**Nomogram-Based Preoperative Score for Predicting Clinical Outcome in Unilateral Primary Aldosteronism**

**Running Title:** NBPS and Clinical Outcome in Unilateral PA

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**Supplemental methods**

**Criteria for case detection, confirmation tests and adrenal venous sampling (AVS) interpretation**

In the Chongqing cohort, the cut-off for case detection is a ARR higher than 2.0 ng·dL−1/mU·L−1, and the cut-off for confirmation tests is a plasma aldosterone concentration (PAC) of 6 ng/dL for the fludrocortisone suppression test (FST), 8 ng/dL for the saline infusion test (SIT) and 11 ng/dL for the captopril challenge test (CCT). In the present study, SIT were performed in 136 cases of UPA patients, 144 for CCT and 112 for FST. For the determination of lateralization, AVS with or without adrenocorticotropic hormone (ACTH) use were both used. For AVS interpretation, the successful cannulation of the adrenal veins was defined as the selectivity index (SI) >2 without ACTH use or SI >3 with ACTH stimulation. The diagnosis of unilateral PA was made if the lateralization index (LI) >2 without ACTH use and LI >4 with ACTH stimulation (1).

In the centers from Torino, the screening test was considered to be positive when the ARR was higher than 30 (PAC in ng/dl and PRA in ng/ml\*h). The confirmation test was considered to be positive when a PAC post SIT greater than 5 ng/dL. For the determination of lateralization, Unstimulated and AVS with continuous ACTH infusion were both used. For AVS interpretation, the successful cannulation of the adrenal veins was defined as the SI≧3. The diagnosis of unilateral PA was made if the LI≧4 (2).

In the centers from Munich, the cut-off for case detection is an ARR higher than 1.12 ng·dL−1/mU·L−1, and the cut-off for confirmation tests is a PAC 5 ng/dL for the saline infusion test (SIT). For the determination of lateralization, bilateral simultaneous AVS without ACTH stimulation were used. For AVS interpretation, the successful cannulation of the adrenal veins was defined as the SI≧2. The diagnosis of unilateral PA was made if the LI≧4 (3).

**Blood Pressure Measurement**

In both cohorts, blood pressure of UPA patients were measured in the office, as refer to European Society of Hypertension/European Society of Cardiology guidelines for the management of arterial hypertension (4,5). The detail methods were previously described (1,6). Briefly, the patient was seated, rested for at least 5 minutes, and avoided stimulation such as coffee, exercise and smoking for at least 30 minutes. BP were recorded in both arms, and the arm that gives the higher reading were used for subsequent readings. Another measurement is required and separate by 2 min. The average of 2 readings were recorded as the blood pressure levels. The patients were also asked if the measurement were similar with the blood pressure at home to exclude white coat hypertension. Blood pressure (BP) were determined using an electronic sphygmomanometer in the training cohort (Omron, HBP-9020) and a mercury sphygmomanometer in the validation cohort. The sphygmomanometers were regularly recalibrated according to manufacturers’ instructions.

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**Supplemental Table 1. Preoperative clinical and biochemical characteristics of patients with UPA in the validation cohort.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Complete Clinical Success (n=57)** | **Absent + Partial Clinical Success (n=108)** | ***P* Value** |
| Age (years) | 44.9 ± 10.4 | 52.9 ± 10.3 | <0.001 |
| Sex (M/F) | 20/37 (64.9%) | 73/35 (32.4%) | <0.001 |
| Duration of HT (years) | 5.1 (1.3, 7.6) | 8.0 (3.0, 13.5) | <0.001 |
| History of hypokalemia (Yes/No) | 44/13 (77.2%) | 90/18 (83.3%) | 0.403 |
| BMI (kg/m2) | 25.0 ± 4.3 | 28.3 ± 4.5 | <0.001 |
| SBP (mmHg) | 155.2 ± 20.9 | 164.8 ± 26.2 | 0.019 |
| DBP (mmHg) | 98.2 ± 13.8 | 98.2 ± 14.5 | 0.999 |
| Serum K+ (mmol/l) | 2.8 ± 0.6 | 2.9 ± 0.5 | 0.294 |
| PAC (Pg/ml) | 392.7 (240.0, 526.4) | 277.6 (180.9, 481.7) | 0.013 |
| ARR (pg.ml-1/mIU.l-1) | 178.3 (84.2, 291.0) | 56.3 (15.0, 145.5) | <0.001 |
| DDD of anti-hypertensive medication | 2.1 (1.5, 4.2) | 4.00 (2.0, 5.6) | 0.001 |
| Target organ damage (Yes/No) | 29/28 (50.9%) | 88/20 (81.5%) | <0.001 |
| Left Ventricular Hypertrophy (Yes/No) | 42.1% | 71.3% | <0.001 |
| Microalbuminuria (Yes/No) | 34.0% | 41.7% | 0.383 |
| Size of largest nodule at imaging (mm) | 15.1 (10.0, 21.5) | 14.0 (9.0, 16.7) | 0.014 |

Data were expressed as mean ± SD, median (interquartile range) and proportion (%), proportions indicate females, presence of hypokalemia, and presence of target organ damage . HT, hypertension; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Serum K+, concentration of serum potassium; PAC, plasma aldosterone concentration; ARR, aldosterone to renin ratio; DDD, defined daily dose.

**Supplemental Table 2. Comparison of preoperative clinical and biochemical data of patients with UPA between the training and validation cohorts.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Training cohort (n=150)** | **Validation cohort (n=165)** | ***P* Value** |
| Complete clinical success (Yes/No) | 97/53 (64.7%) | 57/108 (34.5%) | <0.001 |
| Age (years) | 45.5 ± 12.3 | 50.2 ± 11.0 | <0.001 |
| Sex (M/F) | 51/99 (66.0%) | 93/72 (43.6%) | <0.001 |
| Duration of HT (years) | 4.0 (1.0,10.0) | 7.4 (3.2,14.6) | <0.001 |
| History of hypokalemia (Yes/No) | 128/22 (85.3%) | 134/31(81.2%) | 0.367 |
| BMI (kg/m2) | 23.5 ± 3.2 | 27.2 ± 4.8 | <0.001 |
| SBP (mmHg) | 156.0 ± 17.9 | 161.5 ± 24.9 | 0.026 |
| DBP (mmHg) | 96.3 ± 13.3 | 98.2 ± 14.3 | 0.212 |
| Serum K+ (mmol/l) | 3.0 ± 0.6 | 2.9 ± 0.6 | 0.119 |
| PAC (pg/ml) | 342.5 (234.5,525.3) | 331.9 (207.4, 499.3) | 0.168 |
| ARR (pg.ml-1/mIU.l-1) | 201.6 (56.6, 445.6) | 87.4 (27.8, 219.2) | <0.001 |
| DDD of anti-hypertensive medication | 2.0 (1.0, 2.7) | 3.3 (2.0, 5.0) | <0.001 |
| Target organ damage (Yes/No) | 101/49 (67.3%) | 117/48 (70.9%) | 0.542 |
| Left Ventricular Hypertrophy (Yes/No) | 53.3% | 61.2% | 0.172 |
| Microalbuminuria (Yes/No) | 51.3% | 39.2% | 0.090 |
| Size of largest nodule at imaging (mm) | 13.5 (10.4, 16.1) | 15.0 (10.0, 18.0) | 0.414 |

Data were expressed as mean ± SD, median (interquartile range) and proportion (%), proportions indicate complete clinical success, females, presence of hypokalemia, and presence of target organ damage. HT, hypertension; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Serum K+, concentration of serum potassium; PAC, plasma aldosterone concentration; ARR, aldosterone to renin ratio; DDD, defined daily dose.

**Supplemental Table 3. Summary of nomogram-based preoperative score (NBPS), ARS and PASO scores in UPA patients in the training and validation cohorts.**

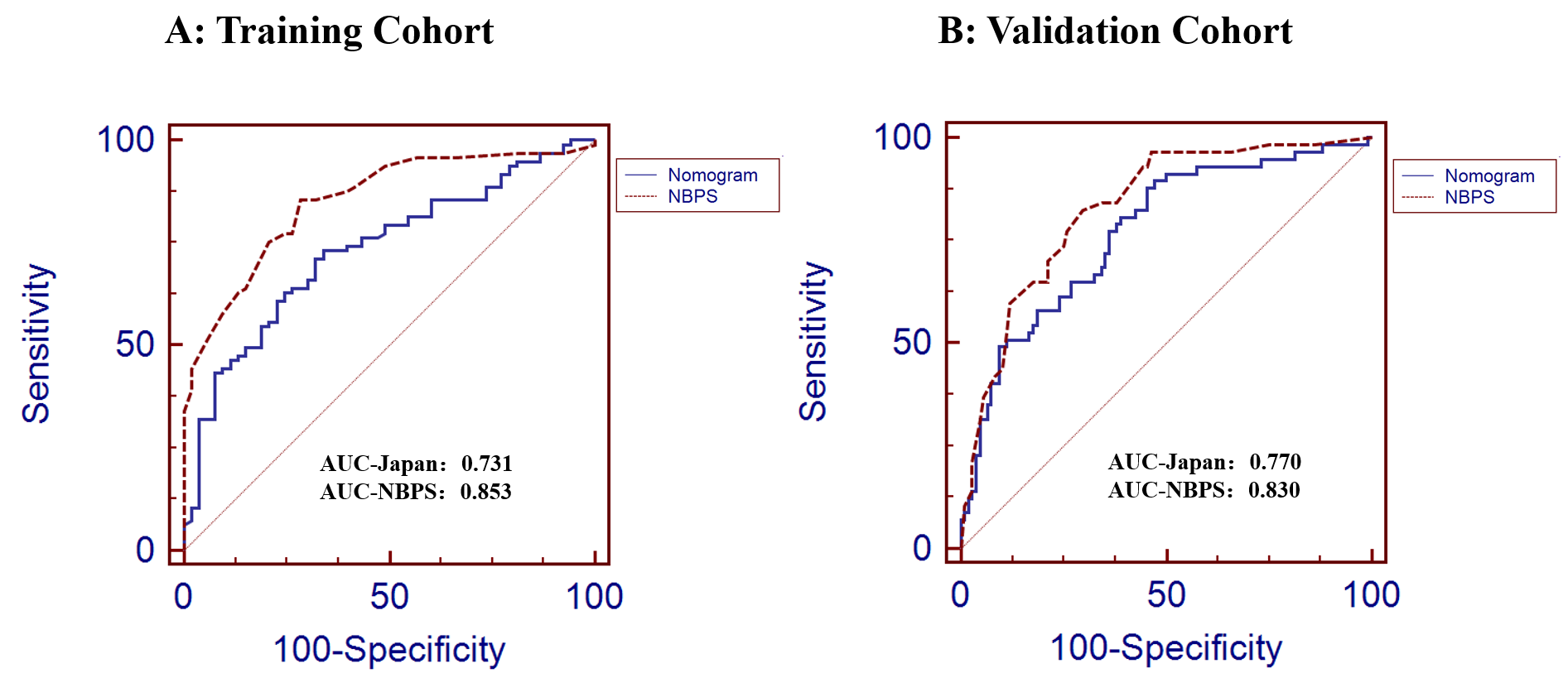
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Predictive models** | **Training Cohort** | | | **Validation Cohort** | | |
| **Complete Clinical Success (n=97)** | **Absent + Partial Clinical Success (n=53)** | ***P* Value** | **Complete Clinical Success(n=57)** | **Absent + Partial Clinical Success(n=108)** | ***P* Value** |
| ARS | 4.0 (3.0-5.0) | 3.0 (2.0-4.0) | <0.001 | 3.00 (2.00-4.50) | 1.00 (0.00-2.00) | <0.001 |
| PASO score | 19.0 (16.0-21.0) | 15.0 (12.5-17.0) | <0.001 | 18.00 (14.50-21.75) | 12.00 (9.13-14.38) | <0.001 |
| NBPS | 16.5 (13.5-19.5) | 8.5 (6.0-12.5) | <0.001 | 14.5 (10.5-17.0) | 6.0 (3.5-10.5) | <0.001 |

Data were expressed as median (interquartile range). NBPS, nomogram-based preoperative score; ARS, aldosteronoma resolution score; PASO, primary aldosteronism surgical outcome.

**Supplemental Table 4.** **Sensitivity,** **specificity, positive predictive value and negative predictive value of different cut-offs of NBPS in predicting complete clinical success in the training cohort.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cut-offs** | **Sensitivity** | **Specificity** | **Positive predictive value** | **Negative predictive value** |
| **≥8.5** | **95.9%** | **43.4%** | **75.6%** | **85.2%** |
| **≥11.5** | **85.6%** | **71.7%** | **84.7%** | **73.1%** |
| **≥16.5** | **51.5%** | **94.3%** | **94.3%** | **51.5%** |

**Supplemental** **Figure 1. Comparison of NBPS with previous nomogram developed by the Japanese team for the preoperative estimation of hypertension remission in UPA patients in the training and validation cohorts.**



ROC curve analysis was used to compare the NBPS with the nomogram developed by the Japanese team for the estimation of hypertension remission in the training (A) and validation cohorts (B). The AUC is indicated. Nomogram indicates the nomogram previous developed by the Japanese team. ROC curve, receiver operating characteristic curve; NBPS, nomogram-based preoperative score.