

1
2
3 **Online appendix 1** Surgical technique and post-operative course for all the study population,
4 according to their R status.
5

| | All patients N=160 | R0 >0.1cm N=113 | R0+ ≤0.1cm N=34 | R1 0cm N=13 | P-value |
|-----------------------------|-----------------------|-----------------------|-----------------------|-------------------|---------|
| Type of resection | | | | | 0.157 |
| Lewis Santy | 133 (83.1) | 94 (83.2) | 9 (69.2) | 29 (85.3) | |
| McKeown | 19 (11.9) | 15 (13.3) | 2 (15.4) | 2 (5.9) | |
| Transhiatal | 9 (5.6) | 4 (3.5) | 2 (15.4) | 3 (8.8) | |
| Minimally invasive approach | | | | | |
| Laparoscopy | 130 (81.3) | 91 (80.5) | 10 (76.9) | 29 (85.3) | 0.858 |
| Thoracoscopy | 80 (50.0) | 58 (51.3) | 5 (38.5) | 17 (50.0) | 0.680 |
| Severe complication | 56 (35.0) | 39 (34.5) | 4 (30.8) | 13 (38.2) | 0.874 |
| Anastomotic leakage | 58 (36.3) | 41 (36.3) | 4 (30.8) | 13 (38.2) | 0.893 |

25 Categorical variables are expressed as N (%).
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

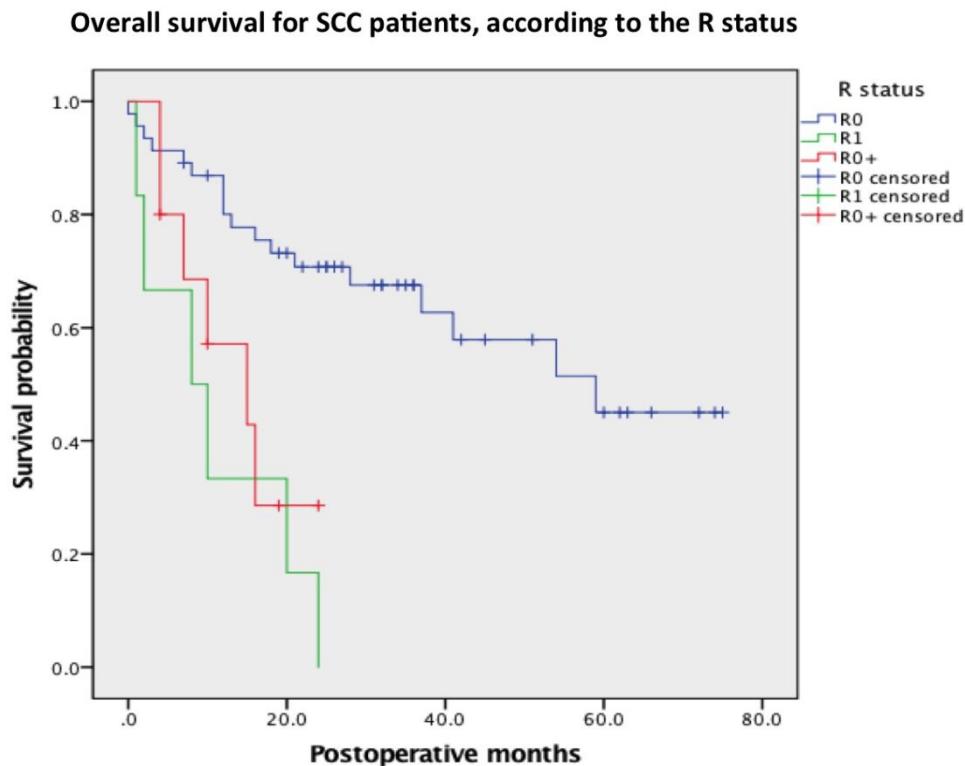
1
2
3
4 **Online appendix 2 Subgroup analysis for squamous cell carcinoma patients (SCC)**
5
6

| | All patients N=62 | R0 N=46 | R0+ ≤0.1cm N=10 | R1 0cm N=6 | P-value |
|----------------------|----------------------|------------|-----------------------|------------------|---------|
| Male gender | 45 (72.6) | 31 (67.4) | 10 (100) | 4 (66.7) | 0.105 |
| Age, years | 64.1 [8.7] | 63 [8] | 70 [8.6] | 62.7 [11.7] | 0.066 |
| ASA class | | | | | 0.436 |
| 1-2 | 36 (58.1) | 28 (60.9) | 7 (70) | 1 (16.7) | |
| 3-4 | 26 (41.9) | 18 (39.1) | 3 (30) | 5 (83.3) | |
| SUVmax (g/l) | 13.9[9.6] | 13.3 [8.9] | 14.7 [10.8] | 17.3 [13.5] | 0.679 |
| cT stage | | | | | 0.324 |
| 1 | 7 (11.3) | 7 (15.2) | 0 (0) | 0 (0) | |
| 2 | 11 (17.7) | 9 (19.6) | 2 (20) | 0 (0) | |
| 3 | 44 (71) | 30 (65.2) | 8 (80) | 6 (100) | |
| cN stage | | | | | 0.770 |
| 0 | 27 (43.5) | 21 (45.7) | 3 (30) | 3 (50) | |
| 1 | 28 (45.2) | 19 (41.3) | 6 (60) | 3 (50) | |
| 2 | 6 (9.7) | 5 (10.9) | 1 (10) | 0 (0) | |
| NAT | 50 (80.6) | 36 (78.3) | 8 (80) | 6 (100) | 0.447 |
| NAT type | | | | | 0.541 |
| Chemotherapy | 2 (3.2) | 1 (2.2) | 0 (0) | 1 (16.7) | |
| Chemoradiation | 47 (75.8) | 34 (73.9) | 8 (80) | 5 (83.3) | |
| Surgical approach | | | | | 0.867 |
| Lewis | 41 (66.1) | 31 (67.4) | 7 (70) | 3 (50) | |
| McKeown | 16 (25.8) | 12 (26.1) | 2 (20) | 2 (33.3) | |
| Transhiatal | 5 (8.1) | 3 (6.5) | 1 (10) | 1 (16.7) | |
| Severe complications | 23 (37.1) | 17 (37) | 2 (20) | 4 (66.7) | 0.964 |
| Anastomotic leakage | 27 (43.5) | 19 (41.3) | 5 (50) | 3 (50) | 0.833 |
| pT stage | | | | | <0.001 |
| 0 | 22 (35.5) | 22 (47.9) | 0 (0) | 0 (0) | |
| 1 | 16 (25.8) | 15 (32.6) | 1 (10) | 0 (0) | |

| | | | | | 0.003 |
|----|-------------------------|-----------|-----------|--------|----------------|
| 1 | 2 | 3 (4.8) | 3 (6.5) | 0 (0) | 0 (0) |
| 2 | 3 | 21 (33.9) | 6 (13) | 9 (90) | 6 (100) |
| 3 | pN stage | | | | |
| 4 | 0 | 48 (77.4) | 37 (80.4) | 7 (70) | 4 (66.7) |
| 5 | 1 | 10 (16.1) | 8 (17.4) | 1 (10) | 1 (16.7) |
| 6 | 2 | 1 (1.6) | 0 (0) | 0 (0) | 1 (16.7) |
| 7 | 3 | 2 (3.2) | 0 (0) | 2 (20) | 0 (0) |
| 8 | TRG | | | | 0.001 |
| 9 | 1-2 | 27 (43.5) | 24 (52.2) | 2 (20) | 1 (16.7) |
| 10 | 3-5 | 17 (27.4) | 6 (13) | 6 (60) | 5 (83.3) |
| 11 | Early recurrence | 16 (25.8) | 7 (15.2) | 4 (40) | 5 (83.3) 0.001 |
| 12 | Locoregional recurrence | 16 (25.8) | 10 (21.7) | 2 (20) | 4 (66.7) 0.059 |
| 13 | Distant recurrence | 14 (22.6) | 8 (17.4) | 3 (30) | 3 (50) 0.179 |

Categorical variables are expressed as N (%), and continuous variables as median [IQR].

1
 2
Online appendix 3 Survival analysis for squamous cell carcinoma (SCC)
 3
 4
 5
 6
 7

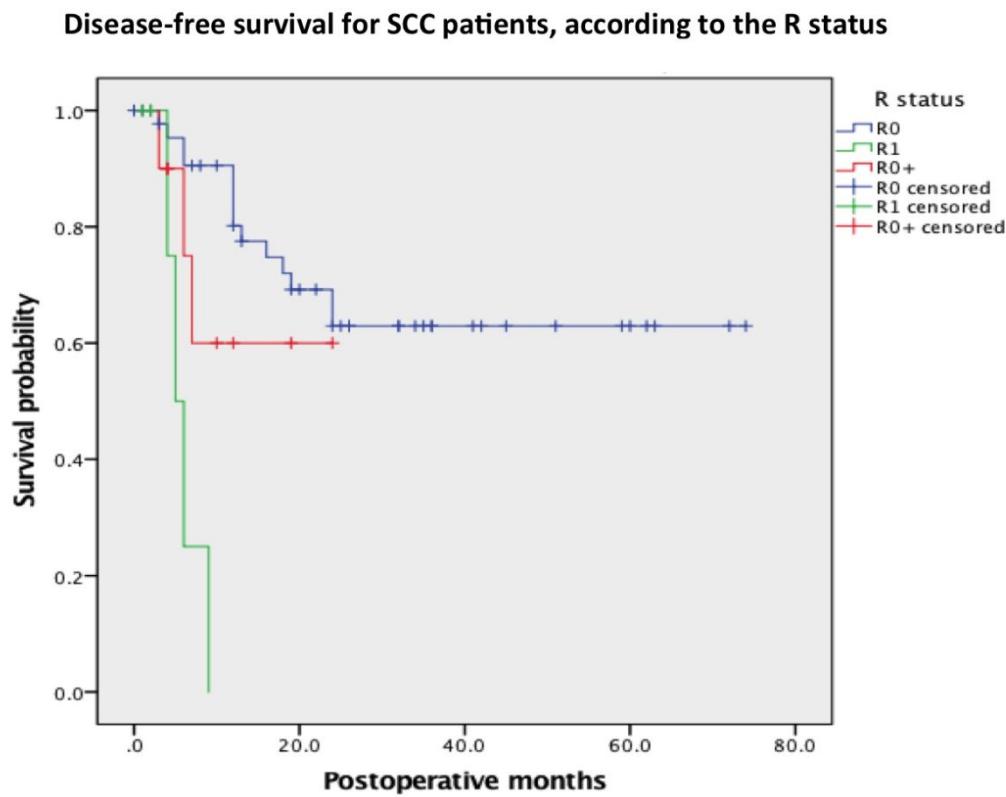


| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 45 | 30 | 13 | 6 | 0 |
| R0+ | 9 | 1 | 0 | 0 | 0 |
| R1 | 5 | 1 | 0 | 0 | 0 |

41
 42
 43
 44
 45
 46
 47
 48
 49
 50
 51
 52
 53
 54
 55
 56
 57
 58
 59
 60

Figure legend: R0 patients had a mean OS of 48.6 months (95%CI 39.4-57.7), significantly better than R0+ (median 15 months 95%CI 3.0-26.9, p=0.012) and R1 patients (median 8 months, 95%CI 0-17.6, p<0.001). The difference was not significant between R0+ and R1 patients (p=0.391).

R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm



| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 45 | 23 | 9 | 4 | 0 |
| R0+ | 9 | 1 | 0 | 0 | 0 |
| R1 | 5 | 0 | 0 | 0 | 0 |

Figure legend: R0 patients had a mean DFS of 51.6 months (95%CI 42.1-61.0), not significantly different from R0+ (mean 16.6 months 95%CI 10.1-23.2, p=0.298) and significantly better than R1 patients (median 5 months, 95%CI 3.0-6.9, p<0.001). R0+ patients had a significantly better DFS than R1 (p=0.049).

R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm

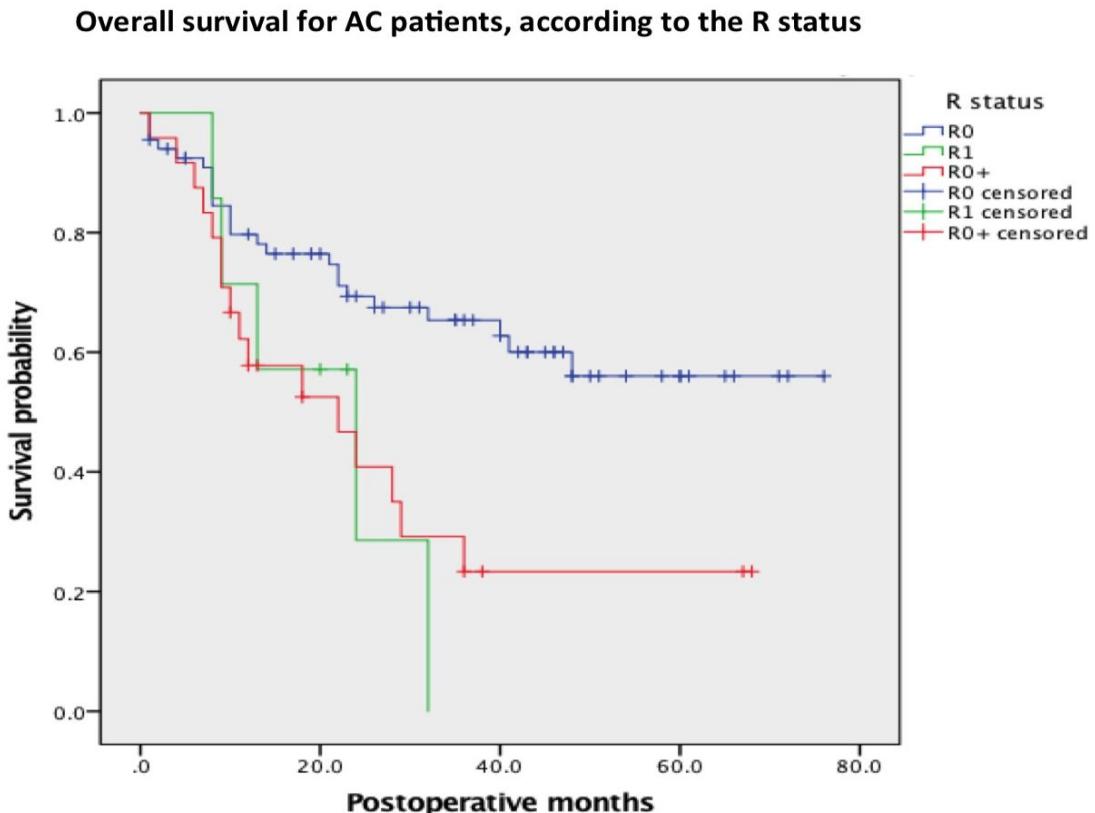
1
2
3
4 **Online appendix 4 Subgroup analysis for adenocarcinoma patients (AC)**
5
6
7

| | All patients N=98 | R0 >0.1cm N=67 | R0+ ≤0.1cm N=24 | R1 0cm N=7 | P-value |
|----------------------|----------------------|----------------------|-----------------------|------------------|---------|
| Male gender | 82 (83.7) | 55 (82.1) | 20 (83.3) | 7 (100) | 0.475 |
| Age, years | 61.5[10.2] | 60.4 [9.4] | 65.3 [11.7] | 59 [10.0] | 0.101 |
| ASA class | | | | | 0.281 |
| 1-2 | 62 (63.3) | 43 (64.2) | 17 (70.8) | 2 (28.6) | |
| 3-4 | 36 (36.7) | 24 (35.8) | 7 (29.2) | 5 (71.4) | |
| SUVmax (g/l) | 13.8[8.8] | 14.5 [10] | 12.3 [5.8] | 13.4 [4.7] | 0.581 |
| cT stage | | | | | 0.276 |
| 1 | 9 (9.2) | 9 (13.4) | 0 (0) | 0 (0) | |
| 2 | 11 (11.2) | 8 (12) | 2 (8.3) | 1 (14.3) | |
| 3 | 78 (79.6) | 50 (74.6) | 22 (91.7) | 6 (85.7) | |
| cN stage | | | | | 0.637 |
| 0 | 32 (32.7) | 22 (32.8) | 9 (37.5) | 1 (14.3) | |
| 1 | 54 (55.1) | 37 (55.2) | 11 (45.8) | 6 (85.7) | |
| 2-3 | 10 (10.2) | 6 (9) | 4 (16.7) | 0 (0) | |
| NAT | 84 (85.7) | 55 (82.1) | 22 (91.7) | 7 (100) | 0.134 |
| NAT type | | | | | 0.138 |
| Chemotherapy | 22 (22.4) | 12 (17.9) | 6 (25) | 4 (57.1) | |
| Chemoradiation | 59 (60.2) | 40 (59.7) | 16 (66.7) | 3 (42.9) | |
| Surgical approach | | | | | 0.250 |
| Lewis | 91 (92.8) | 63 (94) | 22 (91.7) | 6 (85.7) | |
| McKeown | 3 (3.1) | 3 (4.5) | 0 (0) | 0 (0) | |
| Transhiatal | 4 (4.1) | 1 (1.5) | 2 (8.3) | 1 (14.3) | |
| Severe complications | 33 (33.7) | 22 (32.8) | 9 (37.5) | 2 (28.6) | 0.878 |
| Anastomotic leakage | 31 (31.6) | 22 (32.8) | 8 (33.3) | 1 (14.3) | 0.591 |
| pT stage | | | | | <0.001 |
| 0 | 11 (11.2) | 11 (16.5) | 0 (0) | 0 (0) | |

| | | | | | |
|----|--------------------|-----------|-----------|-----------|----------|
| | | | | | |
| 1 | | | | | |
| 2 | | | | | |
| 3 | 1 | 24 (24.5) | 23 (34.3) | 1 (4.2) | 0 (0) |
| 4 | 2 | 9 (9.2) | 9 (13.4) | 0 (0) | 0 (0) |
| 5 | 3 | 54 (55.1) | 24 (35.8) | 23 (95.8) | 7 (100) |
| 6 | | | | | |
| 7 | | | | | |
| 8 | pN stage | | | | 0.001 |
| 9 | 0 | 59 (60.2) | 50 (74.6) | 8 (33.3) | 1 (14.3) |
| 10 | 1 | 20 (20.4) | 9 (13.4) | 8 (33.3) | 3 (42.9) |
| 11 | 2 | 11 (11.2) | 6 (9) | 4 (16.7) | 1 (14.3) |
| 12 | 3 | 8 (8.2) | 2 (3) | 4 (16.7) | 2 (28.6) |
| 13 | | | | | |
| 14 | | | | | |
| 15 | | | | | |
| 16 | TRG | | | | 0.001 |
| 17 | 1-2 | 49 (50) | 23 (34.3) | 20 (83.3) | 6 (85.6) |
| 18 | 3-5 | 33 (33.7) | 29 (43.2) | 3 (12.5) | 1 (14.3) |
| 19 | | | | | |
| 20 | | | | | |
| 21 | Early recurrence | 28 (28.6) | 14 (20.9) | 11 (45.8) | 3 (42.9) |
| 22 | | | | | 0.046 |
| 23 | | | | | |
| 24 | Locoregional | 16 (16.3) | 8 (11.9) | 5 (20.8) | 3 (42.9) |
| 25 | recurrence | | | | 0.043 |
| 26 | | | | | |
| 27 | | | | | |
| 28 | Distant recurrence | 36 (36.7) | 19 (28.4) | 12 (50) | 5 (71.4) |
| 29 | | | | | 0.010 |
| 30 | | | | | |

Categorical variables are expressed as N (%), and continuous variables as median [IQR].

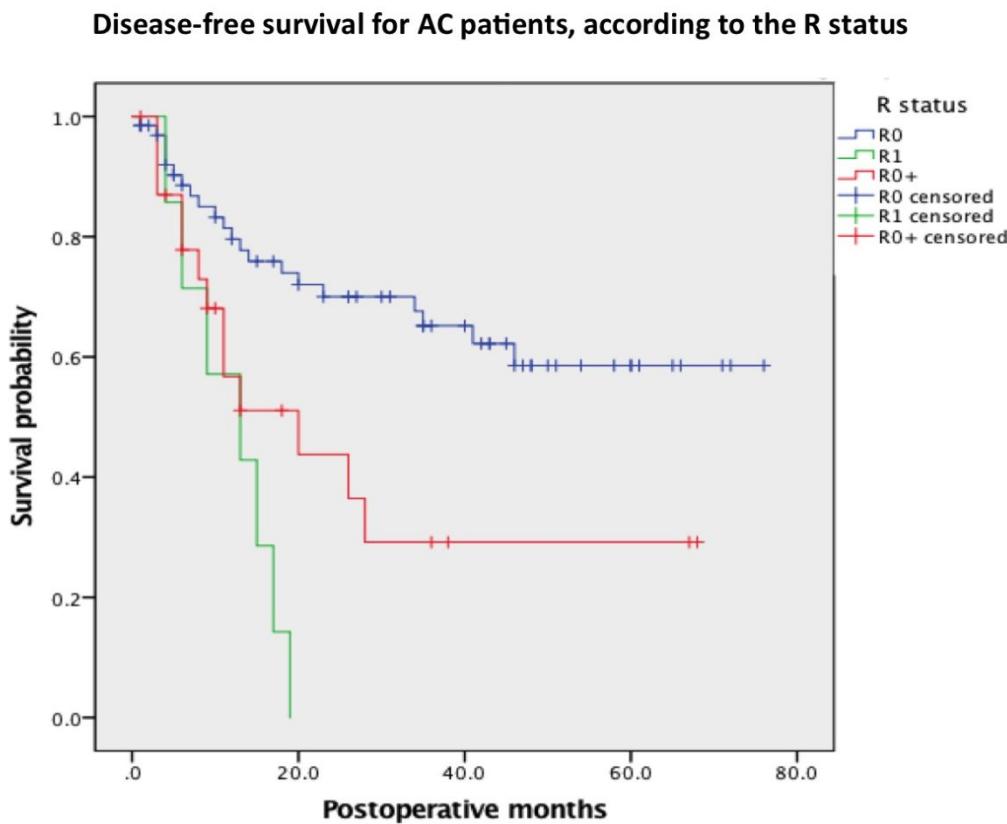
1
 2
Online appendix 5 Subgroup survival analysis for adenocarcinoma (AC)
 3
 4
 5
 6



| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 66 | 43 | 27 | 7 | 0 |
| R0+ | 23 | 4 | 0 | 0 | 0 |
| R1 | 6 | 3 | 0 | 0 | 0 |

43 Figure legend: R0 patients had a mean OS of 51.1 months (95%CI 43.2-58.9), significantly
 44 better than R0+ (median 22 months 95%CI 7.2-40.8, p=0.004) and R1 patients (median 24
 45 months, 95%CI 2.7-23.3, p=0.041). The difference was not significant between R0+ and R1
 46 patients (p=0.818).

47
 48 R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm
 49
 50
 51
 52
 53
 54
 55
 56
 57
 58
 59
 60



| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 65 | 37 | 22 | 6 | 0 |
| R0+ | 23 | 6 | 0 | 0 | 0 |
| R1 | 6 | 0 | 0 | 0 | 0 |

Figure legend: R0 patients had a mean DFS of 52.1 months (95%CI 43.9-60.2), significantly better than R0+ (median 20 months 95%CI 3.9-36.1, p=0.010) and R1 patients (median 13 months, 95%CI 2.7-23.3, p<0.001). The difference was not significant between R0+ and R1 patients (p=0.088).

R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm

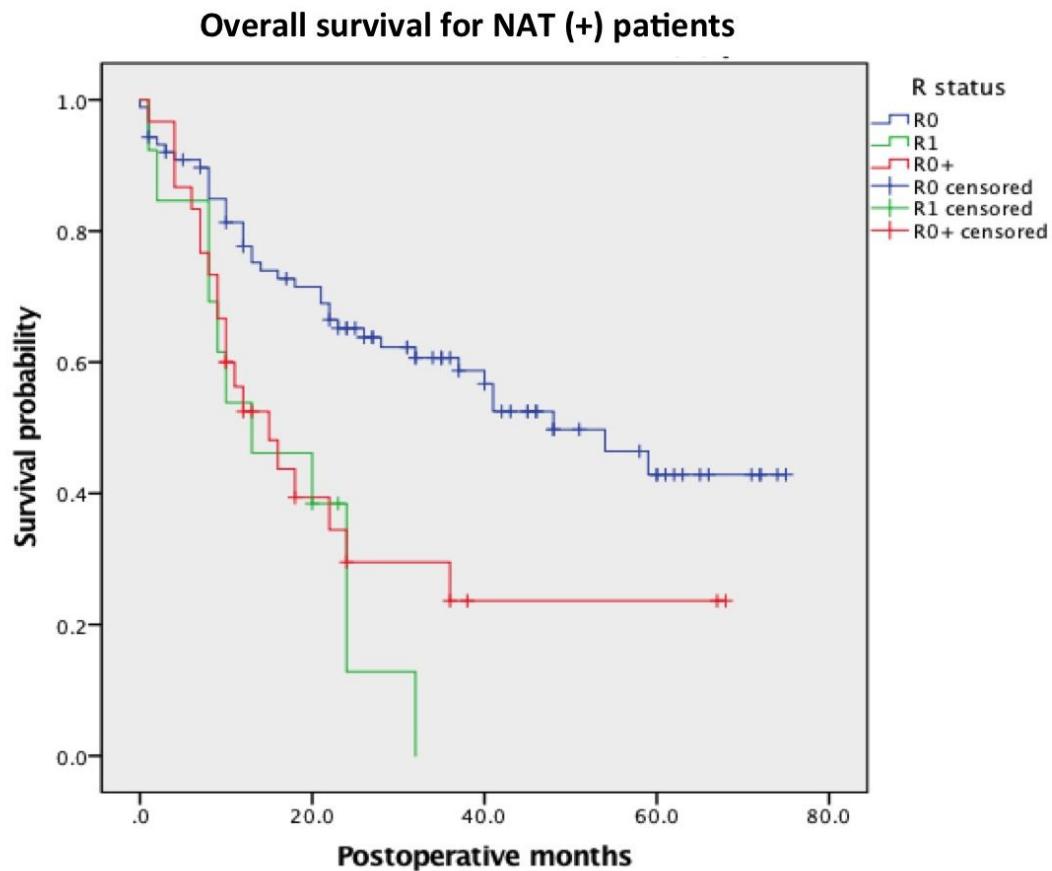
1
 2
3 Online appendix 6 Subgroup descriptive analysis for patients who received NAT (SCC and
4 AC)
 5
 6
 7

| | All patients N=131 | R0 >0.1cm N=88 | R0+ ≤0.1cm N=30 | R1 0cm N=13 | P-value |
|----------------------|-----------------------|----------------------|-----------------------|-------------------|---------|
| Male gender | 103 (78.6) | 66 (75) | 26 (86.7) | 11 (84.6) | 0.346 |
| Age, years | 62.7[9.7] | 61.8 [8.8] | 66.2 [11.4] | 60.7 [10.5] | 0.075 |
| ASA class | | | | | 0.041 |
| 1-2 | 81 (61.8) | 57 (46.8) | 21 (70) | 3 (23.1) | |
| 3-4 | 50 (38.2) | 31 (35.2) | 9 (30) | 10 (76.9) | |
| SUVmax (g/l) | 15.4 [9] | 16.4 [9.5] | 12.9 [7.2] | 15 [9.1] | 0.228 |
| cT stage | | | | | 0.653 |
| 1 | 4 (3.1) | 4 (4.5) | 0 (0) | 0 (0) | |
| 2 | 7 (5.3) | 5 (5.7) | 1 (3.3) | 1 (7.7) | |
| 3 | 120 (91.6) | 79 (89.8) | 29 (96.7) | 12 (92.3) | |
| cN stage | | | | | 0.749 |
| 0 | 31 (23.7) | 18 (20.5) | 9 (30) | 4 (30.8) | |
| 1 | 82 (62.6) | 56 (63.6) | 17 (56.7) | 9 (69.2) | |
| 2-3 | 15 (11.5) | 11 (12.5) | 4 (13.3) | 0 (0) | |
| NAT type | | | | | 0.316 |
| Chemotherapy | 24 (18.3) | 13 (14.8) | 6 (20) | 5 (38.5) | |
| Chemoradiation | 106 (80.9) | 74 (84.1) | 24 (80) | 8 (61.5) | |
| Surgical approach | | | | | 0.200 |
| Lewis | 109 (83.2) | 74 (84.1) | 26 (86.7) | 9 (69.2) | |
| McKeown | 16 (12.2) | 12 (13.6) | 2 (6.7) | 2 (15.4) | |
| Transhiatal | 6 (4.6) | 2 (2.3) | 2 (6.7) | 2 (15.4) | |
| Severe complications | 41 (31.3) | 25 (28.4) | 12 (40) | 4 (30.8) | 0.497 |
| Anastomotic leakage | 47 (35.9) | 32 (36.4) | 11 (36.7) | 4 (30.8) | 0.921 |
| pT stage | | | | | 0.001 |
| 0 | 30 (22.9) | 30 (34.1) | 0 (0) | 0 (0) | |
| 1 | 21 (16) | 20 (22.7) | 1 (3.3) | 0 (0) | |
| 2 | 9 (6.9) | 9 (10.2) | 0 (0) | 0 (0) | |

| | | | | | |
|-------------------------|-----------|-----------|-----------|-----------|-------|
| 3 | 71 (54.2) | 29 (33) | 29 (96.7) | 13 (100) | |
| pN stage | | | | | |
| 0 | 84 (64.1) | 66 (75) | 13 (43.3) | 5 (38.5) | 0.004 |
| 1 | 28 (21.4) | 15 (17) | 9 (30) | 4 (30.8) | |
| 2 | 9 (6.9) | 5 (5.7) | 2 (6.7) | 2 (15.4) | |
| 3 | 10 (7.6) | 2 (2.3) | 6 (20) | 2 (15.4) | |
| TRG | | | | | |
| 1-2 | 65 (49.6) | 29 (33) | 25 (83.3) | 11 (84.6) | 0.001 |
| 3-5 | 59 (45) | 52 (59.1) | 5 (16.7) | 2 (15.4) | |
| Early recurrence | 42 (32.1) | 19 (21.6) | 15 (50) | 8 (61.5) | 0.001 |
| Locoregional recurrence | 30 (22.9) | 16 (18.2) | 7 (23.3) | 7 (53.8) | 0.009 |
| Distant recurrence | 45 (34.4) | 24 (27.3) | 13 (43.3) | 8 (61.5) | 0.017 |

Categorical variables are expressed as N (%), and continuous variables as median (IQR).

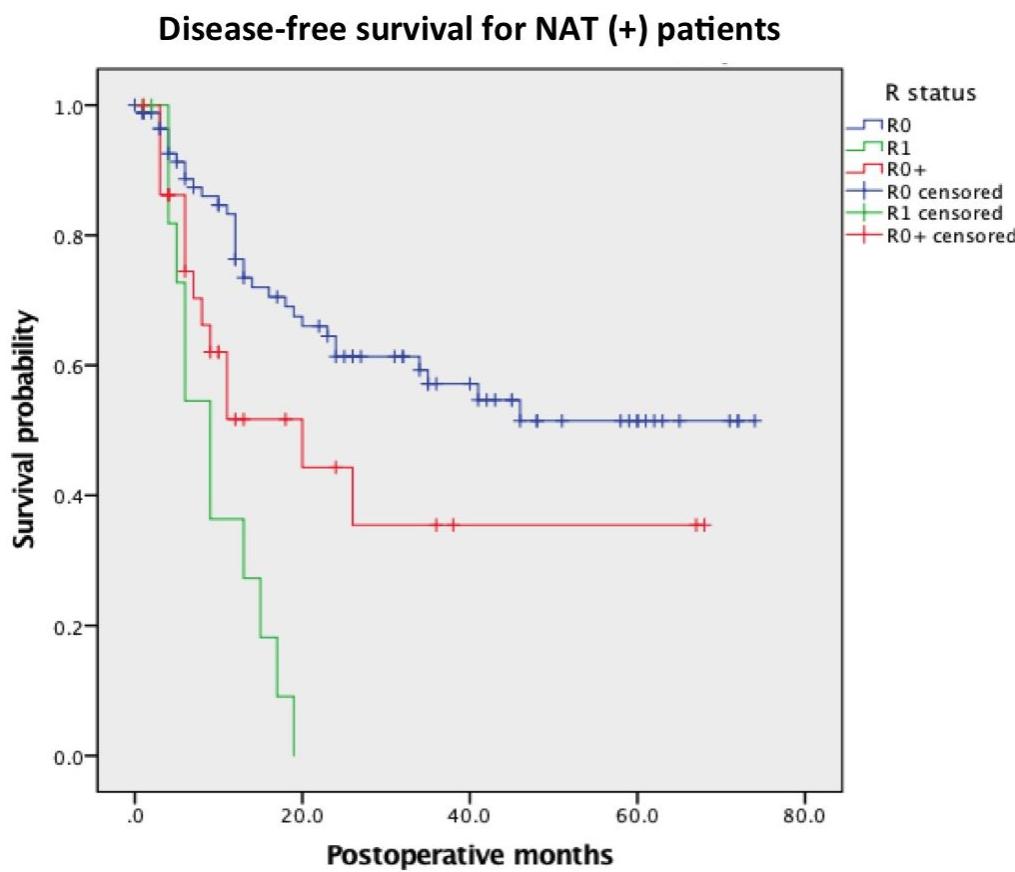
1
 2
Online appendix 7 Subgroup survival analysis for patients **who received NAT (SCC and**
 4 **AC)**
 5
 6
 7



| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 87 | 57 | 27 | 11 | 0 |
| R0+ | 29 | 8 | 1 | 0 | 0 |
| R1 | 12 | 4 | 0 | 0 | 0 |

44 Figure legend: R0 patients had a median OS of 48 months (95%CI 30.9-65.1), significantly
 45 better than R0+ (median 15 months 95%CI 7.5-22.4, p=0.002) and R1 patients (median 13
 46 months, 95%CI 0.1-25.9, p<0.001). The difference was not significant between R0+ and R1
 47 patients (p=0.461).

48
 49 R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm
 50
 51
 52
 53
 54
 55
 56
 57
 58
 59
 60



| Nb at risk | 0 mo | 20 mo | 40 mo | 60 mo | 80 mo |
|------------|------|-------|-------|-------|-------|
| R0 | 86 | 44 | 23 | 8 | 0 |
| R0+ | 29 | 6 | 1 | 0 | 0 |
| R1 | 12 | 0 | 0 | 0 | 0 |

40
41 Figure legend: R0 patients had a mean DFS of 46.6 months (95%CI 39.4-53.7), significantly
42 better than R0+ (median 20 months 95%CI 26.3-33.7, p=0.032) and R1 patients (median 9
43 months, 95%CI 5.9-12.1, p<0.001). R0+ patients had a significantly better survival than R1
44 patients (p=0.015).
45

46 R0: resection margins >1mm R0+: resection margins ≤1mm R1: resection margins 0mm
47
48
49
50
51
52
53
54
55
56
57
58
59
60