Influence of Body Mass Index, Smoking, and Blood Pressure on Survival of Patients with Surgically-Treated, Low Stage Renal Cell Carcinoma: A 14-Year Retrospective Cohort Study

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Received: 5 September 2012
Accepted: 26 December 2012

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INTRODUCTION

Obesity, cigarette smoking, and hypertension are three well-established risk factors for developing renal cell carcinoma (RCC), and epidemiological studies have consistently suggested evidence for an association between these risk factors and the etiology of RCC (1-3). However, the influence of these risk factors on prognosis and survival in patients with RCC has not been well studied, especially before the early 2000s. Recently, a number of studies have provided evidence that being overweight or obese, as measured by the body mass index, is a favorable prognostic factor in patients with RCC (4-11). A few studies have shown that smoking may increase the risk of mortality in patients with RCC (12-14), but there have been very few studies and inconsistent conclusions concerning blood pressure (15, 16). The prognostic value of smoking and blood pressure for RCC survival therefore remains unclear, compared to the increasing awareness of body mass index as a prognostic factor.

The current literature does not contain any studies that fully evaluate the association between these three major risk parameters and overall or cancer-specific survival in patients with RCC.

The association of body mass index, smoking, and blood pressure, which are related to the three well-established risk factors of renal cell carcinoma, and survival in patients with renal cell carcinoma is not much studied. Our objective was to evaluate this association. A cohort of 1,036 patients with low stage (pT1 and pT2) renal cell carcinoma who underwent radical or partial nephrectomy were enrolled. We retrospectively reviewed medical records and collected survival data. The body mass index, smoking status, and blood pressure at the time of surgery were recorded. Patients were grouped according to their obesity grade, smoking status, and hypertension stage. Survival analysis showed a significant decrease in overall (P = 0.001) and cancer-specific survival (P < 0.001) with being underweight, with no differences of smoking status or perioperative blood pressure. On multivariate analysis, perioperative blood pressure ≥ 160/100 mmHg (HR, 2.642; 95% CI, 1.221-5.720) and being underweight (HR, 4.320; 95% CI, 1.557-11.984) were independent predictors of overall and cancer-specific mortality, respectively. Therefore, it is concluded that being underweight and perioperative blood pressure ≥ 160/100 mmHg negatively affect cancer-specific and overall survival, respectively, while smoking status does not influence survivals in patients with renal cell carcinoma.

Key Words: Carcinoma, Renal Cell; Body Mass Index; Smoking; Blood Pressure; Survival

Furthermore, most of the studies in the literature were conducted for RCC with all pathologic T stages (T1-T4). Therefore, the association of the three risk parameters and the survival of low stage (pT1 and pT2) RCC is still unclear. Our objective was to assess the influence of body mass index, smoking, and blood pressure on overall and cancer-specific survival in patients with pT1 and pT2 RCC.

MATERIALS AND METHODS

Data collection
A total of 1,545 patients with RCC who underwent radical or partial nephrectomy between October 1994 and December 2008 were initially selected. The exclusion criteria were: 1) pediatric patients (age under 20 yr); 2) pT3 and pT4 stage renal cell carcinoma; and 3) less than 12 months of follow-up. Patients with clinical lymph node positivity or distant metastasis on preoperative imaging were included because they were not pathologically proven preoperatively. Therefore, a cohort of 1,036 patients was finally enrolled in this study. We retrospectively reviewed the medical records of the cohort, and then followed them to...
obtain survival and the cause of death data available from the Department of Medical Records in our hospital and the Korea National Statistics Office. The designated endpoint date was December 31, 2008. Body mass index, smoking status, and blood pressure at the time of surgery were recorded. The body mass index was calculated by a single author using height and weight of the patients measured preoperatively. Smoking status was interviewed by ward nurses before surgery and recorded on medical records. Blood pressure was measured pre- and postoperatively on a daily basis and a single author calculated the mean value of three consecutive blood pressures measured one day before surgery and two consecutive postoperative days. The duration of survival was calculated from the date of surgery to the date of death or to the study endpoint. Other demographic covariates including cancer stage and Fuhrman grade were collected. The stage for RCC was recorded based on the 2010 7th edition American Joint Committee on Cancer (AJCC) TNM staging system. Pathologic T stage was obtained from the pathologic documentation of surgical specimen. Because not all patients underwent lymphadenectomies or metastasectomies, clinical N and M stage were obtained from preoperative and follow-up imaging studies such as computed tomography and bone scans.

The obesity grade was classified using the World Health Organization (WHO) recommendation for Asians based on body mass index (underweight < 18.5 kg/m²; normal weight ≥ 18.5 to < 23 kg/m²; overweight ≥ 23 to < 27.5 kg/m²; obese ≥ 27.5 kg/m²²) (17). Smoking status was recorded as non-smoker, former smoker, or current smoker. The perioperative blood pressure was classified using the definition of hypertension stage from the Joint National Committee-7 (JNC-7) (blood pressure: normal < 120/80 mmHg; prehypertension 120-139/80-89 mmHg; stage 1 hypertension 140-159/90-99 mmHg; stage 2 hypertension ≥ 160/100 mmHg) (18). All patients were grouped according to these classifications.

Statistical methods
To compare the distribution of important clinical and pathologic covariates across each of the three risk factors, we employed one-way analysis of variance (ANOVA), chi-square tests, and Fisher's exact tests. A life table analysis was conducted by plotting survival curves and statistical significance was deduced by the Gehan’s Wilcoxon test. A Cox proportional hazards regression model was used for multivariate analysis. Step-wise regression techniques were used to build multivariate models using a significance level of 0.15 for the variable to remain in the model. Also, covariates with no significance on univariate analysis were also included in the model if they were those that the authors intended to know the association with patient survival. All analyses were performed using SPSS v.19.0 (SPSS Inc., Chicago, IL, USA), and a P value < 0.05 was considered statistically significant.

Ethics statement
The study protocol was approved by the institutional review board of the Samsung Medical Center (IRB File No. 2011-07-061). Informed consent was waived by the board.

RESULTS
Baseline demographic data of the entire cohort are summarized in Table 1.

### Body mass index
Of the 1,036 cohort in our study, 23 patients (2.2%) were categorized as underweight (< 18.5 kg/m²), 863 (83.3%) categorized as normal weight (≥ 18.5 to < 23 kg/m²), 893 (86.2%) categorized as overweight (≥ 23 to < 27.5 kg/m²), and 893 (86.2%) categorized as obese (≥ 27.5 kg/m²²).

### Smoking status
Smoking status was recorded as non-smoker, former smoker, or current smoker. The perioperative blood pressure was classified using the definition of hypertension stage from the Joint National Committee-7 (JNC-7) (blood pressure: normal < 120/80 mmHg; prehypertension 120-139/80-89 mmHg; stage 1 hypertension 140-159/90-99 mmHg; stage 2 hypertension ≥ 160/100 mmHg) (18). All patients were grouped according to these classifications.

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rized as underweight, 288 (27.8%) as normal weight, 555 (53.6%) as overweight, and 170 (16.4%) as obese (Table 2). Significant differences were noted in age, sex, the American Society of Anesthesiologists (ASA) class, perioperative blood pressure, history of hypertension, type of surgery, and pathologic T stage.

As shown in the life table survival plots (Fig. 1A), the overall and cancer-specific survivals significantly decreased with being underweight compared to being normal, overweight, and obese ($P = 0.001$ for overall survival; $P < 0.001$ for cancer-specific survival). The overall and cancer-specific survivals five years after surgery were 73% and 73% for underweight, 90% and 92% for overweight, and 90% and 93% for obese patients, respectively. There were no significant differences in overall and cancer-specific survival between the normal and overweight, and overweight and obese groups.

### Smoking

A total of 732 patients (70.7%) were categorized as non-smokers, 38 (3.6%) as former smokers, and 266 (25.7%) as current smokers (Table 3). Significant differences were noted in age, sex, ASA class, history of hypertension, type of surgery, and histologic subtype. At survival analysis, the overall and cancer-specific survivals 5 yr after surgery were 90% and 92% for non-smokers, 87% and 92% for former smokers, and 94% and 94% for current smokers, respectively. The life table survival plots did not reveal any significant differences in overall ($P = 0.138$) and cancer-specific survival among the groups classified by obesity grade.

### Table 2. Comparison of clinicopathologic features among groups classified by obesity grade

| Parameters                        | Underweight (n = 23) | Normal weight (n = 288) | Overweight (n = 555) | Obese (n = 170) | $P$ value |
|-----------------------------------|----------------------|-------------------------|----------------------|-----------------|-----------|
| Mean age ± SD, yr                 | 56.7 ± 15.3          | 51.4 ± 12.2             | 54.4 ± 11.6          | 53.3 ± 11.2     | 0.003*    |
| Sex (%)                           |                      |                         |                      |                 |           |
| Female                            | 10 (43.5)            | 111 (38.5)              | 142 (25.8)           | 51 (30.0)       |           |
| Male                              | 13 (66.5)            | 177 (61.5)              | 413 (74.4)           | 119 (70.0)      |           |
| Mean ASA class ± SD               | 1.8 ± 0.6            | 1.5 ± 0.6               | 1.6 ± 0.6            | 1.7 ± 0.6       | 0.015*    |
| Perioperative BP (%)              |                      |                         |                      |                 |           |
| < 120/80 mmHg                     | 8 (34.8)             | 97 (33.7)               | 122 (22.9)           | 27 (15.9)       |           |
| 120-139/80-89 mmHg                | 10 (43.5)            | 127 (44.1)              | 252 (45.4)           | 71 (41.8)       |           |
| 140-159/90-99 mmHg                | 2 (8.7)              | 51 (17.7)               | 130 (23.4)           | 58 (34.1)       |           |
| ≥ 160/100 mmHg                    | 3 (13.0)             | 13 (4.5)                | 51 (9.2)             | 14 (8.2)        |           |
| Smoking (%)                       |                      |                         |                      |                 | 0.812*    |
| Ever (former & current)           | 6 (26.1)             | 90 (31.2)               | 157 (28.3)           | 51 (30.0)       |           |
| Never                             | 17 (73.9)            | 198 (68.8)              | 398 (71.7)           | 119 (70.0)      |           |
| Symptoms at presentation (%)      |                      |                         |                      |                 | 0.107*    |
| Present                           | 11 (47.8)            | 94 (32.6)               | 153 (27.6)           | 49 (28.8)       |           |
| Absent                            | 12 (52.2)            | 194 (67.4)              | 402 (72.4)           | 121 (71.2)      |           |
| History of DM (%)                 |                      |                         |                      |                 | 0.062*    |
| Present                           | 1 (4.3)              | 27 (9.4)                | 66 (11.9)            | 29 (17.1)       |           |
| Absent                            | 22 (95.7)            | 261 (90.6)              | 489 (88.1)           | 141 (82.9)      |           |
| History of hypertension (%)       |                      |                         |                      |                 | < 0.001† |
| Present                           | 4 (17.4)             | 52 (18.1)               | 174 (31.4)           | 72 (42.4)       |           |
| Absent                            | 19 (82.6)            | 236 (81.9)              | 381 (68.6)           | 96 (57.6)       |           |
| Type of surgery (%)               |                      |                         |                      |                 | 0.030†    |
| Radical nephrectomy               | 22 (95.7)            | 239 (83.0)              | 439 (79.1)           | 126 (74.1)      |           |
| Partial nephrectomy               | 1 (4.3)              | 49 (17.0)               | 116 (20.9)           | 44 (25.9)       |           |
| Histologic subtype (%)            |                      |                         |                      |                 | 0.088†    |
| Conventional                      | 17 (73.9)            | 240 (83.3)              | 485 (87.4)           | 151 (88.8)      |           |
| Nonconventional                   | 6 (26.1)             | 48 (16.7)               | 70 (12.6)            | 19 (11.2)       |           |
| Sarcomatoid variant (%)           |                      |                         |                      |                 | 0.975†    |
| Present                           | 0 (0)                | 2 (0.7)                 | 3 (0.5)              | 1 (0.6)         |           |
| Absent                            | 23 (100)             | 286 (99.3)              | 552 (95.5)           | 169 (99.4)      |           |
| Fuhrman grade (%)                 |                      |                         |                      |                 | 0.838†    |
| Low (G1 & G2)                     | 12 (52.2)            | 154 (53.5)              | 302 (54.4)           | 98 (57.6)       |           |
| High (G3 & G4)                    | 11 (47.8)            | 134 (46.5)              | 253 (45.6)           | 72 (42.4)       |           |
| Pathologic T stage (%)            |                      |                         |                      |                 | < 0.001† |
| T1                                | 13 (56.5)            | 221 (76.7)              | 482 (87.9)           | 146 (85.9)      |           |
| T2                                | 10 (43.5)            | 67 (23.3)               | 72 (13.0)            | 24 (14.1)       |           |
| Clinical LN positivity (%)        |                      |                         |                      |                 | 0.655†    |
| Present                           | 3 (13.0)             | 31 (10.8)               | 47 (8.5)             | 15 (8.8)        |           |
| Absent                            | 20 (87.0)            | 257 (89.2)              | 508 (91.5)           | 155 (91.2)      |           |
| Distant metastasis (%)            |                      |                         |                      |                 | 0.216†    |
| Present                           | 2 (8.7)              | 8 (2.8)                 | 11 (2.0)             | 4 (2.4)         |           |
| Absent                            | 21 (91.3)            | 280 (97.2)              | 544 (98.0)           | 166 (97.6)      |           |

*One-way ANOVA; †Chi-square and Fisher’s exact test. SD, standard deviation; ASA, American Society of Anesthesiologists; BP, blood pressure; DM, diabetes mellitus; LN, lymph node.
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Blood pressure

A total of 254 patients (24.5%) were categorized as normal blood pressure (< 120/80 mmHg), 460 (44.4%) as prehypertension (120-139/80-89 mmHg), 241 (23.3%) as stage 1 hypertension (140-159/90-99 mmHg), and 81 (7.8%) as stage 2 hypertension (≥ 160/100 mmHg). Age, sex, ASA class, obesity grade, history of diabetes mellitus, and history of hypertension differed among the four groups (Table 4). At survival analysis, the overall and cancer-specific survivals five years after surgery were 92% and 94% for normal blood pressure, 91% and 93% for prehypertension, 91% and 93% for stage 1 hypertension, and 84% and 92% for stage 2 hypertension, respectively. Life table survival plots

Fig. 1. Life table survival plots according to obesity grade (A), smoking status (B), and perioperative blood pressure (C) with regard to the overall and cancer-specific survival in patients with surgically treated, low stage (pT1 and pT2) renal cell carcinoma.
did not reveal any significant differences in overall \((P = 0.162)\) and cancer-specific survivals \((P = 0.973)\) among the four groups (Fig. 1C).

**Multivariate analysis**

Age, Fuhrman grade, and distant metastasis were common independent predictors affecting both overall and cancer-specific mortalities (Tables 5, 6). Perioperative blood pressure \((P = 0.022)\) was an independent predictor for overall mortality, whereas obesity grade \((P = 0.033)\) and erythrocyte segmentation rate \((P = 0.037)\) were independent predictors for cancer-specific mortality. However, although not statistically significant, there was a strong trend for obesity grade to predict overall mortality \((P = 0.086)\) and perioperative blood pressure to predict cancer-specific mortality \((P = 0.082)\). Specifically, perioperative blood pressure of stage 2 hypertension degree \((\geq 160/100 \text{ mmHg})\) was an independent predictor for overall mortality \((\text{HR, } 2.642; 95\% \text{ CI, } 1.221-5.720)\) compared to normal blood pressure, while being underweight was an independent predictor for cancer-specific mortality \((\text{HR, } 4.320; 95\% \text{ CI, } 1.557-11.984)\) compared to normal weight. However, smoking status was found not to influence overall and cancer-specific mortalities independently.
Table 4. Comparison of clinicopathologic features among groups classified by perioperative blood pressure (mmHg)

| Parameters                        | < 120/80 (n = 254) | 120-139/80-89 (n = 460) | 140-159/90-99 (n = 241) | ≥ 160/100 (n = 81) | P value |
|-----------------------------------|---------------------|--------------------------|-------------------------|-------------------|---------|
| Mean age ± SD, yr                 | 51.4 ± 12.4         | 53.0 ± 11.9              | 55.4 ± 11.3             | 56.7 ± 9.5        | < 0.001*|
| Sex (%)                           |                     |                          |                         |                   | 0.002†  |
| Female                            | 99 (39.0)           | 117 (25.4)               | 75 (31.1)               | 23 (28.4)         |         |
| Male                              | 155 (61.0)          | 343 (74.6)               | 166 (68.9)              | 58 (71.6)         |         |
| Mean ASA class ± SD              | 1.5 ± 0.6           | 1.5 ± 0.5                | 1.6 ± 0.6               | 1.8 ± 0.5         | < 0.001*|
| Obesity grade (%)                 |                     |                          |                         |                   | < 0.001†|
| Underweight                       | 8 (3.1)             | 10 (2.2)                 | 2 (0.8)                 | 3 (3.7)           |         |
| Normal weight                     | 97 (38.2)           | 127 (27.6)               | 51 (21.2)               | 13 (16.0)         |         |
| Overweight                        | 122 (48.0)          | 252 (54.8)               | 130 (53.9)              | 51 (63.0)         |         |
| Obese                             | 27 (10.6)           | 71 (15.4)                | 56 (24.1)               | 14 (17.3)         |         |
| Smoking (%)                       |                     |                          |                         |                   | 0.125†  |
| Ever (former & current)           | 66 (26.0)           | 148 (32.2)               | 62 (25.7)               | 28 (34.6)         |         |
| Never                             | 188 (74.0)          | 312 (67.8)               | 179 (74.3)              | 53 (65.4)         |         |
| Symptoms at presentation (%)      |                     |                          |                         |                   | 0.161†  |
| Present                           | 68 (26.8)           | 129 (28.0)               | 80 (33.2)               | 30 (37.0)         |         |
| Absent                            | 186 (73.2)          | 331 (72.0)               | 161 (66.8)              | 51 (63.0)         |         |
| History of DM (%)                 |                     |                          |                         |                   | 0.029†  |
| Present                           | 22 (8.7)            | 50 (10.9)                | 41 (17.0)               | 10 (12.3)         |         |
| Absent                            | 232 (91.3)          | 410 (89.1)               | 200 (83.0)              | 71 (87.7)         |         |
| History of hypertension (%)       |                     |                          |                         |                   | < 0.001*|
| Present                           | 41 (16.1)           | 112 (24.3)               | 101 (41.9)              | 48 (59.3)         |         |
| Absent                            | 213 (83.9)          | 348 (75.7)               | 140 (58.1)              | 33 (40.7)         |         |
| Type of surgery (%)               |                     |                          |                         |                   | 0.237†  |
| Radical nephrectomy               | 199 (78.3)          | 358 (77.8)               | 201 (83.4)              | 68 (84.0)         |         |
| Partial nephrectomy               | 55 (21.7)           | 102 (22.2)               | 40 (16.6)               | 13 (16.0)         |         |
| Histologic subtype (%)            |                     |                          |                         |                   | 0.912†  |
| Conventional                     | 216 (85.0)          | 400 (87.0)               | 207 (85.9)              | 70 (86.4)         |         |
| Nonconventional                  | 38 (15.0)           | 60 (13.0)                | 34 (14.1)               | 11 (13.6)         |         |
| Sarcomatoid variant (%)           |                     |                          |                         |                   | 0.496†  |
| Present                           | 0 (0)               | 3 (0.7)                  | 2 (0.8)                 | 1 (1.2)           |         |
| Absent                            | 254 (100)           | 457 (99.3)               | 239 (99.2)              | 80 (98.8)         |         |
| Fuhrman grade (%)                 |                     |                          |                         |                   | 0.475†  |
| Low (G1 & G2)                    | 134 (52.8)          | 262 (57.0)               | 124 (51.5)              | 46 (56.8)         |         |
| High (G3 & G4)                   | 120 (47.2)          | 198 (43.0)               | 117 (48.5)              | 35 (43.2)         |         |
| Pathologic T stage (%)            |                     |                          |                         |                   | 0.056†  |
| T1                                | 217 (85.4)          | 392 (85.2)               | 193 (80.1)              | 61 (75.3)         |         |
| T2                                | 37 (14.6)           | 68 (14.8)                | 48 (19.9)               | 20 (24.7)         |         |
| Clinical LN positivity (%)        |                     |                          |                         |                   | 0.295†  |
| Present                           | 25 (9.8)            | 38 (8.3)                 | 21 (8.7)                | 12 (14.8)         |         |
| Absent                            | 229 (90.2)          | 422 (91.7)               | 220 (91.3)              | 69 (85.2)         |         |
| Distant metastasis (%)            |                     |                          |                         |                   | 0.427†  |
| Present                           | 8 (3.1)             | 12 (2.6)                 | 5 (2.1)                 | 0 (0)             |         |
| Absent                            | 246 (96.9)          | 448 (97.4)               | 236 (97.9)              | 81 (100)          |         |

†One-way ANOVA; †Chi-square and Fisher’s exact test; SD, standard deviation; ASA, American Society of Anesthesiologists; DM, diabetes mellitus; LN, lymph node.

DISCUSSION

A number of recent studies have provided evidence indicating that being overweight and/or obese, as indicated by body mass index, are favorable prognostic factors in patients with RCC (4-11). By a similar context, other studies have reported that being underweight is an unfavorable prognostic factor (19-21). Several explanations for why being overweight and/or obese are associated with a better prognosis, or why being underweight is associated with a worse prognosis have been suggested. Yu et al. (22), in their first report of obesity as a favorable prognostic factor in RCC, postulated that the increased amount of fat between the kidney and the Gerota’s fascia in obese patients might function as a barrier to further invasion of cancer cells. Haferkamp and associates (19) suggested cachexia as one reason for underweight patients having a poorer prognosis. They reported that up-regulated tissue catabolism and impaired anabolism, release of tumor-derived catabolic factors and inflammatory cytokines, and neuroendocrine dysfunction could possibly affect patient survival. This hypothesis was supported by a study by Kim et al. (23) who reported that cachexia-like symptoms independently predicted a worse prognosis. Another possible explanation was suggested by Rasmussen and colleagues (24), who reported that serum insulin-like growth factor-1 in obese patients might be associated with in...
creased survival. The association between body mass index and tumor characteristics can be another factor to consider, but is still uncertain. Parker et al. (6) reported that patients with a body mass index ≥ 25 kg/m² had less aggressive tumors. Naya and associates (25) revealed that visceral adipose tissue, as assessed by computed tomography, in patients with stage 1 disease was significantly greater than that in patients with more advanced disease. In contrast, Schips and colleagues (26) could not affirm that being overweight and/or obese are favorable prognostic factors independently, irrespective of the tumor stage. It is likely that body mass index can affect patient survival independently for pathologic T and clinical N and M stage (Table 6). Thus, it is likely that body mass index can affect cancer-specific mortality after adjustment for pathologic T stage occurred than T1 stage as the obesity grade decreased (Table 2). This difference might be regarded as a biased phenomenon because one may think that the difference in patient survival was not affected by obesity grade but by pathologic T stage. But our multivariate analysis showed that obesity grade independently affected cancer-specific mortality after adjustment for pathologic T and clinical N and M stage (Table 6). As mentioned above, most of the current literatures have stated that being overweight and/or obese are favorable prognostic factors.

Table 5. Univariate and multivariate analysis of variables influencing overall mortality

| Variables                  | Univariate |          | Multivariate |          |
|---------------------------|------------|----------|--------------|----------|
|                           | HR (95% CI)| P value  | HR (95% CI)  | P value  |
| Age                       | 1.063 (1.043-1.083) | < 0.001 | 1.049 (1.026-1.073) | < 0.001 |
| ASA class                  |            | 0.002    |              | 0.956    |
| 1                         | 1          |          | 1            |          |
| 2                         | 2.077 (1.296-3.329) | 0.002   | 1.177 (0.667-2.079) | 0.574    |
| 3                         | 3.694 (1.768-7.719) | 0.001   | 1.163 (0.467-2.897) | 0.745    |
| 4                         | 0.000 (0.000-0.086) | 0.969   | 0.000 (0.000-3.003) | 0.974    |
| Obesity grade             |            |          | 0.033        | 0.086    |
| Normal                    | 1          |          |              |          |
| Overweight                | 0.816 (0.506-1.317) | 0.405   | 1.130 (0.628-2.033) | 0.684    |
| Obese                     | 0.950 (0.507-1.779) | 0.873   | 1.632 (0.791-3.366) | 0.185    |
| Underweight               | 2.964 (1.226-6.168) | 0.016   | 3.250 (1.207-4.752) | 0.020    |
| Smoking                   |            | 0.141    | 0.000        | 0.795    |
| Never                     | 1          |          |              |          |
| Former                    | 1.210 (0.523-2.798) | 0.655   | 0.657 (0.192-2.525) | 0.504    |
| Current                   | 0.610 (0.362-1.029) | 0.064   | 1.005 (0.505-2.002) | 0.989    |
| Perioperative blood pressure |            |          | 0.022        | 0.010    |
| < 120/80 mmHg             | 1          |          | 0.723        | 0.389    |
| 120-139/80-89 mmHg        | 1.109 (0.625-1.971) | 0.723   | 1.330 (0.695-2.543) | 0.526    |
| 140-159/90-99 mmHg        | 1.002 (0.520-1.929) | 0.996   | 0.785 (0.371-1.660) | 0.004    |
| ≥ 160/100 mmHg            | 2.372 (1.219-4.615) | 0.011   | 2.642 (1.221-5.720) | 0.014    |
| Alcohol intake            |            | 0.004    | 0.240        |          |
| Never                     | 1          |          |              |          |
| Former                    | 1.075 (0.392-2.949) | 0.888   | 1.178 (0.276-5.033) | 0.825    |
| Current                   | 0.407 (0.239-0.692) | 0.001   | 0.569 (0.288-1.127) | 0.106    |
| History of diabetes mellitus |            | 0.035    | 1.444 (0.703-2.969) | 0.317    |
| History of hypertension   | 1.320 (0.858-2.030) | 0.207   | 0.751 (0.429-1.315) | 0.317    |
| Fasting blood glucose     | 1.006 (1.001-1.010) | 0.007   | 1.002 (0.996-1.008) | 0.501    |
| Hemoglobin level          | 0.795 (0.720-0.878) | < 0.001 | 0.931 (0.796-1.088) | 0.368    |
| Serum creatinine          | 1.238 (1.068-1.436) | 0.005   | 1.176 (0.971-1.424) | 0.097    |
| Serum albumin             | 0.488 (0.351-0.679) | < 0.001 | 1.136 (0.713-1.810) | 0.591    |
| Serum ALP                 | 1.012 (1.008-1.016) | < 0.001 | 1.004 (0.997-1.010) | 0.248    |
| ESR                       | 1.022 (1.016-1.027) | < 0.001 | 1.008 (0.999-1.017) | 0.088    |
| Symptoms at presentation  | 2.303 (1.523-3.483) | < 0.001 | 1.200 (0.736-1.956) | 0.464    |
| Type of surgery           |            | 0.015    | 0.224        |          |
| Radical nephrectomy       | 1          |          |              |          |
| Partial nephrectomy       | 0.325 (0.131-0.803) | 0.015   | 0.507 (0.170-1.516) | 0.224    |
| Sarcomatoid variant       | 5.587 (1.366-22.855) | 0.017   | 2.009 (0.437-9.232) | 0.370    |
| Furhman grade             |            |          |              |          |
| Low (G1 + G2)             | < 0.001    |          |              |          |
| High (G3 + G4)            | 2.528 (1.651-3.871) | < 0.001 | 1.831 (1.108-3.024) | 0.018    |
| Pathologic T stage        |            |          |              |          |
| T1                        | 1          |          |              |          |
| T2                        | 2.654 (1.734-4.064) | < 0.001 | 1.212 (0.701-2.095) | 0.491    |
| Clinical LN positivity    | 1.983 (1.121-3.507) | 0.019   | 1.506 (0.634-2.807) | 0.876    |
| Distant metastasis        | 15.229 (7.713-26.617) | < 0.001 | 10.537 (3.391-20.595) | < 0.001 |

HR, hazard ratio; CI, confidence interval; ASA, American Society of Anesthesiologists; ALP, alkaline phosphatase; ESR, erythrocyte segmentation rate; LN, lymph node.
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Factors for cancer-specific survival, but not for overall survival (4, 6-11). Few studies have focused on the effect of being underweight in the prognosis of patients with RCC. A study by Haferkamp and colleagues (19) concluded that being underweight worsened the prognosis by more than four times (HR, 4.27; 95% CI, 1.557-11.984). However, in our study, being underweight was the only statistically significant factor for cancer-specific survival, but not for overall survival (HR, 4.320; 95% CI, 1.47-12.4), which is very similar to our study (HR, 4.147; 95% CI, 1.557-11.984). However, in our study, being underweight was the only statistically significant factor for cancer-specific survival, while being overweight or obese showed no statistical significance. Although unclear, the difference might have resulted from limiting the cohort to low stage (pT1 and pT2) diseases in our study, while most of other studies included the whole pathologic T stages.

There are few studies of the association between smoking and RCC survival. At the Memorial Sloan-Kettering Cancer Center, investigators reviewed 25,436 tumor registry records and reported that smokers had an overall lower rate of survival than non-smokers, with a significant association in several solid cancers, but not in renal cancer (27). Parker et al. (15) did not find an association between smoking status and RCC survival despite adjustment for age and tumor stage. Other studies showed that smokers, with a significant association in several solid cancers, showed no statistical significance. Although unclear, the difference might have resulted from limiting the cohort to low stage (pT1 and pT2) diseases in our study, while most of other studies included the whole pathologic T stages.

Table 6. Univariate and multivariate analysis of variables influencing cancer-specific mortality

| Variables                                    | Univariate | Multivariate |
|----------------------------------------------|------------|--------------|
|                                              | HR (95% CI) | P value      | HR (95% CI)   | P value     |
| Age                                          | 1.060 (1.038-1.082) | < 0.001 | 1.043 (1.018-1.070) | 0.001       |
| ASA class                                    | 0.019 | 0.326 |          |              |
| 1                                            |            |      | 1.224 (0.642-2.329) | 0.540       |
| 2                                            | 2.073 (1.224-3.511) | 0.007 | 3.239 (0.476-3.711) | 0.587       |
| 3                                            | 3.155 (1.328-7.499) | 0.009 | 4.320 (1.557-11.984) | 0.005       |
| 4                                            | 0.000 (0.000-2.065) | 0.971 | 0.001 (0.000-6.375) | 0.982       |
| Obesity grade                                |            |      |              |              |
| Normal                                       |            |      | 0.522-1.979 | 0.961       |
| Overweight                                   | 0.731 (0.430-1.241) | 0.246 | 1.017 (0.089-1.583) | 0.182       |
| Obese                                        | 0.745 (0.356-1.559) | 0.435 | 1.279 (0.555-2.944) | 0.563       |
| Underweight                                   | 3.496 (1.427-8.567) | 0.006 | 4.320 (1.557-11.984) | 0.005       |
| Smoking                                      |            |      |              |              |
| Never                                        |            |      |              |              |
| Former                                       | 1.003 (0.362-2.780) | 0.996 | 0.375 (0.089-1.583) | 0.182       |
| Current                                      | 0.628 (0.353-1.117) | 0.113 | 0.928 (0.439-1.991) | 0.848       |
| Perioperative blood pressure                 |            |      |              |              |
| < 120/80 mmHg                                 |            |      |              |              |
| 120-139/80-89 mmHg                            | 1.211 (0.633-2.314) | 0.563 | 1.445 (0.708-2.949) | 0.312       |
| 140-159/90-99 mmHg                            | 1.090 (0.524-2.269) | 0.817 | 0.848 (0.368-1.955) | 0.699       |
| ≥ 160/100 mmHg                                | 2.015 (0.916-4.431) | 0.081 | 2.394 (0.977-5.863) | 0.056       |
| Alcohol intake                               |            |      |              |              |
| Never                                        |            |      |              |              |
| Former                                       | 1.048 (0.327-3.357) | 0.938 | 1.733 (0.325-9.227) | 0.520       |
| Current                                      | 0.461 (0.260-0.818) | 0.008 | 0.682 (0.323-1.441) | 0.315       |
| History of diabetes mellitus                 | 1.834 (1.037-3.242) | 0.037 | 1.461 (0.666-3.208) | 0.345       |
| History of hypertension                      | 1.298 (0.799-2.111) | 0.292 | 0.856 (0.449-1.634) | 0.638       |
| Fasting blood glucose                        | 1.065 (1.000-1.010) | 0.055 | 1.001 (0.995-1.007) | 0.763       |
| Hemoglobin level                             | 0.809 (0.724-0.905) | < 0.001 | 0.947 (0.791-1.154) | 0.557       |
| Serum albumin                                | 0.543 (0.373-0.791) | 0.001 | 1.335 (0.788-2.261) | 0.283       |
| Serum ALP                                    | 1.013 (1.009-1.017) | < 0.001 | 1.005 (0.997-1.012) | 0.227       |
| ESR                                          | 1.024 (1.017-1.030) | < 0.001 | 1.011 (1.001-1.021) | 0.037       |
| Symptoms at presentation                     | 2.534 (1.587-4.044) | < 0.001 | 1.244 (0.710-2.179) | 0.446       |
| Type of surgery                              | 0.038 | 0.677 |          |              |
| Radical nephrectomy                          |            |      |              |              |
| Partial nephrectomy                          |            |      |              |              |
| Fuhrman grade                                | 0.343 (0.125-0.945) | 0.038 | 0.798 (0.276-2.309) | 0.677       |
| Low (G1 + G2)                                | < 0.001 | 0.026 |          |              |
| High (G3 + G4)                               | 2.710 (1.672-4.390) | < 0.001 | 1.916 (1.082-3.394) | 0.026       |
| Pathologic T stage                           | < 0.001 | 0.216 |          |              |
| T1                                           |            |      |              |              |
| T2                                           | 3.320 (2.079-5.301) | < 0.001 | 1.473 (0.798-2.720) | 0.216       |
| Clinical LN positivity                       | 2.443 (1.339-4.549) | 0.004 | 1.247 (0.601-2.589) | 0.553       |
| Distant metastasis                           | 18.761 (10.174-34.598) | < 0.001 | 10.991 (5.257-22.980) | < 0.001     |

HR, hazard ratio; CI, confidence interval; ASA, American Society of Anesthesiologists; ALP, alkaline phosphatase; ESR, erythrocyte segmentation rate; LN, lymph node.
ate analysis (13, 14). We were similarly unable to find an association between smoking status and overall and cancer-specific survivals.

Studies of an association with blood pressure are also scarce. In a 1993 cohort study authors found increased mortality due to RCC among hypertensive patients (28). Two more recent studies have reported contradictory conclusions; Parker and authors (15) reported a positive association between hypertension and RCC-specific survival, whereas Grossman et al. (16) showed a negative association. Grove and associates (29), in a 20-yr prospective study of a cohort of 8,006 patients, found no association between blood pressure and RCC death. In our study, the life table survival plot did not show a significant association between perioperative blood pressure levels and overall or cancer-specific survival. However, the multivariate analysis revealed that the perioperative blood pressure was an independent predictor for overall mortality with adjusting the past history of hypertension as a covariate. Specifically, the perioperative blood pressure of a stage 2 hypertension degree (≥ 160/100 mmHg) was found to be an independent predictor for overall mortality.

We admit that our study had several limitations which should be discussed. It had a retrospective design and was performed at a single institution. There is the possibility of selection bias associated with referral patterns to a tertiary medical center. The significant differences in basic demographic data such as age, sex, and ASA class between groups classified by the obesity grade, smoking status, or perioperative blood pressure levels could be the weakest point of our study. Although these demographic variables were adjusted for in the multivariate analysis, these differences may still have affected our findings.

In conclusion, overall and cancer-specific survivals significantly decrease with being overweight in patients with low stage RCC. Perioperative blood pressure ≥ 160/100 mmHg and being overweight are unfavorable independent predictors of overall and cancer-specific survival, respectively, while smoking status does not influence overall or cancer-specific survival.

ACKNOWLEDGMENTS

The authors have no conflicts of interest to disclose.

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