Figure S1. Flowchart of cases.
Table S1. Association of demographics and clinical characteristics of OC cancers and HPV positivity according to three different HPV-relatedness definitions: HPV-DNA, HPV-E6*I mRNA detection, and HPV-DNA/p16\(^{INK4a}\).

| Characteristics | OC samples (n = 165) | HPV-DNA detection | HPV-E6*I mRNA detection | HPV-DNA AND p16\(^{INK4a}\) detection |
|-----------------|----------------------|-------------------|--------------------------|---------------------------------------|
|                 | Positive (n = 10)   | OR crude (95%CI) | OR adjusted\(^c\)       | Positive (n = 3)                        |
| Age at diagnosis| No. (%)\(^a\)       | No. (%)\(^b\)    | OR crude (95%CI)         | OR adjusted\(^c\)                    |
| 17–54 y         | 71 (43.0)           | 5 (7.0)           | 0.99 (0.95–1.03)         | 1.02 (0.95–1.10)                     |
| 55–62 y         | 28 (17.0)           | 2 (7.1)           | 1.01 (0.9–5.57)          | 0.98 (0.93–1.05)                     |
| 63–70 y         | 27 (16.4)           | 2 (7.4)           | 1.06 (0.19–5.80)         | 0.98 (0.93–1.05)                     |
| 71–94 y         | 39 (23.6)           | 1 (2.5)           | 0.34 (0.04–3.08)         | 0.98 (0.93–1.05)                     |
| Gender          | Male 99 (60.0)      | 6 (6.1)           | 1.00 (0.27–3.69)         | 1.00 (0.27–3.69)                     |
|                 | Female 66 (40.0)    | 4 (6.1)           | 1.50 (0.07–8.39)         | 1.50 (0.07–8.39)                     |
| Period of diagnosis | 2000–2003 49 (29.7) | 1 (2.0)           | 1.19 (0.95–1.50)         | 1.19 (0.95–1.50)                     |

\(^a\) No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\) | No. (%)\(^b\)

\(^c\) Adjusted for age and gender.

1
|                | 2004–2007 | 2008–2010 |
|----------------|-----------|-----------|
|                | 68 (41.2) | 48 (29.1) |
|                | 5 (7.4)   | 4 (8.3)   |
|                | 3.81 (0.43–33.69) | 4.36 (0.47–40.55) |
|                | 2 (2.9)   | 1 (2.0)   |
|                | 1.42 (0.13–16.17) | Ref.       |
|                | 3 (4.5)   | 1 (2.1)   |
|                | 2.20 (0.322–21.84) | Ref.       |

**Tobacco behaviour**

| Category           | 2004–2007 | 2008–2010 |
|--------------------|-----------|-----------|
| Non-smoker         | 62 (37.6) | 67 (40.6) |
|                    | 4 (6.5)   | 5 (7.5)   |
|                    | Ref.      | 2.18 (0.50–9.46) |
|                    | 1 (1.6)   | 1 (1.5)   |
|                    | Ref.      | 0.62 (0.05–7.00) |
|                    | 1 (1.6)   | 1 (1.5)   |
|                    | Ref.      | Ref.      |
| Former smoker      | 31 (18.8) | 84 (50.9) |
|                    | 2 (6.5)   | 3 (3.6)   |
|                    | (0.17–5.78) | (0.08–2.69) |
|                    | 2 (6.5)   | 2 (2.4)   |
|                    | (0.37–48.31) | Ref.       |
|                    | 2 (6.5)   | 2 (2.4)   |
|                    | (0.37–48.31) | Ref.      |
| Smoker             | 63 (38.2) | 11 (6.7)  |
|                    | 2 (3.2)   | 2 (18.2)  |
|                    | (0.08–2.69) | 0 (0.0)   |
|                    | 0 (0.0)   | 0 (0.0)   |
|                    | 4.21 (0.37–48.31) | Ref.      |
| Unknown            | 9 (5.4)   | 11 (6.7)  |
|                    | 2 (22.2)  | 2 (18.2)  |
|                    | 0 (0.0)   | 0 (0.0)   |
|                    | 1 (11.1)  | 1 (9.1)   |

**Alcohol behaviour**

| Category          | 2004–2007 | 2008–2010 |
|-------------------|-----------|-----------|
| Non-drinker       | 67 (40.6) | 67 (40.6) |
|                   | 5 (7.5)   | 5 (7.5)   |
|                   | 2.18 (0.50–9.46) | 0.62 (0.05–7.00) |
|                   | 1 (1.5)   | 1 (1.5)   |
|                   | Ref.      | Ref.      |
| Former drinker    | 3 (1.8)   | 3 (1.8)   |
|                   | 0 (0.0)   | 0 (0.0)   |
|                   | –         | –         |
|                   | 0 (0.0)   | 0 (0.0)   |
|                   | –         | –         |
| Drinker           | 84 (50.9) | 84 (50.9) |
|                   | 3 (3.6)   | 3 (3.6)   |
|                   | Ref.      | Ref.      |
|                   | 2 (2.4)   | 2 (2.4)   |
|                   | Ref.      | Ref.      |
| Unknown           | 11 (6.7)  | 11 (6.7)  |
|                   | 2 (18.2)  | 2 (18.2)  |
|                   | 0 (0.0)   | 0 (0.0)   |
|                   | 1 (9.1)   | 1 (9.1)   |

**Subsite**

| Subsite          | 2004–2007 | 2008–2010 |
|------------------|-----------|-----------|
| Proximal to oropharynx | 50 (30.3) | 115 (69.7) |
|                   | 6 (12.0)  | 4 (3.5)   |
|                   | 3.78 (1.02–14.06) | 3.78 (1.02–14.06) |
|                   | 2 (4.0)   | 1 (0.9)   |
|                   | 4.75 (0.42–53.63) | Ref.      |
|                   | 2 (4.0)   | 2 (1.7)   |
|                   | 2.40 (0.33–17.58) | Ref.      |
| Distal to oropharynx | 115 (69.7) | 115 (69.7) |
|                   | 4 (3.5)   | 4 (3.5)   |
|                   | Ref.      | Ref.      |
|                   | Ref.      | Ref.      |
|                   | Ref.      | Ref.      |
|                   | Ref.      | Ref.      |
## Stage (7th edition TNM)

| Stage | Count(%) | Ref. | 1 (%) | Ref. | 1(%) | Ref. |
|-------|----------|------|-------|------|------|------|
| I     | 52(31.5) | 4(7.7) | Ref.  | 1(1.9) | Ref.  | 1(1.9) | Ref.  |
|       | (0.57)   |       |       |       |       |       |
|       | II       | 22(13.3) | 1(4.5) | 0(0.0) | –      | 0(0.0) | –      |
|       | (0.06–5.42) |       |       |       |       |       |
|       | III      | 28(17.0) | 2(7.1) | 0(0.0) | –      | 1(3.7) | 1.96(0.11–32.64) |
|       | (0.16–5.38) |       |       |       |       |       |
|       | IVa      | 62(37.6) | 3(4.8) | 2(3.2) | (0.15–19.30) | 2(3.2) | (0.15–19.29) |
|       | (0.13–2.86) |       |       |       |       |       |
|       | IVb      | 0(0.0) | –    | –     | –      | –      | –      |
|       | IVc      | 1(0.6) | 0(0.0) | –     | 0(0.0) | –      | 0(0.0) | –      |

## Treatment

| Treatment | Count(%) | Ref. | 1(%) | Ref. | 1(%) | Ref. |
|-----------|----------|------|------|------|------|------|
| Only surgery | 85(51.5) | 5(5.9) | 1.42 | (0.33–6.15) | 1(1.2) | 0.83 | (0.05–13.571) | 1(1.2) | Ref. |
| Surgery + others | 71(43.0) | 3(4.2) | Ref. | 1(1.4) | Ref. | 2(2.8) | 2.41 | (0.22–27.42) |
| No surgery | 2(1.2) | 2(100) | –    | 1(50.0) | 70.00 | (2.33–2103.43) | 1 | (100.0) | – |
| Only radio | 1(0.6) | 0(0.0) | –    | 0(0.0) | 0(0.0) | –      | – |
| Unknown    | 6(3.6) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | – |

## Histological diagnosis

| Histological diagnosis | Count(%) | Ref. | 1(%) | Ref. | 1(%) | Ref. |
|------------------------|----------|------|------|------|------|------|
| SCC                    | 112(67.9) | 5(4.5) | Ref. | 0(0.0) | – | 1 (0.9) | Ref. |
|                | Conventional non ker. | SCC Other | Other non-SCC |       |       |
|----------------|-----------------------|-----------|---------------|-------|-------|
|                | 47 (28.5)             | 6 (3.6)   | 0 (0.0)       | 2.55 (0.70–9.25) | 7.74 (0.78–76.50) |

**Tumour differentiation**

| Grade         | Count (%)        | OR     | CI       | Count (%)        | OR     | CI       |
|---------------|------------------|--------|----------|------------------|--------|----------|
| Grade 1       | 72 (43.6)        | Ref.   | 0.25     | 1 (1.4)          | Ref.   | 1.33     |
| Grade 2       | 54 (32.7)        | 1 (1.9)| 2.94     | 1 (1.9)          | Ref.   | 4.06     |
| Grade 3       | 38 (20.3)        | 2 (5.3)| 2.94     | 2 (5.4)          |       | 46.28    |
| Unknown       | 1 (0.6)          | 0 (0.0)| 0 (0.0)  | 0 (0.0)          |       | 4 (2.4)  |
| **Total**     | 165 (100.0)      | 3 (1.8)|          | 4 (2.4)          |       |          |

OC: oral cavity cancer; OR: odds ratio; Distal to oropharynx: C02 and C02.0 and C02.1 and C02.2 and C02.3 and C03.1 and C04.1 and C04.9 and C06.0; Proximal to oropharynx: C02.8 and C02.9 and C05.8 and C06.2; a column percentage. b row Percentage. c adjusted logistic regressions model using Backward Method initially including variables with crude p-value ≤ 0.25, and finally selecting variables with p-value < 0.05; bold represents statistically significant categories.
Table S2. Association of demographics and clinical characteristics of OPC cancers and HPV positivity according to three different HPV-relatedness definitions: HPV-DNA, HPV-E6*I mRNA detection, and HPV-DNA/p16\(^{INK4a}\).

| Characteristic          | OPC samples (n = 109) | HPV-DNA detection | HPV-E6*I mRNA detection | HPV-DNA AND p16\(^{INK4a}\) detection |
|-------------------------|-----------------------|-------------------|--------------------------|-----------------------------------------|
|                         | No. (%)\(^a\)         | OR crude (95%CI)  | OR adjusted\(^c\) (95%CI)| OR crude (95%CI) | OR adjusted\(^c\) (95%CI)| OR positive (n = 47) | OR adjusted\(^c\) (95%CI) |
| **Age at diagnosis**    |                       |                   |                          |                          |                          |                          |                          |
| 17–54 y                 | 25 (22.9)             | 0.97 (0.93–1.01)  | 0.94 (0.90–0.99)         | 1.00 (0.96–1.04)         | 0.99 (0.95–1.02)         |
| 55–62 y                 | 38 (34.8)             | 0.47 (0.16–1.34)  | 0.83 (0.29–2.31)         | 16 (43.2)                | 0.59 (0.22–1.66)         |
| 63–70 y                 | 24 (22.0)             | 0.28 (0.07–0.92)  | 0.63 (0.19–2.03)         | 8 (33.3)                 | 0.39 (0.12–1.25)         |
| 71–94 y                 | 22 (20.2)             | 0.39 (0.12–1.28)  | 1.06 (0.34–3.36)         | 9 (42.9)                 | 0.59 (0.18–1.89)         |
| **Gender**              |                       |                   |                          |                          |                          |                          |                          |
| Male                    | 85 (78.0)             | 42 (49.4)         | 34 (40.0)                | 37 (44.1)                |                          |                          |                          |
| Female    | 24 (22.0) | 13 (54.2) | 1.21 (0.49–3.00) | 10 (41.7) | 1.07 (0.43–2.69) | 10 (43.5) | 0.97 (0.38–2.48) |
|-----------|-----------|-----------|------------------|-----------|------------------|-----------|------------------|
| Period of diagnosis | | | | | | | |
| 2000–2003 | 41 (37.3) | 14 (34.2) | Ref. | 10 (24.4) | Ref. | 10 (25.0) | Ref. |
| 2004–2007 | 46 (42.7) | 26 (56.5) | 2.51 (1.05–5.98) | 20 (43.5) | 2.38 (0.95–5.99) | 24 (52.2) | 3.27 (1.30–8.21) |
| 2008–2010 | 22 (20.0) | 15 (68.2) | 4.13 (1.37–12.48) | 14 (63.6) | 5.43 (1.76–16.69) | 13 (61.9) | 4.85 (1.57–15.16) |
| Tobacco behaviour | | | | | | | |
| Non-smoker | 21 (19.3) | 13 (61.9) | 3.35 (1.17–9.60) | 3.95 (1.26–12.39) | 12 (57.1) | 4.97 (1.67–14.79) | 5.15 (1.65–16.08) | 13 (61.9) | 5.76 (1.91–17.41) | 5.91 (1.88–18.65) |
| Former smoker | 22 (20.2) | 16 (72.3) | 5.49 (1.82–16.54) | 7.22 (2.15–24.21) | 13 (59.1) | 5.38 (1.83–15.85) | 5.32 (1.65–10.08) | 15 (68.2) | 7.59 (2.48–23.26) | 7.69 (2.36–25.05) |
| Smoker | 52 (47.7) | 17 (32.7) | Ref. | Ref. | 11 (21.2) | Ref. | Ref. | 11 (22.0) | Ref. | Ref. |
| Unknown | 14 (12.8) | 9 (64.3) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) | 8 (57.1) |
|                | 26 (23.8) | 15 (57.7) | 1.59 (0.64–4.02) | 12 (46.2) | 1.49 (0.59–3.76) | 14 (53.8) | 1.92 (0.76–4.88) |
|----------------|-----------|-----------|------------------|-----------|------------------|-----------|------------------|
| Non-drinker    |           |           |                  |           |                  |           |                  |
| Former drinker | 3 (2.8)   | 0 (0.0)   | –                | 0 (0.0)   | –                | 0 (0.0)   | –                |
| Drinker        | 63 (57.8) | 29 (46.0) | Ref.             | 36.5      | Ref.             | 37.7      | Ref.             |
| Unknown        | 17 (15.6) | 11 (64.7) | (52.9)           |           |                  | (58.8)    |                  |

**Subsite**

|                | 49 (45.0) | 30 (61.2) | 3.32 (1.29–8.55) | 27 (55.1) | 5.11 (1.78–14.67) | 27 (56.3) | 5.14 (1.78–14.86) |
|----------------|-----------|-----------|------------------|-----------|------------------|-----------|------------------|
| Tonsil         |           |           |                  |           |                  |           |                  |
| BOT            | 28 (26.6) | 15 (51.7) | 2.25 (0.79–6.41) | 11 (37.9) | 2.54 (0.79–8.16) | 14 (48.3) | 3.73 (1.18–11.83) |
| Other          | 31 (28.4) | 10 (32.3) | Ref.             | 19.4      | Ref.             | 20.0      | Ref.             |
| oropharynx     |           |           |                  |           |                  |           |                  |

**Stage (7th edition TNM)**

|                | 12 (11.0) | 7 (58.3) | Ref.             | 3 (25.0) | Ref.             | 4 (33.3) | Ref.             |
|----------------|-----------|-----------|------------------|-----------|------------------|-----------|------------------|
| I              |           |           |                  |           |                  |           |                  |
| II             | 12 (11.0) | 4 (33.3)  | 0.36 (0.07–1.88) | 3 (25.0) | 1.00 (0.15–6.34) | 3 (25.0) | 0.67 (0.11–3.93) |
| III            | 22 (20.2) | 13 (59.1) | 1.03 (0.25–4.30) | 12 (54.6) | 3.60 (0.76–17.01)| 11 (55.0) | 2.44 (0.55–10.83) |
| IVa  | 51 (46.8) | 27 (52.9) | 0.80 (0.23–2.87) | 22 (43.1) | 2.28 (0.55–9.41) | 25 (49.0) | 1.92 (0.51–7.20) |
|-----|---------|---------|-----------------|---------|-----------------|---------|-----------------|
| IVb  | 8 (7.3) | 3 (37.5) | 0.43 (0.07–2.68) | 3 (37.5) | 1.80 (0.26–12.5) | 3 (37.5) | 1.20 (0.19–7.77) |
| IVc  | 4 (3.7) | 1 (25.0) | 0.24 (0.02–3.01) | 1 (25.0) | 1.00 (0.07–13.64) | 1 (25.0) | 0.67 (0.05–8.64) |

| Treatment                  |                |                |                |                |                |                |                |
|---------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Only surgery              | 22 (20.2)      | 8 (36.4)       | 1.33 (0.27–6.65) | 3 (13.6)       | 0.37 (0.06–2.27) | 6 (27.3)       | 0.88 (0.17–4.54) |
| Surgery + others          | 41 (37.6)      | 20 (48.8)      | 2.22 (0.50–9.81) | 16 (39.0)      | 1.49 (0.34–6.63) | 18 (43.9)      | 1.83 (0.41–8.07) |
| No surgery                | 29 (26.6)      | 20 (69.0)      | **5.19 (1.08–24.79)** | 19 (65.5) | 4.43 (0.94–20.98) | 17 (62.9)      | 3.97 (0.83–18.91) |
| Only radio                | 10 (9.2)       | 3 (30.0)       | Ref.            | 3 (30.0)       | Ref.            | 3 (30.0)       | Ref.            |
| Unknown                   | 7 (6.4)        | 4 (57.1)       |                | 3 (42.9)       |                | 3 (42.9)       |                |

| Histological diagnosis   |                |                |                |                |                |                |                |
|--------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| SCC                      | 28 (25.7)      | 10 (35.7)      | Ref.           | 2 (7.1)        | Ref.           | 4 (14.3)       | Ref.           |
| Conventional keratinizing|               |                |                |                |                |                |                |
| Type          | Value 1 | Value 2 | Value 3  |
|--------------|---------|---------|----------|
| SCC Conventional non ker. | 52 (47.7) | 23 (44.2) | 1.43 (0.55–3.68) |
| SCC Other     | 22 (20.2) | 18 (81.8) | 8.10 (2.14–30.65) |
| Other non-SCC | 7 (6.4)   | 4 (57.1)  | 2.40 (0.45–12.94) |

**Tumour differentiation**

| Grade | Value 1 | Value 2 | Value 3   |
|-------|---------|---------|-----------|
| Grade 1 | 9 (8.3) | 3 (33.3) | Ref. (0.0) |
| Grade 2 | 30 (27.5) | 16 (53.3) | 2.29 (0.48–10.88) |
| Grade 3 | 67 (61.5) | 34 (50.8) | 2.06 (0.48–8.93) |
| Unknown | 3 (2.7)  | 2 (66.7)  | Ref. (66.7) |

OPC: oropharyngeal cancer; OR: odds ratio; Tonsil: C02.4 and C09.0 and C09.1 and C09.9; BOT: base of the tongue (C01); Other oropharynx: C10 and C10.0 and C10.2 and C10.3 and C10.8 and C10.9; *column percentage; row percentage; adjusted logistic regressions model using Backward Method initially including variables with crude p-value ≤ 0.25, and finally selecting variables with p-value < 0.05; bold represents statistically significant categories.
Table S3. Association of demographics and clinical characteristic of LC cancers and HPV positivity according to three different HPV-relatedness definitions: HPV-DNA, HPV-E6*I mRNA detection, and HPV-DNA/p16\(^{INK4a}\).

| Characteristics       | LC samples (n = 401) | HPV-DNA detection (n = 29) | HPV-E6*I mRNA detection (n = 9) | HPV-DNA AND p16\(^{INK4a}\) detection (n = 7) |
|-----------------------|----------------------|-----------------------------|-------------------------------|---------------------------------|
|                       | Positive | OR crude | (95%CI) | Positive | OR crude | (95%CI) | Positive | OR crude | (95%CI) |
| Age at diagnosis      |          |          |         |          |          |         |          |          |         |
| 17–54 y               | 70 (17.5) | 9 (12.9) | 1.84 (0.67–5.03) | 5 (7.1) | 8.23 (0.94–72.02) | 4 (5.8) | 6.58 (0.72–60.19) |
| 55–62 y               | 115 (28.7) | 9 (7.8) | 1.06 (0.39–2.86) | 3 (2.6) | 2.87 (0.29–27.98) | 2 (1.7) | 1.89 (0.17–21.19) |
| 63–70 y               | 108 (26.9) | 3 (2.8) | 0.36 (0.92–1.38) | 0 (0.0) | – | 0 (0.0) | – |
| 71–94 y               | 108 (26.9) | 8 (7.4) | Ref. | 1 (0.9) | Ref. | 1 (0.9) | Ref. |          |          |
| Gender                |          |          |         |          |          |         |          |          |         |
| Male                  | 355 (88.5) | 25 (7.0) | Ref. | 6 (1.7) | Ref. | 5 (1.4) | Ref. |          |          |
| Female                | 46 (11.5) | 4 (8.7) | 1.26 (0.42–3.79) | 3 (6.5) | 4.06 (0.98–16.82) | 2 (4.4) | 3.26 (0.61–17.28) |
| Period of diagnosis   |          |          |         |          |          |         |          |          |         |
| 2000–2003             | 147 (36.7) | 6 (4.1) | Ref. | 2 (1.4) | Ref. | 0 (0.0) | – |          |          |
| 2004–2007             | 170 (42.4) | 17 (10.0) | 2.61 (1.00–6.81) | 4 (2.4) | 1.75 (0.32–9.68) | 4 (2.4) | Ref. |          |          |
|                | 2008–2010 | 2008–2010 | 2008–2010 | 2008–2010 | 2008–2010 | 2008–2010 |
|----------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                |           |           |           |           |           |           |
| Tobacco        |           |           |           |           |           |           |
| behaviour      |           |           |           |           |           |           |
| Non-smoker     | 84 (20.9)| 6 (7.1)   | 1.81 (0.56–5.79) | 3 (3.6) | 2.69 (0.44–16.40) | 3 (3.6) | 1.52 (0.33–6.99) |
| Former smoker  | 11 (2.7) | 2 (18.2)  | 3.42 (0.70–16.82) | 2 (18.2) | 13.15 (2.33–74.29) | 20.11 (2.77–145.58) | 1 (10.0) | 7.91 (0.83–74.81) |
| Smoker         | 361 (90.0)| 22 (6.1)  | 3.35 (1.16–9.66) | 1 (3.6) | 2.19 (0.25–18.87) | 5.11 (0.51–50.86) | 1 (3.6) | 2.64 (0.30–23.38) |
| Unknown        | 1 (0.2)  | 0 (0.0)   | Ref.       | Ref.      | 6 (1.7)   | Ref.      | 5 (1.4) | Ref.    |
| Alcohol        |           |           |           |           |           |           |
| behaviour      |           |           |           |           |           |           |
| Non-drinker    | 28 (7.0) | 5 (17.9)  | 3.35 (1.16–9.66) | 1 (3.6) | 2.19 (0.25–18.87) | 5.11 (0.51–50.86) | 1 (3.6) | 2.64 (0.30–23.38) |
| Former drinker | 3 (0.7)  | 1 (33.3)  | –          | 0 (0.0)   | –         | 1 (33.3)  | Ref.    | Ref.    |
| Drinker        | 115 (28.7)| 6 (5.2)   | 0.70 (0.27–1.79) | 3 (2.6) | 1.44 (0.34–6.13) | 2 (1.7) | 1.19 (0.21–6.59) |
| Unknown        | 3 (0.7)  | 1 (33.3)  | –          | 0 (0.0)   | –         | 1 (33.3)  | Ref.    | Ref.    |
| Subsite        |           |           |           |           |           |           |
| Proximal to    | 97 (24.2)| 7 (7.2)   | 1.00 (0.41–2.43) | 4 (4.1) | 2.57 (0.68–9.78) | 3 (3.1) | 2.42 (0.53–11.00) |
| oropharynx     | 304 (75.8)| 22 (7.2)  | Ref.       | 5 (1.6)   | Ref.      | 4 (1.3) | Ref.    | Ref.    |
| Distal to      |           |           |           |           |           |           |
| oropharynx     |           |           |           |           |           |           |
| Stage (7th edition TNM) | | | | | | |
| I              | 158 (39.4)| 8 (5.1)   | Ref.       | 3 (1.9)   | Ref.      | 2 (1.3) | Ref.    |
| II             | 98 (24.4)| 8 (8.2)   | 1.67 (0.60–4.60) | 2 (2.0) | 1.08 (0.18–6.56) | 1 (1.0) | 0.80 (0.07–8.99) |
|                  | III     | IVa     | IVb     | IVc     | Treatment                | Histological diagnosis | Tumour differentiation |
|------------------|---------|---------|---------|---------|--------------------------|------------------------|------------------------|
|                  | 77 (19.2) | 63 (15.7) | 5 (1.2) | 0 (0.0) | 267 (66.6) | 195 (48.6) | 106 (26.4) |
|                  | 8 (10.4)  | 5 (7.9)  | 0 (0.0) | –       | 18 (6.7)    | 12 (6.2)   | 3 (2.8)    |
|                  | 2.17 (0.78–6.03) | 1.62 (0.51–5.14) | –       | –       | 2 (2.6)    | 1.44 (0.64–3.25) | 0.97 (0.26–3.59) | 3.81 (0.39–36.82) |
|                  | 19.4 (0.23–8.42) | 2.3 (0.58–9.12) | –       | –       | 1.38 (0.52–19.33) | 0.51 (0.10–2.67) | 0.78 (0.09–6.79) | 9.5 (0.89–101.06) | 1 (20.0) |
|                  | 3 (3.9) | 2 (3.2) | 0 (0.0) | –       | 3 (0.78) | 2 (1.3) | 1 (2.0) |
|                  | 3.16 (0.52–19.33) | 1.69 (0.28–10.39) | –       | –       | 0.85 (0.35–23.48) | 0.51 (0.10–2.67) | 0.78 (0.09–6.79) | 9.5 (0.89–101.06) | 1 (20.0) |
|                  | 6 (2.2) | 0 (0.0) | 0 (0.0) | –       | 0 (0.0) | 0 (0.0) | 1 (20.0) |
|                  | 0 (0.0) | –       | 0 (0.0) | –       | 0 (0.0) | 1 (12.5) | 1 (20.0) |
|                  | 0.0 | 0.0 | 0.0 | –       | 0.0 | 1 (12.5) | 1 (20.0) |

**Histological diagnosis**

|                  | SCC Conventional keratinizing | SCC Conventional non keratinizing | SCC Other | Other non-SCC |
|------------------|-------------------------------|---------------------------------|-----------|---------------|
|                  | 195 (48.6) | 151 (37.7) | 50 (12.5) | 5 (1.2) |
|                  | 12 (6.2) | 13 (8.6) | 3 (6.0) | 1 (20.0) |
|                  | Ref. | Ref. | 0.97 (0.26–3.59) | 3.81 (0.39–36.82) |
|                  | 0.51 (0.10–2.67) | 2 (1.3) | 1 (2.0) | 1 (20.0) |
|                  | 2 (1.3) | 2 (1.3) | 1 (2.0) | 1 (20.0) |
|                  | 0.86 (0.14–5.24) | 1.31 (0.13–12.83) | 16.00 (1.35–189.21) | 16.00 (1.35–189.21) |

**Tumour differentiation**

|                  | Grade 1 |
|------------------|---------|
|                  | 106 (26.4) | 1 (20.0) |
|                  | 3 (2.8) | 1 (20.0) |
|                  | Ref. | Ref. |
|                  | 1 (0.9) | 0 (0.0) |
|        | Grade 2 | Grade 3 | Unknown | Total |
|--------|---------|---------|---------|-------|
|        |         |         |         |       |
| n      | 162 (40.4) | 128 (31.9) | 5 (1.2) | 401 (100.0) |
| %      | 12 (7.4) | 14 (10.9) | 0 (0.0) | 29 (7.2)  |
|        | 2.75 (0.76–9.98) | 4.22 (1.18–15.09) | 4 (3.1) | 9 (2.2)  |
| OR     | 2.66 (0.29–24.11) | 3.39 (0.37–30.77) | 5 (3.9) | 7 (1.8)  |
| CI     | 2 (1.2) | 5 (3.9) | 0 (0.0) |       |

LC: laryngeal cancer; OR: odds ratio; Distal to oropharynx: C02 and C02.0 and C02.1 and C02.2 and C02.3 and C03.1 and C04.1 and C04.9 and C06.0; Proximal to oropharynx: C02.8 and C02.9 and C05.8 and C06.2; a column percentage; b row percentage; c adjusted logistic regressions model using Backward Method initially including variables with crude p-value ≤ 0.25, and finally selecting variables with p-value < 0.05; bold represents statistically significant categories.

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