Statistical Analysis of Lung Cancer Treatment Efficacy

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Introduction

The statistical analysis in question pertains to the comparison of the efficacy of two treatment approaches: Treatment 1, which involves the administration of Drug 1 and Drug 2 in combination with chemotherapy, and Treatment 2, which represents standard chemotherapy. The analysis aimed to verify baseline statistics for all patients included in the study, both collectively and in consideration of subgroup divisions. These subgroup divisions encompassed gender, age with a threshold at 65 years, smoking status, cancer stage, and treatment arm. Furthermore, survival analyses were conducted, with an additional focus on the age of the subjects, as well as efficacy analyses within these subgroup divisions.

Methods

For continuous data, descriptive statistics were used to characterize the study group, including measures such as mean, median, standard deviation (SD), as well as the first and third quartiles (IQR) and range. For categorical data, the frequency distribution of individual responses was presented, using both the count of each category and their percentage distribution.

Various statistical tests were employed in the analysis. The Mann-Whitney U test, a non-parametric test, was used to assess differences in distribution between two groups. The Kruskal-Wallis test, also a non-parametric test, was employed to compare the distribution of a variable among multiple groups. To examine the relationship between categorical variables, the chi-squared test or Fisher's test was utilized.

The impact of the type of therapy used in the study on patient survival was evaluated through survival analysis. Kaplan-Meier curves were employed for this purpose, which depict the probability of survival up to a specific time. These curves are step functions, and confidence intervals around the curves are constructed based on the standard error and logarithmic transformation. One of the key values describing Kaplan-Meier curves is the median survival time, indicating the point in time at which it is expected that 50% of patients will have experienced an event (e.g., death).

The efficacy of treatment was determined as the mean difference in the percentage of deaths among all individuals and subgroups, categorized by treatment type.

The percentage of deaths in subgroups was presented on forest plot-type graphs, which show the differences in the percentage of deaths between the two compared therapies, along with their 95% confidence interval. Additionally, a vertical line denoting 0% efficacy was included.

A significance level of $p=0.05$ was adopted, but results that were statistically significant at $p=0.01$ and $p=0.001$ levels were also indicated. P-values indicating statistically significant results were presented in bold. In cases where $p<0.001$, the notation $p<0.001$ was always used.

All calculations and graphs were generated using the R statistical package, version 4.0.2.

Baseline Characteristics

Table 1 presents the baseline characteristics of the patients. The study included 200 patients, with 53.5% being female and 46.5% male. The average age was around 56 years (±13.84, standard deviation), with 46.5% of patients being over 65 years, and 53.5% being 65 years or younger. The youngest individual was 27 years old, while the oldest was 77 years old. The study included individuals at various stages of cancer, almost evenly distributed in terms of the number of patients. Additionally, 66.5% of the participants were current or former smokers.

Patients were divided into two equally sized groups based on their treatment arm, with 100 individuals in each group. The average time from diagnosis to the end of treatment or death for both groups was approximately 240 days (±43.54). Among all patients enrolled in the study, 36 individuals experienced mortality, constituting 18%.

Table 1. General Descriptive Characteristics

Variable	Parameter	Total (N=200)
Gender	Male	46,5% (N=93)
	Female	53,5% (N=107)
Age	N	200
	Mean (SD)	56,14 (13,84)
	Median (IQR)	59 (40 - 69)
	Range	27 - 77
Age Relative to 65 Years	Over 65 years	46,5% (N=93)
	65 years or younger	53,5% (N=107)
Cancer Stage	1	25,5% (N=51)
	2	23,5% (N=47)
	3	24% (N=48)
	4	27% (N=54)
Smoking Status	Former Smoker	32,5% (N=65)
	Current Smoker	34% (N=68)
	Non-Smoker	33,5% (N=67)
Mortality	Yes	18% (N=36)
	No	82% (N=164)

Variable	Parameter	Total (N=200)
Time from Diagnosis to End of Treatment/Death	N	200
	Mean (SD)	240,48 (43,54)
	Median (IQR)	239 (205,75 - 275)
	Range	152 - 326
Treatment Arm	Treatment 1	50% (N=100)
	Treatment 2	50% (N=100)

The study considered the presence of the following chronic diseases: hypertension, diabetes, obesity, chronic obstructive pulmonary disease (COPD), atherosclerosis, ischemic heart disease, gallstone disease, kidney stones, and peptic ulcer disease. Among the patients, hypertension was the most common (20%). Other common coexisting conditions were diabetes (13%) and obesity (12%). The remaining comorbidities occurred in less than 10% of cases.

Table 2. Descriptive Characteristics of Chronic Diseases

Variable	Parameter	Total (N=200)
Hypertension	Yes	20% (N=40)
	No	80% (N=160)
Diabetes	Yes	13% (N=26)
	No	87% (N=174)
Obesity	Yes	12% (N=24)
	No	88% (N=176)
Chronic Obstructive Pulmonary Disease (COPD)	Yes	9,5% (N=19)
	No	90,5% (N=181)
Atherosclerosis	Yes	8% (N=16)
	No	92% (N=184)
Ischemic Heart Disease	Yes	4,5% (N=9)
	No	95,5% (N=191)
Gallstone Disease	Yes	6,5% (N=13)
	No	93,5% (N=187)
Kidney Stones	Yes	5% (N=10)

Variable	Parameter	Total (N=200)
	No	95% (N=190)
Peptic Ulcer Disease	Yes	9,5% (N=19)
	No	90,5% (N=181)

Table 3 presents the descriptive characteristics of patient test results at the start of treatment, which are used to assess the patient's condition. The following parameters were considered: leukocytes [cells/μL], neutrophils [cells/μL], erythrocyte sedimentation rate (ESR) [mm/h], C-reactive protein (CRP) [mg/L], glucose [mg/dL], creatinine [mg/dL], and alkaline phosphatase [U/L]. It is worth noting that the average values for leukocytes, neutrophils, ESR, and CRP are elevated compared to the normal range, which is characteristic of lung cancer.

Table 3. Descriptive Characteristics of Patient Test Results Before Starting Treatment

Variable	Parameter	Total (N=200)
Leukocytes [cells/μL]	N	200
	Mean (SD)	11793,07 (1555,54)
	Median (IQR)	12090,5 (10411 - 13104,75)
	Range	9011 - 14481
Neutrophils [cells/μL]	N	200
	Mean (SD)	8766,58 (2352,83)
	Median (IQR)	9137,5 (7855,25 - 10562)
	Range	2040 - 11483
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	200
	Mean (SD)	54,67 (9,39)
	Median (IQR)	56 (46 - 62,25)
	Range	40 - 70
C-reactive Protein (CRP) [mg/L]	N	200
	Mean (SD)	321,34 (116,95)
	Median (IQR)	329,5 (223,5 - 421,5)
	Range	102 - 500
Glucose [mg/dL]	N	200
	Mean (SD)	86,75 (11,84)
	Median (IQR)	84,5 (78 - 94)
	Range	70 - 128
Creatinine [mg/dL]	N	200
	Mean (SD)	1,22 (0,19)
	Median (IQR)	1,2 (1 - 1,4)
	Range	0,9 - 1,6

Variable	Parameter	Total (N=200)
Alkaline Phosphatase [U/L]	N	200
	Mean (SD)	97,36 (29,75)
	Median (IQR)	98 (70,75 - 121)
	Range	50 - 149

Among the adverse effects included in the study characteristics, four of the most commonly occurring were considered: neutropenia, anemia, diarrhea, and rash. Neutropenia was the most frequent, occurring in 14% of cases. The other adverse effects were observed in the range of 10-12%.

Table 4. Descriptive Characteristics of the Most Common Adverse Effects

Variable	Parameter	Total (N=200)
Neutropenia	Yes	14% (N=28)
	No	86% (N=172)
Anemia	Yes	12% (N=24)
	No	88% (N=176)
Diarrhea	Yes	11% (N=22)
	No	89% (N=178)
Rash	Yes	10% (N=20)
	No	90% (N=180)

Characteristics by Gender

No significant differences in parameters were observed within the cohort divided by gender.

Table 5. Descriptive Characteristics by Gender

Variable	Parameter	Male (N=93)	Female (N=107)	test	p-value
Age	N	93	107	U Mann-Whitney	0,0645
	Mean (SD)	54,59 (13,2)	57,49 (14,3)		
	Median (IQR)	58 (40 - 66)	66 (40 - 69)		
	Range	27 - 77	27 - 77		
Age Relative to 65 Years	Over 65 years	38,7% (N=36)	53,3% (N=57)	Chi-square	0,0552
	65 years or younger	61,3% (N=57)	46,7% (N=50)		
Cancer Stage	1	30,1% (N=28)	21,5% (N=23)	Chi-square	0,4351
	2	24,7% (N=23)	22,4% (N=24)		

Variable	Parameter	Male (N=93)	Female (N=107)	test	p-value
	3	21,5% (N=20)	26,2% (N=28)		
	4	23,7% (N=22)	29,9% (N=32)		
Smoking Status	Former Smoker	29% (N=27)	35,5% (N=38)	Chi-square	0,1615
	Current Smoker	40,9% (N=38)	28% (N=30)		
	Non-Smoker	30,1% (N=28)	36,4% (N=39)		
Hypertension	Yes	17,2% (N=16)	22,4% (N=24)	Chi-square	0,4567
	No	82,8% (N=77)	77,6% (N=83)		
Diabetes	Yes	8,6% (N=8)	16,8% (N=18)	Chi-square	0,1302
	No	91,4% (N=85)	83,2% (N=89)		
Obesity	Yes	9,7% (N=9)	14% (N=15)	Chi-square	0,4689
	No	90,3% (N=84)	86% (N=92)		
Chronic Obstructive Pulmonary Disease	Yes	10,8% (N=10)	8,4% (N=9)	Chi-square	0,7478
	No	89,2% (N=83)	91,6% (N=98)		
Atherosclerosis	Yes	10,8% (N=10)	5,6% (N=6)	Chi-square	0,2817
	No	89,2% (N=83)	94,4% (N=101)		
Ischemic Heart Disease	Yes	2,2% (N=2)	6,5% (N=7)	Fisher	0,1795
	No	97,8% (N=91)	93,5% (N=100)		
Gallstone Disease	Yes	8,6% (N=8)	4,7% (N=5)	Fisher	0,3893
	No	91,4% (N=85)	95,3% (N=102)		
Kidney Stones	Yes	5,4% (N=5)	4,7% (N=5)	Fisher	1

Variable	Parameter	Male (N=93)	Female (N=107)	test	p-value
	No	94,6% (N=88)	95,3% (N=102)		
Peptic Ulcer Disease	Yes	6,5% (N=6)	12,1% (N=13)	Chi-square	0,2589
	No	93,5% (N=87)	87,9% (N=94)		
Mortality	Yes	15,1% (N=14)	20,6% (N=22)	Chi-square	0,4085
	No	84,9% (N=79)	79,4% (N=85)		
Time from Diagnosis to End of Treatment/Death	N	93	107	U Mann-Whitney	0,1929
	Mean (SD)	236,19 (44,05)	244,2 (42,95)		
	Median (IQR)	234 (203 - 270)	243 (215 - 279)		
	Range	153 - 323	152 - 326		
Neutropenia	Yes	12,9% (N=12)	15% (N=16)	Chi-square	0,8318
	No	87,1% (N=81)	85% (N=91)		
Anemia	Yes	10,8% (N=10)	13,1% (N=14)	Chi-square	0,7734
	No	89,2% (N=83)	86,9% (N=93)		
Diarrhea	Yes	10,8% (N=10)	11,2% (N=12)	Chi-square	1
	No	89,2% (N=83)	88,8% (N=95)		
Rash	Yes	11,8% (N=11)	8,4% (N=9)	Chi-square	0,5707
	No	88,2% (N=82)	91,6% (N=98)		
Treatment Arm	Treatment 1	53,8% (N=50)	46,7% (N=50)	Chi-square	0,395
	Treatment 2	46,2% (N=43)	53,3% (N=57)		

Variable	Parameter	Male (N=93)	Female (N=107)	test	p-value
Leukocytes [cells/µL]	N	93	107	U Mann-Whitney	0,1547
	Mean (SD)	11622,11 (1569,99)	11941,66 (1534,73)		
	Median (IQR)	11331 (10185 - 12618)	12128 (10536 - 13255)		
	Range	9049 - 14426	9011 - 14481		
Neutrophils [cells/µL]	N	93	107	U Mann-Whitney	0,0658
	Mean (SD)	8389,73 (2561,94)	9094,11 (2112,62)		
	Median (IQR)	8633 (7504 - 10364)	9628 (8001,5 - 10588,5)		
	Range	2040 - 11459	2154 - 11483		
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	93	107	U Mann-Whitney	0,6239
	Mean (SD)	55,04 (9,58)	54,35 (9,26)		
	Median (IQR)	56 (46 - 64)	54 (46,5 - 61,5)		
	Range	40 - 70	40 - 70		
C-reactive Protein (CRP) [mg/L]	N	93	107	U Mann-Whitney	0,141
	Mean (SD)	308,71 (112,38)	332,32 (120,23)		
	Median (IQR)	313 (220 - 410)	349 (224,5 - 431)		
	Range	107 - 497	102 - 500		
Glucose [mg/dL]	N	93	107	U Mann-Whitney	0,6292
	Mean (SD)	87,31 (12,14)	86,26 (11,62)		
	Median (IQR)	86 (78 - 94)	84 (77,5 - 93,5)		
	Range	71 - 128	70 - 128		
Creatinine [mg/dL]	N	93	107	U Mann-Whitney	0,8467
	Mean (SD)	1,22 (0,19)	1,22 (0,2)		

Variable	Parameter	Male (N=93)	Female (N=107)	test	p-value
	Median (IQR)	1,3 (1 - 1,4)	1,2 (1 - 1,4)		
	Range	0,9 - 1,6	0,9 - 1,5		
Alkaline Phosphatase [U/L]	N	93	107	U Mann-Whitney	0,4912
	Mean (SD)	98,68 (27,7)	96,21 (31,5)		
	Median (IQR)	99 (75 - 119)	97 (66 - 121,5)		
	Range	50 - 149	50 - 149		

Characteristics by Age

The analysis of dependencies in age groups showed significant differences in the following variables:

- Hypertension (chi-square p-value <0.001);
- Diabetes (chi-square p-value = 0.0018);
- Obesity (chi-square p-value = 0.0198);
- Kidney stone (Fisher p-value = 0.0471);
- Peptic ulcer disease (Fisher p-value = 0.0154);
- Diarrhea (Fisher p-value = 0.0472);
- Rash (Fisher p-value = 0.0027).

Comorbidities such as hypertension, diabetes, obesity, peptic ulcer disease were more common among individuals over 65 years of age than those below 65 years. However, kidney stones were significantly more common in individuals younger than 65 years compared to those over 65 years.

In individuals over 65 years, diarrhea and rash were more frequent than in individuals under 65 years.

Table 6. Descriptive Characteristics Stratified by Age

Variable	Parameter	Over 65 years (N=93)	65 years and younger (N=107)	test	p-value
Gender	Male	38,7% (N=36)	53,3% (N=57)	Chi-square	0,0552
	Female	61,3% (N=57)	46,7% (N=50)		
Cancer Stage	1	26,9% (N=25)	24,3% (N=26)	Chi-square	0,4224
	2	18,3% (N=17)	28% (N=30)		
	3	26,9% (N=25)	21,5% (N=23)		
	4	28% (N=26)	26,2% (N=28)		
Smoking Status	Former Smoker	32,3% (N=30)	32,7% (N=35)	Chi-square	0,6394
	Current Smoker	31,2% (N=29)	36,4% (N=39)		
	Non-Smoker	36,6% (N=34)	30,8% (N=33)		
Hypertension	Yes	33,3% (N=31)	8,4% (N=9)	Chi-square	**<0,001**
	No	66,7% (N=62)	91,6% (N=98)		
Diabetes	Yes	21,5% (N=20)	5,6% (N=6)	Chi-square	**0,0018**
	No	78,5% (N=73)	94,4% (N=101)		
Obesity	Yes	18,3% (N=17)	6,5% (N=7)	Chi-square	**0,0198**
	No	81,7% (N=76)	93,5% (N=100)		

Variable	Parameter	Over 65 years (N=93)	65 years and younger (N=107)	test	p-value
Chronic Obstructive Pulmonary Disease	Yes	12,9% (N=12)	6,5% (N=7)	Chi-square	0,1976
	No	87,1% (N=81)	93,5% (N=100)		
Atherosclerosis	Yes	8,6% (N=8)	7,5% (N=8)	Chi-square	0,975
	No	91,4% (N=85)	92,5% (N=99)		
Ischemic Heart Disease	Yes	6,5% (N=6)	2,8% (N=3)	Fisher	0,3082
	No	93,5% (N=87)	97,2% (N=104)		
Gallstone Disease	Yes	7,5% (N=7)	5,6% (N=6)	Chi-square	0,7936
	No	92,5% (N=86)	94,4% (N=101)		
Kidney Stones	Yes	8,6% (N=8)	1,9% (N=2)	Fisher	**0,0471**
	No	91,4% (N=85)	98,1% (N=105)		
Peptic Ulcer Disease	Yes	15,1% (N=14)	4,7% (N=5)	Fisher	**0,0154**
	No	84,9% (N=79)	95,3% (N=102)		
Mortality	Yes	19,4% (N=18)	16,8% (N=18)	Chi-square	0,7791
	No	80,6% (N=75)	83,2% (N=89)		
Time from Diagnosis to End of Treatment/Death	N	93	107	U Mann-Whitney	0,4147
	Mean (SD)	242,77 (43,38)	238,48 (43,78)		

Variable	Parameter	Over 65 years (N=93)	65 years and younger (N=107)	test	p-value
	Median (IQR)	244 (209 - 280)	235 (203 - 270,5)		
	Range	155 - 326	152 - 326		
Neutropenia	Yes	18,3% (N=17)	10,3% (N=11)	Chi-square	0,1551
	No	81,7% (N=76)	89,7% (N=96)		
Anemia	Yes	17,2% (N=16)	7,5% (N=8)	Chi-square	0,0583
	No	82,8% (N=77)	92,5% (N=99)		
Diarrhea	Yes	18,3% (N=17)	4,7% (N=5)	Fisher	**0,0027**
	No	81,7% (N=76)	95,3% (N=102)		
Rash	Yes	15,1% (N=14)	5,6% (N=6)	Chi-square	**0,0472**
	No	84,9% (N=79)	94,4% (N=101)		
Treatment Arm	Treatment 1	50,5% (N=47)	49,5% (N=53)	Chi-square	1
	Treatment 2	49,5% (N=46)	50,5% (N=54)		
Leukocytes [cells/µL]	N	93	107	U Mann-Whitney	0,3872
	Mean (SD)	11893,23 (1526,86)	11706,02 (1582,02)		
	Median (IQR)	12115 (10619 - 13164)	11945 (10248 - 13083,5)		
	Range	9011 - 14430	9150 - 14481		

Variable	Parameter	Over 65 years (N=93)	65 years and younger (N=107)	test	p-value
Neutrophils [cells/µL]	N	93	107	U Mann-Whitney	0,6969
	Mean (SD)	8844,75 (2317,05)	8698,63 (2392,29)		
	Median (IQR)	9486 (7903 - 10560)	8918 (7854,5 - 10555)		
	Range	2379 - 11481	2040 - 11483		
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	93	107	U Mann-Whitney	0,3196
	Mean (SD)	55,39 (9,32)	54,05 (9,46)		
	Median (IQR)	56 (47 - 62)	53 (45,5 - 62,5)		
	Range	40 - 70	40 - 70		
C-reactive Protein (CRP) [mg/L]	N	93	107	U Mann-Whitney	0,4043
	Mean (SD)	327,2 (121,6)	316,24 (113,09)		
	Median (IQR)	336 (226 - 443)	313 (221,5 - 413,5)		
	Range	102 - 500	107 - 498		
Glucose [mg/dL]	N	93	107	U Mann-Whitney	0,3992
	Mean (SD)	85,86 (11,03)	87,52 (12,5)		
	Median (IQR)	83 (78 - 93)	86 (78 - 94)		
	Range	70 - 128	70 - 128		
Creatinine [mg/dL]	N	93	107	U Mann-Whitney	0,4678
	Mean (SD)	1,23 (0,2)	1,21 (0,19)		
	Median (IQR)	1,3 (1 - 1,4)	1,2 (1 - 1,4)		

Variable	Parameter	Over 65 years (N=93)	65 years and younger (N=107)	test	p-value
	Range	0,9 - 1,6	0,9 - 1,5		
Alkaline Phosphatase [U/L]	N	93	107	U Mann-Whitney	0,8967
	Mean (SD)	97,08 (29,46)	97,6 (30,13)		
	Median (IQR)	99 (72 - 118)	97 (67,5 - 122)		
	Range	50 - 149	50 - 149		

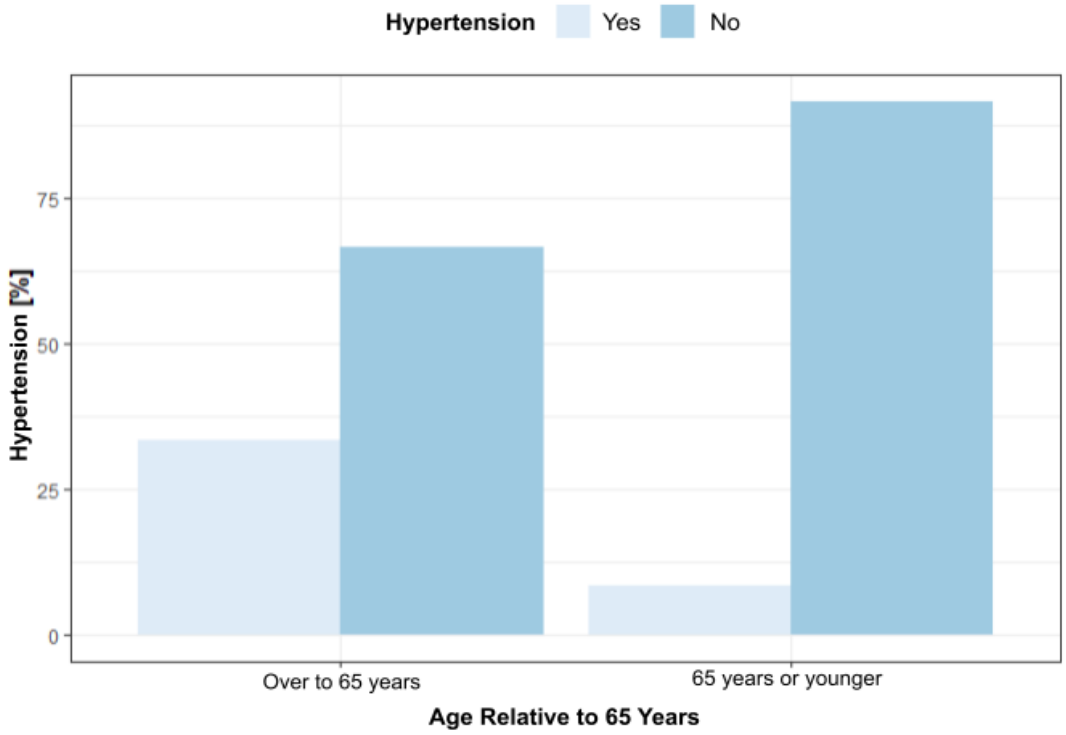

Figure 1. Relationship between the occurrence of hypertension and age group (%)

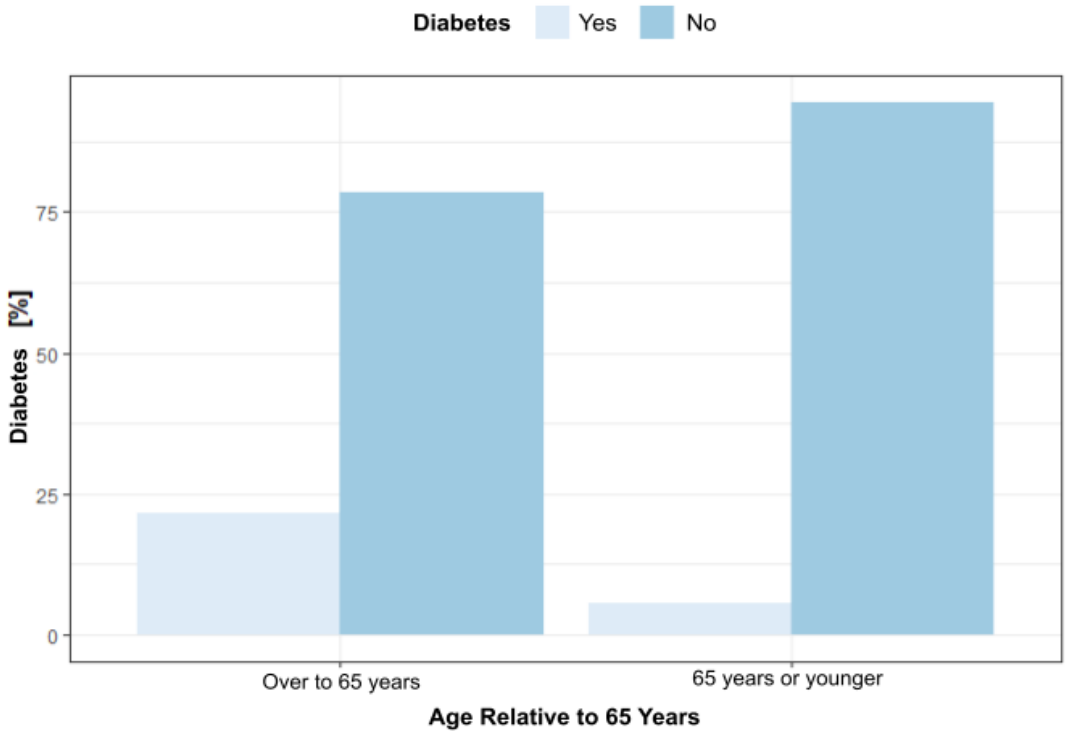

Figure 2. Relationship between the occurrence of diabetes and age group (%)

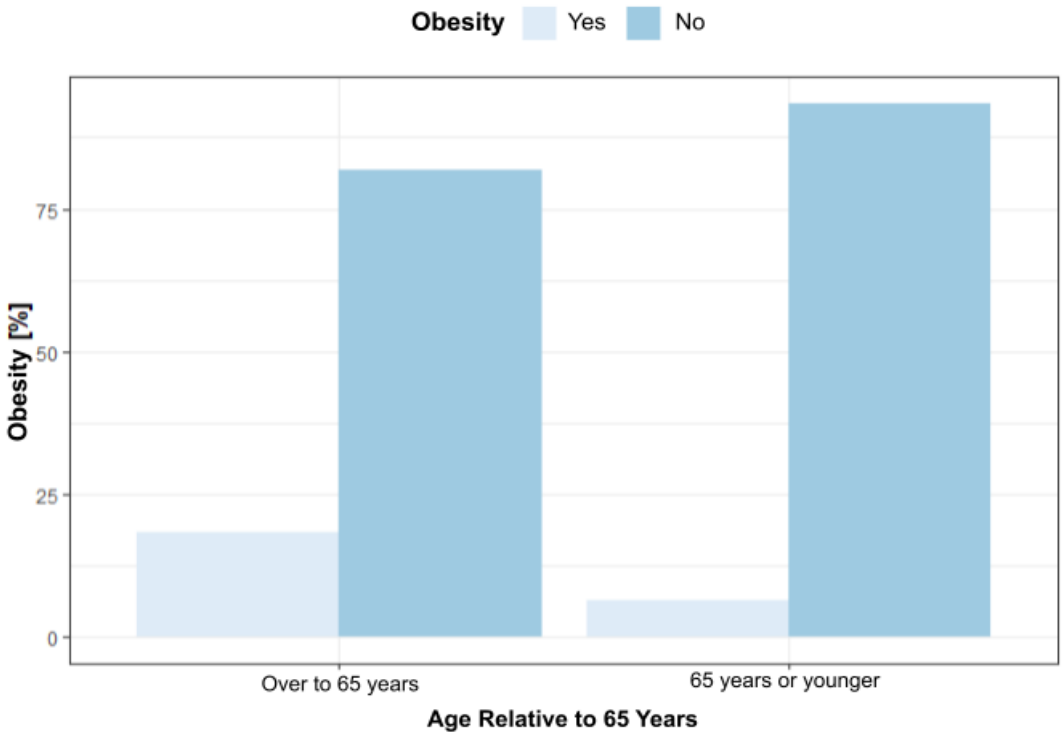

Figure 3. Relationship between the occurrence of obesity and age group (%)

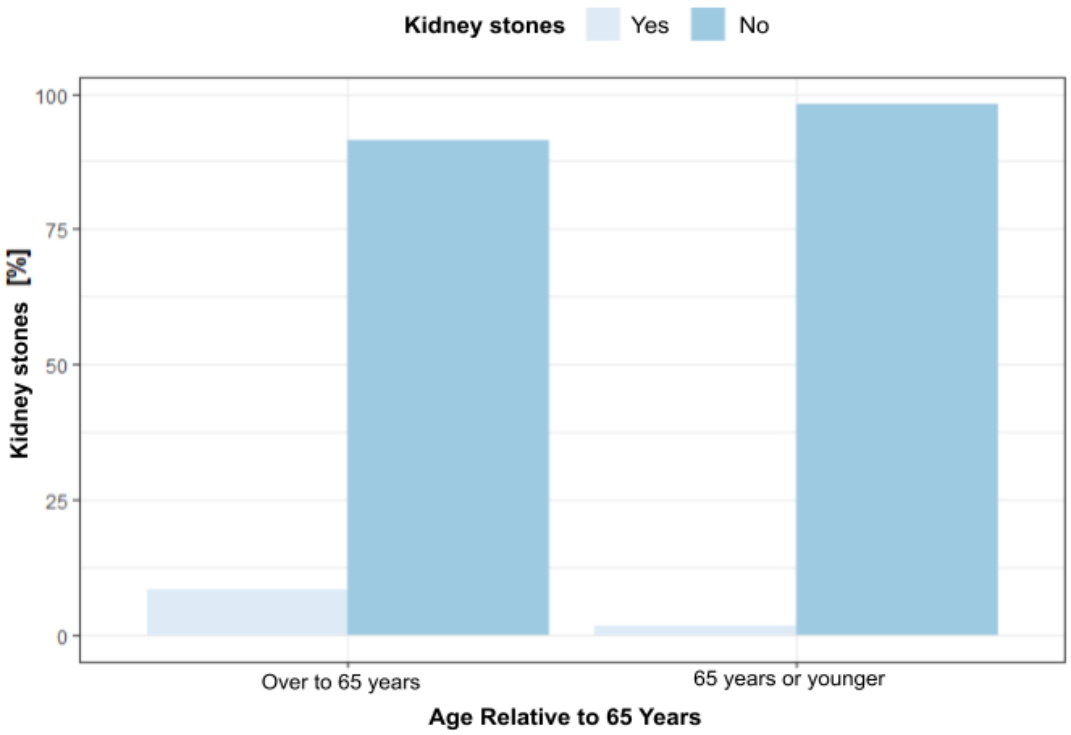

Figure 4. Relationship between the occurrence of kidney stones and age group (%)

Figure 5. Relationship between the occurrence of peptic ulcer disease and age group (%)

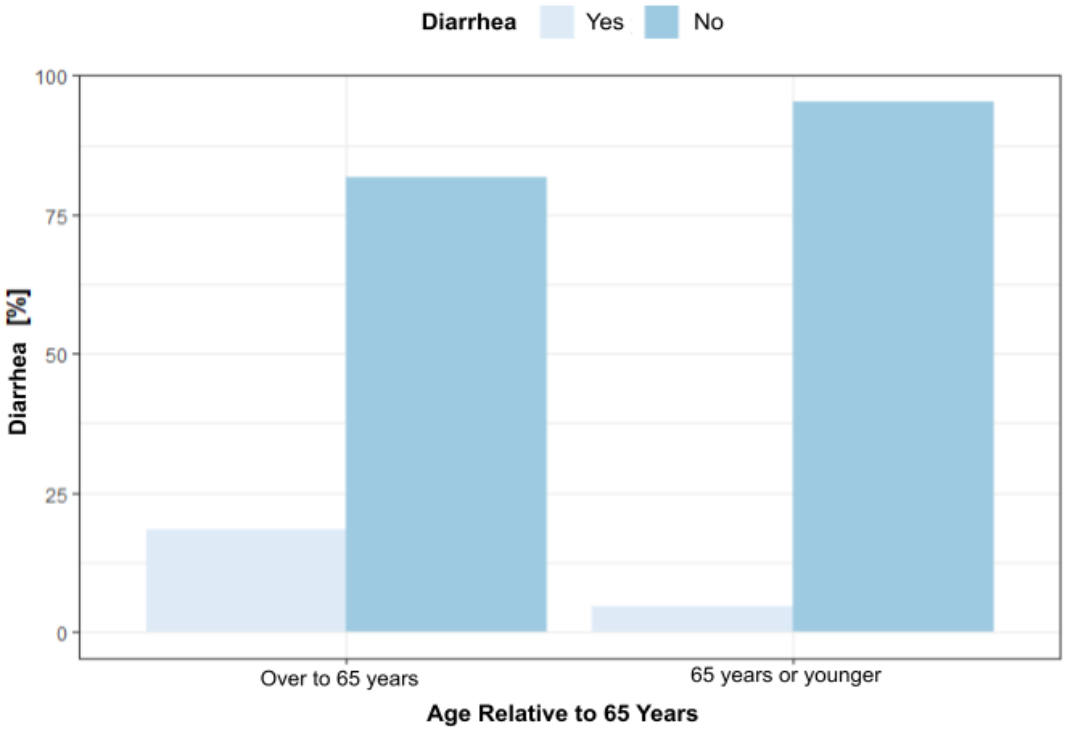

Figure 6. Relationship between the occurrence of diarrhea and age group (%)

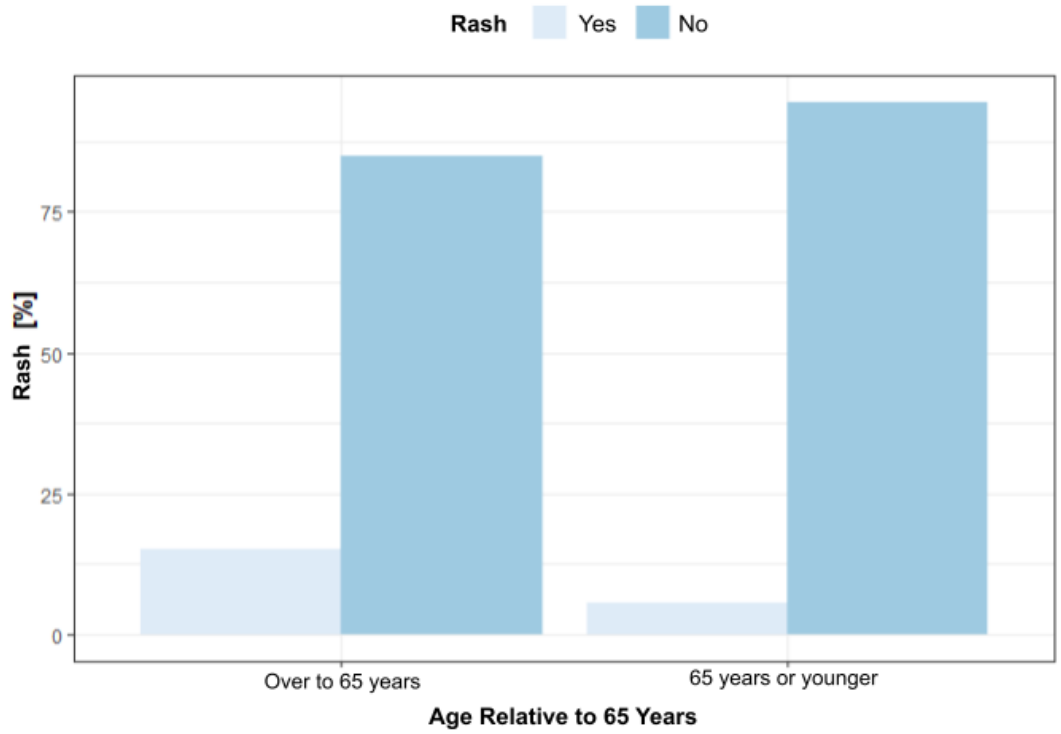

Figure 7. Relationship between the occurrence of rash and age group (%)

Characteristics by Smoking Status

Characteristics by Smoking Status

Significant differences were observed between former smokers, current smokers, and non-smokers in the following variables:

- Diabetes (Fisher p-value = 0.0376)
- Chronic Obstructive Pulmonary Disease (COPD) (Fisher p-value = 0.0042)
- Atherosclerosis (Fisher p-value = 0.0223)
- Peptic Ulcer Disease (Fisher p-value = 0.0289)
- Mortality (chi-square p-value = 0.0305)

Diabetes was most commonly found in non-smokers and least commonly in smokers.

Chronic Obstructive Pulmonary Disease (COPD), atherosclerosis, and peptic ulcer disease were most common among smokers and least common among non-smokers.

Twice as many people died in the smoking group compared to the other groups.

Table 7. Descriptive Characteristics by Smoking Status

Variable	Parameter	Former Smoker (N=65)	Current Smoker (N=68)	Non-Smoker (N=67)	test	p-value
Gender	Male	41,5% (N=27)	55,9% (N=38)	41,8% (N=28)	Chi-square	0,1615
	Female	58,5% (N=38)	44,1% (N=30)	58,2% (N=39)		
Age	N	65	68	67	Kruskal-Wallis	0,3542
	Mean (SD)	55,72 (14,45)	54,71 (14,05)	58 (13)		
	Median (IQR)	59 (40 - 69)	59 (40 - 67)	66 (42,5 - 69)		
	Range	27 - 77	27 - 77	39 - 77		
Age Relative to 65 Years	Over 65 years	46,2% (N=30)	42,6% (N=29)	50,7% (N=34)	Chi-square	0,6394
	65 years or younger	53,8% (N=35)	57,4% (N=39)	49,3% (N=33)		
Cancer Stage	1	30,8% (N=20)	20,6% (N=14)	25,4% (N=17)	Chi-square	0,5058
	2	26,2% (N=17)	20,6% (N=14)	23,9% (N=16)		
	3	24,6% (N=16)	23,5% (N=16)	23,9% (N=16)		
	4	18,5% (N=12)	35,3% (N=24)	26,9% (N=18)		
Hypertension	Yes	24,6% (N=16)	16,2% (N=11)	19,4% (N=13)	Chi-square	0,472
	No	75,4% (N=49)	83,8% (N=57)	80,6% (N=54)		
Diabetes	Yes	12,3% (N=8)	5,9% (N=4)	20,9% (N=14)	Fisher	**0,0376**
	No	87,7% (N=57)	94,1% (N=64)	79,1% (N=53)		
Obesity	Yes	7,7% (N=5)	8,8% (N=6)	19,4% (N=13)	Fisher	0,09

Variable	Parameter	Former Smoker (N=65)	Current Smoker (N=68)	Non-Smoker (N=67)	test	p-value
	No	92,3% (N=60)	91,2% (N=62)	80,6% (N=54)		
Chronic Obstructive Pulmonary Disease	Yes	6,2% (N=4)	19,1% (N=13)	3% (N=2)	Fisher	**0,0042**
	No	93,8% (N=61)	80,9% (N=55)	97% (N=65)		
Atherosclerosis	Yes	9,2% (N=6)	13,2% (N=9)	1,5% (N=1)	Fisher	**0,0223**
	No	90,8% (N=59)	86,8% (N=59)	98,5% (N=66)		
Ischemic Heart Disease	Yes	7,7% (N=5)	2,9% (N=2)	3% (N=2)	Fisher	0,4356
	No	92,3% (N=60)	97,1% (N=66)	97% (N=65)		
Gallstone Disease	Yes	4,6% (N=3)	7,4% (N=5)	7,5% (N=5)	Fisher	0,8201
	No	95,4% (N=62)	92,6% (N=63)	92,5% (N=62)		
Kidney Stones	Yes	4,6% (N=3)	4,4% (N=3)	6% (N=4)	Fisher	0,9241
	No	95,4% (N=62)	95,6% (N=65)	94% (N=63)		
Peptic Ulcer Disease	Yes	9,2% (N=6)	16,2% (N=11)	3% (N=2)	Fisher	**0,0289**
	No	90,8% (N=59)	83,8% (N=57)	97% (N=65)		
Mortality	Yes	13,8% (N=9)	27,9% (N=19)	11,9% (N=8)	Chi-square	**0,0305**
	No	86,2% (N=56)	72,1% (N=49)	88,1% (N=59)		
Time from Diagnosis to End of Treatment/Death	N	65	68	67	Kruskal-Wallis	0,1457
	Mean (SD)	231,98 (46,62)	247,75 (35,68)	241,33 (46,79)		

Variable	Parameter	Former Smoker (N=65)	Current Smoker (N=68)	Non-Smoker (N=67)	test	p-value
	Median (IQR)	232 (189 - 270)	243 (223,75 - 273)	246 (201,5 - 278)		
	Range	153 - 322	175 - 326	152 - 326		
Neutropenia	Yes	15,4% (N=10)	19,1% (N=13)	7,5% (N=5)	Fisher	0,1286
	No	84,6% (N=55)	80,9% (N=55)	92,5% (N=62)		
Anemia	Yes	12,3% (N=8)	16,2% (N=11)	7,5% (N=5)	Fisher	0,2779
	No	87,7% (N=57)	83,8% (N=57)	92,5% (N=62)		
Diarrhea	Yes	15,4% (N=10)	8,8% (N=6)	9% (N=6)	Chi-square	0,3884
	No	84,6% (N=55)	91,2% (N=62)	91% (N=61)		
Rash	Yes	13,8% (N=9)	7,4% (N=5)	9% (N=6)	Fisher	0,4653
	No	86,2% (N=56)	92,6% (N=63)	91% (N=61)		
Treatment Arm	Treatment 1	50,8% (N=33)	54,4% (N=37)	44,8% (N=30)	Chi-square	0,5283
	Treatment 2	49,2% (N=32)	45,6% (N=31)	55,2% (N=37)		
Leukocytes [cells/µL]	N	65	68	67	Kruskal-Wallis	0,0657
	Mean (SD)	11495,23 (1520,79)	12082,94 (1547,19)	11787,82 (1564,92)		
	Median (IQR)	11689 (10142 - 12455)	12180,5 (10646,75 - 13565,75)	12123 (10266,5 - 13169,5)		
	Range	9011 - 14430	9152 - 14426	9150 - 14481		
Neutrophils [cells/µL]	N	65	68	67	Kruskal-Wallis	0,4871

Variable	Parameter	Former Smoker (N=65)	Current Smoker (N=68)	Non-Smoker (N=67)	test	p-value
	Mean (SD)	8716,42 (2085,89)	8890,87 (2465,11)	8689,09 (2505,77)		
	Median (IQR)	8897 (7856 - 10225)	9955,5 (7926,5 - 10763)	9154 (7771,5 - 10575)		
	Range	2377 - 11352	2103 - 11483	2040 - 11459		
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	65	68	67	Kruskal-Wallis	0,6691
	Mean (SD)	53,88 (9,42)	55,35 (9,55)	54,75 (9,29)		
	Median (IQR)	53 (45 - 63)	56 (48 - 64)	55 (46,5 - 60,5)		
	Range	40 - 69	40 - 70	40 - 70		
C-reactive Protein (CRP) [mg/L]	N	65	68	67	Kruskal-Wallis	0,1175
	Mean (SD)	302,72 (111,69)	341,07 (122,01)	319,37 (115,26)		
	Median (IQR)	315 (213 - 399)	361 (250,25 - 449,5)	323 (223 - 423)		
	Range	107 - 493	102 - 500	113 - 496		
Glucose [mg/dL]	N	65	68	67	Kruskal-Wallis	0,6756
	Mean (SD)	85,82 (10,45)	86,34 (12,18)	88,07 (12,79)		
	Median (IQR)	83 (78 - 95)	84 (78 - 93)	87 (78,5 - 94,5)		
	Range	70 - 118	71 - 128	70 - 128		
Creatinine [mg/dL]	N	65	68	67	Kruskal-Wallis	0,4692
	Mean (SD)	1,2 (0,21)	1,24 (0,18)	1,21 (0,2)		
	Median (IQR)	1,2 (1 - 1,4)	1,3 (1,1 - 1,4)	1,2 (1 - 1,35)		
	Range	0,9 - 1,5	0,9 - 1,6	0,9 - 1,5		
Alkaline Phosphatase [U/L]	N	65	68	67	Kruskal-Wallis	0,4591
	Mean (SD)	94,45 (31,88)	100,28 (29,66)	97,21 (27,8)		

Variable	Parameter	Former Smoker (N=65)	Current Smoker (N=68)	Non-Smoker (N=67)	test	p-value
	Median (IQR)	93 (63 - 122)	100 (73 - 124,5)	100 (75,5 - 117)		
	Range	50 - 147	54 - 149	50 - 149		

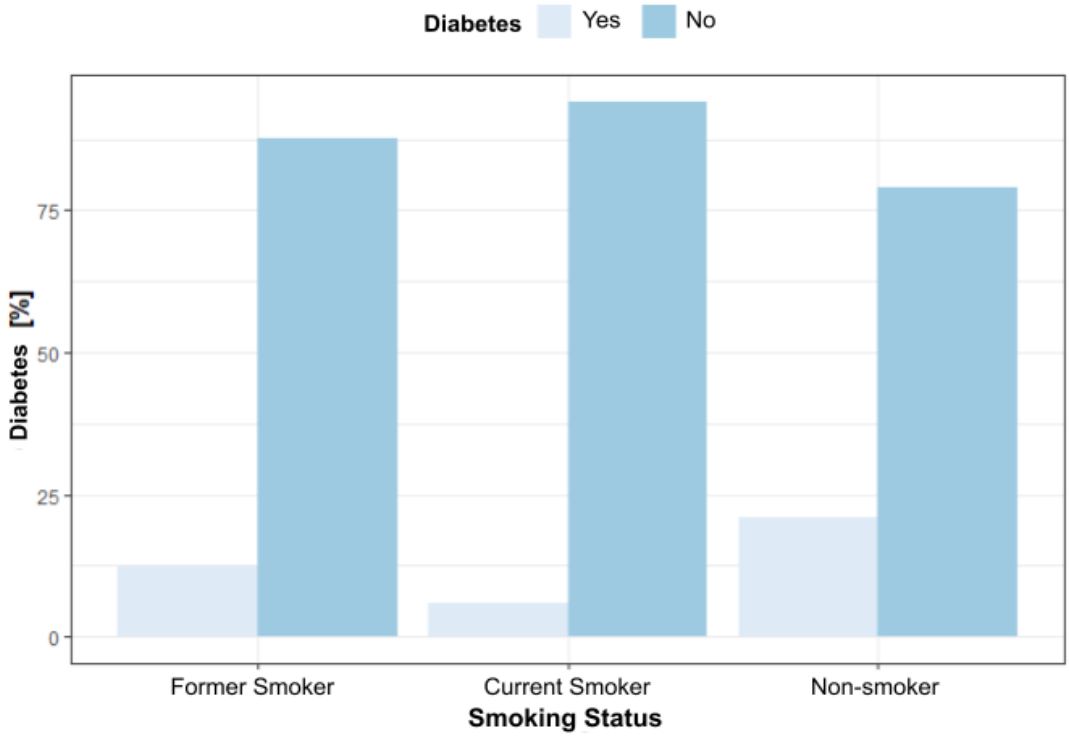

Figure 8. Relationship between the occurrence of diabetes and smoking status (%)

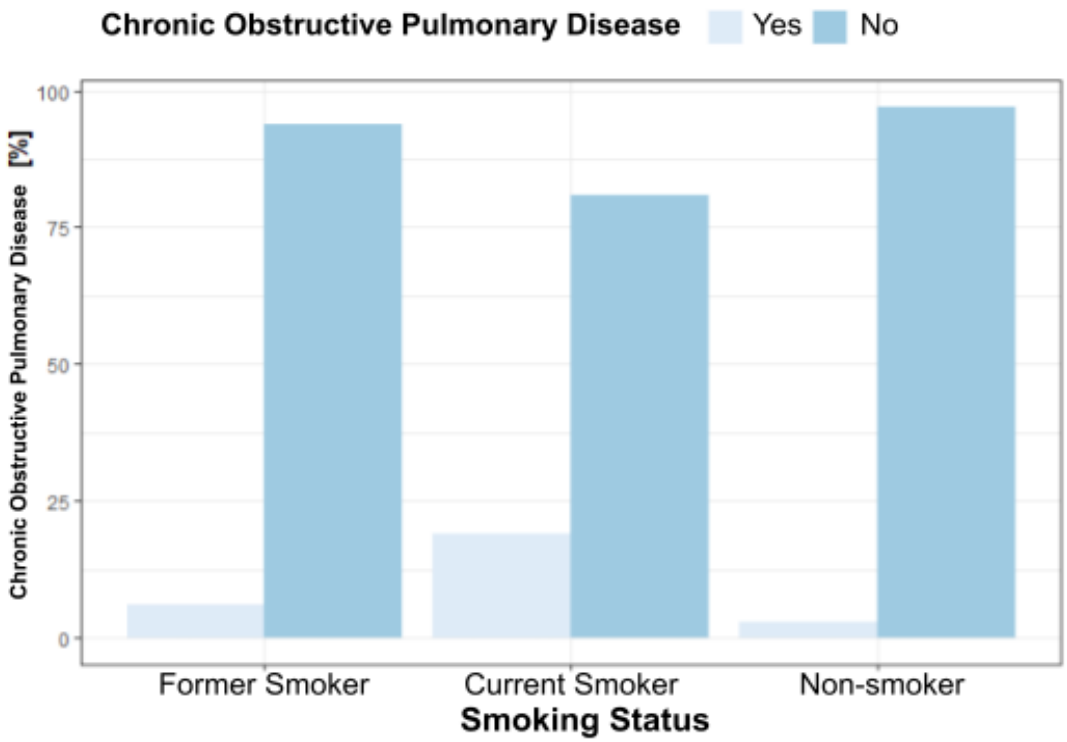

Figure 9. Relationship between the occurrence of Chronic Obstructive Pulmonary Disease (COPD) and smoking status (%)

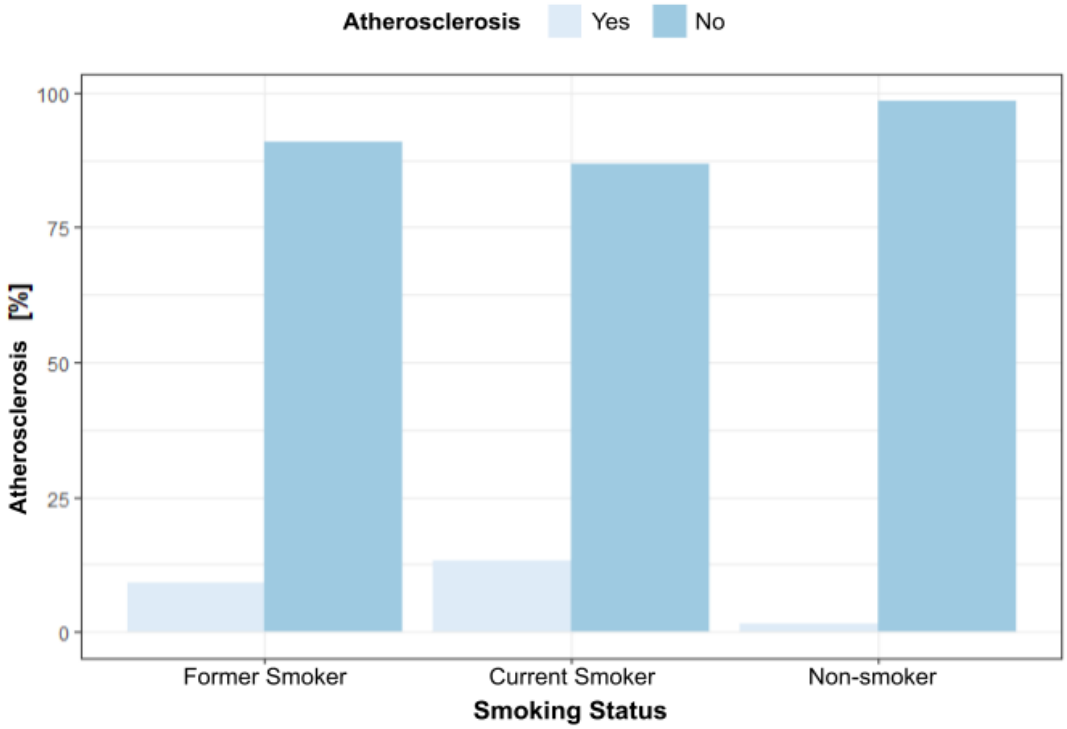

Figure 10. Relationship between the occurrence of atherosclerosis and smoking status (%)

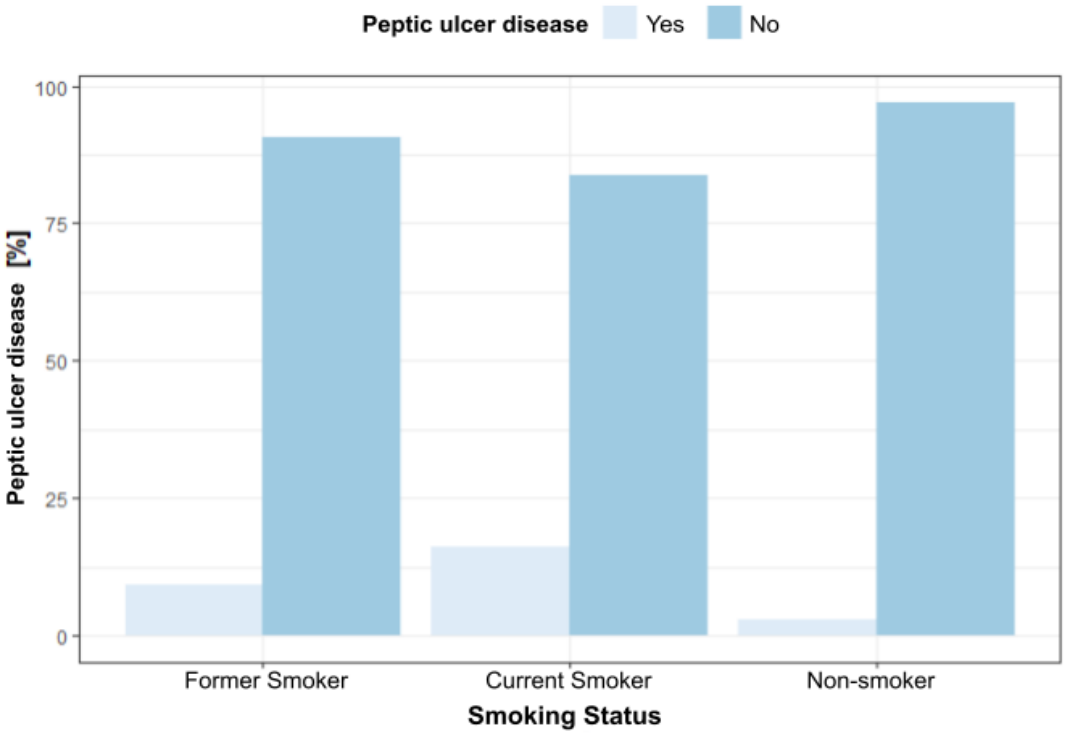

Figure 11. The relationship between the occurrence of peptic ulcer disease and smoking status (%)

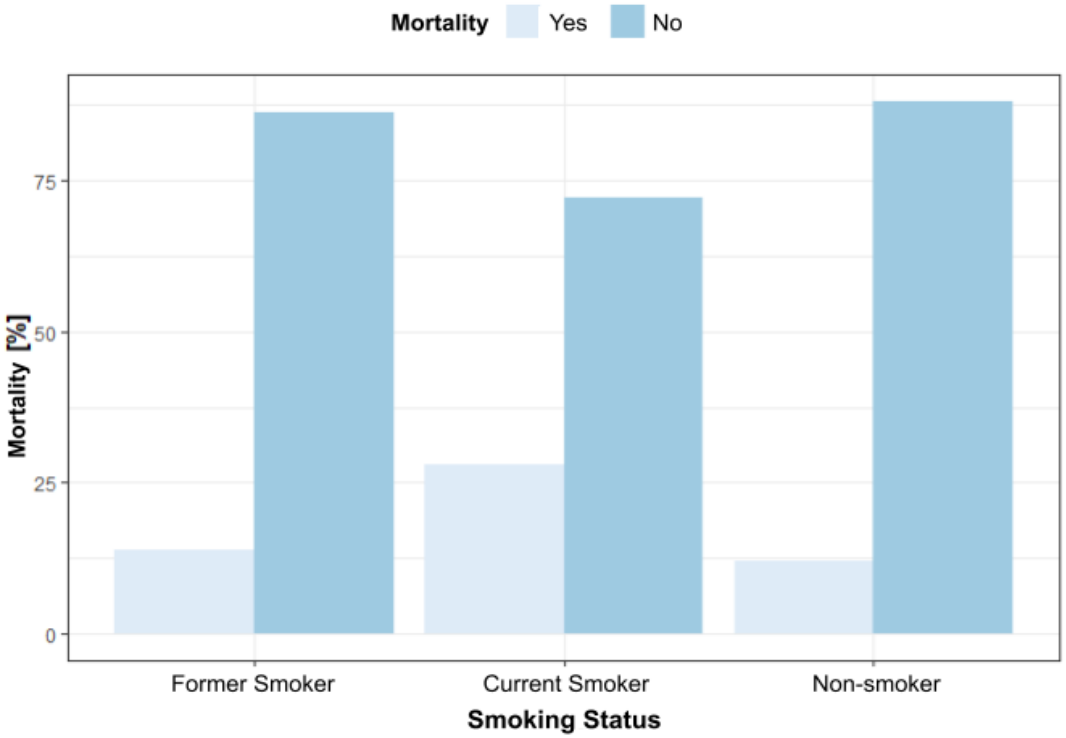

Figure 12. Relationship between the occurrence of mortality and smoking status (%)

Characteristic based on cancer stage

Significant differences between cancer stages were observed for the following variables:

- Diabetes (Fisher p-value = 0.0357);
- Kidney stones (Fisher p-value = 0.0274);
- Death (Fisher p-value < 0.001);
- Time from diagnosis to end of treatment/death (Kruskal-Wallis p-value < 0.001);
- Leukocytes [count/μL] (Kruskal-Wallis p-value < 0.001);
- Neutrophils [count/μL] (Kruskal-Wallis p-value < 0.001);
- CRP (C-reactive protein) [mg/L] (Kruskal-Wallis p-value < 0.001).

Diabetes and kidney stones were significantly more common among individuals in the third stage of the disease compared to the other groups. The highest mortality rate was found in the fourth stage, while the lowest was in the first stage. The duration of treatment was longest in the fourth stage and shortest in the first stage. The highest levels of the parameters: leukocytes [count/μL], neutrophils [count/μL], and CRP [mg/L] were observed in the fourth stage group, while the lowest levels of these parameters were observed in the first stage group.

Table 8. Descriptive characteristics categorized by cancer stage

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
Gender	Male	54,9% (N=28)	48,9% (N=23)	41,7% (N=20)	40,7% (N=22)	Chi-square	0,4351
	Female	45,1% (N=23)	51,1% (N=24)	58,3% (N=28)	59,3% (N=32)		
Age	N	51	47	48	54	Kruskal-Wallis	0,3156
	Mean (SD)	56,39 (13,94)	53,62 (14,1)	59,27 (13,18)	55,31 (13,93)		
	Median (IQR)	59 (42 - 69)	55 (40 - 67)	66 (43,75 - 69,25)	59 (40 - 67)		
	Range	27 - 77	27 - 77	39 - 77	34 - 77		
Age Relative to 65 Years	Over 65 years	49% (N=25)	36,2% (N=17)	52,1% (N=25)	48,1% (N=26)	Chi-square	0,4224

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
	65 years or younger	51% (N=26)	63,8% (N=30)	47,9% (N=23)	51,9% (N=28)		
Smoking Status	Former smoker	39,2% (N=20)	36,2% (N=17)	33,3% (N=16)	22,2% (N=12)	Chi-square	0,5058
	Current smoker	27,5% (N=14)	29,8% (N=14)	33,3% (N=16)	44,4% (N=24)		
	Non-smoker	33,3% (N=17)	34% (N=16)	33,3% (N=16)	33,3% (N=18)		
Hypertension	Yes	25,5% (N=13)	8,5% (N=4)	20,8% (N=10)	24,1% (N=13)	Fisher	0,1171
	No	74,5% (N=38)	91,5% (N=43)	79,2% (N=38)	75,9% (N=41)		
Diabetes	Yes	5,9% (N=3)	8,5% (N=4)	25% (N=12)	13% (N=7)	Fisher	**0,0357**
	No	94,1% (N=48)	91,5% (N=43)	75% (N=36)	87% (N=47)		
Obesity	Yes	13,7% (N=7)	8,5% (N=4)	16,7% (N=8)	9,3% (N=5)	Fisher	0,5797
	No	86,3% (N=44)	91,5% (N=43)	83,3% (N=40)	90,7% (N=49)		
Chronic Obstructive Pulmonary Disease	Yes	9,8% (N=5)	4,3% (N=2)	10,4% (N=5)	13% (N=7)	Fisher	0,5042
	No	90,2% (N=46)	95,7% (N=45)	89,6% (N=43)	87% (N=47)		
Atherosclerosis	Yes	15,7% (N=8)	4,3% (N=2)	8,3% (N=4)	3,7% (N=2)	Fisher	0,1189
	No	84,3% (N=43)	95,7% (N=45)	91,7% (N=44)	96,3% (N=52)		
Ischemic Heart Disease	Yes	2% (N=1)	8,5% (N=4)	4,2% (N=2)	3,7% (N=2)	Fisher	0,4888
	No	98% (N=50)	91,5% (N=43)	95,8% (N=46)	96,3% (N=52)		

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
Gallstone Disease	Yes	7,8% (N=4)	6,4% (N=3)	2,1% (N=1)	9,3% (N=5)	Fisher	0,4942
	No	92,2% (N=47)	93,6% (N=44)	97,9% (N=47)	90,7% (N=49)		
Kidney Stones	Yes	3,9% (N=2)	4,3% (N=2)	12,5% (N=6)	0% (N=0)	Fisher	**0,0274**
	No	96,1% (N=49)	95,7% (N=45)	87,5% (N=42)	100% (N=54)		
Peptic Ulcer Disease	Yes	11,8% (N=6)	6,4% (N=3)	6,2% (N=3)	13% (N=7)	Fisher	0,5798
	No	88,2% (N=45)	93,6% (N=44)	93,8% (N=45)	87% (N=47)		
Mortality	Yes	3,9% (N=2)	6,4% (N=3)	22,9% (N=11)	37% (N=20)	Fisher	**<0,001**
	No	96,1% (N=49)	93,6% (N=44)	77,1% (N=37)	63% (N=34)		
Time from Diagnosis to End of Treatment/Death	N	51	47	48	54	Kruskal-Wallis	**<0,001**
	Mean (SD)	190,29 (20,59)	224 (19,87)	254,69 (27,22)	289,57 (20,38)		
	Median (IQR)	189 (175 - 206)	226 (207 - 239)	252 (235,5 - 276,25)	285,5 (273 - 302,75)		
	Range	152 - 226	190 - 272	163 - 310	262 - 326		
Neutropenia	Yes	11,8% (N=6)	6,4% (N=3)	25% (N=12)	13% (N=7)	Fisher	0,0754
	No	88,2% (N=45)	93,6% (N=44)	75% (N=36)	87% (N=47)		
Anemia	Yes	7,8% (N=4)	8,5% (N=4)	12,5% (N=6)	18,5% (N=10)	Fisher	0,3477
	No	92,2% (N=47)	91,5% (N=43)	87,5% (N=42)	81,5% (N=44)		

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
Diarrhea	Yes	11,8% (N=6)	8,5% (N=4)	12,5% (N=6)	11,1% (N=6)	Fisher	0,9405
	No	88,2% (N=45)	91,5% (N=43)	87,5% (N=42)	88,9% (N=48)		
Rash	Yes	9,8% (N=5)	8,5% (N=4)	14,6% (N=7)	7,4% (N=4)	Fisher	0,6781
	No	90,2% (N=46)	91,5% (N=43)	85,4% (N=41)	92,6% (N=50)		
Treatment Arm	Treatment 1	47,1% (N=24)	48,9% (N=23)	50% (N=24)	53,7% (N=29)	Chi-square	0,9202
	Treatment 2	52,9% (N=27)	51,1% (N=24)	50% (N=24)	46,3% (N=25)		
Leukocytes [cells/µL]	N	51	47	48	54	Kruskal-Wallis	**<0,001**
	Mean (SD)	10014,94 (567,7)	10945,17 (787,1)	12304,94 (486,01)	13755,41 (439,74)		
	Median (IQR)	10098 (9593,5 - 10477,5)	10771 (10266,5 - 11449,5)	12273,5 (12134,25 - 12489)	13821 (13323,75 - 14133,75)		
	Range	9011 - 10989	9920 - 13560	9558 - 12974	13042 - 14481		
Neutrophils [cells/µL]	N	51	47	48	54	Kruskal-Wallis	**<0,001**
	Mean (SD)	6936,41 (1655,13)	8286,09 (1784,1)	8834,15 (2603,3)	10853,2 (1249,12)		
	Median (IQR)	7489 (7108 - 7867,5)	8756 (8349,5 - 9061)	9975,5 (9605 - 10118,75)	11078 (10755,5 - 11260,25)		

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
	Range	2633 - 8399	2040 - 10632	2377 - 10430	2103 - 11483		
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	51	47	48	54	Kruskal-Wallis	0,2961
	Mean (SD)	56,08 (8,75)	52,64 (9,84)	55,38 (9,43)	54,48 (9,49)		
	Median (IQR)	57 (48 - 64)	51 (44,5 - 57,5)	55 (47,75 - 64)	57 (46,25 - 61)		
	Range	40 - 69	40 - 70	40 - 70	40 - 70		
C-reactive Protein (CRP) [mg/L]	N	51	47	48	54	Kruskal-Wallis	**<0,001**
	Mean (SD)	170,24 (44,76)	280,02 (48,62)	370,15 (49,81)	456,63 (30,39)		
	Median (IQR)	167 (126,5 - 207)	278 (242,5 - 313,5)	371 (341,5 - 400,5)	459,5 (430,5 - 485,25)		
	Range	102 - 250	206 - 432	172 - 450	402 - 500		
Glucose [mg/dL]	N	51	47	48	54	Kruskal-Wallis	0,9889
	Mean (SD)	86,55 (10,64)	85,85 (9,91)	87,42 (12,98)	87,13 (13,56)		
	Median (IQR)	84 (78 - 93)	85 (79 - 92)	85 (77,75 - 94,25)	83,5 (77,25 - 94,5)		
	Range	71 - 123	71 - 117	70 - 128	70 - 128		
Creatinine [mg/dL]	N	51	47	48	54	Kruskal-Wallis	0,0992
	Mean (SD)	1,18 (0,19)	1,19 (0,19)	1,26 (0,21)	1,25 (0,19)		
	Median (IQR)	1,2 (1 - 1,3)	1,2 (1 - 1,4)	1,3 (1,08 - 1,4)	1,3 (1,1 - 1,4)		
	Range	0,9 - 1,5	0,9 - 1,5	0,9 - 1,6	0,9 - 1,5		

Variable	Parameter	1 (N=51)	2 (N=47)	3 (N=48)	4 (N=54)	test	p-value
Alkaline Phosphatase [U/L]	N	51	47	48	54	Kruskal-Wallis	0,6271
	Mean (SD)	100,18 (31,06)	92,91 (27,37)	99,71 (29,33)	96,46 (31,11)		
	Median (IQR)	107 (70 - 123)	93 (72,5 - 114)	104,5 (73,5 - 123,75)	92 (70,25 - 122,75)		
	Range	50 - 149	50 - 149	50 - 147	52 - 149		

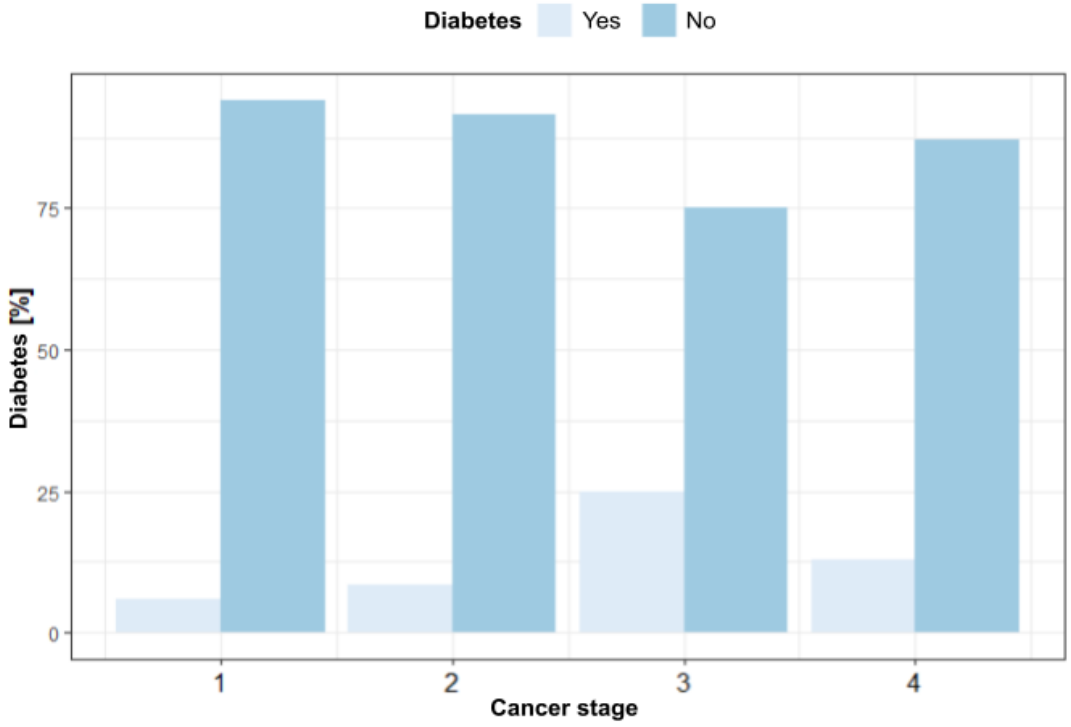

Figure 13. The relationship between the occurrence of diabetes and cancer stage (%)

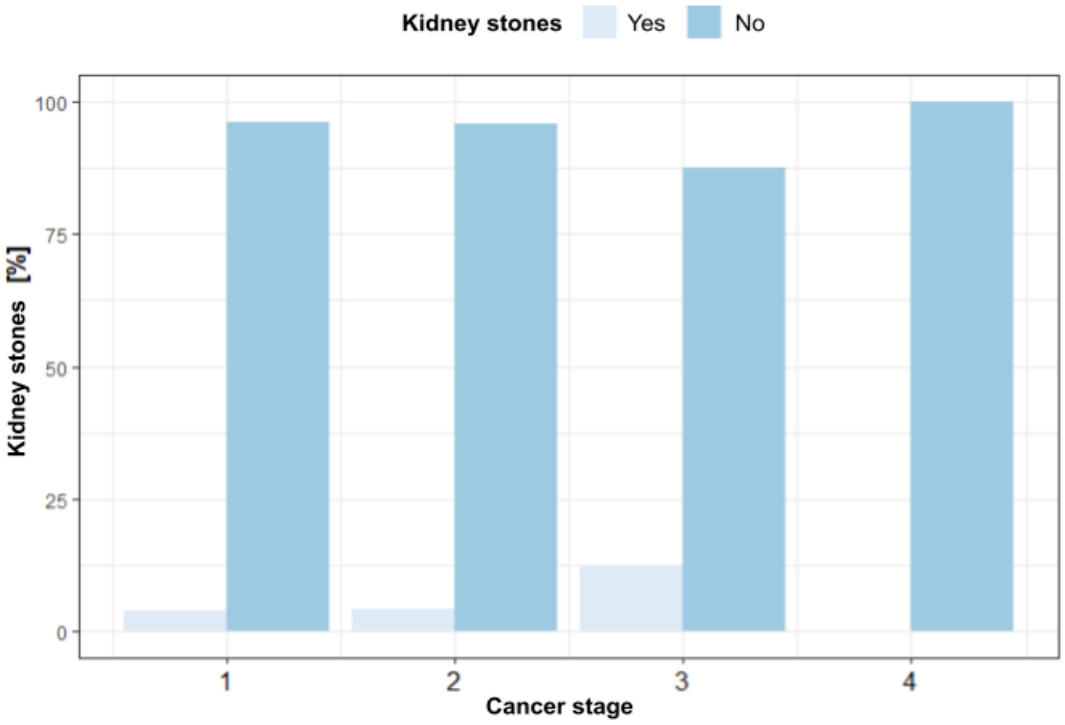

Figure 14. The relationship between the occurrence of kidney stones and cancer stage (%)

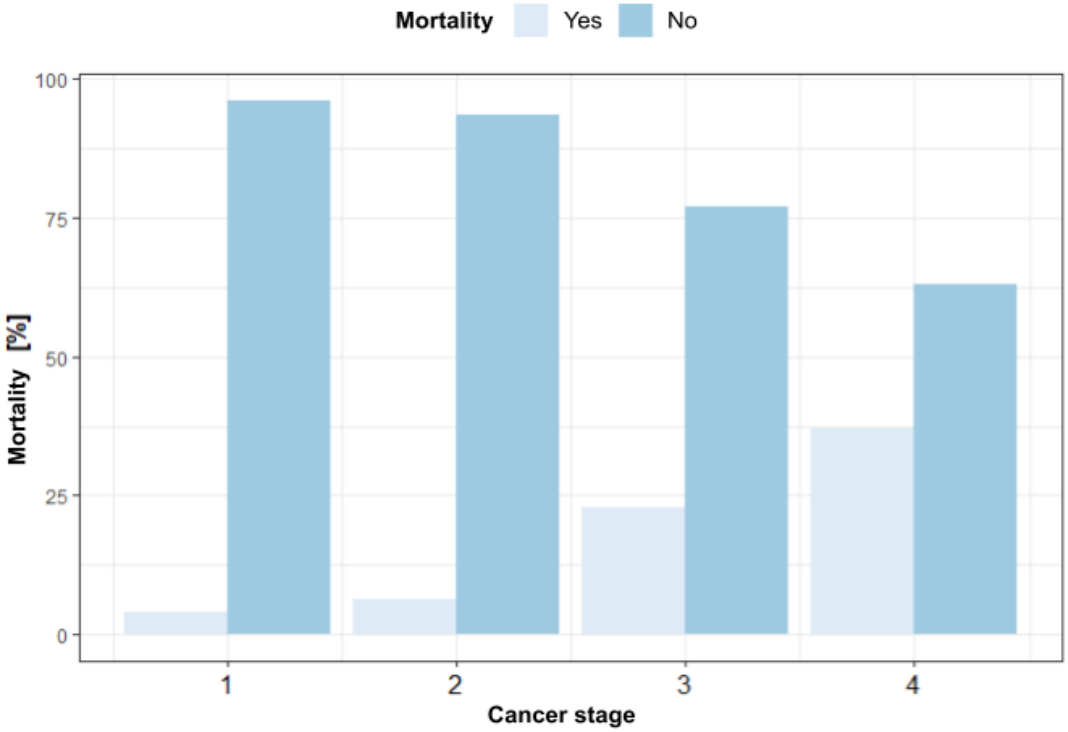

Figure 15. The relationship between the occurrence of death and cancer stage (%)

Characteristic by Treatment Arm

Statistically significant differences were detected among patients for variables in the analysis of two treatment arms, such as:

- Neutropenia (chi-square p-value = 0.025);
- Anemia (chi-square p-value = 0.0167);
- Drug 1 dosage (U Mann-Whitney p-value < 0.001);
- Drug 2 dosage (U Mann-Whitney p-value < 0.001).

Neutropenia and anemia were more than twice as common in treatment arm 2 compared to treatment arm 1. Dosages of drug 1 and drug 2 were only present in treatment arm 1.

Table 9. Descriptive Characteristics Stratified by Treatment Type

Variable	Parameter	Treatment 1 (N=100)	Treatment 2 (N=100)	test	p-value
Gender	Male	50% (N=50)	43% (N=43)	Chi-square	0,395
	Female	50% (N=50)	57% (N=57)		
Age	N	100	100	U Mann-Whitney	0,468
	Mean (SD)	56,44 (13,44)	55,84 (14,29)		
	Median (IQR)	59 (40 - 69)	59 (40 - 67,5)		
	Range	34 - 77	27 - 77		
Age Relative to 65 Years	Over 65 years	47% (N=47)	46% (N=46)	Chi-square	1
	65 years or younger	53% (N=53)	54% (N=54)		
Cancer Stage	1	24% (N=24)	27% (N=27)	Chi-square	0,9202
	2	23% (N=23)	24% (N=24)		
	3	24% (N=24)	24% (N=24)		
	4	29% (N=29)	25% (N=25)		
Smoking Status	Former Smoker	33% (N=33)	32% (N=32)	Chi-square	0,5283
	Current Smoker	37% (N=37)	31% (N=31)		

Variable	Parameter	Treatment 1 (N=100)	Treatment 2 (N=100)	test	p-value
	Non-Smoker	30% (N=30)	37% (N=37)		
Hypertension	Yes	17% (N=17)	23% (N=23)	Chi-square	0,3768
	No	83% (N=83)	77% (N=77)		
Diabetes	Yes	12% (N=12)	14% (N=14)	Chi-square	0,8335
	No	88% (N=88)	86% (N=86)		
Obesity	Yes	8% (N=8)	16% (N=16)	Chi-square	0,1277
	No	92% (N=92)	84% (N=84)		
Chronic Obstructive Pulmonary Disease	Yes	10% (N=10)	9% (N=9)	Chi-square	1
	No	90% (N=90)	91% (N=91)		
Atherosclerosis	Yes	9% (N=9)	7% (N=7)	Chi-square	0,7944
	No	91% (N=91)	93% (N=93)		
Ischemic Heart Disease	Yes	6% (N=6)	3% (N=3)	Fisher	0,4977
	No	94% (N=94)	97% (N=97)		
Gallstone Disease	Yes	8% (N=8)	5% (N=5)	Fisher	0,5679
	No	92% (N=92)	95% (N=95)		
Kidney Stones	Yes	6% (N=6)	4% (N=4)	Fisher	0,7475
	No	94% (N=94)	96% (N=96)		
Peptic Ulcer Disease	Yes	11% (N=11)	8% (N=8)	Chi-square	0,6296
	No	89% (N=89)	92% (N=92)		
Mortality	Yes	14% (N=14)	22% (N=22)	Chi-square	0,1976
	No	86% (N=86)	78% (N=78)		
Time from Diagnosis to End of Treatment/Death	N	100	100	U Mann-Whitney	0,8431
	Mean (SD)	241,21 (43,13)	239,74 (44,15)		
	Median (IQR)	238,5 (212,75 - 273)	240,5 (203 - 277,25)		
	Range	153 - 326	152 - 326		
Neutropenia	Yes	8% (N=8)	20% (N=20)	Chi-square	**0,025**
	No	92% (N=92)	80% (N=80)		

Variable	Parameter	Treatment 1 (N=100)	Treatment 2 (N=100)	test	p-value
Anemia	Yes	6% (N=6)	18% (N=18)	Chi-square	**0,0167**
	No	94% (N=94)	82% (N=82)		
Diarrhea	Yes	9% (N=9)	13% (N=13)	Chi-square	0,4978
	No	91% (N=91)	87% (N=87)		
Rash	Yes	6% (N=6)	14% (N=14)	Chi-square	0,099
	No	94% (N=94)	86% (N=86)		
Drug 1 dosage	N	100	100	U Mann-Whitney	**<0,001**
	Mean (SD)	360 (0)	0 (0)		
	Median (IQR)	360 (360 - 360)	0 (0 - 0)		
	Range	360 - 360	0 - 0		
Drug 2 dosage	N	100	100	U Mann-Whitney	**<0,001**
	Mean (SD)	73,23 (14,26)	0 (0)		
	Median (IQR)	73 (64,75 - 80,25)	0 (0 - 0)		
	Range	50 - 131	0 - 0		
Leukocytes [cells/µL]	N	100	100	U Mann-Whitney	0,5213
	Mean (SD)	11875,87 (1630,64)	11710,27 (1480,2)		
	Median (IQR)	12143 (10258,5 - 13261,5)	11800 (10464,5 - 12991)		
	Range	9011 - 14481	9150 - 14430		
Neutrophils [cells/µL]	N	100	100	U Mann-Whitney	0,6814
	Mean (SD)	8620,89 (2550,39)	8912,26 (2140,13)		
	Median (IQR)	9120,5 (7780,5 - 10585,25)	9212,5 (7923,5 - 10454,75)		

Variable	Parameter	Treatment 1 (N=100)	Treatment 2 (N=100)	test	p-value
	Range	2040 - 11459	2377 - 11483		
Erythrocyte Sedimentation Rate (ESR) [mm/h]	N	100	100	U Mann-Whitney	0,8296
	Mean (SD)	54,79 (10,01)	54,55 (8,78)		
	Median (IQR)	56 (45 - 64)	55 (48 - 61,25)		
	Range	40 - 70	40 - 70		
C-reactive Protein (CRP) [mg/L]	N	100	100	U Mann-Whitney	0,601
	Mean (SD)	324,93 (118,68)	317,75 (115,69)		
	Median (IQR)	335 (224,75 - 430,5)	323 (219 - 417,25)		
	Range	107 - 500	102 - 498		
Glucose [mg/dL]	N	100	100	U Mann-Whitney	0,8059
	Mean (SD)	86,33 (11,08)	87,17 (12,6)		
	Median (IQR)	84,5 (78 - 93)	84,5 (78 - 94)		
	Range	70 - 123	70 - 128		
Creatinine [mg/dL]	N	100	100	U Mann-Whitney	0,2335
	Mean (SD)	1,2 (0,2)	1,24 (0,19)		
	Median (IQR)	1,2 (1 - 1,4)	1,3 (1,1 - 1,4)		
	Range	0,9 - 1,5	0,9 - 1,6		
Alkaline Phosphatase [U/L]	N	100	100	U Mann-Whitney	0,5824
	Mean (SD)	98,46 (29,96)	96,25 (29,64)		
	Median (IQR)	104 (69,25 - 121,25)	94,5 (71,75 - 119,25)		
	Range	50 - 149	50 - 147		

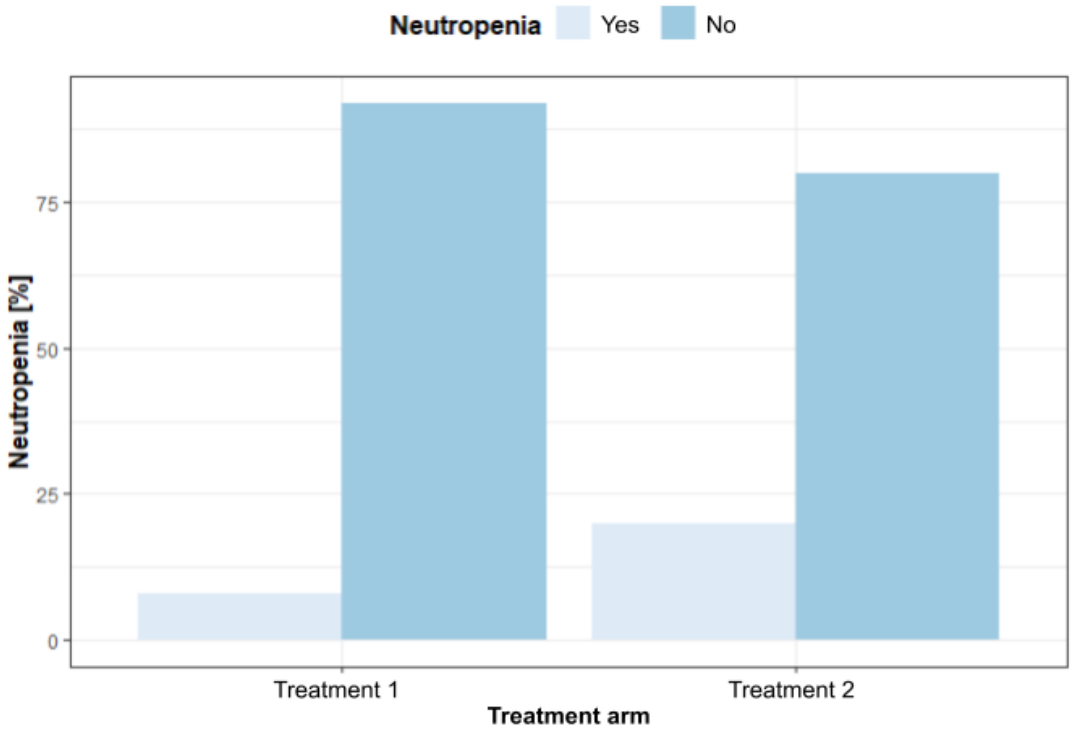

Figure 16. The relationship between the occurrence of neutropenia and treatment arm (%)

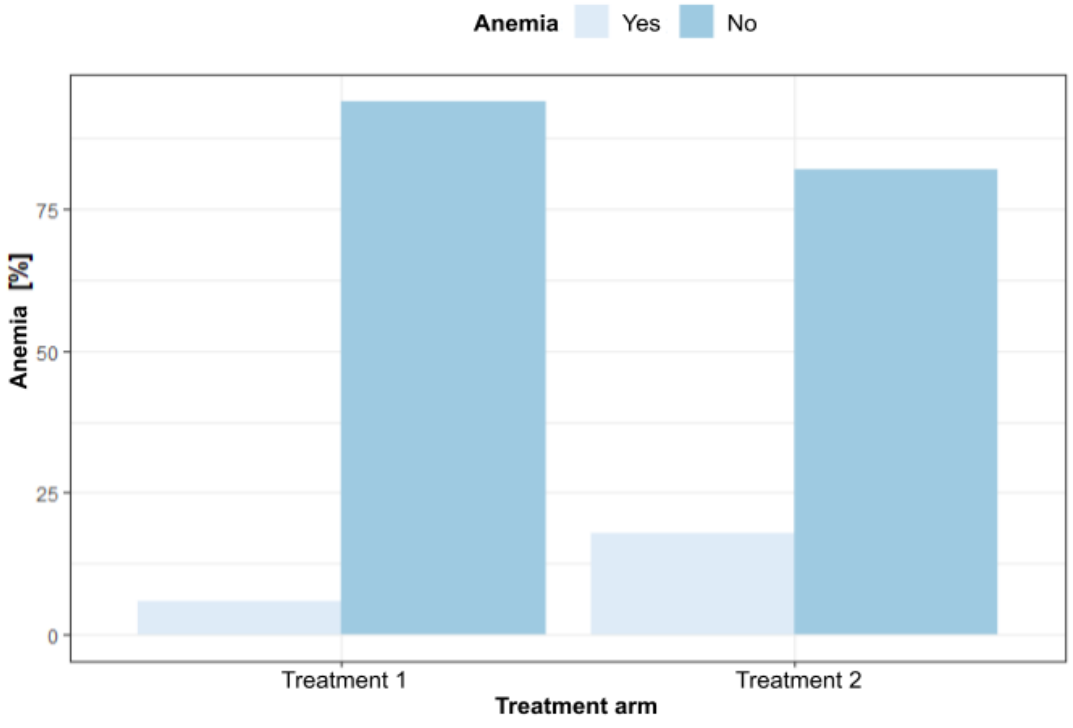

Figure 17. The relationship between the occurrence of anemia and treatment arm (%)

Characteristics of Drug Dosages by Subgroups

Significant differences in drug dosages were observed for the second drug, categorized by gender and age group. Women received lower dosages of the drug more frequently than men. In the age group over 65, the dosage of the second drug was higher than in the group of individuals aged 65 or less.

Table 10. Descriptive Characteristics of Drug Dosages Stratified by Gender

Variable	Parameter	Male (N=50)	Female (N=50)	test	p-value
Drug 1 dosage	N	50	50	U Mann-Whitney	N/A
	Mean (SD)	360 (0)	360 (0)		
	Median (IQR)	360 (360 - 360)	360 (360 - 360)		
	Range	360 - 360	360 - 360		
Drug 2 dosage	N	50	50	U Mann-Whitney	**<0,001**
	Mean (SD)	80,78 (12,7)	65,68 (11,54)		
	Median (IQR)	78,5 (73 - 86)	64,5 (57,25 - 72,75)		
	Range	65 - 131	50 - 100		

Table 11. Descriptive Characteristics of Drug Dosages Stratified by Age Group

Variable	Parameter	Over 65 years (N=47)	65 years and younger (N=53)	test	p-value
Drug 1 dosage	N	47	53	U Mann-Whitney	N/A
	Mean (SD)	360 (0)	360 (0)		
	Median (IQR)	360 (360 - 360)	360 (360 - 360)		
	Range	360 - 360	360 - 360		
Drug 2 dosage	N	47	53	U Mann-Whitney	**0,0184**
	Mean (SD)	69,21 (12)	76,79 (15,23)		
	Median (IQR)	70 (59,5 - 76)	73 (68 - 83)		
	Range	50 - 90	50 - 131		

Table 12. Descriptive Characteristics of Drug Dosages Stratified by Smokers, Former Smokers, and Non-Smokers

Zmienna	Parameter	Former Smokers (N=33)	Current Smokers (N=37)	Non-smokers (N=30)	test	p-value
Drug 1 dosage	N	33	37	30	Kruskal-Wallis	N/A
	Mean (SD)	360 (0)	360 (0)	360 (0)		
	Median (IQR)	360 (360 - 360)	360 (360 - 360)	360 (360 - 360)		
	Range	360 - 360	360 - 360	360 - 360		
Drug 2 dosage	N	33	37	30	Kruskal-Wallis	0,2955
	Mean (SD)	76,79 (17,25)	72,27 (12,41)	70,5 (12,3)		
	Median (IQR)	73 (70 - 83)	73 (62 - 80)	68 (64,25 - 76)		
	Range	50 - 131	50 - 106	50 - 98		

Table 13. Descriptive Characteristics of Drug Dosages Stratified by Cancer Stage

Variable	Parameter	1 (N=24)	2 (N=23)	3 (N=24)	4 (N=29)	test	p-value
Drug 1 dosage	N	24	23	24	29	Kruskal-Wallis	
	Mean (SD)	360 (0)	360 (0)	360 (0)	360 (0)		
	Median (IQR)	360 (360 - 360)	360 (360 - 360)	360 (360 - 360)	360 (360 - 360)		
	Range	360 - 360	360 - 360	360 - 360	360 - 360		
Drug 2 dosage	N	24	23	24	29	Kruskal-Wallis	0,2271
	Mean (SD)	77,08 (14,33)	73,48 (15,07)	74,04 (16)	69,17 (11,45)		
	Median (IQR)	75,5 (70,5 - 85)	72 (62 - 80,5)	73 (65 - 77,75)	70 (61 - 79)		
	Range	50 - 120	50 - 106	50 - 131	50 - 90		

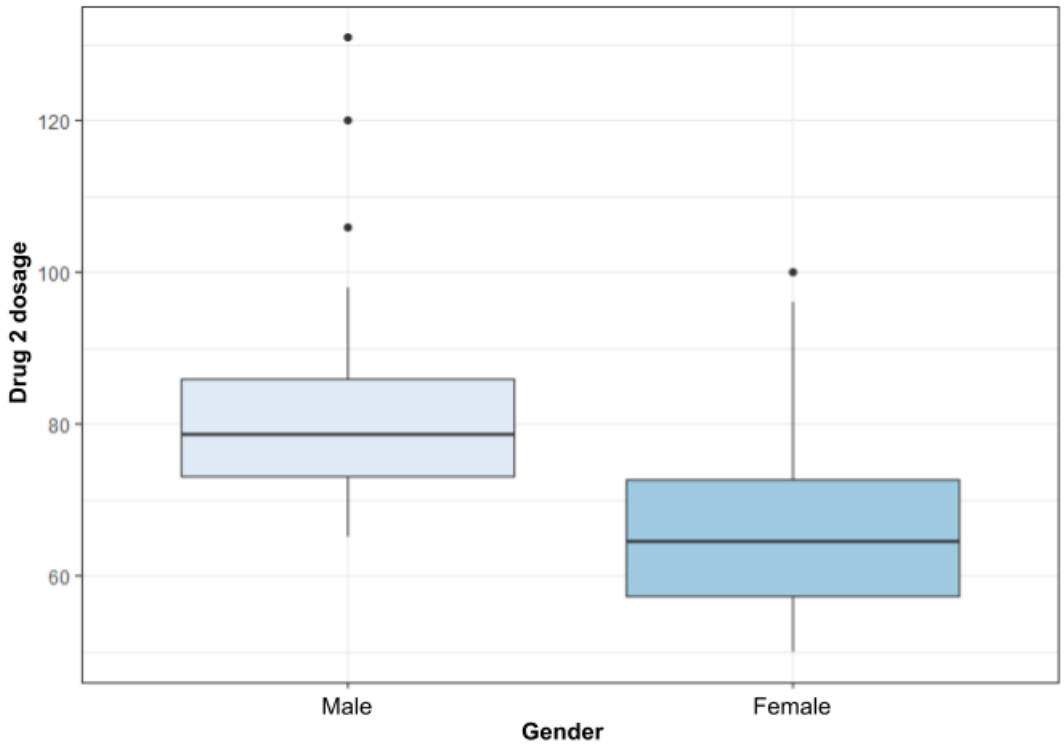

Figure 18. Relationship between the dosage of drug 1 and gender

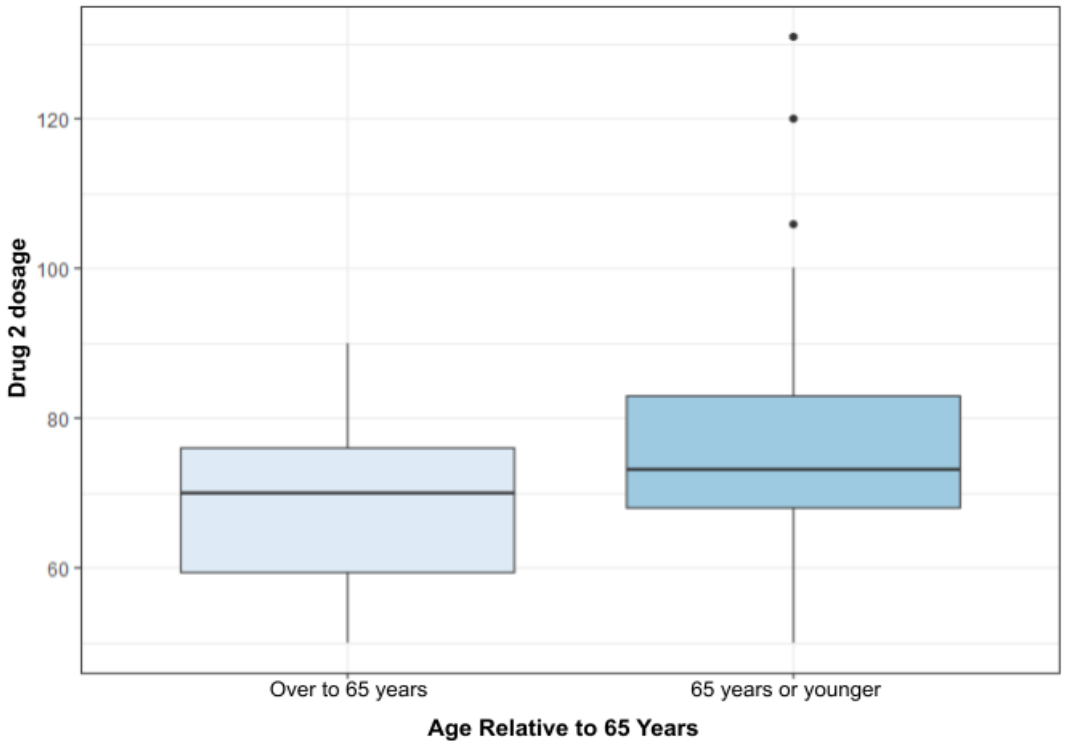

Figure 19. Relationship between the dosage of drug 1 and age group

Survival Analysis

Survival analyses were conducted based on age stratification at 65 years and the type of therapy administered (Figures 20 and 21). Subsequently, Figures 22 and 23 display survival rates according to the type of therapy within specific age groups.

No statistically significant reduction in mortality was observed among patients treated with therapy 1. Survival curves, regardless of the subgroup, were very similar, with a median survival of approximately 300 (±20) days.

Figure 20. Survival Analysis by Age

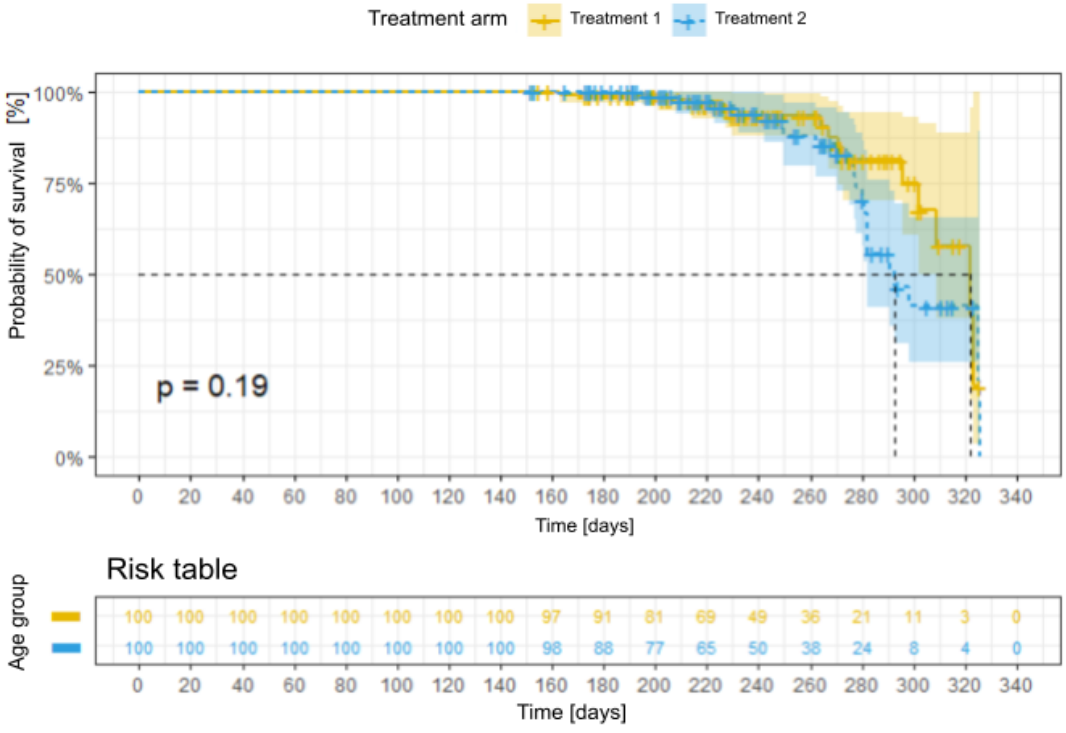

Figure 21. Survival Analysis by Type of Treatment

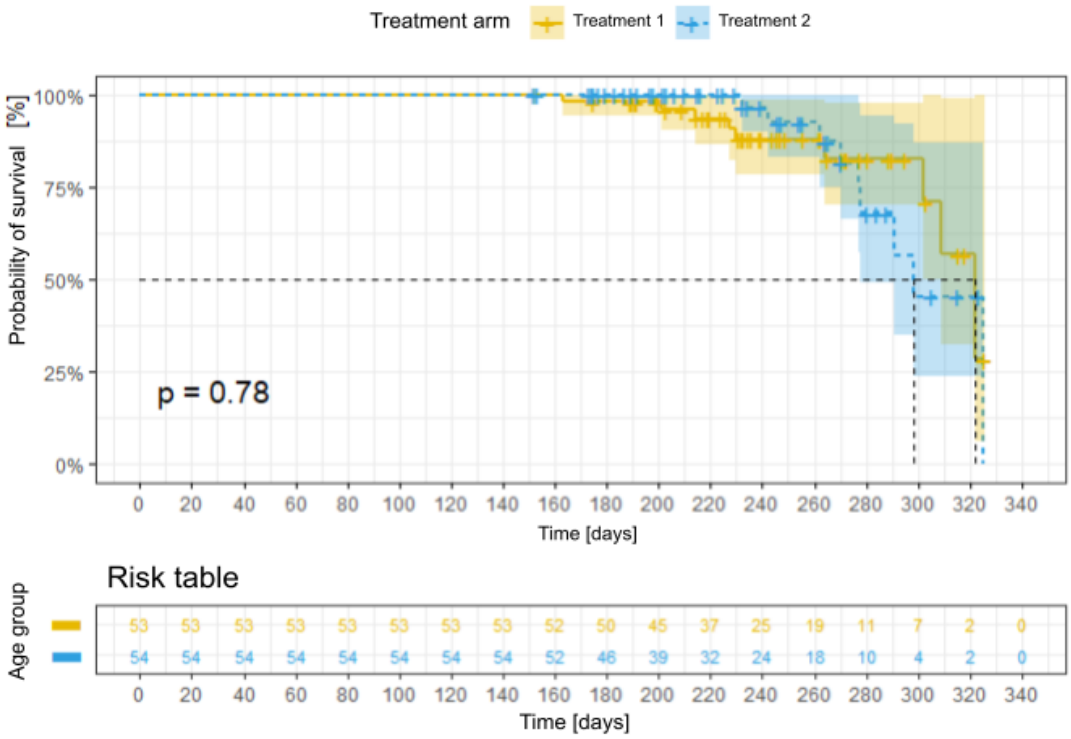

Figure 22. Survival analysis by treatment in the group aged 65 and under

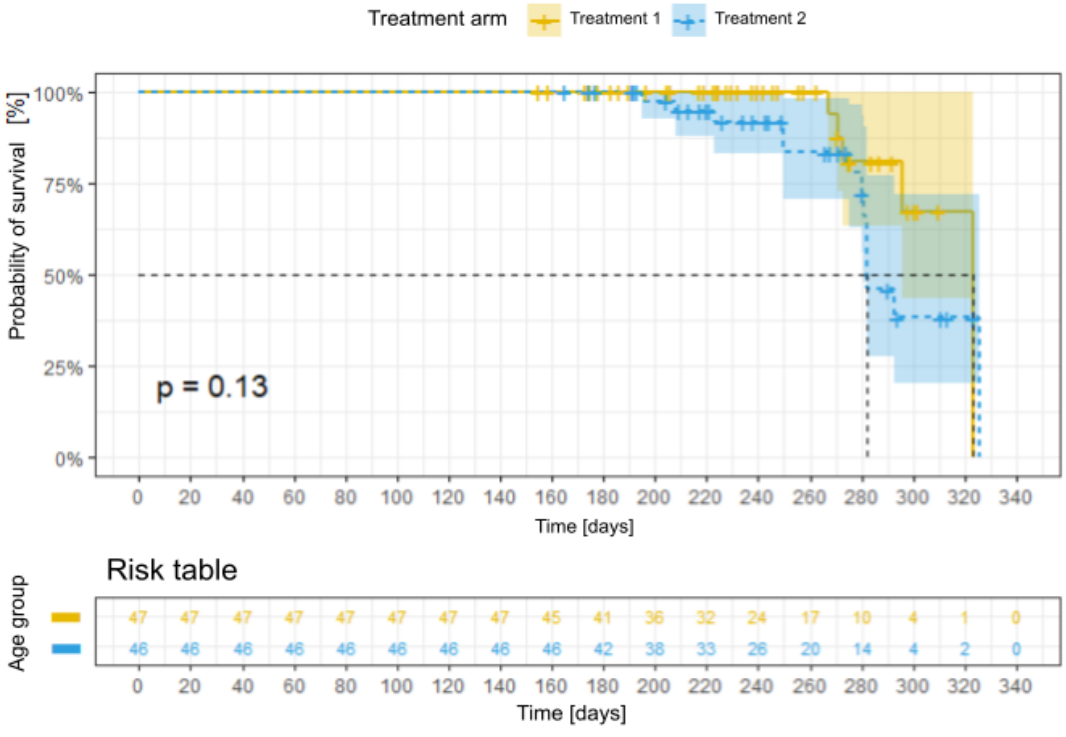

Figure 23. Survival analysis by treatment in the group aged over 65

Efficacy Analysis

The analysis also examined differences in mortality rates between the two treatment arms. Such comparisons were also prepared in subgroups characterizing the patients. In most cases, it can be observed that therapy 1 is associated with a lower mortality rate for patients, with exceptions in subgroups: those aged 65 and under and those in stage 1. However, regardless of these observations, the differences are not statistically significant because the confidence intervals for these differences intersect with the vertical line marked at 0% on the chart. Only in the case of individuals aged over 65 is the relationship on the verge of statistical significance.

Table 14. Efficacy in Subgroups

	Treatment 1	Treatment 2	Confidence interval
Total	14% (14/100)	22% (22/100)	-0,2 , 0,04
Female	16% (8/50)	24,56% (14/57)	-0,26 , 0,08
Male	12% (6/50)	13,95% (8/43)	-0,23 , 0,1
Age > 65 lat	10,64% (5/47)	28,26% (13/46)	-0,35 , 0
Age ≤ 65 lat	16,98% (9/53)	16,67% (9/54)	-0,14 , 0,15
Former smokers	12,12% (4/33)	15,62% (5/32)	-0,23 , 0,16
Non-smokers	6,67% (2/30)	16,22% (6/37)	-0,38 , 0,11
Current smokers	21,62% (8/37)	35,48% (11/31)	-0,27 , 0,08
Individuals in Stage 1	4,17% (1/24)	3,7% (1/27)	-0,11 , 0,12
Individuals in Stage 2	4,35% (1/23)	8,33% (2/24)	-0,22 , 0,14
Individuals in Stage 3	16,67% (4/24)	29,17% (7/24)	-0,4 , 0,15
Individuals in Stage 4	27,59% (8/29)	48% (12/25)	-0,5 , 0,09

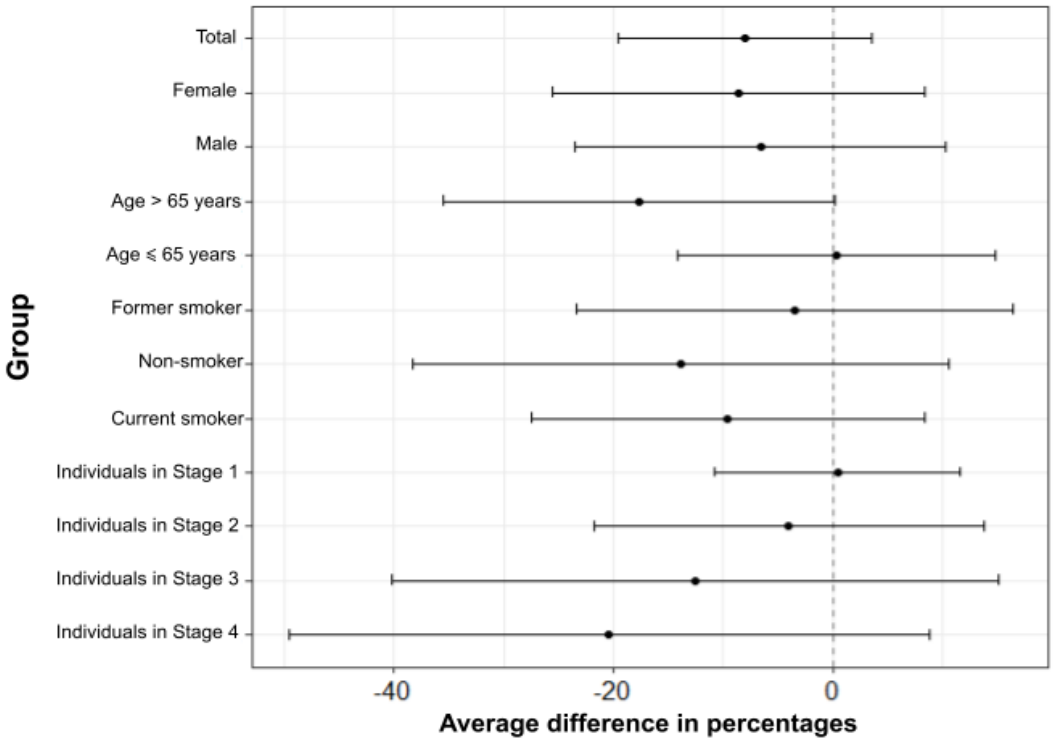

Figure 24. Efficacy in Subgroups

Summary

The statistical analysis conducted, comparing the efficacy of two treatments, did not demonstrate a clear advantage for Therapy 1, which involved the administration of Drug 1 and Drug 2 in combination with chemotherapy, over Therapy 2, the standard chemotherapy. The overall and subgroup characteristics showed some differences in various parameters, but they were not sufficient to draw conclusions about the significant superiority of one method over the other. One of the few differences that could be pointed out is the lower occurrence of adverse effects, particularly neutropenia and anemia, in Therapy 1 compared to the use of only Therapy 2. Survival analysis based on the type of therapy and efficacy analysis did not show that Therapy 1 was more effective or had a significant impact on patient survival.

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