

Analysis of Selected Nutritional Parameters in Patients with HPV-Related and HPV- not Related Oropharyngeal Cancer Before and After Radiotherapy Alone or Combined with Chemotherapy

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Table S1. Laboratory results in patients before and after treatment.

	All	HPV(-)	HPV(+)	p	p HB
CRP 0 [g/l]	5.15±7.07 (0.16-36.90)	6.79±8.39 (0.16-36.90)	3.40±4.80 (0.17-27.20)	0.008	0.088
CRP 1 [g/l]	26.60±35.93 (0.17-197.00)	30.96±44.43 (0.20-197.00)	22.00±23.50 (0.17-87.20)	0.179	1.000
Albumin 0 [g/l]	41.67±3.68 (33.00-50.00)	41.58±3.65 (33.00-49.00)	41.77±3.74 (32.00-50.00)	0.778	1.000
Albumin 1 [g/l]	36.95±3.92 (30.00-49.00)	37.05±4.11 (30.00-47.00)	36.84±3.75 (30.00-49.00)	0.778	1.000
Prealbumin 0 [g/l]	0.28±0.08 (0.13-0.52)	0.26±0.09 (0.13-0.52)	0.29±0.07 (0.18-0.45)	0.092	0.920
Prealbumin 1 [g/l]	0.20±0.08 (0.08-0.49)	0.19±0.07 (0.08-0.35)	0.21±0.09 (0.09-0.49)	0.223	1.000
Haemoglobin 0 [g/dl]	13.97± 1.50 (10.60-17.40)	14.05±1.51 (12.85-15.35)	13.88±1.51 (10.80-16.90)	0.530	1.000
Haemoglobin 1 [g/dl]	12.70± 1.50 (9.40-16.30)	12.29±1.46 (9.40-16.30)	12.03±1.54 (9.50-15.80)	0.331	1.000

TLC 0 [/mm ³]	1.90±0.72 (0.57-4.84)	1.91±0.71 (0.65-3.94)	1.89±0.73 (0.57-4.54)	0.842	0.842
TLC 1 [/mm ³]	0.62±0.37 (0.11-2.84)	0.71±0.44 (0.11-2.84)	0.52±0.24 (0.17-1.34)	0.004	0.048
PNI 0	41.68±3.68 (32.00-50.00)	41.59±3.65 (33.01-49.01)	41.78±3.74 (32.00-50.00)	0.778	1.000
PNI 1	36.95±3.92 (30.00-49.00)	37.05±4.11 (30.00-47.00)	36.85±3.75 (30.00-49.00)	0.777	1.000

Values are presented as means and standard deviations.

0, before treatment, 1 after treatment; CRP, C-reactive protein; TLC, total lymphocyte count; PNI, prognostic nutritional index.

H-B Holm-Bonferroni correction for multiple testing

Table S2. Weight, BMI and laboratory results: differences before and after treatment in HPV- and HPV+ groups undergoing RT and CRT separately (comparison of values before and after RT/CRT within individual HPV- and HPV+ subgroups + separately).

	CRT		<i>p</i>	<i>p</i> H-B	RT		<i>p</i>	<i>p</i> H-B
	HPV(-)	HPV(+)			HPV(-)	HPV(+)		
Weight 0-1 [kg]	4.11±3.75	5.76±4.27	0.142	1.000	4.89±3.68	4.83±4.21	1.000	1.000
Weight [%]	5.62±5.24	7.32±5.24	0.221	1.000	5.73±3.74	5.13±4.55	1.000	1.000
BMI 0-1 [kg/m ²]	1.44±1.34	1.99±1.40	0.127	1.000	1.84±1.37	1.81±1.70	1.000	1.000
CRP 0-1 [g/l]	-19.70±37.60	-17.92±22.07	0.623	1.000	-32.39±55.67	-24.79±32.97	0.803	1.000
Albumin 0-1 [g/l]	4.89±4.37	5.00±5.05	0.774	1.000	3.75±4.33	5.14±4.53	0.221	1.000
Prealbumin 0-1 [g/l]	0.059±0.101	0.088±0.098	0.237	1.000	0.079±0.087	0.002±0.116	0.431	1.000
Haemoglobin 0-1 [g/dl]	2.10±1.54	2.04±1.55	0.943	1.000	1.10±1.05	0.44±1.13	0.249	1.000
TLC 0-1 [/mm ³]	1.22±0.77	1.36±0.70	0.438	1.000	1.15±0.63	1.46±0.69	0.351	1.000
PNI 0-1	4.90±1.37	5.01±5.06	0.739	1.000	3.76±4.33	5.15±4.53	0.213	1.000

Table S3. Weight, BMI and laboratory results before and after treatment in HPV- and HPV+ groups undergoing RT and CRT separately (comparison of difference values between two subgroups according to HPV status).

	CRT		<i>p</i>	<i>p</i> H-B	RT		<i>p</i>	<i>p</i> H-B
	HPV(-)	HPV(+)			HPV(-)	HPV(+)		

Weight 0 [kg]	72.60±14.13	78.58±14.92	0.091	1.000	71.99±17.04	85.53±11.43	0.050	1.000
Weight 1[kg]	68.96±13.24	72.10±14.71	0.560	1.000	75.08±13.44	86.73±9.72	0.276	1.000
BMI 0 [kg/m ²]	25.11±4.00	27.78±4.31	0.007	0.241	26.92±5.69	30.52±3.58	0.103	1.000
BMI 1 [kg/m ²]	23.56±3.21	25.40±4.10	0.090	1.000	27.91±4.53	30.91±3.47	0.350	1.000
NRS 2002 0	0.36±0.84	0.20±0.40	0.883	1.000	0.50±0.93	0.86±1.46	0.615	1.000
NRS 2002 1	3.06±1.15	3.40±1.12	0.217	1.000	2.73±0.90	3.33±0.58	0.314	1.000
CRP 0 [g/l]	7.18±9.76	2.94±3.77	0.016	0.546	6.02±4.84	6.81±9.24	0.730	1.000
CRP 1 [g/l]	27.13±35.78	20.66±22.49	0.770	1.000	38.63±58.38	31.59±30.05	0.978	1.000
Albumin 0 [g/l]	42.05±3.91	41.92±3.93	0.949	1.000	40.67±2.96	40.71±1.80	0.957	1.000
Albumin 1 [g/l]	37.23±4.16	37.02±3.77	0.899	1.000	36.71±4.10	35.57±3.60	0.454	1.000
Prealbumin 0 [g/l]	0.277±0.079	0.301±0.070	0.117	1.000	0.230±0.098	0.213±0.029	0.861	1.000
Prealbumin 1 [g/l]	0.213±0.072	0.217±0.081	0.965	1.000	0.150±0.048	0.200±0.120	0.536	1.000
Haemoglobin 0 [g/dl]	14.08±1.50	13.85±1.56	0.466	1.000	14.00±1.54	14.09±1.10	0.887	1.000
Haemoglobin 1 [g/dl]	11.98±1.40	11.82±1.41	0.450	1.000	12.87±1.41	13.64±1.65	0.249	1.000
TLC 0 [/mm ³]	1.91±0.78	1.89±0.75	0.840	1.000	1.91±0.56	1.85±0.57	0.723	1.000
TLC 1 [/mm ³]	0.69±0.47	0.53±0.25	0.084	1.000	0.74±0.38	0.40±0.16	0.006	0.234
PNI 0	42.06±3.91	41.93±3.93	0.936	1.000	40.68±2.96	40.72±1.80	1.000	1.000
PNI 1	37.23±4.16	37.02±3.77	0.820	1.000	36.72±4.10	35.57±3.60	0.265	1.000

Table S4. Comparison of selected clinicopathological factors between groups with low and high prognostic nutritional index (PNI).

	All				HPV(-)				HPV(+)			
	PNI<41.68	PNI≥41.68	p	p HB	PNI<41.59	PNI≥41.59	p	p HB	PNI<41.78	PNI≥41.78	p	p HB
Age [years]	62.8	58.5	0.004	0.076	62.5	59.2	0.031	1.00	57.7	63.2	0.004	0.148
Gender			0.235	1.00			0.764	1.00			0.184	1.00
M	38 (64.4%)	45 (75.0%)			24 (75.0%)	24 (80.0%)			14 (51.9%)	21 (70.0%)		
F	21 (35.6%)	15 (25.0%)			8 (25.0%)	6 (20.0%)			13 (48.1%)	9 (30.0%)		

General location			0.004	0.072			0.033	1.00			0.093	1.00
Tonsil	36 (61.0%)	51 (85.0%)			17 (53.1%)	24 (80.0%)			19 (70.4%)	27 (90.0%)		
Others	23 (39.0%)	9 (15.0%)			15 (46.9%)	6 (20.0%)			8 (29.6%)	3 (10.0%)		
Detailed location			0.005	0.085			0.031	1.00			0.120	1.00
1. tonsil	36 (61.0%)	51 (85.0%)			17 (53.1%)	24 (80.0%)			19 (70.4%)	27 (90.0%)		
2. palate	8 (13.6%)	1 (1.7%)			8 (25.0%)	1 (3.3%)						
3. root of the tongue	12 (20.3%)	8 (13.3%)			7 (21.9%)	5 (16.7%)			5 (18.5%)	3 (10.0%)		
4. other oropharynx	3 (5.1%)	0 (0%)			0	0			3 (11.1%)	0		
Histological grading			0.346	1.00			0.515	1.00			0.367	1.00
G1	3 (8.1%)	4 (10.8%)			3 (15.0%)	3 (14.3%)			0	1 (6.3%)		
G2	27 (73.0%)	21 (56.8%)			15 (75.0%)	13 (61.9%)			12 (70.6%)	8 (50.0%)		
G3	7 (18.9%)	12 (32.4%)			2 (10.0%)	5 (23.8%)			5 (29.4%)	7 (43.8%)		
			0.287	1.00			0.410	1.00			0.481	1.00
G1-2	30 (81.1%)	25 (67.6%)			18 (90.0%)	16 (76.2%)			12 (70.6%)	9 (56.3%)		
G3	7 (18.9%)	12 (32.4%)			2 (10.0%)	5 (23.8%)			5 (29.4%)	7 (43.8%)		
Tumor depth (T)			0.257	1.00			0.107	1.00			0.733	1.00
T1	5 (8.5%)	6 (10.0%)			3 (9.4%)	3 (10.0%)			2 (7.4%)	3 (10.0%)		
T2	19 (32.2%)	21 (35.0%)			13 (40.6%)	11 (36.7%)			6 (22.2%)	10 (33.3%)		
T3	18 (30.5%)	25 (41.7%)			7 (21.9%)	14 (46.7%)			11 (40.7%)	11 (36.7%)		
T4	16 (27.1%)	8 (13.3%)			8 (25.0%)	2 (6.7%)			8 (29.6%)	6 (20.0%)		
Tx	1 (1.7%)	0			1 (3.1%)	0						
			0.714	1.00			0.805	1.00			0.410	1.00
T1-2	24 (40.7%)	27 (45.0%)			16 (50.0%)	14 (46.7%)			8 (29.6%)	13 (43.3%)		
T3-4	34 (59.3%)	33 (55.0%)			16 (50.0%)	16 (53.3%)			19 (70.4%)	17 (56.7%)		
Lymph node metastasis (N)			0.366	1.00			0.771	1.00			0.476	1.00
N0	13 (22.0%)	10 (16.7%)			10 (31.3%)	7 (23.3%)			3 (11.1%)	3 (10.0%)		
N1	8 (13.6%)	16 (26.7%)			6 (18.8%)	9 (30.0%)			2 (7.4%)	7 (23.3%)		
N2	29 (49.2%)	26 (43.3%)			12 (37.5%)	10 (33.3%)			17 (63.0%)	16 (53.3%)		
N3	8 (13.6%)	8 (13.3%)			4 (12.5%)	4 (13.3%)			4 (14.8%)	4 (13.3%)		
Nx	1 (1.7%)	0							1 (3.7%)	0		
			0.455	1.00			0.805	1.00			0.241	1.00
N0-1	21 (35.6%)	26 (43.3%)			16 (50.0%)	16 (53.3%)			5 (18.5%)	10 (33.3%)		
N2-3	38 (64.4%)	34 (56.7%)			16 (50.0%)	14 (46.7%)			22 (81.5%)	20 (66.7%)		
Treatment duration [days]			0.233	1.00	43.3	44.9	0.292	1.00	47.7	49.4	0.233	1.00

General treatment regimen				0.394	1.00			0.598	1.00			0.697	1.00
RT	16 (27.1%)	12 (20.0%)				12 (37.5%)	9 (30.0%)			4 (14.8%)	3 (10.0%)		
CRT	43 (72.9%)	48 (80.0%)				20	21			23 (85.2%)	27 (90.0%)		
Weight loss				0.282	1.00			0.751	1.00			0.260	1.00
1. Stable													
2. Weight loss ≤ 5%	21 (50.0%)	17 (37.0%)				10 (50.0%)	8 (42.1%)			11 (50.0%)	9 (33.3%)		
3. Weight loss > 5%	21 (50.0%)	29 (63.0%)				10 (50.0%)	11 (57.9%)			11 (50.0%)	18 (66.7%)		
Initial BMI [kg/m ²]				27.0	26.8	0.922	1.00	25.5	26.0	0.816	1.00	27.6	28.8
BMI groups						0.679	1.00			1.00	1.00		0.474
1. <18.5	3 (5.1%)	2 (3.3%)				2 (6.3%)	2 (6.7%)			1 (3.7%)	0		
2. ≥18.5	56 (94.9%)	58 (96.7%)				30 (93.8%)	28 (93.3%)			26 (96.3%)	30 (100%)		
NRS 2002 (mean value)													
NRS 2002				0.547	1.00			0.701	1.00			0.145	1.00
0	43 (72.9%)	47 (79.7%)				25 (78.1%)	22 (73.3%)			18 (66.7%)	25 (86.2%)		
1.	13 (22.0%)	7 (11.9%)				5 (15.6%)	3 (10.0%)			8 (29.6%)	4 (13.8%)		
2.	1 (1.7%)	3 (5.1%)				1 (3.1%)	3 (10.0%)						
3.	1 (1.7%)	1 (1.7%)				1 (3.1%)	1 (3.3%)						
4.	1 (1.7%)	1 (1.7%)				0	1 (3.3%)			1 (3.7%)	0		
5.													
NRS 2002 (division into groups)					1.00			0.607				0.482	
1. <3	57 (96.6%)	57 (96.6%)			1.00	31 (96.9%)	28 (93.3%)		1.00	26 (96.3%)	29 (100%)		1.00
2. ≥3	2 (3.4%)	2 (3.3%)				1 (3.1%)	2 (6.7%)			1 (3.7%)	0		
Smoking				1.00	1.00			0.589	1.00			0.410	1.00
Yes	30 (50.8%)	30 (50.0%)				23 (71.9%)	19 (63.3%)			7 (25.9%)	11 (36.7%)		
No	29 (49.2%)	30 (50.0%)				9 (28.1%)	11 (36.7%)			20 (74.1%)	19 (63.3%)		
Alcohol abuse				1.00	1.00			0.607	1.00				
Yes	1 (1.7%)	2 (3.3%)				1 (3.1%)	2 (6.7%)			0	0		
No	58 (98.3%)	58 (96.7%)				31 (96.9%)	28 (93.3%)			27 (100%)	30 (100%)		

RT, radiotherapy; CRT, chemoradiotherapy, BMI, body mass index; NRS 2002, Nutritional Risk Score.

Table S5. Overall survival (OS) in patients: univariate and multivariate analysis for pre-treatment parameters.

Variable	Univariate analysis			Multivariate analysis	
	n	HR (95%CI)	p-value	HR (95%CI)	p-value
CRP >3.50 vs. ≤3.50	120	2.50 (1.28-4.88)	0.007	2.22 1.12-4.42	0.023
Albumin [g/l] >40.0 vs. ≤40.0	119	1.41 (0.70-2.83)	0.337		
Hb 0 [g/dl] >13.5 vs. ≤13.5	127	0.82 (0.43-1.55)	0.544		
TLC 0 [/mm ³] >1.28 vs. ≤1.28	127	0.62 (0.30-1.28)	0.196		
PNI >39.01 vs. ≤39.01	119	1.08 (0.50-2.30)	0.845		
Age >60 vs. ≤60	127	0.86 (0.46-1.63)	0.653		
Gender F vs. M	127	0.49 (0.22-1.07)	0.073	0.32 0.13-0.82	0.017
General location tonsil vs. others	127	1.60 (0.73-3.49)	0.239	3.20 1.19-8.60	0.021
Tumor depth (T) T3-4 vs. T1-2	126	1.02 (0.53-1.94)	0.962		
Lymph node metastasis N 2-3 vs. N 0-1	126	1.09 (0.57-2.09)	0.791		
Radiotherapy vs. Radiochemotherapy	127	1.28 (0.63-2.58)	0.493		

BMI 0 >24.53 vs. <24.53	127	0.37 (0.19-0.70)	0.003	0.32 0.14-0.72	0.006
NRS 2002 >1 vs. ≤1	126	3.99 (1.66-9.62)	0.002		
Smoking Yes vs. No	127	1.40 (0.74-2.67)	0.306	0.48 0.22-1.07	0.074
Alcohol abuse Yes vs. No	127	6.38 (1.89-21.51)	0.003	3.86 1.00-14.86	0.050
HPV+ vs. HPV-	127	0.31 (0.16-0.63)	0.001	0.36 0.16-0.80	0.012

0, before treatment; Hb, haemoglobin level; TLC, lymphocyte count .

Table S6. Disease-free survival (DFS) in patients: univariate and multivariate analysis for pre-treatment parameters.

Variable	Univariate analysis			Multivariate analysis	
	n	HR (95%CI)	p-value	HR (95%CI)	p-value
CRP >3.50 vs. 3.50	120	4.00 1.87-8.56	0.0004	3.53 1.50-8.32	0.004
Albumin [g/l] >40.0 vs. <40.0	119	0.86 0.42-1.77	0.677		
Hb 0 [g/dl] >13.5 vs. <13.5	127	0.50 (0.25-1.00)	0.051		
TLC 0 [/mm ³] >1.28 vs. <1.28	127	0.44 (0.21-0.92)	0.028		
PNI >39.01 vs. <39.01	119	0.48 0.23-0.99	0.046	0.47 0.21-1.06	0.070
Age >60 vs. ≤60	127	0.83 0.42-1.65	0.604		

Gender F vs. M	127	0.86 0.41-1.81	0.693		
General location tonsil vs. others	127	1.33 0.60-2.94	0.489	2.74 0.97-7.70	0.056
Tumor depth (T) T3-4 vs. T1-2	126	1.22 0.61-2.45	0.578		
Lymph node metastasis N 2-3 vs. N 0-1	126	2.11 (0.98-4.54)	0.057	3.28 (1.33-8.12)	0.010
Radiotherapy vs. Radiochemotherapy	127	0.93 (0.42-2.06)	0.854		
BMI 0 >24.53 vs. <24.53	127	0.32 0.16-0.64	0.001		
NRS 2002 >1 vs. ≤1	126	5.05 2.07-12.34	0.0004	5.92 1.84-19.05	0.003
Smoking Yes vs. No	127	1.39 0.70-2.78	0.346		
Alcohol abuse Yes vs. No	127	4.35 1.03-18.35	0.046	5.78 1.04-31.97	0.045
HPV+ vs. HPV-	127	0.28 (0.12-0.62)	0.002	0.33 0.14-0.81	0.015

0, before treatment; Hb, haemoglobin level; TLC, lymphocyte count .

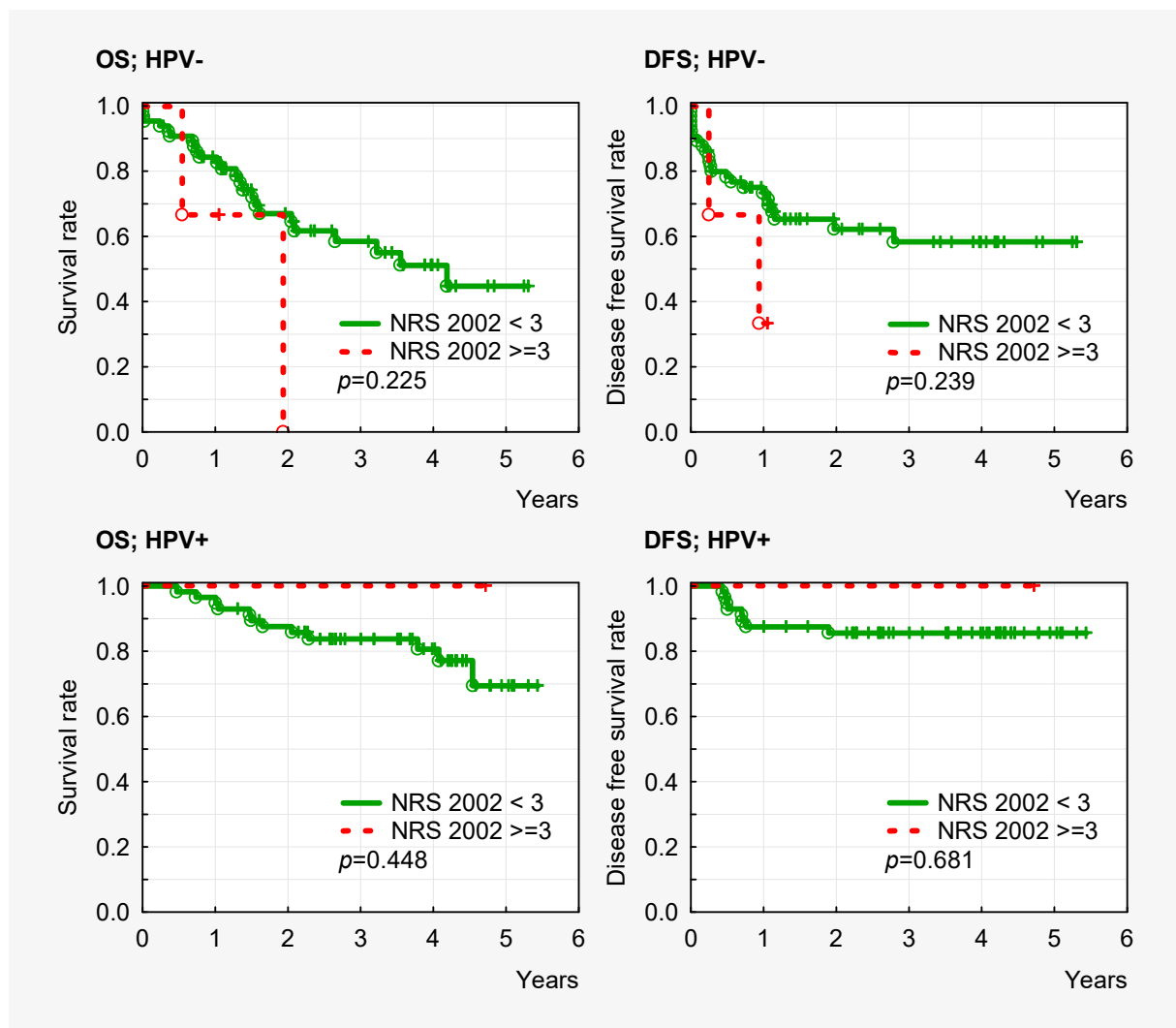


Figure S1. Overall and disease-free survival in HPV- and HPV+ patients depending on NRS 2002 (NRS 2002<3 vs. NRS 2002≥3).

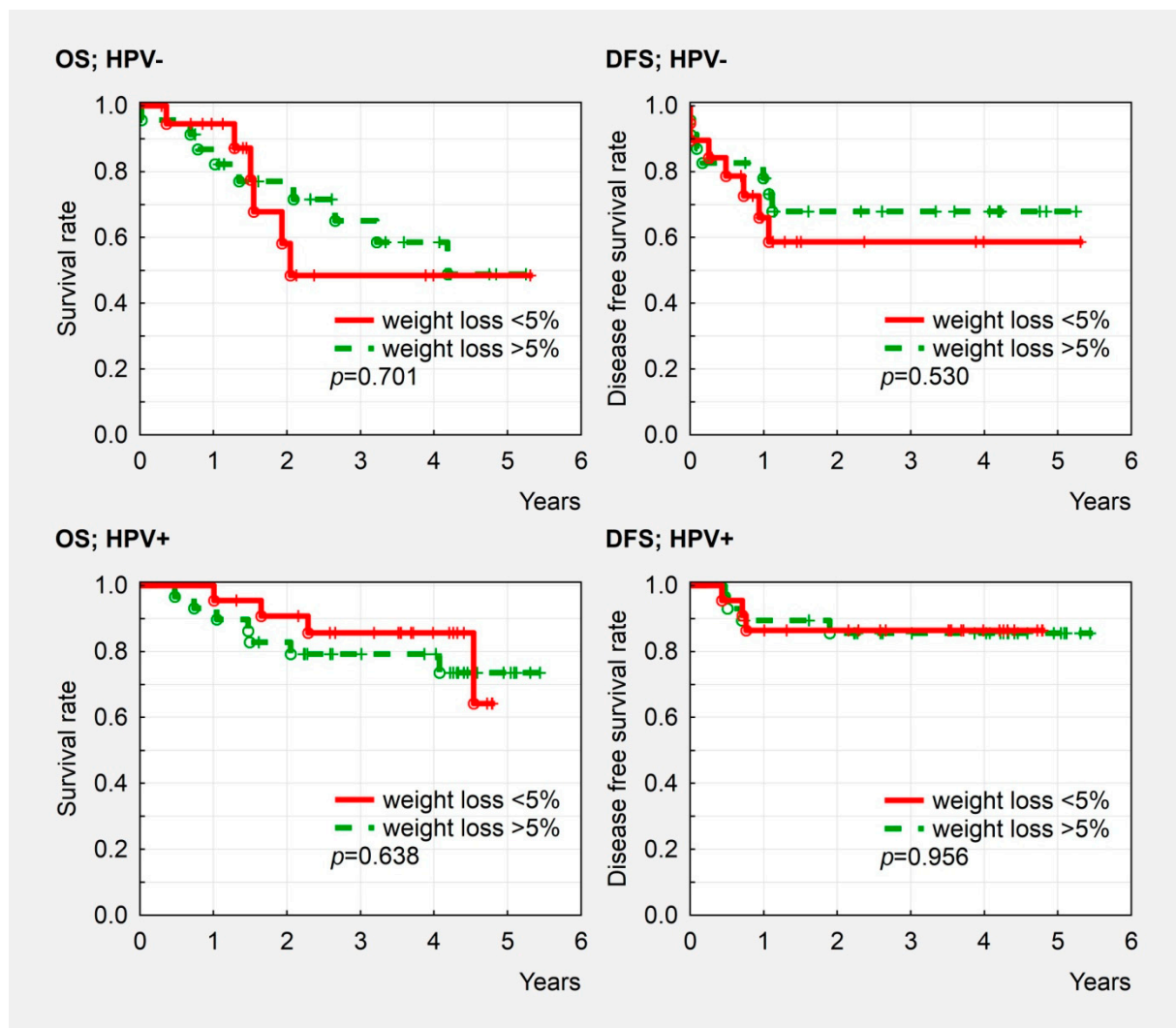


Figure S2. Overall and disease-free survival in HPV- and HPV+ patients depending on NRS 2002 (weight loss<5% vs. weight loss>5%).