**Table 1.** General characteristics of the studies included in the systematic review.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Country** | **Study Design** | **Ultrasound signs** | **Reference standard** | **Associated major CHDs** | **GA at US** | **Fetuses (n)** | **CoA**  **(n)** |
| Arya (14) | 2016 | United States | Retrospective | AoI d z-score, RV/LV d ratio, RV/LV length ratio, TV/LV area ratio, RV/LV volume ratio, DA/AoI flow ratio, DAo/AoI d ratio, MPA/AoI d ratio, LCSA, Aao/Dao angle, TAo-DAo angle | Post-natal echocardiography, surgery | Excluded | 32.8 ± 4.2 | 40 | 20 |
| Toole (15) | 2015 | United States | Retrospective | TV z-score, MV z-score, PV z-score AoV z-score, AAo z-score, TAoA z-score, AoI z-score, RV length, LV length, AoV/PV ratio, RV/LV area ratio, AoI/DA ratio, MV/TV ratio, PLSVC, Isthmus-ductal angle, AoI PSV, AoI PI | Post-natal echocardiography, surgery | Excluded | 33.9(30.4-36.0) | 62 | 27 |
| Mărginean (16) | 2015 | Romania | Prospective | AoI z-score, Aao z-score, AD/AoI ratio, PA/Ao ratio, Ao d, AoI d, RV/LV ratio, PLSVC, BAV, VSD | Post-natal echocardiography, surgery | Excluded | 36 (32-39) | 32 | 9 |
| Durand (17) | 2015 | France | Prospective | Ventricular and/or great vessels disproportion, AoV z-score (FL and GA), AoV d (mm), PSLVC, VSD, bicuspid AoV, hypoplastic and/or angular AoA | Post-natal echocardiography, surgery | Excluded | 36w±3d | 285 | 41 |
| Sivanandam (18) | 2015 | United States | Retrospective | CSI, AoI z-score, MV z-score, AoV z-score | Post-natal echocardiography, surgery | Excluded | 25,6 (20-35) | 31 | 11 |
| Gomez-Montes (19) | 2014 | Spain | Retrospective | TV z-score, MV z-score, TV/MV ratio, PV z-score, AoV z-score, MPA z-score, AA z-score, Isthmus z-score, AD z-score, Isthmus/AD ratio, hypoplastic arch, PLSVC, midflow at AoA, bidirectional flow at FO | Post-natal echocardiography, surgery | Excluded | 27.6±6.6 | 115 | 52 |
| Rizzo (20) | 2010 | Italy | Prospective | PA/AO ratio | Post-natal echocardiography, surgery | Excluded | 30 (26–34) | 18 | 8 |
| Slodki (21) | 2009 | Poland/United States | Retrospective | AoI d (mm), AAo d (mm), PA d (mm), PA/AoA ratio | Post-natal echocardiography, surgery | Excluded | 33.0±3.8 | 52 | 12 |
| Axt-Fliedner (22) | 2008 | Germany | Retrospective | PLSVC, VSD | Autopsy, post-natal echocardiography, surgery | Excluded | 31w+4d (13+2-38+6) | 61 | 37 |
| Matsui (23) | 2008 | UK | Retrospective | Vascular disproportion, PLSVC, VSD, BAV, shelf, Doppler anomalies, AoI Z-score, AoI/AD ratio | Autopsy, post-natal echocardiography, surgery | Excluded | 22w+0d (15+4-38+4) | 44 | 20 |
| Head (24) | 2004 | United Kingdom | Retrospective | VSD, PLSVC, | Autopsy, post-natal echocardiography, surgery | Excluded | Not stated | 144 | 43 |
| Hornung (25) | 2001 | United Kingdom | Retrospective | VSD, BAV | Post-natal echocardiography, surgery | Excluded | 29 (16–38) | 38 | 3 |

Ao: aorta, AAo: ascending aorta, AD: arterial duct, AoA: aortic arch, AoI: aortic isthmus, BAV: bicuspid aortic valve, CSI: carotid subclavian index, DAo: descending aorta,LCSA:left common carotid-to-left subclavian artery distanceLV: left ventricle, MV: mitral valve, PA: pulmonary artery, PI: pulòsatility index, PV: pulmonary valve, PLSVC: persistent left superior vena cava, RV: right ventricle, TAoA: transverse aortic arch, TV: tricuspid valve, VSD: ventricular septal defect,

**Table 2.** Quality assessment of the included studiesaccording to Newcastle-Ottawa Scale (NOS) a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Author** | **Year** | **Selection** | **Comparability** | **Outcome** |
| Arya (14) | 2016 |  |  |  |
| Toole (15) | 2016 |  |  |  |
| Mărginean (16) | 2015 |  |  |  |
| Durand (17) | 2015 |  |  |  |
| Sivanandam (18) | 2015 |  |  |  |
| Gomez-Montes (19) | 2015 |  |  |  |
| Rizzo (20) | 2014 |  |  |  |
| Slodki (21) | 2010 |  |  |  |
| Axt-Fliedner (22) | 2009 |  |  |  |
| Matsui (23) | 2008 |  |  |  |
| Head (24) | 2008 |  |  |  |
| Hornung (25) | 2002 |  |  |  |

**Table 3**. Results of the meta-analyses comparing the echocardiographic parameters of different cardiac structures in fetuses with diagnosis of coarctation of the aorta versus normal fetuses.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Continuous Parameters*** | **N. studies**  **(total sample)** | **Reference** | **n/N\*** | **Mean difference**  **(95% CI)** | **p** | **I2**, % |
|  |  |  |  |  |  |  |
| ***1. Atrio-ventricular valves*** |  |  |  |  |  |  |
| - Tricuspid valve z-score | 2 (177) | (15,19) | 79 / 98 | 0.40 (0.09; 0.71) | **0.01** | 0 |
| - Mitral valve z-score | 3 (208) | (15,18,19) | 90 / 118 | -0.97 (-1.43; -0.51) | **<0.001** | 0 |
|  |  |  |  |  |  |  |
| ***2. Outflow tracts*** |  |  |  |  |  |  |
| - Aortic valve z-score (based upon GA) | 4 (383) | (15,17-19) | 130 / 253 | -1.19 (-1.56; -0.82) | **<0.001** | 32 |
| - Ascending aorta z-score (based upon GA) | 2 (177) | (15,19) | 79 / 98 | -0.95 (-1.97; 0.07) | 0.07 | 85 |
| - Ascending aorta diameter, mm | 2 (84) | (16,21) | 21 / 63 | -0.78 (-2.86; 1.31) | 0.47 | 87 |
| - Aortic isthmus z-score (sagittal view) | 4 (248) | (14,15,18,19) | 110 / 138 | -1.24 (-2.27; -0.22) | **0.02** | 82 |
| - Aortic isthmus z-score (3-vessel view) | 3 (178) | (16,18,19) | 72 / 106 | -1.47 (-2.27; -0.68) | **<0.001** | 74 |
| - Aortic isthmus diameter, mm | 2 (84) | (16,21) | 21 / 63 | -0.99 (-1.21; -0.77) | **<0.001** | 0 |
| - Pulmonary valve z-score | 2 (177) | (15,19) | 79 / 98 | 0.73 (0.32; 1.13) | **<0.001** | 0 |
|  |  |  |  |  |  |  |
| ***4. Ratios*** |  |  |  |  |  |  |
| - Right ventricle/left ventricle (diameters, mm) | 2 (72) | (14,16) | 29 / 43 | 0.21 (0.04; 0.39) | **0.02** | 0 |
| - Right ventricle/left ventricle (areas, mm2) | 2 (102) | (14,15) | 47 / 55 | 0.25 (-0.01; 0.51) | 0.06 | 0 |
| - Pulmonary artery/ascending aorta (diameters, mm) | 4 (217) | (15,19-21) | 81 / 136 | 0.43 (0.07; 0.78) | **0.02** | 90 |
| - Aortic isthmus/arterial duct (diameters, mm) | 2 (161) | (15,19) | 63 / 98 | -0.13 (-0.19; -0.08) | **<0.001** | 0 |
| - Arterial duct/aortic isthmus (diameters, mm) | 2 (70) | (14,16) | 28 / 42 | 0.24 (-0.17; 0.65) | 0.25 | 82 |

GA = Gestational age.

\*: n: overall number of fetuses affected by CoA; N: overall number of fetuses not affected by CoA.

**Table 4**. Likelihood of presenting each cardiovascular anomaly in fetuses with a diagnosis of coarctation of the aorta versus normal fetuses. For each parameter, summary estimates of sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR-) and diagnostic odds ratio (DOR) to predict coarctation of the aorta were also computed. Depending on the number of studies, computations were based upon DerSimonian-Laird random-effect (Ψ) or hierarchical summary receiver operating characteristic (HSROC) model (Ω).

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Categorical***  ***Parameters*** | **N.**  **studies** | **Reference** | **Total**  **Sample** | **OR**  **(95% CI)** | **p** | **I2(%)** | **Sensitivity**  **% (95% CI)** | **Specificity**  **% (95% CI)** | **DOR**  **(95% CI)** | **LR+**  **(95% CI)** | **LR-**  **(95% CI)** |
| **PLSVC** | 8 Ω | (14-17,19,22-24) | 662 | 1.08  (0.48-2.42) | 0.85 | 51 | 11.7  (7.39-18.0) | 89.6  (79.4-95.1) | 1.14  (0.57-2.30) | 1.12  (0.60-2.10) | 0.98  (0.92-1.06) |
| **VSD** | 8 Ω | (14,16-18,22-25) | 554 | 2.33  (0.80-6.80) | 0.12 | 73 | 26.9  (16.5-40.6) | 87.2  (77.9-91.7) | 2.30  (0.83-6.34) | 1.95  (0.87-4.36) | 0.85  (0.68-1.05) |
| **Shelf** | 2 Ψ | (18, 23) | 75 | 26.0  (4.42-153) | **<0.001** | 0 | 48.4  (30.2-66.9) | 97.7  (88.0-99.9) | 26.0  (4.42-153) | 13.9  (2.76-69.6) | 0.54  (0.39-0.76) |
| **Hypoplastic aortic arch** | 5 Ω | (14,17,19,23,24) | 506 | 38.2  (3.01-486) | **0.005** | 90 | 90.0  (48.6-98.8) | 87.1  (59.4-96.9) | 60.8  (3.16-1169) | 6.99  (1.73-28.2) | 0.12  (0.014-0.91) |
| **Bicuspid aortic valve** | 6 Ω | (14,16-18,23,25) | 360 | 4.79  (0.45-51.2) | 0.20 | 84 | 24.8  (14.9-38.4) | 95.7  (75.4-99.4) | 7.35  (0.90-59.9) | 5.78  (0.81-41.4) | 0.78  (0.66-0.94) |

PLSVC: persistent left superior vena cava; VSD: ventricular septal defect

**Table 5.** Predictive models for CoA integrating multiple risk factors.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Predictive model** | **AUC (95% CI)** | **Sensitivity (95% CI)** | **Specificity (95% CI)** |
| Arya*et al.*(14) | 2016 | AAo-DAo angle+TAo-DAo angle | NS | 95 (75-100) | 100 (83-100) |
| Toole*et al.*(15) | 2015 | MV d+MV/TV ratio+ IDD+IDA+IDD | 0.92 (0.80-1.00) | 85 (66-96) | 60 (42-76) |
| Mărginean*et al.*(16) | 2015 | RV/LV<1.5+AoI <4.2 mm + AD/AoI >1.4 | NS | 56 (21-86) | 87 (66-97) |
| Gomez-Montes *et al.* (19) | 2014 | z-score AAo + z-score AoI (Sagittal view) (≤28w) | 0.88 (0.72–1.00) | 60 (41–77) a | 78 (45–94) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AAo + z-score AoI (3VT view) (≤28w) | 0.98 (0.94–1.00) | 91 (76–97) a | 91 (62–98) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AAo + TV/MV ratio (≤28w) | 0.85 (0.71–0.99) | 44 (29–59) a | 69 (42–87) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AAo + MPA/AAo ratio (≤28w) | 0.87 (0.76–0.99) | 78 (63–88) a | 62 (36–82) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AoI (Sagittal view) + z-score AoI (3VT view) (≤28w) | 0.97 (0.91–1.00) | 86 (65–95) a | 89 (57–98) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AoI (sagittal view) + TV/MV ratio (≤28w) | 0.82 (0.63–1.00) | 23 (11–42) a | 70 (40–89) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AoI (sagittal view) + MPA/AAo ratio (≤28w) | 0.85 (0.72–0.98) | 68 (48–83) a | 44 (19–73) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AoI (3VT view) + TV/MV ratio (≤28w) | 0.94 (0.84–1.00) | 87 (71–95) a | 83 (55–95) b |
| Gomez-Montes *et al.*(19) | 2014 | z-score AoI (3VT view) + MPA/AAo ratio (≤28w) | 0.89 (0.75–1.00) | 48 (32–65) a | 82 (52–95) b |
| Gomez-Montes *et al.*(19) | 2014 | TV/MV ratio + MPA/AAo ratio (≤28w) | 0.82 (0.67–0.96) | 44 (29–59) a | 54 (29–77) b |
| Gomez-Montes *et al.*(19) | 2014 | GA+ z-score AAo + z-score isthmus (3VT view) + PV/AV (≤28w) | 0.85 (0.73–0.98) | 40 (26–54) a | 64 (39–84) b |
| Gomez-Montes *et al.*(19) | 2014 | TV/MV ratio +MPA/AAo ratio (>28w) | 0.84 (0.67–1.00) | 63 (31–86) a | 43 (30–58) b |
| Gomez-Montes *et al.*(19) | 2014 | GA+ z-score AAo + z-score AoI (3VT view) + PV/AV (>28w) | 0.90 (0.83–0.98) | 44 (19–73) a | 82 (69–90) b |

a: for 10% false positive rate

b: for 10% false negative rate