**Supplementary Table 1.** NOS risk of bias scale for included cohort studies

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Selection |  |  |  |  | Outcome |  |  |
| First author / Year | Representativeness of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Outcome of interest not present at start of study | Comparability | Assessment of outcome | Adequacy of duration of follow-up | Adequacy of completeness of follow-up | Total score(0-9) |
| Kaya 2017 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Nunez 2015 (Ca125 Gal3) | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Durak-Nalbantic 2013 | 1 | 0 | 1 | 1 | 1 (age) | 1 | 1 | 1 | 7 |
| Nunez 2012 (RS) | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Davutoglu 2010 | 1 | 0 | 1 | 1 | 1 (age) | 1 | 1 | 1 | 7 |
| Nunez 2010 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Mansour 2010 | 1 | 0 | 1 | 1 | 1 (age) | 1 | 1 | 1 | 7 |
| Nunez 2007 | 1 | 0 | 1 | 1 | 1 (age) | 1 | 1 | 1 | 7 |
| Kouris 2006 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Sir 2017 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 5 |
| Jang 2017 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 4 |
| Ratkovic 2016 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 4 |
| Santas 2016 | 1 | 0 | 1 | 1 | 1 (age) | 1 | 1 | 1 | 7 |
| Nunez 2015 (Ca125 BNP) | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 5 |
| Josa-Laorden 2015 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 4 |
| Liu 2012 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 5 |

**Supplementary Table 2.** Characteristics of the 16 studies included in this meta-analysis.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First author / Year | Study design | CA125 cut-off (U/ml) | Sample size (n) | Male (n) | Age (yrs) | Follow-up (months) | LVEF (%) | Variables in multivariate model | Ref |
| Kaya 2017 | Prospective cohort | 48 | 300 | 184 | 68 | 4 | 37 (10-65) | Atrial fibrillation, sodium, creatinine, age, diabetes mellitus, left atrial diameter, right ventricular dilatation, systolic pulmonary arterial pressure, pericardial effusion, blood urea nitrogen, potassium, albumin, beta blocker, diuretic, positive inotropic support, left ventricular ejection fraction  | [1] |
| Nunez 2016 | Randomized controlled trial | 35 | 380 | 212 | 74 | 12 | 46 (30-62) | (Univariate) | [2] |
| Nunez 2015 (Ca125 Gal3) | Prospective cohort | 67 | 264 | 131 | 73 | 24 | 49 (28-70) | Charlson comorbidity index, wide QRS (>120 msec), hemoglobin and Gal-3 | [3] |
| Durak-Nalbantic 2013 | Prospective cohort | - | 50 | 25 | 73 | - | - | - | [4] |
| Davutoglu 2010 | Prospective cohort | 50 | 100 | 59 | 65 | 6 | 33 (27-40) | Smoking, angiotensin converting enzyme, diuretic | [5] |
| Nunez 2010 | Prospective cohort | 60 | 1111 | 544 | 73 | 6 | 51 (41-61) | age (year), gender, prior admission for AHF, AHF category (acute decompensate heart failure vs. others), admission systolic blood pressure (mmHg), admission heart rate (b.p.m.), atrial fibrillation, evidence of pleural effusion, left ventricular ejection fraction, 50%, serum creatinine (mg/dL), serum sodium ≤ 130 mEq/L, and treatment with angiotensin receptor blockers and beta-blockers. | [6] |
| Mansour, 2010 | Prospective cohort | 35 | 172 | 105 | 56 | 40 | 29 (5-54) | Age, ischemic heart disease, glomerular filtration rate, left ventricular ejection fraction  | [7] |
| Nunez, 2007 | Prospective cohort | 35 | 529 | 249 | 73 | 6 | - (40% have LVEF (45%) | age, gender, diabetes and their interaction with gender and diabetes, New York Heart Association class III/IV, aetiology of valvular heart disease, systolic blood pressure, serum creatinine and haemoglobin | [8] |
| Kouris 2006 | Prospective cohort | - | 95 | 95 | 70 | 15 | 27 (20-34) | Left ventricular ejection fraction, early filling deceleration time, right ventricular systolic pressure | [9] |
| Sir 2017 | Prospective cohort | 64 | 100 | 59 | 72 | - | - | - | [10] |
| Jang 2017 | Retrospective cohort | continuous | 457 | 236 | 64 | 36 | - | Age, gender, New York Heart Association class, systolic blood pressure, beta blocker, inotropic, NT-proBNP | [11] |
| Ratkovic 2016 | Prospective cohort | - | 86 | - | - | - | - | - | [12] |
| Bosch Campos 2016 | Prospective cohort | 25 | 1869 | - | - | - | - | - | [13] |
| Santas 2016 | Prospective cohort | - | 1827 | 895 | 73 | 12 | 50 (30-70) | - | [14] |
| Nunez 2015 (Ca125 BNP) | Prospective cohort | Continuous | 846 | - | - | 32 | - | Well-established risk factors, NT-proBNP | [15] |
| Josa-Laorden 2015 | Prospective cohort | 60 | 200 | 101 | 79 | 6 | - | - | [16] |
| Liu 2012 | Prospective cohort | 35 | 444 | - | - | 24 | - | Red cell distribution width, NT-proBNP | [17] |

Abbreviations: NT-proBNP: N-terminal pro B-type natriuretic peptide.

**References**

[1] Kaya H, Kurt R, Beton O, Zorlu A, Yucel H, Gunes H, et al. Cancer Antigen 125 is Associated with Length of Stay in Patients with Acute Heart Failure. Tex Heart Inst J. 2017;44:22-8.

[2] Nunez J, Llacer P, Bertomeu-Gonzalez V, Bosch MJ, Merlos P, Garcia-Blas S, et al. Carbohydrate Antigen-125-Guided Therapy in Acute Heart Failure: CHANCE-HF: A Randomized Study. JACC Heart Fail. 2016;4:833-43.

[3] Nunez J, Rabinovich GA, Sandino J, Mainar L, Palau P, Santas E, et al. Prognostic value of the interaction between galectin-3 and antigen carbohydrate 125 in acute heart failure. PLoS One. 2015;10:e0122360.

[4] Durak-Nalbantic A, Resic N, Kulic M, Pecar E, Zvizdic F, Dzubur A, et al. Serum level of tumor marker carbohydrate antigen-CA125 in heart failure. Med Arch. 2013;67:241-4.

[5] Davutoglu V, Yildirim C, Kucukaslan H, Yuce M, Sari I, Tarakcioglu M, et al. Prognostic value of pleural effusion, CA-125 and NT-proBNP in patients with acute decompensated heart failure. Kardiol Pol. 2010;68:771-8.

[6] Nunez J, Sanchis J, Bodi V, Fonarow GC, Nunez E, Bertomeu-Gonzalez V, et al. Improvement in risk stratification with the combination of the tumour marker antigen carbohydrate 125 and brain natriuretic peptide in patients with acute heart failure. Eur Heart J. 2010;31:1752-63.

[7] Mansour IN, Napan S, Tarek Alahdab M, Stamos TD. Carbohydrate antigen 125 predicts long-term mortality in African American patients with acute decompensated heart failure. Congest Heart Fail. 2010;16:15-20.

[8] Nunez J, Nunez E, Consuegra L, Sanchis J, Bodi V, Martinez-Brotons A, et al. Carbohydrate antigen 125: an emerging prognostic risk factor in acute heart failure? Heart. 2007;93:716-21.

[9] Kouris NT, Kontogianni DD, Papoulia EP, Goranitou GS, Zaharos ID, Grassos HA, et al. Clinical and prognostic value of elevated CA125 levels in patients with congestive heart failure. Hellenic J Cardiol. 2006;47:269-74.

[10] Sir JJ, Lee SA, Choi SM, Joo SB. The prognostic value of carbohydrate antigen 125 level in patients with acute decompensated heart failure: Correlation with echocardiographic parameters. European Journal of Heart Failure. 2017;19:44.

[11] Jang SY, Yang DH, Kim CY, Kim NG, Bae MH, Lee JH, et al. Prognostic value of CA-125 in combination with N-terminal pro-brain natriuretic peptide in patients with acute decompensated heart failure. European Journal of Heart Failure. 2017;18:247.

[12] Ratkovic N, Danijela V, Slobodan O, Miodrag S, Lidija T, Ristic A, et al. Serum concentrations of tumor markers carbohydrate antigen 125 (CA 125) in acute heart failure - clinical implications. European Journal of Heart Failure. 2016;18:242.

[13] Bosch Campos MJ, Santas E, Bondanza L, Merlos MP, Palau P, Sanchis J, et al. Antigen carbohydrate 125 predicts 30-day readmission in acute heart failure. European Heart Journal. 2016;35:1010.

[14] Santas E, Sandino J, Chorro FJ, Méndez J, Miñana G, Núñez E, et al. Prognostic implications of pericardial effusion in acute heart failure: Does size matter? International Journal of Cardiology. 2015;184:259-61.

[15] Nunez J, Nunez E, Minana G, Sanchis J, Santas E, Escribano D, et al. Mortality prediction following an admission for acute heart failure: a longitudinal comparison between N-terminal brain natriuretic peptide and carbohydrate antigen 125. European Journal of Heart Failure 2015;17:261.

[16] Josa-Laorden C, Torres-Courchoud I, Martinez-Marin M, Gimenez-Lopez I, Sanchez-Marteles M, Garces-Horna V, et al. Glycoprotein CA125 as short and long term prognostic biomarker in heart failure. European Journal of Heart Failure. 2015;17:99.

[17] Liu MY, Zhang H, Zhu W, Yang XM, Shen H, Wei M. Determining the prognostic value of red cell distribution width and carbohydrate antigen 125 in acute decompensated heart failure patients. European Journal of Heart Failure. 2013;15:S130.