**Adolescents and adults with Fontan circulation: insights from the PREpArE-Fontan registry**

**Supplementary material**

Lars Søndergaard, Jamil Aboulhosn, Yves d’Udekem, Céline Faure, Wayne J Franklin, Alfred Hager, YY Kim, Erwan Muros-Le Rouzic, Daniel Rosenberg, Markus Schwerzmann, Paul Clift

**Supplementary Table 1.** Details of study enrolment by country

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **USA** | **Denmark** | **Germany** | **Switzerland** | **UK** |
| Date of first registration visit | May 3, 2016 | February 16, 2016 | November 7, 2016 | July 28, 2016 | July 28, 2016 |
| Date of last registration visit | April 27, 2017 | January 26, 2017 | April 28, 2017 | April 25, 2017 | April 20, 2017 |
| Number of patients in the enrolled population | 99 | 38 | 44 | 14 | 71 |

**Supplementary Table 2.** Relevant medical history, as defined in the PREpArE-Fontan registry

|  |  |
| --- | --- |
| **Event or condition** | **Inclusion period** |
| Severe extra-cardiac congenital defect | Ongoing at registration visit |
| Neurological deficit |
| Pacemaker |
| Ascites | Within 2 years prior to registration visit |
| Clinically significant peripheral oedema |
| Significant collateral circulation |
| Postural orthostatic tachycardia syndrome |
| Thromboembolic event |
| Symptomatic coronary artery disease |
| Myocardial infarction |
| Stenosis in Fontan circulation |
| Life-threatening arrhythmia |
| Relapsing tachyarrhythmia |
| Pericardial constriction |
| Severe ventricular dysfunction with elevated single ventricular end diastolic pressure (>12 mmHg) |
| Severe atrio-ventricular valve regurgitation |
| Aortic regurgitation |
| Valvular defect due to systemic inflammatory disease |
| Syncope during exercise |
| Initiation or change in diuretic medication |

Any instance of the above-listed events or conditions was considered relevant medical history and recorded in the electronic case report form by the investigator.

**Supplementary Table 3.** Selected cardiopulmonary parameters and medications by CrCl

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CrCl <90 mL/min****n=81** | **CrCl ≥90 mL/min****n=75** | **Total population**†**n=156** | **P-value** |
| Heart rate, bpm Missing, n | 77.7 (13.4)0 | 78.8 (13.9)1 | 78.2 (13.6)1 | 0.683 |
| Arrhythmia, n (%) Missing, n | 14 (17.5)1 | 20 (27.4)2 | 34 (22.4)3 | 0.141 |
| NYHA FC, n (%) I II III Missing, n | 55 (67.9)22 (27.2)4 (4.9)0 | 50 (66.7)21 (28.0)4 (5.3)0 | 105 (67.3)43 (27.6)8 (5.1)0 | 1.000 |
| Systolic blood pressure, mmHg Missing, n | 116 (13)0 | 118 (14)1 | 117 (13)1 | 0.854 |
| Diastolic blood pressure, mmHg Missing, n | 73 (8)1 | 70 (10)1 | 71 (9)2 | 0.074 |
| SpO2 at rest, % Missing, n | 93 (4)2 | 93 (5)1 | 93 (4)3 | 0.762 |
| SpO2 during exercise, % Missing, n | 89 (5)58 | 89 (7)36 | 89 (7)94 | 0.720 |
| Medications initiated or ongoing at registration visit, n (%)  Anticoagulant ACE inhibitor ARB  Antiplatelet Beta-blocker Diuretic Anti-arrhythmic Pulmonary hypertension medication Iron supplementation Missing, n  | 50 (61.7)51 (63.0)1 (1.2)25 (30.9)23 (28.4)17 (21.0)18 (22.2)4 (4.9)1 (1.2)0 | 28 (37.3)31 (41.3)2 (2.7)40 (53.3)23 (30.7)10 (13.3)7 (9.3)8 (10.7)1 (1.3)0 | 78 (50.0)82 (52.6)3 (1.9)65 (41.7)46 (29.5)27 (17.3)25 (16.0)12 (7.7)2 (1.3)0 | 0.0020.0070.6080.0040.7560.2070.0280.1801.000 |

Values are mean (SD) unless otherwise noted. P-values relate to exploratory analyses of correlations and associations between renal dysfunction and laboratory parameters, patient demographics or clinical characteristics undertaken, stratified by CrCl (<90, ≥90 mL/min). Analyses included unpaired *t*-test (or Mann-Whitney-Wilcoxon test when assumptions were not met) for continuous variables, the chi-squared test (or Fisher exact test when assumptions were not met) for categorical nominal variables and the Mann-Whitney-Wilcoxon or Cochran Mantel Haenszel test for categorical ordinal variables.

†Patients with non-missing CrCl data.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; bpm, beats per minute; CrCl, creatinine clearance; NYHA FC, New York Heart Association functional class; SpO2, oxygen saturation.

**Supplementary Table 4.** Logistic regression analysis of the patient characteristics associated with renal dysfunction

|  |  |  |
| --- | --- | --- |
| **Parameter**  | **Univariate analysis** | **Multivariate analysis** |
| **P-value** | **Odds ratio** | **95% CI lower** | **95% CI upper** | ***p*-value** |
| Region: Europe (reference [1.000]) or USA | 0.018 |  |  |  |  |
| Age at Fontan completion (years)  | 0.007 |  |  |  |  |
| Type of Fontan surgery: ECC (reference [1.000]) or LT | <0.001 | 4.777 | 2.113 | 10.799 | 0.0002 |
| Haemoglobin level¶: abnormal (reference [1.000]) or normal  | 0.247 |  |  |  |  |
| Serum albumin (g/L)  | 0.001 |  |  |  |  |
| Serum protein§: abnormal (reference [1.000]) or abnormal | 0.072 |  |  |  |  |
| Arrhythmia: no (reference [1.000]) or yes | 0.141 |  |  |  |  |
| Diastolic blood pressure at rest (mmHg)  | 0.074 |  |  |  |  |
| Neurological deficit: no (reference [1.000]) or yes | 0.017 |  |  |  |  |
| Thromboembolic event: no (reference [1.000]) or yes | 0.230 |  |  |  |  |
| ACE inhibitor use: no (reference [1.000]) or yes | 0.007 |  |  |  |  |
| Diuretic use: no (reference [1.000]) or yes | 0.207 |  |  |  |  |
| Anti-arrhythmic medication: no (reference [1.000]) or yes | 0.028 | 0.284 | 0.093 | 0.866 | 0.0270 |
| Antiplatelet medication: no (reference [1.000]) or yes | 0.004 | 2.492 | 1.102 | 5.635 | 0.0283 |
| Pulmonary hypertension medication: no (reference [1.000]) or yes | 0.180 |  |  |  |  |
| Abdominal ultrasound: no (reference [1.000]) or yes | 0.007 | 2.991 | 1.302 | 6.870 | 0.0096 |
| Cardiac catheterization: no (reference [1.000]) or yes | 0.129 |  |  |  |  |

Based on the analysis population (n=125) with available data. The analysis population was subdivided into two groups by renal function (creatine clearance <90 and ≥90 mL/min) and the patient characteristics associated with renal dysfunction were investigated by multivariate logistic regression analyses. Multivariate model includes all patient characteristics that, in the univariate regression, had p<0.25 (remaining characteristics are greyed out in multivariate columns). Additional parameters were excluded from the analysis due to high levels of missing data.

¶For males, normal: 13–17 g/dL; abnormal: <13 or >17 g/dL. For females, normal: 12–15 g/dL; abnormal: <12 or >15 g/dL.

§Normal: 60–80 g/L; abnormal: <60 or >80 g/L.

ACE, angiotensin converting enzyme; CI, confidence interval; ECC, extra-cardiac conduit; LT, lateral tunnel.