe	Extremely severe
All	Low	n	136	17	0	0	0	1
		%	84,5	31,5	0,0	0,0	0,0	6,3
	Medium	n	25	37	53	63	10	0
		%	15,5	68,5	98,1	74,1	25,0	0,0
	High	n	0	0	1	22	30	15
		%	0,0	0,0	1,9	25,9	75,0	93,8
Men	Low	n	21	3	0	0	0	0
		%	65,6	16,7	0,0	0,0	0,0	0,0
	Medium	n	11	15	14	12	1	0
		%	34,4	83,3	100,0	66,7	11,1	0,0
	High	n	0	0	0	6	8	5
		%	0,0	0,0	0,0	33,3	88,9	100,0
Women	Low	n	115	14	0	0	0	1
		%	89,1	38,9	0,0	0,0	0,0	9,1
	Medium	n	14	22	39	51	9	0
		%	10,9	61,1	97,5	76,1	29,0	0,0
	High	n	0	0	1	16	22	10
		%	0,0	0,0	2,5	23,9	71,0	90,9

Table 66: Frequency distribution of patients according to Beck Depression Inventory and PHQ-9 depression test

Excerpt	PHQ-9 depression test	Frequency	Beck Depression Inventory					
			No	Mild	Mild to moderate	Moderate to severe	Severe	Extremely severe
All	No	n	143	9	0	0	0	0
		%	88,8	16,7	0,0	0,0	0,0	0,0
	Mild	n	14	33	10	0	0	0
		%	8,7	61,1	18,5	0,0	0,0	0,0
	Moderate	n	3	12	35	13	1	0
		%	1,9	22,2	64,8	15,3	2,5	0,0
	Moderate to severe	n	1	0	8	66	21	1
		%	0,6	0,0	14,8	77,6	52,5	6,3
	Severe	n	0	0	1	6	18	15
		%	0,0	0,0	1,9	7,1	45,0	93,8
Men	No	n	27	2	0	0	0	0
		%	84,4	11,1	0,0	0,0	0,0	0,0
	Mild	n	2	9	0	0	0	0
		%	6,3	50,0	0,0	0,0	0,0	0,0
	Moderate	n	2	7	12	2	0	0
		%	6,3	38,9	85,7	11,1	0,0	0,0
	Moderate to severe	n	1	0	2	15	6	0
		%	3,1	0,0	14,3	83,3	66,7	0,0
	Severe	n	0	0	0	1	3	5
		%	0,0	0,0	0,0	5,6	33,3	100,0
Women	No	n	116	7	0	0	0	0
		%	89,9	19,4	0,0	0,0	0,0	0,0
	Mild	n	12	24	10	0	0	0
		%	9,3	66,7	25,0	0,0	0,0	0,0
	Moderate	n	1	5	23	11	1	0
		%	0,8	13,9	57,5	16,4	3,2	0,0
	Moderate to severe	n	0	0	6	51	15	1
		%	0,0	0,0	15,0	76,1	48,4	9,1
	Severe	n	0	0	1	5	15	10
		%	0,0	0,0	2,5	7,5	48,4	90,9

Table 67: Frequency distribution of patients according to the PHQ-9 depression test and Beck's Inventory

Excerpt	Beck Depression Inventory	Frequency	PHQ-9 depression test				
			No	Mild	Moderate	Moderate to severe	Severe
All	No	n	143	14	3	1	0
		%	94,1	24,6	4,7	1,0	0,0
	Mild	n	9	33	12	0	0
		%	5,9	57,9	18,8	0,0	0,0
	Mild to moderate	n	0	10	35	8	1
		%	0,0	17,5	54,7	8,2	2,5
	Moderate to severe	n	0	0	13	66	6
		%	0,0	0,0	20,3	68,0	15,0
	Severe	n	0	0	1	21	18
		%	0,0	0,0	1,6	21,6	45,0
	Extremely severe	n	0	0	0	1	15
		%	0,0	0,0	0,0	1,0	37,5
Men	No	n	27	2	2	1	0
		%	93,1	18,2	8,7	4,2	0,0
	Mild	n	2	9	7	0	0
		%	6,9	81,8	30,4	0,0	0,0
	Mild to moderate	n	0	0	12	2	0
		%	0,0	0,0	52,2	8,3	0,0
	Moderate to severe	n	0	0	2	15	1
		%	0,0	0,0	8,7	62,5	11,1
	Severe	n	0	0	0	6	3
		%	0,0	0,0	0,0	25,0	33,3
	Extremely severe	n	0	0	0	0	5
		%	0,0	0,0	0,0	0,0	55,6
Women	No	n	116	12	1	0	0
		%	94,3	26,1	2,4	0,0	0,0
	Mild	n	7	24	5	0	0
		%	5,7	52,2	12,2	0,0	0,0
	Mild to moderate	n	0	10	23	6	1
		%	0,0	21,7	56,1	8,2	3,2
	Moderate to severe	n	0	0	11	51	5
		%	0,0	0,0	26,8	69,9	16,1
	Severe	n	0	0	1	15	15
		%	0,0	0,0	2,4	20,5	48,4
	Extremely severe	n	0	0	0	1	10
		%	0,0	0,0	0,0	1,4	32,3

Table 68: Frequency distribution of patients according to the PHQ-9 depression test and the Taylor test

Excerpt	Taylor test (anxiety levels)	Frequency	PHQ-9 depression test				
			No	Mild	Moderate	Moderate to severe	Severe
All	Low	n	133	19	1	1	0
		%	87,5	33,3	1,6	1,0	0,0
	Medium	n	19	37	62	66	4
		%	12,5	64,9	96,9	68,0	10,0
	High	n	0	1	1	30	36
		%	0,0	1,8	1,6	30,9	90,0
Men	Low	n	20	4	0	0	0
		%	69,0	36,4	0,0	0,0	0,0
	Medium	n	9	7	23	14	0
		%	31,0	63,6	100,0	58,3	0,0
	High	n	0	0	0	10	9
		%	0,0	0,0	0,0	41,7	100,0
Women	Low	n	113	15	1	1	0
		%	91,9	32,6	2,4	1,4	0,0
	Medium	n	10	30	39	52	4
		%	8,1	65,2	95,1	71,2	12,9
	High	n	0	1	1	20	27
		%	0,0	2,2	2,4	27,4	87,1

Task 11:To look for the presence of prognostic groups and other relations.

In order to differentiate prognostic groups for the expected postoperative pain, we applied binary logistic regression analysis. Taking into account the results so far, as potential factors influencing the occurrence of pain over 5 on VAS were tested: gender, residence, marital status, surgical method, surgery type, polymorphism, Taylor's test (in categorical form) and the quantitative - age, Beck Depression Inventory and PHQ-9 tests, time for surgery and time for anesthesia. Limit 5 was chosen experimentally so as take into account the influence of the maximum number of potential factors.

As the studied quantitative features do not have a normal distribution, therefore, we cannot use them directly in the binary logistic regression analysis, and we had to apply ROC curve analysis in order to establish threshold values distinguishing the patients with values of postoperative pain on VAS up to and above 5. The obtained results (Fig. 30-33) show that for all studied indicators a statistically significant threshold value can be established. The largest area under the curve (0.852) is Beck Depression Inventory, and the smallest is age (0.600), (Table 69).

Table 69: Age thresholds, Beck Depression Inventory and PHQ-9 depression tests, surgery time and anesthesia time to limit the existing VAS postoperative pain values up to and above 5, and criteria values for screening test validation

Indicator	Threshold value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	% correct answers
Age (years)	≥60,5	48	68	61	56	58
Beck Depression Inventory	≥11,5	82	74	77	80	78
PHQ-9 test	≥5,5	85	72	76	82	79
Surgery time (min)	≥147,5	70	65	68	68	68
Anesthesia time (min)	≥167,5	70	63	66	67	67

In Table 70 it is seen that:

- All studied indicators are significant **risk** factors for the occurrence of postoperative pain over 5 on VAS;
- With the greatest risk impact is the presence of a high level of anxiety in the Taylor test compared to those with low level – the risk is 62 times higher;
- The second largest is the risk impact of open surgery compared to the other two (laparoscopic and robotic); we found that the risk is about 44 times higher. The combination of laparoscopic and

robotic methods was necessary due to the fact that in the robotic surgeries there is not a single patient with postoperative pain over 5;

- In last place is the residence and age in terms of risks below 2.

In order to take into account the combined influence of the indicators studied and to eliminate possible blurring factors, we placed together in the regression equation the indicators having significant risk relations. After applying the procedure “Backward conditional” in the final version of the equation, 6 of the studied indicators entered. Table 70 shows that:

- Patients with open surgery are at the highest risk (52 times) for postoperative pain compared to those with the other two types of surgery, followed by patients with the GG allele versus the AA allele in SNP 118 genetic polymorphism by about 6.5 times;
- The male sex has the lowest significant ratio of chances compared to the female one - the risk is about twice as high;
- The current model allows 86% accurate classification, which is a very good result.

Table 70: Risk ratio and 95% CI of the studied indicators as factors for values of VAS postoperative pain above 5

Indicators	Comparison	Individual				Group			
		OR	95% CI		P	OR	95% CI		P
			Lower limit	Upper limit			Lower limit	Upper limit	
Surgical method	Open surgery/ laparoscopy or robotic surgery	44,397	23,602	83,515	**<0,001**	52,059	20,937	129,442	**<0,001**
SNP 118 polymorphism	≥60,5	48	68	61	56	58	≥60,5	48	68
	≥11,5	82	74	77	80	78	≥11,5	82	74
COMT 1947 polymorphism	≥5,5	85	72	76	82	79	≥5,5	85	72
	≥147,5	70	65	68	68	68	≥147,5	70	65
MDR1 polymorphism	≥167,5	70	63	66	67	67	≥167,5	70	63
	≥60,5	48	68	61	56	58	≥60,5	48	68
Taylor's test for anxiety level	≥11,5	82	74	77	80	78	≥11,5	82	74
	≥5,5	85	72	76	82	79	≥5,5	85	72
Gender	≥147,5	70	65	68	68	68	≥147,5	70	65
Beck's Inventory	≥167,5	70	63	66	67	67	≥167,5	70	63
PHQ-9 test	≥60,5	48	68	61	56	58	≥60,5	48	68
Surgery time (minutes)	≥11,5	82	74	77	80	78	≥11,5	82	74
Surgery type	≥5,5	85	72	76	82	79	≥5,5	85	72
Anethesia (minutes)	≥147,5	70	65	68	68	68	≥147,5	70	65
	≥167,5	70	63	66	67	67	≥167,5	70	63
Marital status	≥60,5	48	68	61	56	58	≥60,5	48	68
	≥11,5	82	74	77	80	78	≥11,5	82	74
Age	≥5,5	85	72	76	82	79	≥5,5	85	72
Residence	≥147,5	70	65	68	68	68	≥147,5	70	65

Prognostic groups

Based on the results of table. 68, three prognostic groups were distinguished (Table 71):

1. Low risk of pain over 5 on the VAS scale - operative method - robotic or laparoscopic surgery; SNP 118 polymorphism, AA allele; polymorphism COMT 1947, GG allele; MDR1 polymorphism, TT allele; Taylor's test - low level of anxiety; gender - no matter.
2. Medium risk for pain over 5 on VAS - surgical method - robotic or laparoscopic surgery; SNP 118 polymorphism, AG or GG allele; COMT 1947 polymorphism, allele GA or AA; MDR1 polymorphism, CT or CC allele; Taylor's test - medium or high level of anxiety; gender - no matter.
3. High risk of pain over 5 on the VAS scale - surgery method - open surgery.

Table 71: Prognostic groups

Low risk for pain over 5 on VAS	Medium risk for pain over 5 on VAS	High risk for pain over 5 on VAS
1. Surgery method - robotic or laparoscopic surgery	1. Surgery method - robotic or laparoscopic surgery	1. Surgery method - open surgery
2. SNP 118 polymorphism, allele AA	2. SNP 118 polymorphism, allele AG or GG	
3. COMT 1947 polymorphism, allele GG	3. COMT 1947 polymorphism, allele GA or AA	
4. MDR1 polymorphism, allele TT	4. MDR1 polymorphism, allele CT or CC	
5. Taylor's test - low level of anxiety	5. Taylor's test - medium or high level of anxiety	
6. Gender - no matter	6. Gender - no matter	

V. DISCUSSION:

Generalized anxiety disorder is the most commonly diagnosed anxiety disorder in the population of patients with chronic pain. The coexistence of pain and anxiety should not surprise us - both signals warn of danger and aim the individual to cope with the impending threat. Anxiety disorders are at second place - after the depression in the population of patients with chronic pain. While anxiety is a normal response in all people, clinical anxiety leads to increased intensity and prolongation of the feeling of horror interfering with normal functioning (Adam K. M. et al.).

Preoperative anxiety is associated with stronger postoperative pain in many surgical interventions. In hospitals, anxiety is exacerbated by sleep disturbances in the postoperative period due to visits by staff for observation, by other patients in the rooms, and for perfoming the appointments. This vicious circle is closed by the fear of complications, loss of control and feelings of helplessness. Hospital admission and forthcoming surgery are highly stressful events for most individuals (Adam K. M. et al.).

Preoperative depression, which is characterized by the classic triad of slow thought process, abulia and dysthymia, also increases the intensity of pain and the need to use opiates to relieve it (regardless of the route of administration) in the postoperative period. Another common phenomenon in depressed patients is the high level of dissatisfaction with analgesia, (Hartung

T. et al., ANZCA Acute Pain Management: Scientific Evidence: Australian & New Zealand College of Anesthetists; (2nd ed.) 2005).

In our study, in task two, we proved that postoperative pain on the pain scale (VAS) correlates unidirectionally and strongly in strength with all the three considered psychological tests.

In female patients, we found a stronger relation between the postoperative pain strength and preoperative Taylor anxiety ($p<0.001$) compared to men, which is confirmed by the results obtained from Bukberg J. et al., Halan O. et al. , Afivi M. et al. and Riecher Rössler et al

Quite logically, we reported that the higher the degree of preoperative anxiety and preoperative and postoperative depression, the greater the pain intensity experienced by patients in the early postoperative period, with no difference between the two genders (respectively for the Taylor test). - SD = 12.56, PHQ-9 test - SD = 6.23 and Beck Inventory - SD = 26, 70) - Table 14.

We found that postoperative pain on VAS correlated unidirectionally and strongly with all three psychological tests used (Taylor Test, Beck Depression Inventory, PHQ-9 Preoperative Depression Questionnaire). That is, with low levels of anxiety and depression, there is less pain in the early postoperative period. Conversely, the higher the level of anxiety and depression, the stronger the intensity of the pain experienced.

We have shown that postoperative pain on VAS correlates unilaterally and strongly in strength with all three psychological tests used (Taylor Test, Beck Depression Inventory, PHQ-9 Preoperative Depression Questionnaire). That is, with low levels of anxiety and depression, there is less pain in the early postoperative period. Conversely, the higher the level of anxiety and depression, the stronger the intensity of the pain experienced.

Pain stimulus sensitivity and pain tolerance are genetically determined (Moseng T. et al., Norbury T.A. et al., Nielsen C.S. et al., Hocking L.J. et al., Grøholt E.K. et al.).

Genetic polymorphisms contribute to a number of specific pain phenotypes.

Identifying the relevant genes can help to understand the basic biological mechanisms and the search for therapeutic goals.

In most people, experience and susceptibility to pain are the result of a complex interaction between several genetic variants involved in different stages of neuronal processing of nociceptive information with the additional contribution of other genetic or psychosocial factors, sociocultural environment and prior learning (Lotsch J. et al.).

In addition, variuos genes can be involved in the various types of pain, their sensory and affective variable dimensions, all of which are intertwined with others, leading to highly variable responses in humans, (Edwards R. et al., Turk D. et al.).

In performing the third task in our study, we found that the postoperative pain (measured by the visual analog scale - VAS) is directly dependent on the SNP OPRM1, COMT 1947 and MDR1 ABCB1 genetic polymorphisms.

In the SNP OPRM1 genetic polymorphism (in the whole sample), we registered a lower mean value of postoperative pain in patients with the AA allele compared to those with the AG and GG alleles (AA- $\overline{X}$ -4.99; AG- $\overline{X}$ - 6.37; GG- $\overline{X}$ - 6.76).

In people with COMT 1947 genetic polymorphism (in the whole sample), it is noticeable that the weakest pain is reported in those havinig the GG allele ($\overline{X}$ - 4.86), compared to the other two alleles: AA ($\overline{X}$ - 5.62) and GA ($\overline{X}$ - 5.77).

In patients with MDR1 ABCB1 genetic polymorphism (in the whole sample), the strongest pain was demonstrated in those with the CC allele ($\overline{X}$ - 6.16).
In SNP OPRM1 (for men and women), the strongest pain was recorded in patients with the AG and GA alleles, and the weakest - in those with the AA allele.
In COMT 1947 G>A genetic polymorphism, the strongest pain in the postoperative period was reported in patients with the AA and GA alleles, and the weakest in those who were homozygous for the normal GG allele.
The strongest pain in the MDR1 ABCB1 genetic polymorphism was given by the studied patients with the CC allele. This was observed in both genders.
A number of genes have been tested for association with anxiety-related traits, including monoamine oxidase type A, cytochrome P 450 2D6 isoenzyme, GABA-A receptor alpha-6-subunit, and in a number of studies catechol-methyltransferase (Eley T. et al. Jorm A. et al., Roberts R. et al., Sen S. et al., Enoch M. et al., Henderson A. et al.).
In our study of the Taylor test and analyzing the results obtained in the fourth task, we concluded that among the whole group of subjects (men and women) with SNP OPRM1 genetic polymorphism there is a lower level of anxiety in these of them who have the AA allele.
By gender, in SNP OPRM1 it was proved that in men with the GG allele the relative share of the mean level of anxiety is statistically credibly lower than those of the other two levels, who do not show a difference between them - Table 14.
In men and women with COMT 1947 genetic polymorphism, no statistically significant difference was found in the Taylor anxiety level in the three alleles. The lack of such difference is also observed in MDR1 ABCB1 genetic polymorphism.
Based on the study performed, we found that there is a link between pre- and postoperative depression (PHQ-9 test and Beck Depression Inventory) and various genetic polymorphisms.
In patients with SNP OPRM1 genetic polymorphism, a lower mean value of preoperative depression (according to the results of the PHQ-9 test) is found in people with AA polymorphism ($\overline{X}$ -8.69; SD-6.27), Table 13.
In COMT 1947 polymorphism, in both genders with the GG allele, we found a lower level of preoperative depression compared to the other two alleles (($\overline{X}$ - 8.07 - for the sample, $\overline{X}$ - 8.55 for men and $\overline{X}$ -7.95 for women).
In the MDR1 ABCB1 genetic polymorphism, in the general sample of patients, the highest percentage of preoperative depression had the patients with the CC allele ($\overline{X}$ -10.82; SD-6.98), and with the lowest those with the TT allele ($\overline{X}$ -8.81; SD- 6.72) - Table 13.
By gender, men with the GA allele have the highest rate of “Severe Depression” according to the PHQ-9 Depression Questionnaire (77.8%). The women repeated the frequency distribution of the whole sample for all three alleles of the considered genetic polymorphism - Table 18.
In COMT 1947 genetic polymorphism, in women with the AA allele a higher percentage of “Moderate to severe depression’ was proved (29.0%), while in men, the difference in the frequency distribution of the depression levels is statistically insignificant - Table 19.
Regarding the MDR1 ABCB1 polymorphism, we found that women with the TT allele had the lowest level of anxiety (9.7%) compared to the other alleles. In male patients, no

significant difference was found in the frequency distribution of the different depression levels in all the three alleles - Table 20.

Patients with SNP OPRM1 genetic polymorphism with the AA allele reported milder postoperative pain, lower Taylor Anxiety, Beck Depression Inventory and PHQ-9 Depression Questionnaire.

Conversely, the other two alleles AG and GG showed milder pain and, respectively, higher degree of anxiety and depression.

"Severe" depression is common in patients with AG and GG alleles.

In COMT 1947 G> A, patients with GG allele have the lowest level of anxiety and depression. They also reported milder pain in the postoperative period, regardless the diagnosis, surgery method used, and surgery type.

Respectively, the other two alleles AA and GA had higher anxiety, depression, and pain intensity. This is observed in patients of both genders.

In terms of anxiety, in MDR1 ABCB1 polymorphism, there is no difference in the frequency distribution between the three alleles: CC, CT and TT.

However, this is not the case when it comes to depression. Patients with the TT allele have a higher rate of "Missing" to "Mild" depression and less pain than the other two alleles, CC and CT.

5. Psychological factors that are relevant to the postoperative pain strength can be divided into three subcategories: anxiety, psychological stress and coping strategies.

Anxiety is the most common predictor of postoperative pain, as the positive correlation with the intensity of the patient's pain has been confirmed. This is evidenced in six studies conducted in recent years on gastrointestinal surgery, five in obstetric and gynecological surgery, two in mixed surgery, one in breast surgery and one in thoracic surgery, (Rudin A. et al., Taenzer P. et al., Caumo W. et al.).

In our study in task five, we found that the number of anesthetics administered correlated with the pain strength experienced in the postoperative period.

A correlation was also found between the subjects and the three tests for pre- and postoperative anxiety and depression, the number of painkillers per 24 hours and the postoperative pain severity.

In patients with SNP OPRM1 genetic polymorphism, patients with the AA allele ($\overline{X}$ -1.86, SD-1.04) have a lower need (number of analgesics per 24 hours).

In patients with COMT 1947 genetic polymorphism, in both genders and all three types of alleles, there was no difference in the number of analgesics for 24 hours, while male subjects with the GA allele showed a more frequent need of postoperative analgesia in the early postoperative period.

In patients with MDR1 and SNP OPRM1 genetic polymorphism, it was found that in both genders who have the CT allele are characterized by the need of more frequent analgesia in the first 24 hours after surgery ($\overline{X}$ for the whole sample - 2.28, SD - 1.04; $\overline{X}$ men - 2.67, SD men - 0.88; $\overline{X}$ women - 2.13, SD women - 1.07) - Table 22.

This poses a risk of a number of adverse side effects as a result of Morphine used for postoperative analgesia.

The only study that supports the relation between nausea and vomiting and preoperative anxiety is that of Quinn et al., (Quinn A. et al.).
In our study, in the entire sample of patients and women, the frequency of nausea was directly proportional to the intensity of pain experienced (VAS), the number of analgesics administered and the pre- and postoperative psychological state of patients. This was not found in the male patients studied. In them, such a dependence is proved only in terms of the number of anesthetics applied, ie. they lack of relation between the psychological status and the pain strength - Table 23.
In the other common complication, vomiting, it was proved that in the whole sample and in women there is a significant relation between mental state, pain, and the number of painkillers and the vomiting, while in men again a difference is found, namely, in them these values are higher in terms of pain and number of analgesics, ie. the pre- and postoperative psychological state are not so significant for this side effect resulting from the anesthesia applied with the opioid analgesic Morphine - Table 24.
Another team that confirms our results is that of Stadler M. et al., who argue that female gender and general anesthesia are a prerequisite for more frequent postoperative nausea and vomiting (Stadler M. et al.).
The third common complication of analgesia is respiratory depression.
A number of studies have shown that there is an increased risk of developing ORID in patients who have major heart or lung disease, ie. they have a reduced cardio-respiratory reserve, which increases the sensitivity to opioid analgesics (Weingarten T. et al., Ramachandran S. et al.).
A study by Albert M. et al. and Sarton E. et al. prove that in women opiates have greater analgesic power and greater influence on vector control, (Albert M. et al., Sarton E. et al.).
In our study, respiratory depression as a complication was more common in the women studied, who had higher levels of preoperative anxiety, preoperative and postoperative depression, and increased pain intensity, requiring more frequent analgesia.
In men in the studied subjects, this is less pronounced and the differences in the reported indicators and the frequency of postoperative depression have no statistical significance - Table 29.
It has been proved that preoperative anxiety and fear can lead to increased levels of stress hormones, leading to metabolic side effects before anesthesia, including the appearance of high systemic levels of catecholamines, which cause an increase in blood pressure and heart rate. (Weissman C. et al., Fell D. et al.).
The last complications we studied arose as a result of the applied anesthesia are cardiovascular complications (hypotension, hypertension, arrhythmias, etc.). Here, too, a directly proportional relation (in both genders) is found between all studied indicators (pre- and postoperative psychological condition, postoperative pain and number of analgesia applied within the first 24 hours) on cardiovascular complications - Table 30.
In addition to establishing the psychological state of the studied contingent of patients, it was important for us to look for a connection between the studied genetic polymorphisms and the complications that occurred as a result of analgesia.

We proved that in the studied women with the GG allele of the SNP OPRM1 genetic polymorphism, the frequency of vomiting resulting from frequent morphine analgesia was higher compared to the other two alleles (p-0.156) - Table 28.

The analysis of the relation between the three types of genetic polymorphism (SNP OPRM1, COMT 1947 and MDR1) on the occurrence of nausea and respiratory depression as a result of the opioid analgesic Morphine found that the difference between the relative shares of patients with and without these two complications is statistically insignificant - Table 27 and Table 29.

Patients with the AG allele were more likely to develop cardiovascular complications (38.4%; p- 0.002), while the lowest reported incidence of this type of complication was demonstrated in patients with the SNP OPRM1 genetic polymorphism, allele AA (71.4%; p- 0.001) - Table 30.

In women, the difference between the relative shares of patients with and without cardiovascular complications in all three types of isomorphism and alleles is statistically insignificant - Table 30.

In men, this dependence persists. The lowest percentage of cardiovascular complications was registered in genetic polymorphism SNP OPRM1, allele AA (84.8%; p- 0.004), and the highest - in the same genetic polymorphism and allele AG (41.3%; p-0.001) - Table 28.

Much effort has been made to identify predictors of postoperative pain. Unfortunately, the factor of “education status” has not been studied in depth. However, lower education has been found to be associated with a higher incidence of painful conditions (Jordan K. et al.).

A number of studies have been found that assess the relation between educational qualifications and postoperative pain, but they are unconvincing, ie. they do not show the presence of a connection, as in only one case described in the literature is the presence of a negative association (ie the higher the education, the lower the pain), but this is based only on 40 patients, (Chia Y. et al., Lau H. et al., Taenzer P. et al.)

Studies by Jin S., Park J., Kim D. et al. compare the pain intensity experienced between laparoscopic and robotic partial nephrectomy in patients with renal tumors and the complications’ frequency resulting from Morphine analgesia. The contingent of 963 patients was studied for the period January 2000 - September 2016. They received results proving that there is no statistically significant difference between the groups of laparoscopic and robotic surgery. The incidence of opioid-related complications, including nausea, vomiting, dizziness, urticaria, constipation, headache, and sedation, also did not differ significantly between the two groups. This also applies to the intensity of pain measured by VAS and the length of hospital stay, (Jin S., Park J., Kim D.).

We found that moderate pain was diagnosed in patients diagnosed with sigmoid carcinoma, and those with the mildest pain were diagnosed with endometrial hyperplasia.

There is a tendency to reduce the pain intensity from open to robotic surgery.

In the open surgical method, patients with SNP OPRM1 genetic polymorphism, AG and GG alleles, in COMT 1947 G> A genetic polymorphism, in AA and GA alleles and in MDR1 ABCB1 genetic polymorphism, CC and CT alleles, more pain was found in the postoperative period.

In laparoscopic operations in all three types of polymorphism, the difference between the mean values on VAS of patients with the corresponding alleles is statistically insignificant.

In robotic surgery, only MDR1 ABCB1 polymorphism shows a significant difference between the mean values of postoperative pain. The strongest pain was demonstrated in the operated people having CC and CT alleles, the weakest in those ones with the TT allele.
According to the surgery type, it is proven that the highest mean value of postoperative pain is in patients who have undergone breast surgery.
Between the SNP OPRM1 and COMT 1947 G> A genetic polymorphisms and the type of surgical method, it was found that in abdominal surgeries, a lower mean value was present in normal alleles compared to heterozygotes.
In MDR1 ABCB1 polymorphism, less pain is demonstrated in the TT allele.
There is no statistical representation in breast surgery in all three types of genetic polymorphism.
In small pelvic surgery, the pain mean value in the AA allele of the SNP OPRM1 genetic polymorphism was lowest, while in the MDR1 ABCB1 genetic polymorphism, the pain was strongest in the CC allele.
In female patients, postoperative pain correlates directly with the age and duration of anesthesia and surgery.
No such dependence is found in men.
In SNP OPRM1, the AA allele postoperative pain correlates with the age and the surgery duration.
In the AG allele, surgery and anesthesia correlate.
In the GG allele, there is no relation.
In COMT 1947 G> A, all three alleles showed a directly proportional relation with the surgery duration and the anesthesia, and in people with the GA allele, a relation with the age was also demonstrated.
In MDR1 ABCB1, the TT and CT alleles, a relation was found between pain with the surgery duration and the anesthesia, and in subjects with the CC allele – also with the age.
Mean postoperative pain is stronger in men.
It was proved that in women with SNP OPRM1 genetic polymorphism, allele AA, and in men with COMT 1947 G> A genetic polymorphism, the pain is weaker than in the other alleles. In MDR1 ABCB1 the pain is strongest in the CC allele.
According to the marital status indicator, family patients reported least pain.
According to the residence indicator, more pain was found in patients living in rural areas.
According to the indicator of the presence of children and genetic polymorphisms and postoperative pain strength, it was found that there is no relation between the presence or absence of children and the postoperative pain strength.
Numerous studies in recent years have concluded that women are at increased risk of multiple acute and persistent pain conditions, and that the trajectories of pain treatment outcomes may differ by gender, (Melchior M. et al. , Pereira M. et al., Bartley E. et al., LeResche L., Paller C. et al.).
Many researchers have confirmed that men have low levels of negative affect, which is associated with less postoperative pain up to two weeks after surgery, (Edwards R. et al., Jones A. et al., Edwards R. et al., Barry D. et al., Regan C. et al.).
Our analysis in task seven, of the relation between the three studied genetic polymorphisms, the postoperative pain strength (VAS), the number of analgetics for 24 hours with the

presence of previous surgeries experienced by the patient proved that in people with allele AA and AG of SNP OPRM1 genetic polymorphism, whether or not they have experienced previous surgery, the number of analgesics in those who report moderate to severe pain is higher than in patients with mild to no pain. However, the weakest pain was registered in the GG allele ($\bar{X}$-3) compared to the other two alleles, regardless of the pain intensity reported by the operated patients - Table 49.

In COMT 1947 genetic polymorphism, more frequent analgesia (number of analgesics per 24 hours) was also observed in patients with moderate to severe pain, regardless of whether or not these patients had previous surgery. The highest postoperative pain intensity, respectively more frequent , was found in the operated, who so far have no previous surgeries and are carriers of the GG allele ($\bar{X}$- 2.88) - Table 49.

The presence of previous operations has been shown not to affect the relation between the three genetic polymorphisms, the postoperative pain intensity (VAS) and the number of analgesics per 24 hours.

Our seventh task included an analysis of the relation between the three genetic polymorphisms, the postoperative pain severity and the number of anesthetics per 24 hours relative to the patients' gender.

In men with SNP OPRM1 genetic polymorphism, no significant difference was found in analgesia of pain of varying severity.

In women with genetic polymorphism SNP OPRM1 in alleles AA and AG, the average number of analgesics in severe pain is higher, respectively, in AA ($\bar{X}$- 2.95; p<0.001) - Table 50.

In men with COMT 1947 genetic polymorphism, the difference between the number of analgesics in patients with moderate or severe pain and mild to absent one was found in all alleles: GG ($\bar{X}$- 2.91; p <0.001), GA ($\bar{X}$- 3.05; p <0.001), AA ($\bar{X}$-3.07; p<0.001) - Table 50.

In men with MDR1 polymorphism and CT allele, more pain was demonstrated and the need for more frequent analgesia ($\bar{X}$-2.93; p<0.006) - Table 50.

In women with the same polymorphism, there was a statistically significant difference between the number of analgesics and all types of pain in all three alleles: TT ($\bar{X}$- 2.54; p<0.003), CT ($\bar{X}$- 3.13; p<0.001) and CC ($\bar{X}$- 3.19; p <0.001) -Table 50.

From the data analysis obtained from the three genetic polymorphisms and gender, it can be concluded that significant differences in the number of anesthetics for 24 hours are observed significantly less frequently in men.

A number of studies have shown that reducing cognitive factors preoperatively reduces postoperative pain, (Lazarus R. et al.,).

Clinically, the catastrophization of pain is a recognized phenomenon that is often viewed in the context of depression, (Hirsh A. et al., Sullivan M. et al., Affleck G. et al.).

Pain, depression and catastrophization can be equally important in the multimadal management of these conditions.

Looking for the relation between the three genetic polymorphisms, the postoperative pain strength, the number of analgetics for 24 hours with the presence of catastrophization, we found that in patients with SNP OPRM1 polymorphism and alleles AA and AG, no

catastrophization was found, the pain strength after surgery is greater, which requires more frequent analgesia in the first 24 hours during their stay in intensive care, respectively AA ($\bar{X}$- 3.11; p <0.001), AG ($\bar{X}$-3.11; p<0.001) - Table 51.

In patients with SNP OPRM1 polymorphism and catastrophization with Rumination, the number of analgesia was higher only in the AG allele ($\bar{X}$- 3.15, p<0.001) - Table 51.

In catastrophization with Magnification and SNP OPRM1, more frequent analgesia was demonstrated in moderate to severe pain in the AA allele ($\bar{X}$- 2.44; p <0.6821) - Table 52.

For patients with COMT 1947 polymorphism, in whom no catastrophization was observed, most often the application of analgesia as a result of developed moderate to severe pain was found in the GA allele ($\bar{X}$- 3.20; p <0.001) - Table 51.

In those of them with catastrophization and Rumination, the number of analgesics in 24 hours was highest in the GA alleles ($\bar{X}$-2.88; p<2.88; p<0.006) and AA alleles ($\bar{X}$-3.00; p<0.023) - Table 51.

We also registered patients with COMT 1947 polymorphism and Magnification, as those who wished for more frequent analgesia due to the development of moderate to severe pain in the first 24 hours had the GA allele ($\bar{X}$- 3.09; p<0.020) - Table 52.

For patients with MDR1 genetic polymorphism without catastrophization, it is characteristic that the strongest postoperative pain was confirmed in the CC allele ($\bar{X}$- 3.25; p<0.001) - Table 51.

Rumination and moderate to severe pain was demonstrated in the allele CT ($\bar{X}$- 3.25; p<0.20) - Table 51, and Magnification only in the CT allele at different postoperative pain intensities (strong, medium, mild to absent) - p<0.116 - Table 52.

Unfortunately, the available data in patients with Helplessneses in the three types of polymorphism and in all alleles did not allow a statistically reliable analysis.

In summary, it can be concluded that in all patients with catastrophization with Rumination and Magnification, the differences in the number of analgesia are less significant in nature than in patients in whom the tests applied do not prove the presence of catastrophization.

The open (conventional) surgery method and the genetic polymorphisms are also related to the postoperative pain intensity (according to the VAS) and the number of anesthetics for 24 hours - Table 53.

In SNP OPRM1, the strongest pain was found in alleles AA ($\bar{X}$- 2.83; p<0.008) and AG ($\bar{X}$- 3.10; p 0.008).

In COMT 1947, the strongest pain was demonstrated in alleles GG ($\bar{X}$- 2.85; p - 0.016) and GA ($\bar{X}$- 3.07; p<0.001). In the case of AA allele, the difference in the number of analgesia in severe, moderate, mild to absent pain is insignificant - p-0.067- Table 53.

In MDR1, the pain is strongest in patients undergoing open surgery with alleles CT ($\bar{X}$- 3.09; p <0.001) and CC ($\bar{X}$- 3.06; p - 0.012) - Table 53.

In the patients operated by laparoscopic and robotic surgery methods, due to the lack of statistical representation, no specific analysis can be made of the relation between the three

genetic polymorphisms, the postoperative pain strength (VAS) and the number of anesthetics with the surgery method applied (laproscopic or robotic).

In studies by Shankar N. et al. and Simoni A. et al. the relation between the blood type and the experimentally cold-induced pain was studied. The first study did not show a significant difference between the blood types and the experimentally induced pain in healthy volunteers, while the second study found a difference among the blood types (Shankar N. et al., Simoni A. et al.).

In a study by Simoni A. et al., however, a significant gender difference was demonstrated, with men with blood type B showing a higher pain threshold in this study than women with the same blood type, (Simoni A.).

In our study, there was no evidence of a relation between the blood type, the three genetic polymorphisms and the postoperative pain strength of - Tables 55-58.

Currently, few studies have shown a potential relation between the blood types of ABO system and the preoperative anxiety. In an observational study conducted by Feng Xu et al. however, 352 patients provided strong evidence that blood types from the ABO system were associated with preoperative anxiety (Feng Xu).

They found that patients with AB blood type undergoing elective surgery were more likely to develop anxiety, ie. AB blood type is a risk factor for its preoperative manifestation, (Feng Xu).

Patients with A blood type and with SNP OPRM1 genetic polymorphism, allele AA, COMT 1947 G> A genetic polymorphism, allele GG, show a low degree of anxiety. In the MDR1 ABCB1 genetic polymorphism, a slight difference was found between the values of the three alleles.

In patients with B blood type, SNP OPRM1 genetic polymorphism, AA allele, a low degree of anxiety was demonstrated. In COMT 1947 G> A and SNP OPRM1 polymorphisms, there is no difference between the three alleles.

In patients with AB blood type, the three genetic polymorphisms lacked a statistically significant difference between the three alleles.

In SNP OPRM1 polymorphisms, AA allele has the lowest level of anxiety, while in MDR1 ABCB1 and COMT 1947 G>A, there is no difference between the three alleles.

Regarding Beck Depression Inventory and A blood type, patients with SNP OPRM1 and SNP OPRM1 did not show a difference between the mean values of the respective alleles.

At COMT 1947 G>A, patients with the GG allele have a lower mean value of depression.

In subjects with B blood type, SNP OPRM1, allele AA, COMT 1947 G> A, allele AA, in COMT 1947 G>A genetic polymorphism, allele GG was shown the lowest level of depression.

In MDR1 ABCB1, there is no difference in the mean values of the three alleles.

In AB and 0 blood types, SNP OPRM1 genetic polymorphism, AA allele, there is no depression or a mildly expressed depressive syndrome.

Regarding the PHQ-9 preoperative depression questionnaire, patients with A and B blood types and with SNP OPRM1 genetic polymorphism, in the alleles AA and AG, no differences were found between the different alleles GG. In MDR1 ABCB1, a slight difference was found between the three alleles.

In AB blood type, the SNP OPRM1 genetic polymorphism, AA and AG alleles did not differ.

At COMT 1947 G> A, patients with the GG allele had the lowest depression rate.
In MDR1 ABCB1, the differences between the three alleles are insignificant.
Blood group O, SNP OPRM1, allele AA had the lowest preoperative depression rate.
In COMT 1947 G> A and MDR1 ABCB1, there is no difference between the three alleles.
9. We did not find a statistically dependent relation between the type of medical institution where patients were treated (public or private) and the postoperative pain severity (measured through VAS).
In men, however, it is noticeable that there is a difference, albeit marginally significant ($p<0.1$), as a higher mean value of the pain experienced was found in those of them who had been treated or anesthetized in a state hospital (p-0.052) - Table 67.
10. Comparison of pre- and postoperative anxiety and depression tests (Taylor anxiety test, Beck Depression Inventory, PHQ-9 depression questionnaire) show similar results, which in practice make them interchangeable in the clinical work with patients according to the preferences of the individual anesthesiologist-resuscitator.
11. Based on the results obtained in task eleven, three prognostic groups were identified.
1. Low risk of pain over 5 on VAS - surgery method - robotic or laparoscopic surgery; SNP 118 polymorphism, AA allele; polymorphism COMT 1947, GG allele; MDR1 polymorphism, TT allele; Taylor test - low level of anxiety; gender - no matter.
2. Medium risk of pain over 5 on VAS - surgery method - robotic or laparoscopic surgery; SNP 118 polymorphism, AG or GG allele; COMT 1947 polymorphism, allele GA or AA; MDR1 polymorphism, CT or CC allele; Taylor test - medium or high level of anxiety; gender - no matter.
3. High risk of pain over 5 on VAS - surgery method – open (conventional) surgery.

VI. CONCLUSIONS:

1. The postoperative pain severity correlates with pre- and postoperative anxiety and depression.
2. The relation between postoperative pain and anxiety is more pronounced in female patients.
3. Postoperative pain is directly dependent on genetic polymorphisms (SNP OPRM1, COMT 1947 G> A and MDR1 ABCB1).
4. Low risk of pain over 5 on VAS was found in a surgery method - robotic or laparoscopic surgery; SNP 118 polymorphism, AA allele; polymorphism COMT 1947, GG allele; MDR1 polymorphism, TT allele; Taylor - low level of anxiety; gender - no matter.
5. In patients with SNP OPRM1, COMT 1947 G> A and MDR1 ABCB1 genetic polymorphisms, in open surgery the risk of complications associated with analgesia compared to the other two types of surgical methods (laparoscopic and robotic) is about 44 times higher.
6. With the highest risk (52 times) for the development of postoperative pain over 5 are the patients who underwent open surgery intervention compared to laparoscopic and robotic surgeries.

7. Patients with the SNP OPRM1 genetic polymorphism and AA allele experience less postoperative pain than patients with the other two alleles.
8. In patients with COMT 1947 G>A genetic polymorphism, the strongest pain is experienced by those who carry the AA and GA alleles.
9. Patients with MDR1 ABCB1 genetic polymorphism with the CC allele require more frequent postoperative analgesia due to the stronger pain that is registered in them in the postoperative period.
10. In patients with SNP OPRM1 genetic polymorphism (AA allele), Taylor anxiety is lower than in patients with AG and GG alleles.
11. In COMT 1947 G>A and MDR1 ABCB1, there is no difference in the level of Taylor anxiety in all three alleles.
12. Patients with genetic polymorphisms SNP OPRM1 (AA allele), COMT 1947 G>A (GG allele) and in MDR1 ABCB1 (TT allele) showed the lowest depression level on the PHQ-9 questionnaire for preoperative and postoperative depression on Beck Inventory.
13. Men with MDR1 ABCB1 genetic polymorphism and CC allele have the highest level of anxiety on the PHQ-9 depression test.
14. In patients with COMT 1947 G>A genetic polymorphism, the AA allele has a higher rate of "Moderate to severe" depression.
15. In people with the MDR1 ABCB1 genetic polymorphism, the CC allele has the highest rate of anxiety.
16. The number of analgesia in the postoperative period correlates with the pain strength experienced in the perioperative period.
17. Patients with SNP OPRM1 genetic polymorphism (GG allele), COMT 1947 G>A genetic polymorphism (GA allele) and MDR1 ABCB1 genetic polymorphism (CT allele) need more frequent analgesia.
18. The frequency of postoperative nausea is directly proportional to the postoperative pain intensity.
19. There is a significant relation between mental status, pain intensity and the number of analgesics with the occurrence of postoperative vomiting, respiratory depression and cardiovascular complications resulting from morphine analgesia.
20. Cardiovascular complications in the postoperative period that occurred after morphine analgesia are most common in patients with the SNP OPRM1 genetic polymorphism, allele AG.
21. The strongest postoperative pain is registered in open (conventional) surgeries, followed by laparoscopic and robotic surgeries.
22. In open surgeries, the strongest postoperative pain is registered in patients with SNP OPRM1 genetic polymorphism (AG and GG alleles), COMT 1947 G>A genetic polymorphism (AA and GA allele) and MDR1 ABCB1 genetic polymorphism (CC and CT alleles).
23. According to the type of surgery, patients who have undergone breast surgery have the highest mean value of pain.
24. In patients with SNP OPRM1 genetic polymorphism, AA allele, postoperative pain correlates with the age and surgery duration, and in people carrying the AG allele, it correlates with the surgery duration and anesthesia.

25. In COMT 1947 G>A genetic polymorphism in all three alleles there is a directly proportional relation with the surgery duration and anesthesia, and in people with the GA allele there is a relation with the patients' age.
26. In people operated on, with the MDR1 ABCB1 genetic polymorphism with the TT and CT alleles, there is a relation between the pain, the surgery duration and the anesthesia, and in those with the CC allele also with the age.
27. The weakest postoperative pain is in married patients.
28. More severe pain is found in rural patients.
29. There is no connection between the studied genetic polymorphisms and the presence or absence of children born.
30. In people with the AA and AG alleles of SNP OPRM1 genetic polymorphism, whether or not they have experienced previous surgery, the number of analgesics in those who report moderate to severe pain is higher than in patients with the same alleles, but experiencing mild to no pain.
31. In patients with COMT 1947 G> A genetic polymorphism, without previous surgery and with the GA allele, the number of analgesics is higher in those who report moderate to severe pain.
32. In patients with MDR1 ABCB1 genetic polymorphism without previous surgery, patients with the CT allele require more frequent analgesia.
33. The presence of previous surgeries did not affect the relation between the three genetic polymorphisms, the postoperative pain intensity and the number of analgesics.
34. In all patients with catastrofization with Rumination and Magnification, the difference in the number of analgesia was less significant than in patients in whom the tests provided did not prove the presence of catastrofization.
35. Blood type A and SNP OPRM1 genetic polymorphism (allele AA) and COMT 1947 G>A genetic polymorphism (allele GG) showed a lower level of Taylor anxiety. In the MDR1 ABCB1 genetic polymorphism, there is a slight difference between the values of the different alleles.
36. Blood types B and AB and SNP OPRM1 genetic polymorphism (AA allele) have the lowest level of anxiety.
37. There is no relation between the type of medical institution (public and private) where the patients are treated and the postoperative pain severity. In men treated in a public hospital, the mean pain experienced was borderline.
38. The use of various psychological tests for pre- and postoperative depression and anxiety can clarify the patient's psychological profile, most likely predicting the likelihood of genetic polymorphisms associated with pain, and this will help to develop an optimal plan for surgical treatment and postoperative analgesia.
39. The various psychological tests overlap their results, which allows them to be interchangeable and to use the shorter ones, but sufficiently informative options according to the preferences of the individual anesthesiologist.
40. Robotic surgical interventions with the Da Vinci robotic system with their minimal invasiveness provide a real opportunity in patients with genetic polymorphisms SNP OPRM1, COMT 1947 G> A and MDR1 ABCB1 to achieve an excellent postoperative result associated with less pain in the early postoperative period.

41. The application of the so-called personalized medicine, ie. clinical approach in the patients treatment according to their individual needs and characteristics (genetic, psychological, socio-anthropological, etc.) and the departure from the cliché "gold standard" is the most correct and patient-oriented.

VII. SCIENTIFIC AND APPLIED CONTRIBUTIONS:

1. For the first time in Bulgaria and in the world, the influence of the preoperative anxiety level (Taylor test) and pre- and postoperative depression (Beck Depression Inventory and PHQ-9 test for depression) on the pain intensity was studied after surgery (VAS) in robotic, laparoscopic and conventional surgeries.
2. For the first time in Bulgaria, an assessment of the frequency of SNP OPRM1 118 A>G genetic polymorphism (according to alleles AA, AG, GG), COMT 1947 G> A genetic polymorphism (according to alleles AA, AG, GG), as well as and the MDR1 (C3435T) ABCB1 polymorphism (according to CC allele, CT TT), and their effect on postoperative pain intensity (VAS).
3. For the first time in Bulgaria and in the world, the interrelation SNP 118 A>G of the gene OPRM1 (according to alleles AA, AG, GG), the COMT 1947 G>A genetic polymorphism (according to alleles AA, AG, GG) and the polymorphism MDR1 (C3435T) ABCB1 (according to allele CC, CT TT) was studied and the patients' preoperative psychological state (Taylor Anxiety Test, Beck Depression Inventory and PHQ-9 Depression Test).
4. For the first time in Bulgaria, the connection between the patients' preoperative and postoperative psychological state (Taylor, Beck and PHQ-9) with the SNP 118 A>G genetic polymorphism of the OPRM1 gene (according to alleles AA, AG, GG), COMT 1947 G>A genetic polymorphism (according to alleles AA, AG, GG) and MDR1 (C3435T) ABCB1 polymorphism (according to allele CC, CT TT), VAS for pain and the number of applied analgesia for 24 hours on the frequency and the type of complications resulting from the applied analgesia (nausea, vomiting, respiratory depression and cardiovascular complications).
5. For the first time in Bulgaria and in the world, the relation between diagnosis, surgical method used (open surgery, laparoscopic surgery and robotic surgery), surgery type (abdominal, thoracic and pelvic) and the various socio-anthropological factors is sought (age, gender, BMI, marital status, education, residence, presence of children, education, surgery duration and anesthesia) on the pain strength experienced in the postoperative period (VAS) in patients with COMT 1947 G>A, SNP OPRM 118 A>G and MDR1 (C3435T) ABCB1 genetic polymorphisms.
6. For the first time in Bulgaria and the world, the dependence between the three genetic polymorphisms (SNP OPRM1, COMT 1947 G> A, MDR1 ABCB1), the pain strength (VAS) and the number of analgesics in 24 hours has been studied and analyzed, as well as the presence of previous surgeries experienced by patients with the occurrence of catastrophization (Rumination, Magnification and Helplessness) by gender and surgical method (open surgery, laparoscopic surgery and robotic surgery).

7. For the first time in Bulgaria and in the world, an existing relation was sought between the blood type affiliation, the three genetic polymorphisms and the postoperative pain strength, depression and anxiety.
8. The relation between the presence of pain (VAS) and the type of medical institution where the patients were treated (public and private) was studied.
9. The various psychological tests for anxiety and depression in the perioperative period (Taylor test, Beck Inventory and PHQ-9 depression test) and the possibility of them being interchangeable in clinical practice were evaluated.
10. Several prognostic groups and a number of relations have been found.

List of scientific publications related to the dissertation:

1. Tsvetanova K., Nankov Vl. "Association of the single nucleotide polymorphism of the C3435TbABCB1/MDR1 gene with the opioid sensitivity to Morphine in the treatment of postoperative pain". Magazine "Anesthesiology and Intensive Care". vol. 1/2021 p. 4-9. ISSN: 1310-4284. SCOPUS, SJR 0.1.
2. Tsvetanova K. Influence of the various social, demographic, gender and age factors on postoperative depression in patients with cancer. Magazine "Sestrinsko Delo", vol. 2/2021 p. 20-27. ISSN: 1310-7496. Web of Science.
3. Tsvetanova K. Modern aspects related to postoperative pain, its treatment and its prognosis. Magazine "Sestrinsko Delo", vol. 2/2021 p. 45-51. ISSN: 1310-7496. Web of Science.
4. Tsvetanova K. Influence of preoperative depression, social environment, age and type of surgery method on the postoperative pain strength in patients diagnosed with cervical cancer. Magazine "Anesthesiology and Intensive Care", vol. 2/2021, p. 12-16. ISSN: 1310-4284. SCOPUS, SJR 0.1.
5. Tsvetanova K. Pharmacofenetics Aspects of Anesthesia and Postoperative Anesthesia. International Journal of Science and Research (IJSR), Vol. 10, Issue 2, February 2021. P. 888-891. ISSN: 2319-7064. Google Scholar.
6. Tsvetanova K. The Patient Target of Personalized Medicine. International Journal of Science and Research (IJSR), Vol. 10, Issue 1, January 2021. P. 1551-1553. ISSN: 2319-7064. Google Scholar.