Supplementary Material

# Supplementary Figures and Tables

## Supplementary Tables

**Supplementary Table 1.** PubMed search results.

|  |  |  |  |
| --- | --- | --- | --- |
| Search number | Query | Filters | Results |
| #1 | "Hyperaldosteronism"[Mesh] | - | 9335 |
| #2 | "osteoporosis"[Title/Abstract] OR "BMD"[Title/Abstract] OR "calcium"[Title/Abstract] OR "PTH"[Title/Abstract] | - | 497,653 |
| #3 | "Hyperparathyroidism, Secondary"[Mesh] | - | 8790 |
| #4 | #2 OR #3 | - | 502,306 |
| #5 | #1 AND #4 | - | 339 |
| #6 | #1 AND #4 | English, Humans | 270 |

**Supplementary Table 2**. Other clinical characteristics of studies included in systematic review and meta-analysis.

| Study | Patient and Control | BMI | SBP (mmHg) | DBP (mmHg) | PAC (ng/dL) | PRC (μIU/ml) | PRA (μg/l/h) | Phosphate (mmol/L) | PTH assay method | 25-OHD assay method |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Zavatta, 2022 | PANFA | 27.7±5.028.1±4.5 | 148±23139±17 | 89±1085±8 | 29.80±20.7021.80±13.80 | -- | 0.28±0.111.25±1.32 | 1.00±0.191.10±0.19 | CLA | CLA |
| Tang, 2022 | PASA(GS+BS) | 24.47±4.1921.79±4.55 | -- | -- | 27.00 (16.90, 38.35)16.90(12.25, 21.65) | 1.50(0.60, 2.40)5.40(2.71, 34.55) | -- | 1.09±0.191.24±0.21 | ECLA | ECLA |
| Liu, 2021 | PANFA | 26±427±3 | -- | -- | -- | -- | -- | 1.11±0.561.21±0.18 | ECLIA | ECLIA |
| Kometani, 2021 | (a) unilateral PA bilateral PA | -- | 134±17137±18 | 85±1285±14 | 22.30±23.3016.70±8.00 | -- | 0.50±0.500.60±0.20 | 1.10±0.191.13±0.16 | ECLIA | - |
| (b) unilateral PA bilateral PA | -- | 133±18136±17 | 86±1684±12 | 34.90±19.0016.90±7.80 | -- | 0.40±0.400.60±0.50 | 1.03±0.161.13±0.16 |
| Gravvanis, 2021 | PA before treatmentPA after treatment | 31.44±7.22 | 150(125,230)130(105,156) | 95(75,146)80(65,95) | 16.90(2.94,94.29)32.44(14.57,205.96) | 5.40(1.40,19.80)11.70(1.80,65.88) | -- | 0.99±0.161.04±0.18 | ECLIA | ELISA |
| Yokomoto, 2020 | unilateral PAbilateral PA | 24.6±3.825.0±3.8 | 142±16139±19 | 87±1287±13 | 32.70±18.8018.50±9.00 | -- | 0.20±0.100.40±0.30 | -- | ECLIA | - |
| Tuersun, 2020 | (a) PA EH | 26.57±4.1926.75±4.09 | 148.17±17.23148.60±22.72 | -- | 19.76±6.6816.08±4.76 | -- | 0.55±0.382.24±1.90 | 1.09±0.171.09±0.21 | ECLIA | ECLIA |
| (b) unilateral PA bilateral PA | 25.41±3.2627.64±4.68 | 149.62±19.73147.24±16.56 | 91.72±15.0388.65±13.69 | 22.45±7.1017.24±5.09 | -- | 0.57±0.380.53±0.39 | 1.11±0.171.08±0.18 |
| Asbach, 2020 | (a) unilateral PA bilateral PA | 28.0(25.8,30.9)27.7(25.2,31.0) | 153(140,162)152(135,169) | 94(87,103)96(87,110) | 19.55(14.18,36.40)16.00(10.70,22.10) | 3.90(2.00,6.20)3.90(2.00,7.50) | -- | -- | ECLIA | CLA |
| (b) PA before treatment PA after treatment | 28.64±4.0128.35±3.92 | 149.74±20.44133.08±18.56 | 94.98±15.8986.38±9.71 | 20.97±15.9815.18±16.29 | 3.92±3.5117.05±18.77 | -- | -- |
| Adolf, 2020 | (a) PA HS | 26.0(23.2,30.0)27.0(25.9,34.8) | -- | -- | -- | -- | -- | 1.07(0.94,1.19)1.03(0.97,1.07) | CLA | CLA |
| (b) PA before treatment PA after treatment | 26.0(23.2,30.0)26.2(23.1,30.1) | -- | -- | -- | -- | -- | 1.07(0.94,1.19)1.13(0.97,1.19) |
| Lenzini, 2019 | (a) PA EH | 25.69±4.2525±3 | 149±19143±14 | 92.64±12.5191±6 | 30.06±57.878.40(1.50,15.00) | -- | 1.16±3.580.50(0.10,4.40) | -- | ELISA | - |
| (b) unilateral PA bilateral PA | 25.4±4.126.2±4.6 | 149±18150±22 | 93±1392±12 | 14.20(4.70,93.70)13.70(2.20,24.90) | -- | 0.24(0.10,0.57)0.24(0.10,7.16) | -- |
| (c) PA before treatment PA after treatment | 25.69±4.2524.36±3.06 | 149.36±19.26141.97±22.58 | 92.64±12.5192.91±12.96 | 30.06±57.8711.04±14.07 | -- | 0.31±0.371.01±1.96 | -- |
| Loh, 2018 | (a) PA EH | 27.6(24.5,29.4)27.8(25.9,32.1) | -- | -- | 24.26(14.98,40.38)5.80(3.85,10.85) | -- | 0.38(0.20,0.61)1.30(0.71,2.15) | 1.18(1.03,1.22)1.15(1.02,1.23) | CLIA | ECLIA |
| (b) PA before treatment PA after treatment | -- | -- | -- | -- | -- | -- | 1.18(1.04,1.21)1.18(1.08,1.32) |
| Lim, 2018 | unilateral PAbilateral PA | -- | 149.7±18.8148.9±18.6 | 89.8±13.192.0±11.1 | 42.60±27.0023.20±12.10 | -- | 0.23±0.220.25±0.26 | -- | RIA | Unknown |
| Kim, 2018 | PAAI | 25.28±3.3325.48±4.56 | 135.49±15.72125.41±13.98 | 81.83±10.9377.56±9.73 | 24.60±7.7015.64±6.07 | -- | 0.30±0.191.23±1.42 | -- | - | - |
| Shu, 2018 | OPOEHS | 23.0±2.523.3±2.824.3±3.2 | 118.6±11.6117.9±9.4120.8±10.4 | 72.0±8.472.9±7.173.0±8.3 | 12.10±7.889.17±5.628.18±7.15 | 12.90±13.6013.10±9.8013.20±9.20 | --- | --- | CLIA | CLIA |
| Wu, 2017 | PAEH | -- | -- | -- | -- | -- | -- | -- | - | - |
| Salcuni, 2017 | (a) PA non-PA | 23.9(21)25.6(30.6) | 140(90)120(95) | 83(35)75(55) | 8.76(15.14)4.54(19.43) | -- | -- | 1.01±0.101.11±0.15 | CLIA | RIA |
| (b) OP HS | -- | -- | -- | -- | -- | -- | -- |
| Notsu, 2017 | PAHS | 24.70±4.0023.50±6.30 | 144±21131±18 | 85±1475±13 | 19.94±13.96- | -- | 0.31±0.22- | 1.10±0.191.07±0.16 | CLA | - |
| Zhang, 2016 | PANFA | 26.00±3.3026.70±7.70 | 149±20133±20 | 93±1283±14 | 20.36±7.3811.08±3.22 | -- | 0.27±0.621.11±1.55 | 1.04±0.181.18±0.19 | ECLIA | CLA |
| Jiang, 2016 | (a) PA EH | 24.00(22.20,26.40)25.50(23.0,28.00) | 180(160,190)160(150,180) | 104(100,120)100(90,110) | 48.55(34.06,68.23)21.05(16.15,28.76) | -- | 0.26(0.13,0.52)0.78(0.39,2.60) | 1.10(0.95,1.20)1.26(1.10,1.34) | CLIA | ECLA |
| (b) unilateral PA bilateral PA | 23.14±2.6525.52±3.15 | 177.24±27.21172.97±15.01 | 105.67±7.68103.87±21.76 | 61.28±36.4539.50±17.20 | -- | 0.31±0.290.40±0.49 | 1.07±0.171.08±0.19 |
| (c) PA before treatment PA after treatment | -- | 164.09±27.50123.77±11.07 | 96.05±7.8078.86±5.80 | 44.79±29.3521.80±20.15 | -- | 0.24±0.381.12±1.61 | 1.10±0.191.17±0.26 |
| Petramala, 2014 | (a) PA EH HS | 28.20±4.702900±5.0025.10±2.20 | 138.3±16.8131±18.8119.1±4.2 | 85.9±11.482.4±11.277.2±5.1 | 37.00±25.1022.50±13.009.20±1.70 | --- | 0.90±0.701.40±1.601.10±0.40 | 1.13±0.191.10±0.131.10±0.10 | RIA | CLA |
| (b) unilateral PA bilateral PA | 27.60±4.8028.60±4.60 | 138.8±19.1137.3±14.5 | 88.3±9.683.4±9.6 | 39.80±25.6034.40±24.60 | -- | 0.70±0.601.10±0.80 | 1.10±0.231.16±0.19 |
| Ceccoli, 2013 | (a) PA EH | 27.80±4.8030.10±5.40 | 158±19151±15 | 97±11.293±7.5 | 4.98±3.401.60±1.08 | -- | 0.40(0.20,0.70)1.60±1.40 | -- | ECLIA | CLA |
| (b) PA before treatment PA after treatment | 27.70±4.9028.0±4.20 | 153±17138±21 | 97±1084±11 | -- | -- | -- | -- |
| Salcuni, 2012 | (a) PA NFA | 28.20±3.5027.30±4.30 | 142±20131±12 | 86±1184±7 | 37.16(18.71,279.27)24.69(16.11,55.29) | -- | 0.21(0.01,0.53)0.38(0.01,1.80) | 1.09±0.131.08±0.10 | CLIA | RIA |
| (b) PA before treatment PA after treatment | -- | -- | -- | -- | -- | -- | -- |
| Rossi, 2012 | (a) PA EH | -- | 155±20.94149±16 | 93.59±12.2293±15 | 18.60±10.2913.50(9.40,10.40) | -- | 0.73±0.761.92(0.98,6.20) | 1.00±0.150.91±0.13 | CLIA and CLA | CLA |
| (b) unilateral PA bilateral PA | -- | 155±17155±33 | 94±1092±19 | 19.00(12.20,26.70)17.40(11.80,18.80) | -- | 0.78(0.31,1.31)0.20(0.15,1.00) | 0.99±0.141.06±0.20 |
| (c) PA before treatment PA after treatment | -- | 155±17131±5 | 94±1082±6 | 19.00(12.20,26.70)9.00(6.70,13.50) | -- | 0.78(0.31,1.31)1.30(0.72,1.50) | 0.99±0.140.96±0.15 |
| Pilz, 2012 | (a) PA EH | 31.00±7.1028.50±6.00 | 179±22154±23 | 108±1294±13 | 33.60(24.40,67.80)16.00(12.30,23.40) | 3.10(2.80,4.40)11.90(5.90,28.20) | -- | 0.81±0.220.94±0.18 | ECLIA | CLA |
| (b) PA before treatment PA after treatment | 31.00±7.10- | 179±22149±23 | 108±1296±13 | 33.60(24.40,67.80)31.00(9.10,53.40) | 3.10(2.80,4.40)16.10(10.20,24.10) | -- | 0.81±0.221.00±0.16 |
| Maniero, 2012 | (a) PA EH | -- | 156±19149±18 | 94±1193±15 | 18.50(16.80,28.20)11.10(9.60,14.90) | -- | 0.57(0.21,1.00)2.06(0.80,2.42) | -- | CLIA | RIA |
| (b) PA before treatment PA after treatment | -- | -- | -- | 16.97(11.46,26.56)9.05(7.13,13.28) | -- | 0.57(0.22,0.80)1.10(0.75,1.45) | 1.02±0.180.93±0.15 |
| Rossi, 1998 | PAEH | -- | 161±3157±3 | 105±1102±1 | 29.10±3.1018.40±4.40 | -- | 0.20±0.041.14±0.35 | -- | RIA | - |
| Rossi, 1995 | (a) PA EH HS | 23.10±0.8024.10±1.2624.30±1.50 | 168.4±15.3163.75±13.52121.0±12.2 | 102.70±2.50102.45±4.2272.30±5.30 | 37.20±11.4020.85±8.9719.30±10.00 | --- | 0.10±0.020.87±0.661.28±0.96 | 2.99±0.442.69±0.562.77±0.36 | RIA | - |
| (b) PA before treatment PA after treatment | -- | 171.43±15.23136.71±11.34 | 103.36±2.5384.14±7.75 | 37.89±12.5433.19±20.02 | -- | 0.10±0.021.18±1.36 | -- |
| Lawrence, 1985 | PA | - | - | - | - | - | - | - | - | - |

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, PAC: plasma aldosterone concentration, PRC: plasma renin concentration, PRA: plasma renin activity, NOS: Newcastle-Ottawa Scale, NFA: non-functioning adrenal tumour, SA: secondary aldosteronism, GS: gitelman syndrome, BS: bartter syndrome, AI: adrenal incidentaloma, OP: osteoporosis, OE: osteopenia, HS: healthy subjects, CLA: chemiluminescence assay, ECLA: electro-chemiluminescence assay, ECLIA: electro-chemiluminescence immunoassay, ELISA: enzyme linked immunosorbent assay, CLIA: chemiluminescent immunoassay, RIA: immunoradiometric assays.

**Supplementary Table 3.** Quality of case-control studies included in the systematic review and meta-analysis (NOS scale).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Adequate case definition | Representativeness of the cases | Selection of Controls | Definition of Controls | Study controls for age | Study controls for additional factors | Ascertainment of exposure | Same method of ascertainment for cases and controls | Non-Response rate | Total quality scores |
| Zavatta, 2022 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 8 |
| Tang, 2022 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 7 |
| Liu, 2021 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 6 |
| Kometani, 2021 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 6 |
| Gravvanis, 2021 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Yokomoto, 2020 | 1 | 1 | 0 | 0 | 1 | 1 | 2 | 1 | 0 | 7 |
| Tuersun, 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 8 |
| Asbach, 2020 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Adolf, 2020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 8 |
| Lenzini, 2019 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 7 |
| Loh, 2018 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Lim, 2018 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 8 |
| Kim, 2018 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 8 |
| Shu, 2018 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 8 |
| Salcuni, 2017 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 | 9 |
| Notsu, 2017 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 8 |
| Zhang, 2016 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 1 | 6 |
| Jiang, 2016 | 1 | 1 | 1 | 0 | 1 | 0 | 2 | 1 | 1 | 8 |
| Petramala, 2014 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 6 |
| Ceccoli, 2013 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 7 |
| Salcuni, 2012 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 10 |
| Rossi, 2012 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 | 9 |
| Pliz, 2012 | 1 | 1 | 1 | 1 | 1 | 0 | 2 | 1 | 1 | 9 |
| Maniero, 2012 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 | 9 |
| Rossi, 1998 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 1 | 0 | 7 |
| Rossi, 1995 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 0 | 6 |