

## **Supplementary Information**

### **Article title**

Skeletal muscle status and survival among patients with advanced biliary tract cancer

### **Journal name**

International Journal of Clinical Oncology

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**Supplementary Table 1** Clinical characteristics of patients with advanced biliary tract cancer according to sex-specific quartiles of SMI change or SMD change in two months

| Characteristic <sup>a</sup> | Total<br>(n=297) | SMI change in two months (n=297) <sup>b</sup> |              |              |                           | <i>P</i> value | SMD change in two months (n=248) <sup>b</sup> |              |              |                           | <i>P</i> value |
|-----------------------------|------------------|-----------------------------------------------|--------------|--------------|---------------------------|----------------|-----------------------------------------------|--------------|--------------|---------------------------|----------------|
|                             |                  | Q1<br>More loss<br>(n=75)                     | Q2<br>(n=74) | Q3<br>(n=75) | Q4<br>Less loss<br>(n=73) |                | Q1<br>More loss<br>(n=63)                     | Q2<br>(n=61) | Q3<br>(n=63) | Q4<br>Less loss<br>(n=61) |                |
| Age, years                  | 70.2 ± 10.8      | 71.8 ± 9.8                                    | 70.0 ± 9.4   | 69.1 ± 10.7  | 70.1 ± 12.9               | 0.48           | 72.0 ± 9.6                                    | 67.2 ± 12.0  | 69.7 ± 12.7  | 72.1 ± 9.0                | 0.045          |
| Sex                         |                  |                                               |              |              |                           | 0.99           |                                               |              |              |                           | 0.99           |
| Female                      | 114 (38%)        | 29 (39%)                                      | 28 (38%)     | 29 (39%)     | 28 (38%)                  |                | 24 (38%)                                      | 23 (38%)     | 24 (38%)     | 23 (38%)                  |                |
| Male                        | 183 (62%)        | 46 (61%)                                      | 46 (62%)     | 46 (61%)     | 45 (62%)                  |                | 39 (62%)                                      | 38 (62%)     | 39 (62%)     | 38 (62%)                  |                |
| BMI, kg/m <sup>2</sup>      | 22.1 ± 3.5       | 22.1 ± 3.9                                    | 22.4 ± 2.9   | 22.7 ± 3.9   | 21.5 ± 3.1                | 0.20           | 22.4 ± 3.3                                    | 21.8 ± 3.2   | 22.3 ± 3.8   | 21.9 ± 3.4                | 0.69           |
| Diabetes mellitus           |                  |                                               |              |              |                           | 0.64           |                                               |              |              |                           | 0.18           |
| Absent                      | 221 (74%)        | 58 (77%)                                      | 53 (72%)     | 53 (71%)     | 57 (78%)                  |                | 42 (67%)                                      | 51 (84%)     | 48 (76%)     | 47 (77%)                  |                |
| Present                     | 76 (26%)         | 17 (23%)                                      | 21 (28%)     | 22 (29%)     | 16 (22%)                  |                | 21 (33%)                                      | 10 (16%)     | 15 (24%)     | 14 (23%)                  |                |
| ECOG PS                     |                  |                                               |              |              |                           | 0.13           |                                               |              |              |                           | 0.85           |
| 0                           | 133 (45%)        | 31 (41%)                                      | 34 (46%)     | 42 (56%)     | 26 (36%)                  |                | 26 (41%)                                      | 31 (51%)     | 30 (48%)     | 24 (39%)                  |                |
| 1                           | 146 (49%)        | 39 (52%)                                      | 37 (50%)     | 31 (41%)     | 39 (53%)                  |                | 32 (51%)                                      | 27 (44%)     | 30 (48%)     | 32 (52%)                  |                |
| 2-4                         | 18 (6.1%)        | 5 (6.7%)                                      | 3 (4.1%)     | 2 (2.7%)     | 8 (11%)                   |                | 5 (7.9%)                                      | 3 (4.9%)     | 3 (4.8%)     | 5 (8.2%)                  |                |
| Primary tumor site          |                  |                                               |              |              |                           | 0.99           |                                               |              |              |                           | 0.52           |
| Intrahepatic bile duct      | 82 (28%)         | 21 (28%)                                      | 21 (28%)     | 22 (29%)     | 18 (25%)                  |                | 22 (35%)                                      | 16 (26%)     | 15 (24%)     | 21 (34%)                  |                |
| Extrahepatic bile duct      | 143 (48%)        | 36 (48%)                                      | 33 (45%)     | 36 (48%)     | 38 (52%)                  |                | 24 (38%)                                      | 29 (48%)     | 33 (52%)     | 31 (51%)                  |                |
| Gallbladder                 | 60 (20%)         | 15 (20%)                                      | 16 (22%)     | 14 (19%)     | 15 (21%)                  |                | 16 (25%)                                      | 14 (23%)     | 12 (19%)     | 7 (11%)                   |                |
| Ampulla                     | 12 (4.0%)        | 3 (4.0%)                                      | 4 (5.4%)     | 3 (4.0%)     | 2 (2.7%)                  |                | 1 (1.6%)                                      | 2 (3.3%)     | 3 (4.8%)     | 2 (3.3%)                  |                |
| Cancer status               |                  |                                               |              |              |                           | 0.071          |                                               |              |              |                           | 0.41           |
| Localized                   | 62 (21%)         | 17 (23%)                                      | 13 (18%)     | 13 (17%)     | 19 (26%)                  |                | 11 (17%)                                      | 15 (25%)     | 12 (19%)     | 16 (26%)                  |                |
| Metastatic                  | 119 (40%)        | 36 (48%)                                      | 33 (45%)     | 22 (29%)     | 28 (38%)                  |                | 31 (49%)                                      | 19 (31%)     | 28 (44%)     | 27 (44%)                  |                |
| Recurrent                   | 116 (39%)        | 22 (29%)                                      | 28 (38%)     | 40 (53%)     | 26 (36%)                  |                | 21 (33%)                                      | 27 (44%)     | 23 (37%)     | 18 (30%)                  |                |
| Treatment                   |                  |                                               |              |              |                           | 0.037          |                                               |              |              |                           | 0.31           |
| Gem/CDDP                    | 144 (48%)        | 33 (44%)                                      | 39 (53%)     | 37 (49%)     | 35 (48%)                  |                | 27 (43%)                                      | 32 (52%)     | 29 (46%)     | 32 (52%)                  |                |
| Gem/S-1                     | 21 (7.1%)        | 5 (6.7%)                                      | 9 (12%)      | 2 (2.7%)     | 5 (6.8%)                  |                | 3 (4.8%)                                      | 4 (6.6%)     | 7 (11%)      | 3 (4.9%)                  |                |
| Gem                         | 55 (19%)         | 15 (20%)                                      | 9 (12%)      | 14 (19%)     | 17 (23%)                  |                | 15 (24%)                                      | 8 (13%)      | 12 (19%)     | 14 (23%)                  |                |
| S-1                         | 20 (6.7%)        | 4 (5.3%)                                      | 3 (4.1%)     | 8 (11%)      | 5 (6.8%)                  |                | 2 (3.2%)                                      | 3 (4.9%)     | 4 (6.3%)     | 4 (6.6%)                  |                |

|                                                |                  |                  |                  |                  |                  |        |                  |                  |                  |                  |       |
|------------------------------------------------|------------------|------------------|------------------|------------------|------------------|--------|------------------|------------------|------------------|------------------|-------|
| FOLFIRINOX                                     | 15 (5.1%)        | 3 (4.0%)         | 7 (9.5%)         | 5 (6.7%)         | 0 (0%)           |        | 4 (6.3%)         | 7 (11%)          | 2 (3.2%)         | 2 (3.3%)         |       |
| Radiation                                      | 12 (4.0%)        | 1 (1.3%)         | 2 (2.7%)         | 3 (4.0%)         | 6 (8.2%)         |        | 1 (1.6%)         | 2 (3.3%)         | 5 (7.9%)         | 1 (1.6%)         |       |
| Best supportive care                           | 30 (10%)         | 14 (19%)         | 5 (6.8%)         | 6 (8.0%)         | 5 (6.8%)         |        | 11 (17%)         | 5 (8.2%)         | 4 (6.3%)         | 5 (8.2%)         |       |
| CEACAM5 (CEA), ng/mL                           | 4.6 (2.9-10.9)   | 5.5 (3.5-17.1)   | 5.3 (3.0-11.6)   | 4.0 (2.8-8.1)    | 4.3 (2.8-7.8)    | 0.15   | 7.1 (3.1-33.4)   | 5.1 (2.8-11.3)   | 3.9 (2.9-6.7)    | 4.7 (3.0-10.9)   | 0.079 |
| CA19-9, U/mL                                   | 179<br>(29-775)  | 276<br>(50-1815) | 93<br>(25-788)   | 89<br>(30-619)   | 264<br>(48-722)  | 0.14   | 242<br>(25-1348) | 224<br>(25-743)  | 73<br>(27-630)   | 371<br>(57-1318) | 0.13  |
| mGPS                                           |                  |                  |                  |                  |                  | 0.006  |                  |                  |                  |                  | 0.23  |
| 0                                              | 186 (65%)        | 36 (50%)         | 45 (63%)         | 53 (73%)         | 52 (73%)         |        | 38 (61%)         | 40 (69%)         | 40 (66%)         | 33 (57%)         |       |
| 1                                              | 26 (9.1%)        | 8 (11%)          | 6 (8.5%)         | 10 (14%)         | 2 (2.8%)         |        | 10 (16%)         | 5 (8.6%)         | 2 (3.3%)         | 6 (10%)          |       |
| 2                                              | 75 (26%)         | 28 (39%)         | 20 (28%)         | 10 (14%)         | 17 (24%)         |        | 14 (23%)         | 13 (22%)         | 19 (31%)         | 19 (33%)         |       |
| Cholinesterase, U/L                            | 228<br>(185-277) | 226<br>(177-279) | 229<br>(193-271) | 259<br>(226-314) | 193<br>(147-243) | <0.001 | 231<br>(192-279) | 246<br>(181-279) | 222<br>(185-271) | 206<br>(179-244) | 0.48  |
| Total cholesterol, mg/dL                       | 176<br>(144-211) | 168<br>(144-198) | 169<br>(132-207) | 187<br>(155-216) | 195<br>(147-223) | 0.48   | 191<br>(152-218) | 165<br>(148-206) | 163<br>(134-195) | 185<br>(147-215) | 0.33  |
| NLR                                            | 2.9 (2.0-4.3)    | 3.3 (2.3-4.3)    | 2.6 (2.0-4.4)    | 3.0 (2.1-4.2)    | 2.5 (1.8-4.3)    | 0.57   | 3.3 (2.1-4.3)    | 3.0 (2.3-4.2)    | 2.6 (2.1-3.8)    | 2.8 (1.8-4.3)    | 0.70  |
| Biliary drainage in two months                 |                  |                  |                  |                  |                  | 0.072  |                  |                  |                  |                  | 0.084 |
| Absent                                         | 161 (54%)        | 36 (48%)         | 45 (61%)         | 47 (63%)         | 33 (45%)         |        | 32 (51%)         | 40 (66%)         | 33 (52%)         | 26 (43%)         |       |
| Present                                        | 136 (46%)        | 39 (52%)         | 29 (39%)         | 28 (37%)         | 40 (55%)         |        | 31 (49%)         | 21 (34%)         | 30 (48%)         | 35 (57%)         |       |
| Cholangitis in two months                      |                  |                  |                  |                  |                  | 0.027  |                  |                  |                  |                  | 0.46  |
| Absent                                         | 221 (74%)        | 47 (63%)         | 62 (84%)         | 58 (77%)         | 54 (74%)         |        | 42 (67%)         | 46 (75%)         | 49 (78%)         | 47 (77%)         |       |
| Present                                        | 76 (26%)         | 28 (37%)         | 12 (16%)         | 17 (23%)         | 19 (26%)         |        | 21 (33%)         | 15 (25%)         | 14 (22%)         | 14 (23%)         |       |
| Treatment response                             |                  |                  |                  |                  |                  | 0.073  |                  |                  |                  |                  | 0.11  |
| Partial response                               | 29 (11%)         | 7 (12%)          | 9 (13%)          | 9 (14%)          | 4 (6.5%)         |        | 3 (5.9%)         | 7 (13%)          | 8 (15%)          | 5 (9.1%)         |       |
| Stable disease                                 | 161 (63%)        | 29 (48%)         | 43 (64%)         | 44 (67%)         | 45 (73%)         |        | 27 (53%)         | 32 (59%)         | 36 (67%)         | 39 (71%)         |       |
| Progressive disease                            | 65 (25%)         | 24 (40%)         | 15 (22%)         | 13 (20%)         | 13 (21%)         |        | 21 (41%)         | 15 (28%)         | 10 (19%)         | 11 (20%)         |       |
| Time between baseline and follow-up CT, months | 2.5 (2.0-3.3)    | 2.6 (2.0-3.3)    | 2.3 (2.0-2.8)    | 2.8 (2.1-3.4)    | 2.7 (2.1-3.5)    | 0.023  | 2.4 (2.0-3.0)    | 2.4 (2.1-3.0)    | 2.5 (2.1-3.5)    | 2.7 (2.1-3.4)    | 0.29  |

<sup>a</sup> Data are presented as mean  $\pm$  standard deviation, median (interquartile range), or number of patients (%). Percentage indicates the proportion of patients with a specific characteristic in all cases or in strata of quartiles of SMI change or SMD change in two months.

<sup>b</sup> SMI change in two months were categorized into Q1 (-33.0 to -11.1%), Q2 (-11.0 to -5.6%), Q3 (-5.5 to -0.2%), and Q4 (-0.1 to +16.0%) for males and Q1 (-18.7 to -7.7%), Q2 (-7.6 to -3.1%), Q3 (-3.0 to +2.4%), and Q4 (+2.5 to +34.0%) for females. SMD change in two months were categorized into Q1 (-32.5 to -9.1%), Q2 (-8.8 to -1.7%), Q3 (-1.6 to +4.2%), and Q4 (+4.3 to +31.6%) for males and Q1 (-60.5 to -8.4%), Q2(-8.1 to -0.8%), Q3 (-0.4 to +6.2%), and Q4 (+6.7 to +66.3%) for females.

Abbreviations: BMI, body mass index; CA19-9, carbohydrate antigen 19-9; CDDP, cisplatin; CEA, carcinoembryonic antigen; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; Gem, gemcitabine; mGPS, modified Glasgow prognostic score; NLR, neutrophil-to-lymphocyte ratio; PS, performance status; Q1-4, quartiles 1-4; SMD, skeletal muscle density; SMI, skeletal muscle index

**Supplementary Table 2** Sarcopenia and SMD at baseline in relation to survival among patients with advanced biliary tract cancer (the final multivariable models)

|                                     | Multivariable HR <sup>a</sup> (95% CI) |                              |                 | Multivariable HR <sup>a</sup> (95% CI) |                              |
|-------------------------------------|----------------------------------------|------------------------------|-----------------|----------------------------------------|------------------------------|
|                                     | Progression-free survival              | Overall survival             |                 | Progression-free survival              | Overall survival             |
| Sarcopenia <sup>b</sup> at baseline |                                        |                              | SMD at baseline |                                        |                              |
| Absent                              | 1 (referent)                           | 1 (referent)                 | Q4 (highest)    | 1 (referent)                           | 1 (referent)                 |
| Present                             | 1.56 (1.13-2.17)                       | 1.23 (0.99-1.53)             | Q3              | 1.05 (0.69-1.59)                       | 1.09 (0.78-1.52)             |
|                                     |                                        |                              | Q2              | 1.43 (0.95-2.17)                       | 1.10 (0.79-1.54)             |
|                                     |                                        |                              | Q1 (lowest)     | 1.50 (0.94-2.39)                       | 1.54 (1.09-2.18)             |
| BMI                                 |                                        |                              |                 |                                        |                              |
| 18.5-25.0                           | 1 (referent)                           | Did not remain in this model |                 | Did not remain in this model           | Did not remain in this model |
| <18.5                               | 0.51 (0.31-0.84)                       |                              |                 |                                        |                              |
| >25.0                               | 1.48 (0.98-2.24)                       |                              |                 |                                        |                              |
| ECOG PS                             |                                        |                              |                 |                                        |                              |
| 0                                   | Did not remain in this model           | 1 (referent)                 |                 | Did not remain in this model           | 1 (referent)                 |
| 1-4                                 |                                        | 1.49 (1.19-1.87)             |                 |                                        | 1.48 (1.17-1.88)             |
| Primary tumor site                  |                                        |                              |                 |                                        |                              |
| Intrahepatic                        | 1 (referent)                           | 1 (referent)                 |                 | 1 (referent)                           | 1 (referent)                 |
| Extrahepatic                        | 1.03 (0.71-1.48)                       | 0.95 (0.71-1.27)             |                 | 0.84 (0.58-1.21)                       | 0.92 (0.68-1.25)             |
| Gallbladder                         | 2.23 (1.46-3.40)                       | 1.62 (1.18-2.22)             |                 | 1.87 (1.23-2.86)                       | 1.51 (1.09-2.10)             |
| Ampulla                             | 2.27 (1.11-4.63)                       | 0.70 (0.41-1.20)             |                 | 1.26 (0.53-3.00)                       | 0.62 (0.34-1.14)             |
| Cancer status                       |                                        |                              |                 |                                        |                              |
| Localized or recurrent              | Did not remain in this model           | 1 (referent)                 |                 | Did not remain in this model           | 1 (referent)                 |
| Metastatic                          |                                        | 1.48 (1.14-1.93)             |                 |                                        | 1.59 (1.21-2.09)             |
| Treatment                           |                                        |                              |                 |                                        |                              |
| Combination chemotherapy            | Did not remain in this model           | 1 (referent)                 |                 | Did not remain in this model           | 1 (referent)                 |
| Single agent chemotherapy           |                                        | 1.39 (1.05-1.84)             |                 |                                        | 1.32 (0.98-1.78)             |
| Radiation                           |                                        | 0.58 (0.29-1.18)             |                 |                                        | 0.60 (0.30-1.22)             |
| Best supportive care                |                                        | 2.66 (1.93-3.67)             |                 |                                        | 2.62 (1.86-3.69)             |
| CA19-9                              |                                        |                              |                 |                                        |                              |
| Q1 (lowest)                         | Did not remain                         | 1 (referent)                 |                 | Did not remain                         | 1 (referent)                 |

|              |                  |                  |                  |                  |
|--------------|------------------|------------------|------------------|------------------|
| Q2           | in this model    | 0.90 (0.66-1.22) | in this model    | 0.91 (0.66-1.26) |
| Q3           |                  | 1.15 (0.84-1.57) |                  | 1.21 (0.88-1.68) |
| Q4 (highest) |                  | 1.63 (1.19-2.21) |                  | 1.65 (1.20-2.28) |
| mGPS         |                  |                  |                  |                  |
| 0            | 1 (referent)     | Did not remain   | 1 (referent)     | Did not remain   |
| 1            | 2.11 (1.28-3.46) | in this model    | 1.94 (1.16-3.23) | in this model    |
| 2            | 1.64 (1.15-2.35) |                  | 1.41 (0.99-2.02) |                  |
| NLR          |                  |                  |                  |                  |
| Q1 (lowest)  | Did not remain   | 1 (referent)     | Did not remain   | 1 (referent)     |
| Q2           | in this model    | 1.10 (0.81-1.49) | in this model    | 1.09 (0.79-1.50) |
| Q3           |                  | 1.27 (0.92-1.75) |                  | 1.18 (0.84-1.66) |
| Q4 (highest) |                  | 1.87 (1.35-2.58) |                  | 1.65 (1.17-2.33) |

<sup>a</sup> The multivariable Cox regression model initially included age, sex, body mass index, diabetes mellitus, PS, primary tumor site, cancer status, receipt of treatment, CA19-9, mGPS, and NLR. A backward elimination with a threshold *P* of 0.05 was conducted to select variables for the final models.

<sup>b</sup> Sarcopenia was defined according to the cut-off values of Japan Society of Hepatology guidelines [1]: SMI < 42 cm<sup>2</sup>/m<sup>2</sup> for males and SMI < 38 cm<sup>2</sup>/m<sup>2</sup> for females.

Abbreviations: CA19-9, carbohydrate antigen 19-9; CI, confidential interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; mGPS, modified Glasgow prognostic score; NLR, neutrophil-to-lymphocyte ratio; PS, performance status; Q1-4, quartiles 1-4; SMD, skeletal muscle density; SMI, skeletal muscle index

**Supplementary Table 3** SMI at baseline in relation to survival among patients with advanced biliary tract cancer

|                                        | Progression-free survival |               |                         |                                        | Overall survival |               |                         |                                        |
|----------------------------------------|---------------------------|---------------|-------------------------|----------------------------------------|------------------|---------------|-------------------------|----------------------------------------|
|                                        | No. of cases              | No. of events | Univariable HR (95% CI) | Multivariable HR <sup>a</sup> (95% CI) | No. of cases     | No. of events | Univariable HR (95% CI) | Multivariable HR <sup>a</sup> (95% CI) |
| SMI at baseline                        |                           |               |                         |                                        |                  |               |                         |                                        |
| Q4 (highest)                           | 75                        | 42            | 1 (referent)            | 1 (referent)                           | 96               | 84            | 1 (referent)            | 1 (referent)                           |
| Q3                                     | 77                        | 55            | 1.03 (0.69-1.54)        | 1.09 (0.71-1.68)                       | 97               | 88            | 0.91 (0.68-1.23)        | 0.94 (0.69-1.27)                       |
| Q2                                     | 71                        | 48            | 0.83 (0.55-1.25)        | 0.88 (0.55-1.40)                       | 96               | 85            | 0.79 (0.59-1.07)        | 0.83 (0.61-1.13)                       |
| Q1 (lowest)                            | 68                        | 44            | 1.36 (0.89-2.08)        | 1.86 (1.12-3.09)                       | 97               | 91            | 1.37 (1.02-1.85)        | 1.36 (1.00-1.86)                       |
| <i>P</i> <sub>trend</sub> <sup>b</sup> |                           |               | 0.40                    | 0.16                                   |                  |               | 0.29                    | 0.74                                   |

<sup>a</sup> The multivariable Cox regression model initially included age, sex, body mass index, diabetes mellitus, performance status, primary tumor site, cancer status, receipt of treatment, carbohydrate antigen 19-9, modified Glasgow prognostic score, and neutrophil-to-lymphocyte ratio. A backward elimination with a threshold *P* of 0.05 was conducted to select variables for the final models.

<sup>b</sup> *P*<sub>trend</sub> was calculated by entering quartile-specific median values of SMI at baseline (continuous) in the Cox regression model.

Abbreviations: CI, confidential interval; HR, hazard ratio; Q1-4, quartiles 1-4; SMI, skeletal muscle index

**Supplementary Table 4** SMI change and SMD change in two months in relation to survival among patients with advanced biliary tract cancer (the final multivariable models)

|                           | Multivariable HR <sup>a</sup> (95% CI) |                              |                          | Multivariable HR <sup>a</sup> (95% CI) |                              |
|---------------------------|----------------------------------------|------------------------------|--------------------------|----------------------------------------|------------------------------|
|                           | Progression-free survival              | Overall survival             |                          | Progression-free survival              | Overall survival             |
| SMI change in two months  |                                        |                              | SMD change in two months |                                        |                              |
| Q4 (less loss)            | 1 (referent)                           | 1 (referent)                 | Q4 (less loss)           | 1 (referent)                           | 1 (referent)                 |
| Q3                        | 0.96 (0.63-1.46)                       | 0.84 (0.60-1.20)             | Q3                       | 1.25 (0.78-2.02)                       | 1.17 (0.78-1.75)             |
| Q2                        | 0.97 (0.65-1.45)                       | 0.81 (0.56-1.17)             | Q2                       | 1.33 (0.82-2.16)                       | 0.84 (0.56-1.26)             |
| Q1 (more loss)            | 0.95 (0.60-1.50)                       | 1.65 (1.16-2.35)             | Q1 (more loss)           | 1.83 (1.13-2.95)                       | 1.20 (0.80-1.79)             |
| BMI                       |                                        |                              |                          |                                        |                              |
| 18.5-25.0                 | Did not remain in this model           | Did not remain in this model |                          | 1 (referent)                           | Did not remain in this model |
| <18.5                     |                                        |                              |                          | 0.70 (0.41-1.21)                       |                              |
| >25.0                     |                                        |                              |                          | 1.68 (1.07-2.66)                       |                              |
| Primary tumor site        |                                        |                              |                          |                                        |                              |
| Intrahepatic              | 1 (referent)                           | 1 (referent)                 |                          | 1 (referent)                           | 1 (referent)                 |
| Extrahepatic              | 0.96 (0.67-1.38)                       | 1.13 (0.82-1.55)             |                          | 1.25 (0.80-1.96)                       | 0.97 (0.68-1.37)             |
| Gallbladder               | 1.85 (1.23-2.78)                       | 1.78 (1.23-2.58)             |                          | 2.32 (1.45-3.73)                       | 1.64 (1.09-2.47)             |
| Ampulla                   | 1.76 (0.85-3.65)                       | 1.12 (0.58-2.15)             |                          | 1.71 (0.69-4.28)                       | 0.84 (0.39-1.81)             |
| Cancer status             |                                        |                              |                          |                                        |                              |
| Localized or recurrent    | Did not remain in this model           | Did not remain in this model |                          | 1 (referent)                           | Did not remain in this model |
| Metastatic                |                                        |                              |                          | 1.46 (1.02-2.09)                       |                              |
| Treatment                 |                                        |                              |                          |                                        |                              |
| Combination chemotherapy  | Did not remain in this model           | 1 (referent)                 |                          | Did not remain in this model           | 1 (referent)                 |
| Single agent chemotherapy |                                        | 1.26 (0.94-1.70)             |                          |                                        | 1.23 (0.90-1.69)             |
| Radiation                 |                                        | 0.55 (0.27-1.15)             |                          |                                        | 0.37 (0.15-0.93)             |
| Best supportive care      |                                        | 2.20 (1.39-3.47)             |                          |                                        | 2.38 (1.45-3.90)             |
| CA19-9                    |                                        |                              |                          |                                        |                              |
| Q1 (lowest)               | Did not remain in this model           | 1 (referent)                 |                          | Did not remain in this model           | 1 (referent)                 |
| Q2                        |                                        | 0.90 (0.63-1.29)             |                          |                                        | 0.92 (0.61-1.40)             |
| Q3                        |                                        | 1.06 (0.74-1.51)             |                          |                                        | 1.26 (0.85-1.88)             |
| Q4 (highest)              |                                        | 1.84 (1.30-2.59)             |                          |                                        | 1.81 (1.24-2.64)             |

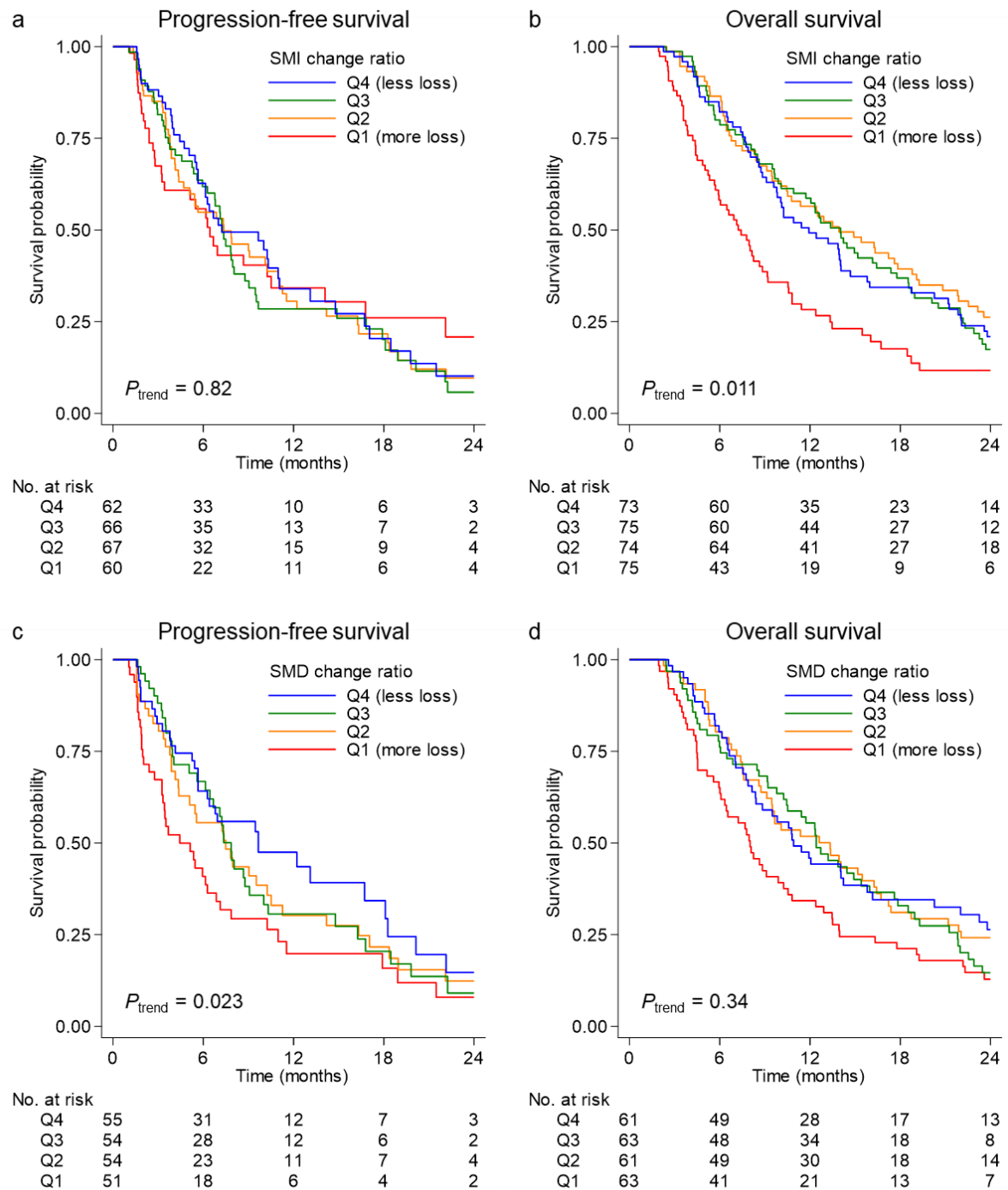
|              |                                 |                                 |                                 |                                 |
|--------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| mGPS         |                                 |                                 |                                 |                                 |
| 0            | 1 (referent)                    | Did not remain<br>in this model | 1 (referent)                    | Did not remain<br>in this model |
| 1            | 2.10 (1.25-3.53)                |                                 | 2.23 (1.30-3.83)                |                                 |
| 2            | 1.54 (1.08-2.19)                |                                 | 1.62 (1.08-2.42)                |                                 |
| NLR          |                                 |                                 |                                 |                                 |
| Q1 (lowest)  | Did not remain<br>in this model | 1 (referent)                    | Did not remain<br>in this model | 1 (referent)                    |
| Q2           |                                 | 1.12 (0.80-1.57)                |                                 | 1.06 (0.73-1.55)                |
| Q3           |                                 | 1.40 (0.98-2.00)                |                                 | 1.32 (0.88-1.98)                |
| Q4 (highest) |                                 | 1.95 (1.34-2.84)                |                                 | 1.85 (1.22-2.80)                |

<sup>a</sup> The multivariable Cox regression model initially included age, sex, body mass index, diabetes mellitus, PS, primary tumor site, cancer status, receipt of treatment, CA19-9, mGPS, and NLR. A backward elimination with a threshold *P* of 0.05 was conducted to select variables for the final models.

Abbreviations: CA19-9, carbohydrate antigen 19-9; CI, confidential interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; mGPS, modified Glasgow prognostic score; NLR, neutrophil-to-lymphocyte ratio; PS, performance status; Q1-4, quartiles 1-4; SMD, skeletal muscle density; SMI, skeletal muscle index

## Reference

1. Nishikawa H, Shiraki M, Hiramatsu A, et al (2016) Japan Society of Hepatology guidelines for sarcopenia in liver disease (1st edition): Recommendation from the working group for creation of sarcopenia assessment criteria. *Hepatol Res* 46:951-63



**Supplementary Fig. 1** Kaplan-Meier survival curves of patients with advanced biliary tract cancer according to serial change of skeletal muscle status. a and b. Progression-free and overall survival, respectively, by SMI change in two months. c and d. Progression-free and overall survival, respectively, by SMD change in two months.

SMD, skeletal muscle density; SMI, skeletal muscle index