# Supplementary Material: Prognostic Impact of Sarcopenia's Occurrence During Radiotherapy in Oropharyngeal Cancer Patients

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## 1. Sarcopenic condition at baseline based on CSA-MM.



(a)



(b)
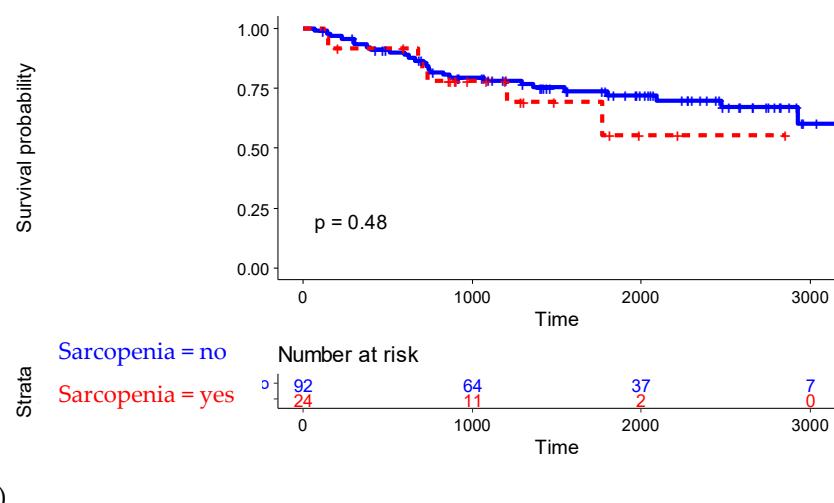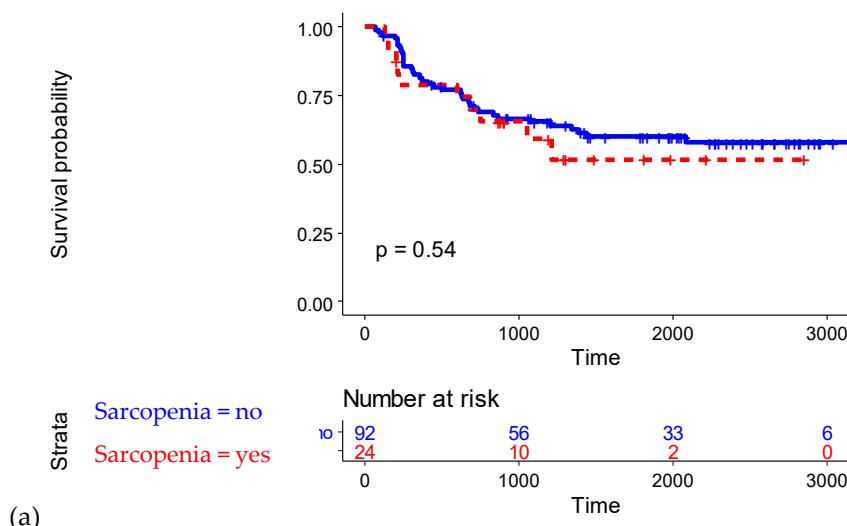
**Figure S1.** KM curves for PFS (a) and OS (b) of sarcopenic patients and not at baseline, based on MM-CSA and the formula validated by Prado et al.[47].

**Table S1.** Sarcopenic condition at baseline and associations with patient characteristics.

| Variable | Overall (*n* = 116) | Sarcopenic Patients at Baseline (*n* = 24, 20.7%) | Non Sarcopenic Patients at Baseline (*n* = 92, 79.3%) | *p*-value |
|---|---|---|---|---|
| Age at RT, median (IQR) | 60 (53–67) | 60.5 (54.2–67.5) | 60 (53–66.2) | 0.83 |
| Sex | | | | |
| Female, *n* (%) | 35 (30.2) | 0 (0) | 35 (38) | 0.0008 |
| Male, *n* (%) | 81 (69.8) | 24 (100) | 57 (62) | |
| Stage | | | | |
| I, *n* (%) | 1 (0.9) | 0 (0) | 1 (1.1) | |
| II, *n* (%) | 4 (3.4) | 0 (0) | 4 (4.3) | |
| III, *n* (%) | 23 (19.8) | 4 (16.7) | 19 (20.6) | 0.70 |
| IV A, *n* (%) | 75 (64.6) | 18 (75) | 57 (61.9) | |
| IV B, *n* (%) | 13 (11.3) | 2 (8.3) | 11 (12.1) | |
| Smoking history | | | | |
| Yes, *n* (%) | 64 (55.2) | 11 (45.8) | 53 (57.6) | |
| No, *n* (%) | 33 (28.4) | 12 (50.0) | 21 (22.8) | 0.06 |
| Missing, *n* (%) | 19 (16.4) | 1 (4.2) | 18 (19.6) | |
| Alcohol history | | | | |
| Yes, *n* (%) | 48 (41.4) | 14 (58.3) | 34 (36.9) | |
| No, *n* (%) | 43 (37.1) | 8 (33.3) | 35 (38.0) | 0.35 |
| Missing, *n* (%) | 25 (21.5) | 2 (8.4) | 23 (25.1) | |
| HPV/p16 status | | | | |
| Negative, *n* (%) | 7 (6.0) | 4 (16.7) | 3 (3.3) | |
| Positive, *n* (%) | 86 (74.1) | 17 (70.8) | 69 (75) | 0.04 |
| Missing, *n* (%) | 23 (19.9) | 3 (12.5) | 20 (21.7) | |
| KPS | | | | |
| <100, *n* (%) | 20 (17.2) | 6 (25) | 14 (15.2) | 0.37 |
| =100, *n* (%) | 96 (82.8) | 18 (75) | 78 (84.8) | |
| Therapy RT, *n* (%) | 11 (9.5) | 3 (12.5) | 8 (8.7) | 0.69 |
| CRT, *n* (%) | 105 (90.5) | 21 (87.5) | 84 (91.3) | |
| NLR | | | | |
| <3 | 50 (43.1) | 6 (25) | 44 (47.8) | 0.05 |
| ≥3 | 62 (56.9) | 18 (75) | 44 (52.2) | |
| Nasogastric tube | | | | |
| Yes | 14 (12.1) | 24 (100) | 78 (84.8) | 0.06 |
| No | 102 (87.9) | 0 (0) | 14 (15.2) | |
| PEG | | | | |
| Yes | 12 (10.3) | 19 (79.2) | 85 (92.4) | 0.07 |
| No | 104 (89.7) | 5 (20.8) | 7 (7.6) | |
| Hb at baseline, median (IQR) | 14.2 (13.2–15.3) | 14.1 (13.5–15.0) | 14.2 (13.0–15.4) | 0.98 |

**Table S2.** Results of multivariable analysis for PFS and OS.

| Variable | PFS | | OS | |
|---|---|---|---|---|
| | **HR (CI 95%)** | ***p*-value** | **HR (CI 95%)** | ***p*-value** |
| Sarcopenia at baseline<br>Yes vs. No | 0.86 (0.38–1.94) | 0.72 | 0.62 (0.20–1.98) | 0.42 |
| Sex<br>M vs. F | 5.25 (1.97–14.0) | 0.0009 | 11.5 (2.64–49.9), | 0.001 |
| KPS<br><100 vs 100 | 2.79 (1.28–6.07) | 0.01 | 6.20 (2.14–18.0) | 0.0008 |
| Nasogastric tube<br>Yes vs. No | 2.20 (0.97–4.97) | 0.057 | 2.69 (1.06–6.86) | 0.04 |
| Hb at baseline<br>Continuous variable | 0.80 (0.64–0.99) | 0.045 | 0.71 (0.54–0.91) | 0.008 |
| PEG<br>Yes vs. No | 2.90 (1.19–6.89) | 0.02 | - | |
| NLR at baseline<br>⩾3 vs. <3 | - | | 4.60 (1.72–12.3) | 0.002 |
| Alcohol<br>Yes vs. No | - | | 5.66 (1.52–21.1) | 0.01 |

## 2. Sarcopenia onset at 50 Gy based on CSA-MM

**Table S3.** Sarcopenic onset during RT and associations with patients characteristics.

| Variable | Overall (*n* = 92) | Sarcopenic Patients at 50 Gy (Not at Baseline) (*n* = 16, 17.4%) | Never Sarcopenic Patients (*n* = 69, 82.6%) | *p*-value |
|---|---|---|---|---|
| Age at RT, median (IQR) | 60 (53–66.2) | 61.5 (51.5–65.2) | 60 (53–66) | 0.90 |
| **Sex** | | | | |
| Female, *n* (%) | 35 (38) | 1 (6.2) | 32 (46.4) | 0.007 |
| Male, *n* (%) | 57 (62.0) | 15 (93.8) | 37 (53.6) | |
| **Stage** | | | | |
| I, *n* (%) | 1 (1.1) | 0 (0) | 1 (1.4) | |
| II, *n* (%) | 4 (4.3) | 1 (6.2) | 3 (4.3) | |
| III, *n* (%) | 19 (20.6) | 5 (31.2) | 14 (20.3) | 0.54 |
| IV A, *n* (%) | 57 (61.9) | 8 (50) | 44 (63.8) | |
| IV B, *n* (%) | 11 (12.1) | 2 (12.6) | 7 (10.2) | |
| **Smoking status** | | | | |
| Yes, *n* (%) | 53 (57.6) | 7 (43.7) | 44 (63.8) | |
| No, *n* (%) | 21 (22.8) | 4 (25) | 15 (21.7) | 0.22 |
| Missing, *n* (%) | 18 (19.6) | 5 (31.3) | 10 (14.5) | |
| **Alcohol status** | | | | |
| Yes, *n* (%) | 34 (36.9) | 9 (56.2) | 24 (34.8) | |
| No, *n* (%) | 35 (38.0) | 2 (12.5) | 31 (44.9) | 0.06 |
| Missing, *n* (%) | 23 (74.9) | 5 (68.7) | 14 (20.3) | |
| **HPV/p16 status 16** | | | | |
| Negative, *n* (%) | 3 (3.3) | 3 (18.7) | 0 (0) | |
| Positive, *n* (%) | 69 (75) | 10 (62.5) | 54 (78.3) | 0.007 |
| Missing, *n* (%) | 20 (21.7) | 3 (18.8) | 15 (21.7) | |
| **KPS** | | | | |
| <100, *n* (%) | 14 (15.2) | 1 (6.2) | 12 (17.4) | 0.46 |
| =100, *n* (%) | 78 (84.8) | 15 (93.8) | 57 (82.6) | |
| **Therapy** | | | | |
| RT, *n* (%) | 8 (8.7) | 0 (0) | 8 (11.6) | 0.21 |
| CRT, *n* (%) | 84 (91.3) | 16 (100) | 61 (88.4) | |
| **NLR** | | | | |
| <3 | 44 (47.8) | 12 (75) | 29 (42.0) | |
| ⩾3 | 44 (47.8) | 4 (25) | 36 (52.2) | 0.05 |
| Missing | 4 (4.3) | 0 (0) | 4 (5.8) | |
| **Nasogastric tube** | | | | |
| Yes | 14 (15.2) | 2 (12.5) | 12 (17.4) | 0.74 |
| No | 78 (84.8) | 14 (87.5) | 57 (82.6) | |
| **PEG** | | | | |
| Yes | 7 (7.6) | 0 (0) | 6 (8.7) | 0.35 |
| No | 85 (92.4) | 16 (100) | 63 (91.3) | |
| Hb at baseline, median (IQR) | 14.2 (13.05–15.4) | 15.1 (12.1–15.6) | 14.1 (13.1–15.4) | 0.41 |
| CCI, median (IQR) | 2 (2–3) | 2(2–2) | 2 (2–3) | 0.42 |

**Table S4.** Sarcopenic onset during RT and associations with blood parameters, both at baseline and at the end of RT.

| | Variable | Sarcopenic Patients at 50 Gy (*n* = 16, 17.4%) Median (IQR) | Never Sarcopenic Patients (*n* = 69, 82.6%) Median (IQR) | *p*-value |
|---|---|---|---|---|
| Baseline | NLR | 2.61 (2.44–3.07) | 3.21 (2.14–3.91) | 0.22 |
| | Hb | 14.1 (13.5–15.0) | 14.2 (13.0–15.4) | 0.98 |
| | PLR | 132.5 (120.2–137.9) | 163.9 (120.3–194.6) | 0.11 |
| | Platelets | 212.0 (169.7–240.5) | 234.0 (199.0–275.0) | 0.12 |
| | Monocytes | 0.61 (0.53–0.74) | 0.59 (0.43–0.78) | 0.41 |
| End of RT | NLR | 9.51 (7.75–14.7) | 12.6 (7.72–17.0) | 0.56 |
| | Hb | 11.9 (10.8–12.4) | 11.9 (11.3–12.9) | 0.41 |
| | PLR | 485.9 (342.7–613.1) | 582.0 (441.2–895.1) | 0.08 |
| | Platelets | 164.5 (156.7–200.5) | 214.0 (153.5–262.0) | 0.05 |
| | Monocytes | 0.62 (0.47–0.68) | 0.52 (0.40–0.73) | 0.58 |

**Table S5.** Sarcopenic onset during RT and associations activation of nutritional counseling during RT.

| Variable | Sarcopenia (yes) (*n* = 16) | Sarcopenia (no) (*n* = 69) | *p*-value |
|---|---|---|---|
| | | | 0.75 |
| Counseling (yes) (*n* = 21) | 3 (14.3) | 18 (85.7) | |
| Counseling (no) (*n* = 64) | 13 (20.3) | 51 (79.7) | |

**3. Sarcopenia onset at 50 Gy based on CSA-C3**

**Table S6.** Sarcopenic onset during RT and associations with blood parameters, both at baseline and at the end of RT.

| Variable | Overall (*n* = 108) | Sarcopenic Patients at 50 Gy (Not at Baseline) (*n* = 14, 13.0%) | Never Sarcopenic Patients (*n* = 94, 87.0%) | *p*-value |
|---|---|---|---|---|
| Age at RT, median (IQR) | 60 (53–67) | 70.5 (64.5–76.7) | 59 (52–64) | <0.001 |
| Sex | | | | |
| Female, *n* (%) | 33 (30.5) | 2 (14.3) | 31 (33.0) | 0.20 |
| Male, *n* (%) | 75 (69.5) | 12 (85.7) | 63 (67.0) | |
| Stage | | | | |
| I, *n* (%) | 1 (0.9) | 0 (0) | 1 (1.1) | |
| II, *n* (%) | 4 (3.7) | 1 (7.1) | 3 (3.2) | |
| III, *n* (%) | 23 (21.3) | 2 (14.3) | 21 (22.3) | 0.74 |
| IV A, *n* (%) | 69 (63.9) | 10 (71.5) | 59 (62.8) | |
| IV B, *n* (%) | 11 (10.2) | 1 (7.1) | 10 (89.4) | |
| Smoking status | | | | |
| Yes, *n* (%) | 62 (57.4) | 8 (57.1) | 53 (56.4) | |
| No, *n* (%) | 31 (28.7) | 4 (28.6) | 27 (28.7) | 0.99 |
| Missing, *n* (%) | 16 (13.9) | 2 (14.3) | 14 (14.9) | |
| Alchol status | | | | |
| Yes, *n* (%) | 47 (43.5) | 6 (42.8) | 41 (43.6) | |
| No, *n* (%) | 40 (37.0) | 4 (28.6) | 36 (38.3) | 0.64 |
| Missing, *n* (%) | 21 (19.5) | 4 (28.6) | 17 (18.1) | |
| HPV status 16 | | | | |
| Negative, *n* (%) | 6 (5.5) | 1 (7.1) | 5 (5.3) | |
| Positive, *n* (%) | 81 (75.0) | 8 (57.1) | 73 (77.6) | 0.22 |
| Missing, *n* (%) | 21 (19.5) | 5 (64.2) | 16 (17.1) | |
| KPS | | | | 0.23 |

| | | | |
|---|---|---|---|
| <100, *n* (%) | 18 (16.7) | 4 (28.6) | 14 (14.9) | |
| =100, *n* (%) | 90 (83.3) | 10 (71.4) | 80 (85.1) | |
| Therapy RT, *n* (%) | 10 (9.3) | 3 (21.4) | 7 (7.5) | 0.12 |
| CRT, *n* (%) | 98 (90.7) | 11 (78.6) | 87 (92.5) | |
| NLR | | | | |
| <3 | 47 (43.5) | 4 (28.6) | 43 (45.7) | 0.41 |
| ≥3 | 57 (52.8) | 9 (64.3) | 48 (51.1) | |
| Missing | 4 (3.7) | 1 (7.1) | 3 (3.2) | |
| Nasogastric tube | | | | |
| Yes | 14 (13.0) | 4 (28.6) | 10 (10.6) | 0.06 |
| No | 94 (87.0) | 10 (71.4) | 84 (89.4) | |
| PEG | | | | |
| Yes | 11 (10.2) | 3 (21.4) | 8 (8.5) | 0.15 |
| No | 97 (89.8) | 11 (78.6) | 86 (91.5) | |
| HB at baseline, median (IQR) | 14.2 (13.2–15.3) | 13.4 (12.6–14.1) | 14.5 (13.3–15.5) | 0.03 |
| CCI median (IQR) | 2 (2–3) | 2(2–2) | 2 (2–3) | 0.76 |

**Table S7.** Associations between becoming sarcopenic at 50 Gy and blood parameters collected at baseline.

| | Variable | Sarcopenic Patients at 50 Gy (*n* = 14, 13%) Median (IQR) | Never Sarcopenic Patients (*n* = 94, 87%) Median (IQR) | *p*-value |
|---|---|---|---|---|
| Baseline | NLR | 3.36 (2.97–4.32) | 3.04 (2.16–3.87) | 0.08 |
| | Hb | 13.4 (12.6–14.1) | 14.5 (13.3–15.5) | 0.03 |
| | PLR | 174.3 (127.5–247.6) | 147 (121.7–192.7) | 0.28 |
| | Platelets | 218 (169–265) | 239 (202–286) | 0.33 |
| | Monocytes | 0.67 (0.55–0.73) | 0.61 (0.47–0.74) | 0.61 |
| End of RT | NLR | 13.2 (10.4–16.1) | 11.6 (7.55–19.5) | 0.57 |
| | Hb | 12 (11.07–12.5) | 11.9 (11.1–12.8) | 0.80 |
| | PLR | 496.5 (424.9–1005.0) | 568.3 (427.5–938.4) | 0.83 |
| | Platelets | 222.5 (178.2–256.2) | 205.5 (157.0–258.5) | 0.43 |
| | Monocytes | 0.60 (0.51–0.75) | 0.54 (0.39–0.74) | 0.40 |

**Table S8.** Sarcopenic onset during RT and associations activation of nutritional counseling during RT.

| Variable | Sarcopenia (yes) (*n* = 14) | Sarcopenia (no) (*n* = 94) | *p*-value |
|---|---|---|---|
| | | | 0.02 |
| Counseling (yes) (*n* = 31) | 8 (25.8) | 23 (79.2) | |
| Counseling (no) (*n* = 77) | 6 (7.8) | 71 (92.2) | |

**Table S9.** Results of multivariable Cox proportional hazard models related to PFS and OS (muscle loss considered as continuous variable).

| | MM-CSA | | C3-CSA | |
|---|---|---|---|---|
| Variable | PFS HR (CI 95%), *p*-value | OS HR (CI 95%), *p*-value | PFS HR (CI 95%), *p*-value | OS HR (CI 95%), *p*-value |
| Sarcopenia at 50 Gy continuous variable | 0.93 (0.87–0.99), 0.02 | 0.89 (0.82–0.96), 0.005 | 1.00 (0.94–1.06), 0.99 | 1.03 (0.95–1.11), 0.51 |
| Sex M vs. F | 13.3 (3.43–51.3), 0.0002 | 16.9 (3.87–73.8), 0.0002 | 4.40 (1.34–14.4), 0.01 | 6.94 (1.45–33.09), 0.01 |
| KPS | 3.82 (1.28–11.4), 0.02 | - | - | 4.34 (1.43–13.1), 0.009 |

| | | | | |
|---|---|---|---|---|
| <100 vs. = 100 | | | | |
| Nasogastric tube<br>Yes vs. No | 2.69 (1.19–6.08), 0.02 | 9.69 (3.46–27.1), <0.001 | 3.18 (1.51–6.70), 0.002 | 3.77 (1.55–9.14), 0.003 |
| Hb at baseline<br>Continuous variable | 0.70 (0.55–0.91), 0.008 | 0.57 (0.41–0.77), 0.0004 | 0.70 (0.57–0.86), 0.0008 | 0.66 (0.50–0.88), 0.004 |
| NLR at baseline<br>≥3 vs. <3 | 2.26 (1.04–4.90), 0.04 | - | - | 4.05 (1.52–10.8), 0.005 |
| CCI<br>Continuous variable | - | 2.57 (1.54–4.30), 0.0003 | - | - |
| Alcohol<br>Yes vs. no | - | - | - | 6.02 (1.30–27.9), 0.02 |