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Reference right ventricular systolic and diastolic function normalized to age, gender and body surface area from steady-state free precession cardiovascular magnetic resonance

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Aims Recent advances in cardiovascular magnetic resonance (CMR) include improved image quality with steady-state free precession (SSFP) sequences and advanced post-processing of high temporal resolution ventricular function. We used these techniques to establish the reference values for right ventricular (RV) volumes and function.

Methods and results We studied 120 healthy subjects (60 men, 60 women; from 20 to 80 years) after exclusion of cardiovascular abnormality. Data were generated from SSFP cines, with three-dimensional modelling. Gender, body surface area (BSA), and age were independent predictors of several RV parameters. Normalized RV mass (RVM) and absolute and normalized RV volumes decreased significantly with age, whereas ejection fraction increased. For diastolic variables, absolute and normalized early peak filling rate (PFR_E) decreased and absolute and normalized active peak filling rate (PFR_A) in males increased, with decreased PFR_E/PFR_A. Increasing BSA was associated with increased RVM, volumes, and PFR_E. Gender significantly influenced absolute and normalized mass and volumes, and absolute and normalized PFR_A.

Conclusion These data using state-of-the-art CMR show that normal values of RV systolic and diastolic parameters vary significantly by gender, BSA, and age. Appropriate reference ranges normalized to all three variables should be used in the determination of normality or severity of abnormality of RV dimensions and function.

Introduction

Cardiovascular magnetic resonance (CMR) has been applied for the measurement of left ventricular (LV) and right ventricular (RV) volumes, systolic function, and mass for several years in the clinical arena, with standardized methods of short-axis multi-slice acquisition.[1] The excellent accuracy,[2] and reproducibility of CMR is well established,[3] making it a gold standard technique that can be very cost-effective.[4] This technique is well suited for the determination of RV parameters, because of the variable configuration of this chamber that requires a three-dimensional volume acquisition. CMR-derived RV volumes show good correlation with *in vivo* standards,[5] and this technique has shown good accuracy[6] and reproducibility[7] for RV measurements. RV normal clinical ranges were established from a spoiled gradient echo sequence.[8] However, in recent years, the steady-state free precession (SSFP) technique has been introduced, which yields significantly improved blood-myocardium contrast, acquisition speed, and the ability to greatly improve the temporal resolution of the cines with improved image quality.[9] SSFP acquisitions yield slightly different results to the spoiled gradient echo sequence for cardiac volumes, because of superior discrimination between blood and endocardium, and between epicardium and epicardial fat.[10] This requires the determination of new reference ranges. The aim of this study was therefore to establish SSFP-based reference values in normal subjects for RV systolic function. In addition, in this study we establish normal values for RV diastolic function.

Methods

Patients

A total of 250 subjects working at the Royal Brompton and Harefield NHS Trust as well as their relatives were initially contacted by e-mail and invited to take part in our study as healthy volunteers, for which they should be asymptomatic, with no known risk factors of coronary artery disease and no history of cardiac disease. Finally, 142 subjects responded positively and agreed to

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participate. Of these, five were rejected after initial assessment (two males found to be hypertensive, one female because of *q*-waves on her electrocardiogram, one female because of morbid obesity, and one male found to have atrial fibrillation). Of the 137 remaining subjects, four finally could not participate because of claustrophobia and another 13 were not included as the target number had been reached before they could take part. Eventually, the study included 120 healthy volunteers, with 10 men and 10 women in each of six age deciles from 20 to 80 years. Data on analysis of LV parameters in these patients has been reported elsewhere.[11] All subjects were completely asymptomatic, with no known risk factors or history of cardiac disease and normal physical examination and ECG. Also measured were the height, weight, blood pressure, total cholesterol, HDL, and B-natriuretic peptide (BNP) (*Table 1*). Body surface area (BSA) was calculated according to the Mosteller formula.[12] With the information, the coronary artery disease risk over 10 years was calculated.[13] The BNP levels were 2.5 $\pm$ 2.1 pg/mL (range 0.5–12.0), and all were in the normal range ($<$100 pg/mL).[14] Moreover, relative stroke volume (SV) comparison with the LV[11] confirmed the lack of shunting in all. Therefore, as far as it was possible to ascertain with conventional non-invasive techniques, all the apparently healthy subjects had a normal cardiovascular system with no evidence of heart failure. The study was approved by the institutional Ethics Committee, and all subjects gave written informed consent.

Cardiovascular magnetic resonance

CMR was performed with a 1.5T scanner (Siemens Sonata) using front and back surface coils and retrospective ECG triggering for capture of the entire cardiac cycle including diastole. All CMR scans were performed by the same operator. SSFP end-expiratory breath-hold cines were acquired in the vertical and horizontal long-axis planes, with subsequent contiguous short-axis cines from the atrioventricular (AV) ring to the apex. Slice thickness was 7 mm. The temporal resolution was 21.6 $\pm$ 1 ms. Sequence parameters included repetition time/echo time of 3.2/1.6 ms, in-plane pixel size of 2.1 $\times$ 1.3 mm, flip angle 60°, and acquisition time of 18 heartbeats.

CMR analysis

Analysis was performed with a personal computer and semi-automated software (CMRTools, Cardiovascular Imaging Solutions, London, UK) with the method described elsewhere.[11] Analysis included three principal steps. First, delineation of RV endocardial and epicardial borders in all planes in all cardiac phases. Second, calculation of the systolic descent and twist of the tricuspid valve from tracking of the valve motion on the long-axis cines, this was used to correct for loss of systolic RV volume due to AV ring descent. Third, delineation of papillary muscles with blood pool thresholding (*Figure 1*). RVM was calculated from the end-diastolic frames. End-systolic (ESV) and end-diastolic (EDV) volumes were calculated from the RV volume/time curve generated from all frames of all cines, and there was no requirement to choose the largest and smallest ventricular frames (*Figure 2*). SV was calculated as the difference between EDV and ESV, and ejection fraction (EF) was calculated as SV/EDV. Papillary muscles were included when measuring mass (equivalent to weighing the RV) and excluded when measuring volumes (equivalent to blood pool techniques). Diastolic function was calculated from the derivative of the time/volume curve, and expressed as peak filling rate (PFR). The early and active peak filling rates (PFR_E and PFR_A) and their ratio were calculated. Longitudinal AV plane descent (AVPD) was measured in the RV septum and lateral wall, and also expressed as a ratio of the ventricular length.

Statistical analysis

All studied parameters except BNP and PFR_E/PFR_A ratio were found to satisfy a normal distribution using the Kolmogorov–Smirnov test and summary data for these variables are presented as mean $\pm$ SD. To determine intraobserver variability, 10 CMR scans were randomly selected and the observer, blinded with respect to the initial values obtained, subsequently re-evaluated copies of these images at least 2 weeks after the first analysis. For each parameter, the mean $\pm$ SD of the differences between the two measurement results was calculated and the coefficient of variability (expressed as a percentage) was calculated as the SD of the differences divided by the mean of the parameter under consideration. To test interobserver variability, the same scans were re-evaluated by a different observer blinded to the results obtained by the previous investigator and the coefficient of variability was obtained in a similar way.

Multivariable analysis was used to determine the dependence of the measured LV parameters on age, gender, and BSA. Simple univariate linear regression against age was then used to construct the presented reference ranges normalized for BSA and divided by

Table 1 Baseline characteristics of normal subjects studied (mean $\pm$ SD)

Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
Males						
Height (cm)	178 $\pm$ 9	181 $\pm$ 9	175 $\pm$ 6	177 $\pm$ 6	175 $\pm$ 8	179 $\pm$ 3
Weight (kg)	71 $\pm$ 9	81 $\pm$ 8	83 $\pm$ 10	78 $\pm$ 12	79 $\pm$ 9	83 $\pm$ 9
BSA (m^2)	1.88 $\pm$ 0.13	2.01 $\pm$ 0.13	1.99 $\pm$ 0.15	1.94 $\pm$ 0.11	1.94 $\pm$ 0.13	2.01 $\pm$ 0.10
Body mass index (kg/m^2)	22 $\pm$ 3	24 $\pm$ 3	27 $\pm$ 2	25 $\pm$ 5	26 $\pm$ 3	26 $\pm$ 3
Systolic blood pressure (mmHg)	125 $\pm$ 7	130 $\pm$ 4	123 $\pm$ 3	123 $\pm$ 9	126 $\pm$ 7	134 $\pm$ 9
Diastolic blood pressure (mmHg)	73 $\pm$ 5	77 $\pm$ 5	73 $\pm$ 4	77 $\pm$ 6	75 $\pm$ 7	77 $\pm$ 7
10-year CAD risk (%)	0.2 $\pm$ 0.2	1.3 $\pm$ 0.9	3.6 $\pm$ 1.2	9.8 $\pm$ 4.4	14.0 $\pm$ 3.4	16.6 $\pm$ 6.5
BNP (pmol/L)	1.2 $\pm$ 1.6	1.4 $\pm$ 1.6	1.5 $\pm$ 1.6	1.7 $\pm$ 2.5	2.1 $\pm$ 2.2	3.4 $\pm$ 2.3
Females						
Height (cm)	166 $\pm$ 11	167 $\pm$ 8	168 $\pm$ 6	165 $\pm$ 5	163 $\pm$ 5	162 $\pm$ 3
Weight (kg)	64 $\pm$ 15	59 $\pm$ 6	64 $\pm$ 9	66 $\pm$ 12	68 $\pm$ 11	70 $\pm$ 16
BSA (m^2)	1.71 $\pm$ 0.23	1.66 $\pm$ 0.11	1.72 $\pm$ 0.11	1.71 $\pm$ 0.11	1.73 $\pm$ 0.13	1.74 $\pm$ 0.16
Body mass index (kg/m^2)	23 $\pm$ 3	21 $\pm$ 2	23 $\pm$ 3	24 $\pm$ 5	25 $\pm$ 5	26 $\pm$ 6
Systolic blood pressure (mmHg)	121 $\pm$ 12	123 $\pm$ 6	115 $\pm$ 13	116 $\pm$ 18	119 $\pm$ 14	135 $\pm$ 12
Diastolic blood pressure (mmHg)	70 $\pm$ 9	68 $\pm$ 4	71 $\pm$ 9	71 $\pm$ 11	73 $\pm$ 6	79 $\pm$ 6
10-year CAD risk (%)	0.0 $\pm$ 0.0	0.3 $\pm$ 0.2	1.6 $\pm$ 0.6	3.2 $\pm$ 2.0	6.2 $\pm$ 2.9	8.3 $\pm$ 4.7
BNP (pmol/L)	1.3 $\pm$ 2.5	1.6 $\pm$ 2.7	1.9 $\pm$ 1.8	1.8 $\pm$ 2.5	2.2 $\pm$ 1.4	2.4 $\pm$ 1.4

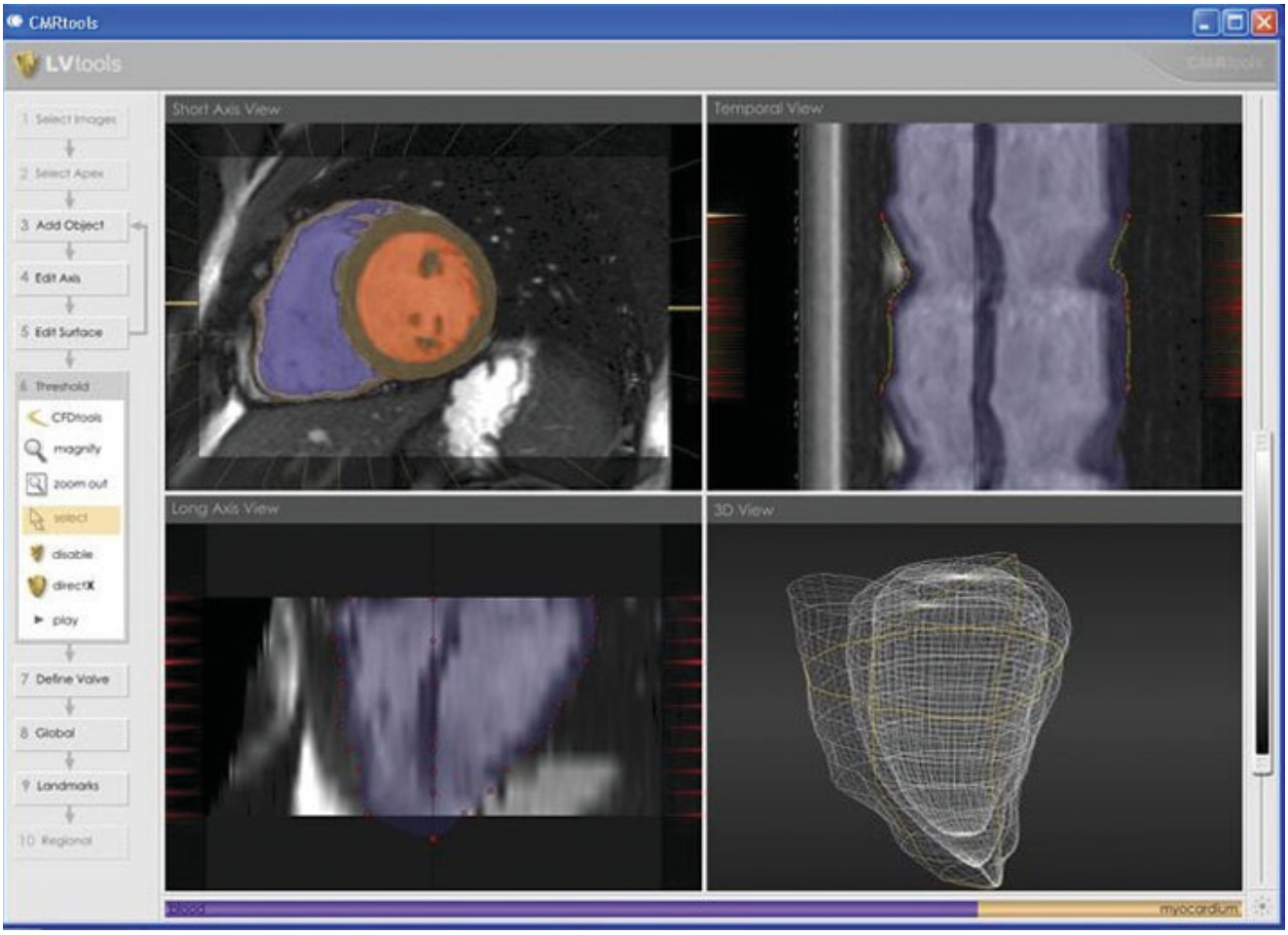

Figure 1 Screenshot showing an example of semi-automated analysis (online supplementary data).

gender, as mean and 95% confidence intervals. BNP and PFR_E/PFR_A data were normally distributed after log-transformation, and after regression, the means and confidence intervals were back-transformed for presentation. Student's paired *t*-test was used to compare RV SV with previously reported LV SV.[11] Two-way ANOVA was used to analyse variations in parameters due to age and gender. *P*-values <0.05 were considered significant.

Results

Baseline characteristics and summary results

Table 1 summarizes the baseline patient characteristics. The results across age deciles, with differentiation into males, females, and all subjects, and sub-division into absolute and BSA-normalized values are shown for systole (*Tables 2–4*) and diastole (*Tables 5–7*). *Table 8* shows the data summarized for the entire study group, and male and female groups, without age breakdown, which has valuable application in research studies of unsorted individuals. *Figures 3* (males) and *4* (females) show the RV systolic and diastolic parameters plotted against age, with the use of absolute values or BSA-normalized values as most appropriate. In order to validate these results, RV SV was compared with LV SV previously obtained, and reported, in the same patients.[11] The mean difference in SV between RV and LV was very small and not significant (LV SV: 95 ± 14 mL vs. RV SV: 94 ± 15 mL, $P = 0.09$). Also, observer variability of this semi-automated technique was tested in a subset of 25 volunteers. The interobserver variability was 6.3% for EDV, 8.6% for ESV, 7% for SV, 4.4% for EF, and 7.8% for RVM. Intraobserver variability was 3.6% for EDV, 6.5% for ESV, 5.9% for SV, 4% for EF, and 5.7% for RVM.

Influence of BSA on RV parameters

On multivariable analysis, BSA was found to have significant independent influence on RVM, EDV, ESV, SV, septal and lateral AVPD, and PFR_E. BSA was significantly higher in males than in females ($P < 0.001$).

Influence of gender on RV parameters

All absolute and normalized RV volumes and mass were significantly larger in males (all $P < 0.001$). No differences were found for RV systolic function between males and females. For RV diastolic function, PFR_E ($P = 0.025$), PFR_A ($P < 0.001$) and PFR_A/BSA ($P = 0.049$) were significantly higher in males. No differences were found in PFR_E/PFR_A. On multivariable analysis, gender had significant independent influence on absolute and normalized RVM, RVEDV and RVSV. It was also independent predictor of absolute and normalized PFR_A (PFR_A, PFR_A/BSA).

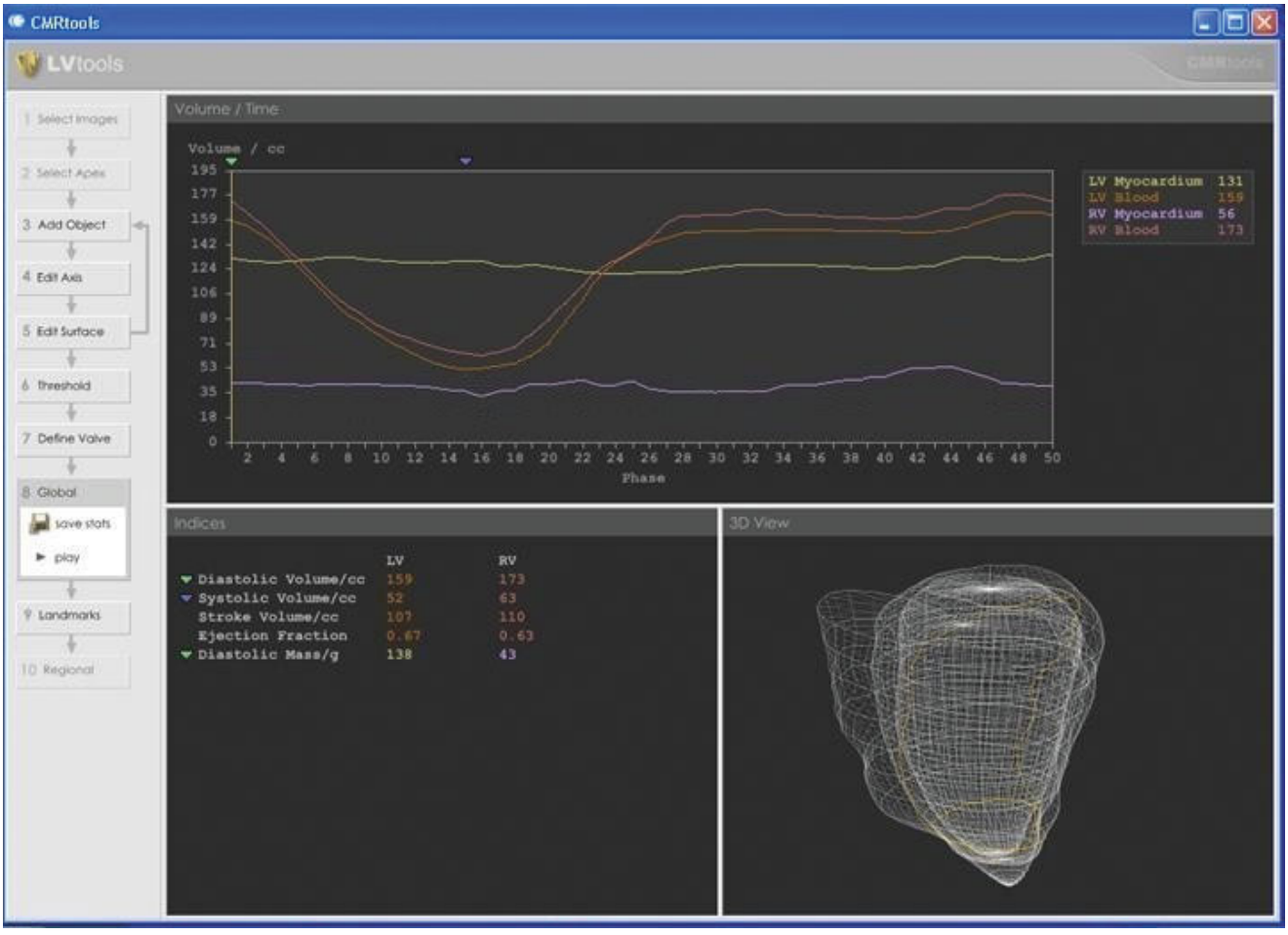

Figure 2 Screenshot showing an example of data output. In the graph above, the RV and LV volume curves are presented. In the table below the main RV and LV dimensions and systolic function parameters are produced (online supplementary data).

Table 2 Males: RV volumes, systolic function and mass (absolute and normalized to BSA) by age decile (mean, 95% confidence interval)

Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
EDV (mL) SD 25.4	177 (127, 227)	171 (121, 221)	166 (116, 216)	160 (111, 210)	155 (105, 205)	150 (100, 200)
ESV (mL) SD 15.2	68 (38, 98)	64 (34, 94)	59 (29, 89)	55 (25, 85)	50 (20, 80)	46 (16, 76)
SV (mL) SD 17.4	108 (74, 143)	108 (74, 142)	107 (73, 141)	106 (72, 140)	105 (71, 139)	104 (70, 138)
EF (%) SD 6.5	61 (48, 74)	63 (50, 76)	65 (52, 77)	66 (53, 79)	68 (55, 81)	70 (57, 83)
Mass (g) SD 14.4	70 (42, 99)	69 (40, 97)	67 (39, 95)	65 (37, 94)	63 (35, 92)	62 (33, 90)
Normalized to BSA						
EDV/BSA (mL/m^2) SD 11.7	91 (68, 114)	88 (65, 111)	85 (62, 108)	82 (59, 105)	79 (56, 101)	75 (52, 98)
ESV/BSA (mL/m^2) SD 7.4	35 (21, 50)	33 (18, 47)	30 (16, 45)	28 (13, 42)	25 (11, 40)	23 (8, 37)
SV/BSA (mL/m^2) SD 8.2	56 (40, 72)	55 (39, 71)	55 (39, 71)	54 (38, 70)	53 (37, 69)	52 (36, 69)
EF/BSA (%/m^2) SD 4	32 (24, 40)	32 (25, 40)	33 (25, 41)	34 (26, 42)	35 (27, 42)	35 (27, 43)
Mass/BSA (g/m^2) SD 6.8	36 (23, 50)	35 (22, 49)	34 (21,48)	33 (20, 46)	32 (19, 45)	31 (18, 44)

Influence of age on RV parameters

There was a significant decrease with increasing age in normalized RVM both in males ($P = 0.005$) and females ($P = 0.003$). There was a significant decrease with age in absolute and normalized EDV and ESV in males and females (EDV $P = 0.026$ and $P = 0.017$; EDV/BSA $P = 0.004$ and $P < 0.001$; ESV $P < 0.001$ and $P = 0.002$; ESV/BSA both $P < 0.001$). For systolic function, there was a significant increase with age in absolute EF both in males and females (EF $P < 0.001$ and $P = 0.004$) and in normalized EF in males ($P < 0.001$). Septal AVPD decreased significantly in females ($P = 0.003$). For diastolic function, absolute and normalized PFR_E decreased significantly with age in males and females (all $P < 0.001$), whereas absolute and

Table 3 Females: RV volumes, systolic function and mass (absolute and normalized to BSA) by age decile (mean, 95% confidence interval)

Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
EDV (mL) SD 21.6	142 (100, 184)	136 (94, 178)	130 (87, 172)	124 (81, 166)	117 (75, 160)	111 (69, 153)
ESV (mL) SD 13.3	55 (29, 82)	51 (25, 77)	46 (20, 72)	42 (15, 68)	37 (11, 63)	32 (6, 58)
SV (mL) SD 13.1	87 (61, 112)	85 (59, 111)	84 (58, 109)	82 (56, 108)	80 (55, 106)	79 (53, 105)
EF (%) SD 6	61 (49, 73)	63 (51, 75)	65 (53, 77)	67 (55, 79)	69 (57, 81)	71 (59, 83)
Mass (g) SD 10.6	54 (33, 74)	51 (31, 72)	49 (28, 70)	47 (26, 68)	45 (24, 66)	43 (22, 63)
Normalized to BSA						
EDV/BSA (mL/m^2) SD 9.4	84 (65, 102)	80 (61, 98)	76 (57, 94)	72 (53, 90)	68 (49, 86)	64 (45, 82)
ESV/BSA (mL/m^2) SD 6.6	32 (20, 45)	30 (17, 43)	27 (14, 40)	24 (11, 37)	21 (8, 34)	19 (6, 32)
SV/BSA (mL/m^2) SD 6.1	51 (39, 63)	50 (38, 62)	49 (37, 61)	48 (36, 60)	46 (34, 58)	45 (33, 57)
EF/BSA (%/m^2) SD 5.2	37 (27, 47)	38 (27, 48)	38 (28, 49)	39 (29, 49)	40 (30, 50)	41 (31, 51)
Mass/BSA (g/m^2) SD 5.2	32 (22, 42)	30 (20, 40)	29 (19, 39)	27 (17, 37)	26 (16, 36)	24 (14, 35)

Table 4 All subjects: RV volumes, systolic function, and mass (absolute and normalized to BSA) by age decile (mean, 95% confidence interval)

All subjects (age in years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
EDV (mL) SD 23.5	159 (113, 206)	154 (107, 200)	148 (102, 194)	142 (96, 188)	136 (90, 182)	130 (84, 177)
ESV (mL) SD 14.3	62 (34, 90)	57 (29, 85)	53 (25, 81)	48 (20, 76)	44 (16, 72)	39 (11, 67)
SV (mL) SD 15.3	98 (68, 128)	96 (66, 126)	95 (65, 125)	94 (64, 124)	93 (63, 123)	92 (61, 122)
EF (%) SD 6.2	61 (49, 73)	63 (51, 75)	65 (53, 77)	67 (54, 79)	68 (56, 81)	70 (58, 83)
Mass (g) SD 12.6	62 (37, 87)	51 (27, 76)	49 (24, 74)	47 (22, 72)	45 (20, 70)	43 (18, 67)
Normalized to BSA						
EDV/BSA (mL/m^2) SD 10.6	88 (67, 108)	84 (63, 105)	80 (60, 101)	77 (56, 98)	73 (52, 94)	70 (49, 90)
ESV/BSA (mL/m^2) SD 7	34 (20, 48)	31 (17, 45)	29 (15, 42)	26 (12, 40)	23 (10, 37)	21 (7, 35)
SV/BSA (mL/m^2) SD 7.2	54 (39, 68)	53 (38, 67)	52 (38, 66)	51 (37, 65)	50 (36, 64)	49 (35, 63)
EF/BSA (%/m^2) SD 4.6	34 (25, 43)	35 (26, 44)	36 (27, 45)	37 (27, 46)	37 (28, 46)	38 (29, 47)
Mass/BSA (g/m^2) SD 6	34 (22, 46)	33 (21, 45)	31 (20, 43)	30 (18, 42)	29 (17, 41)	28 (16, 39)

Table 5 Males: RV diastolic function and AVPD (absolute and normalized values) by age decile (mean, 95% confidence interval)

Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
PFR_E (mL/s) SD137	545 (277, 814)	491 (223, 760)	438 (169, 706)	384 (116, 652)	330 (62, 599)	276 (8, 545)
PFR_A (mL/s) SD 175	366 (23, 709)	413 (70, 756)	461 (118, 804)	508 (165, 852)	556 (213, 899)	604 (260, 947)
PFR_E/PFR_A SD[a] 0.49	1.6 (0.6, 2.5)	1.2 (0.3, 2.2)	1.0 (0.0, 1.9)	0.7 (−0.2, 1.7)	0.6 (−0.4, 1.5)	0.5 (−0.5, 1.4)
Septal AVPD (mm) SD 4.1	16 (8, 24)	15 (7, 24)	15 (7, 23)	14 (6, 22)	14 (6, 22)	13 (5, 21)
Lateral AVPD (mm) SD 4.4	23 (14, 32)	23 (14, 31)	22 (14, 31)	22 (13, 30)	21 (13, 30)	21 (12, 29)
Normalized values						
PFR_E/BSA (mL/s/m^2) SD 71	280 (142, 419)	252 (114, 390)	224 (85, 362)	195 (57, 334)	167 (29, 306)	139 (1, 277)
PFR_E/EDV (/s) SD 0.75	3.1 (1.6, 4.6)	2.8 (1.4, 4.3)	2.6 (1.1, 4.1)	2.3 (0.9, 3.8)	2.1 (0.6, 3.6)	1.9 (0.4, 3.3)
PFR_A/BSA (mL/s/m^2) SD 94	190 (6, 374)	213 (29, 397)	236 (52, 420)	259 (75, 443)	283 (98, 467)	306 (122, 490)
PFR_A/EDV (/s) SD 1.07	2.1 (0.0, 4.2)	2.5 (0.4, 4.6)	2.9 (0.8, 4.9)	3.2 (1.1, 5.3)	3.6 (1.5, 5.7)	4.0 (1.9, 6.1)
Septal AVPD/long length (%) SD 4.5	18 (9, 27)	18 (9, 27)	17 (9, 26)	17 (8, 26)	17 (8, 26)	16 (8, 25)
Lateral AVPD/long length (%) SD 4.1	23 (15, 31)	23 (15, 31)	23 (15, 31)	23 (15, 31)	23 (15, 31)	23 (15, 31)

[a]SD of log transformed data.

normalized PFR_A increased in males (PFR_A $P = 0.007$; PFR_A/BSA $P = 0.01$; PFR_A/EDV $P = 0.001$). Accordingly, PFR_E/PFR_A decreased significantly in males and females (both $P < 0.001$). On multivariable analysis, age was an independent predictor of absolute and normalized ventricular mass and volumes (RVM, EDV, ESV, SV, RVM/BSA, EDV/BSA, ESV/BSA, SV/BSA), and of systolic variables (EF, septal and lateral AV descent). It was also an independent predictor of diastolic variables (PFR_E, PFR_A, PFR_E/PFR_A, PFR_E/EDV, PFR_A/EDV, PFR_E/BSA, PFR_A/BSA).

Table 6 Females: RV diastolic function and AVPD (absolute and normalized values) by age decile (mean, 95% confidence interval)

Age (years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
PFR_E (mL/s) SD 117	471 (241, 701)	419 (189, 649)	368 (137, 598)	316 (86, 546)	264 (34, 494)	213 (-17, 443)
PFR_A (mL/s) SD 153	355 (54, 656)	360 (59, 660)	365 (64, 665)	370 (69, 670)	374 (74, 675)	379 (79, 680)
PFR_E/PFR_A SD[a] 0.46	1.6 (0.7, 2.5)	1.3 (0.4, 2.2)	1.0 (0.1, 1.9)	0.8 (-0.1, 1.7)	0.7 (-0.2, 1.6)	0.5 (-0.4, 1.4)
Septal AVPD (mm) SD 3.0	16 (10, 22)	15 (9, 20)	13 (7, 19)	12 (6, 18)	11 (5, 17)	10 (4, 16)
Lateral AVPD (mm) SD 3.5	22 (15, 29)	21 (14, 28)	21 (14, 28)	20 (13, 27)	20 (13, 27)	19 (12, 26)
Normalized values						
PFR_E/BSA (mL/s/m^2) SD 68	278 (145, 411)	247 (114, 380)	216 (83, 349)	185 (52, 318)	153 (20, 286)	122 (-11, 255)
PFR_E/EDV (/s) SD 0.85	3.4 (1.8, 5.1)	3.1 (1.5, 4.8)	2.8 (1.2, 4.5)	2.5 (0.9, 4.2)	2.2 (0.6, 3.9)	1.9 (0.3, 3.6)
PFR_A/BSA (mL/s/m^2) SD 89	211 (36, 386)	212 (37, 388)	214 (39, 389)	215 (40, 390)	217 (42, 392)	218 (43, 393)
PFR_A/EDV (/s) SD 1.03	2.4 (0.4, 4.4)	2.6 (0.6, 4.6)	2.8 (0.8, 4.8)	3.0 (1.0, 5.0)	3.2 (1.2, 5.2)	3.4 (1.4, 5.4)
Septal AVPD/long length (%) SD 3.9	19 (11, 27)	18 (11, 26)	17 (10, 25)	17 (9, 24)	16 (8, 23)	15 (7, 22)
Lateral AVPD/long length (%) SD 4.0	24 (16, 32)	24 (16, 32)	24 (16, 32)	24 (16, 32)	24 (16, 32)	24 (16, 31)

[a]SD of log transformed data.

Table 7 All subjects: RV diastolic function and AVPD (absolute and normalized values) by age decile (mean ± SD, 95% confidence interval)

All subjects (age in years)	20–29	30–39	40–49	50–59	60–69	70–79
Absolute values						
PFR_E (mL/s) SD 125	508 (264, 753)	455 (211, 700)	403 (158, 647)	350 (105, 594)	297 (53, 542)	244 (0, 489)
PFR_A (mL/s) SD 168	359 (29, 689)	386 (56, 716)	413 (83, 743)	440 (110, 770)	467 (137, 797)	494 (164, 824)
PFR_E/PFR_A SD[a] 0.47	1.6 (0.6, 2.5)	1.2 (0.3, 2.2)	1.0 (0.1, 1.9)	0.8 (−0.1, 1.7)	0.6 (−0.3, 1.6)	0.5 (−0.4, 1.4)
Septal AVPD (mm) SD 3.6	16 (9, 23)	15 (8, 22)	14 (7, 21)	13 (6, 20)	12 (5, 20)	12 (4, 19)
Lateral AVPD (mm) SD 3.9	22 (15, 30)	22 (14, 30)	21 (14, 29)	21 (13, 29)	20 (13, 28)	20 (12, 28)
Normalized values						
PFR_E/BSA (mL/s/m^2) SD 69	279 (144, 414)	249 (114, 385)	220 (85, 355)	190 (55, 325)	160 (25, 296)	131 (-4, 266)
PFR_E/EDV (/s) SD 0.81	3.3 (1.7, 4.9)	3.0 (1.4, 4.6)	2.7 (1.1, 4.3)	2.4 (0.9, 4.0)	2.2 (0.6, 3.8)	1.9 (0.3, 3.5)
PFR_A/BSA (mL/s/m^2) SD 93	200 (17, 382)	212 (30, 395)	225 (43, 407)	238 (55, 420)	251 (68, 433)	263 (81, 446)
PFR_A/EDV (/s) SD 1.05	2.2 (0.2, 4.3)	2.5 (0.5, 4.6)	2.8 (0.8, 4.9)	3.1 (1.1, 5.2)	3.4 (1.4, 5.5)	3.7 (1.7, 5.8)
Septal AVPD/long length (%) SD 4.2	19 (10, 27)	18 (10, 26)	17 (9, 26)	17 (8, 25)	16 (8, 25)	16 (7, 24)
Lateral AVPD/long length (%) SD 4.0	23 (15, 31)	23 (15, 31)	23 (15, 31)	23 (15, 30)	22 (14, 30)	22 (14, 30)

[a]SD of log transformed data.

Table 8 RV summary data for all ages (mean ± SD, 95% confidence interval)

	All	Males	Females
EDV (mL)	144 ± 23 (98, 190)	163 ± 25 (113, 213)	126 ± 21 (84, 168)
EDV/BSA (mL/m^2)	78 ± 11 (57, 99)	83 ± 12 (60, 106)	73±9 (55, 92)
ESV (mL)	50 ± 14 (22, 78)	57 ± 15 (27, 86)	43 ± 13 (17, 69)
ESV/BSA (mL/m^2)	27±7 (13, 41)	29±7 (14, 43)	25±7 (12, 38)
SV (mL)	94 ± 15 (64, 124)	106 ± 17 (72, 140)	83 ± 13 (57, 108)
SV/BSA (mL/m^2)	51±7 (37, 65)	54±8 (38, 70)	48±6 (36, 60)
EF (%)	66±6 (54, 78)	66±6 (53, 78)	66±6 (54, 78)
EF/BSA (%/m^2)	36±5 (27, 45)	34±4 (26, 41)	39±5 (29, 49)
Mass (g)	48 ± 13 (23, 73)	66 ± 14 (38, 94)	48 ± 11 (27, 69)
Mass/BSA (g/m^2)	31±6 (19, 43)	34±7 (20, 47)	28±5 (18, 38)
PFR_E (mL/s)	371 ± 125 (126, 615)	405 ± 137 (137, 674)	337 ± 117 (107, 567)
PFR_E/BSA (mL/m^2)	202 ± 69 (67, 337)	207 ± 70 (68, 345)	197 ± 68 (64, 330)
PFR_E/EDV (/s)	2.6 ± 0.8 (1.0, 4.1)	2.4 ± 0.75 (1.0, 3.9)	2.7 ± 0.85 (1.0, 4.3)
PFR_A (mL/s)	429 ± 168 (99, 759)	489 ± 175 (146, 833)	368 ± 153 (67, 668)
PFR_A/BSA (mL/m^2)	233 ± 93 (50, 415)	250 ± 94 (66, 434)	215 ± 89 (40, 390)
PFR_A/EDV (/s)	3.0 ± 1.0 (1.0, 5.1)	3.1 ± 1.0 (1.0, 5.2)	2.9 ± 1.0 (0.9, 5.0)
PFR_E/PFR_A	0.9 ± 0.47 (-0.1, 1.8)	0.8 ± 0.49 (-0.1, 1.8)	0.9 ± 0.46 (0.0, 1.8)
Septal AVPD (mm)	14 ± 3.6 (6, 21)	15 ± 4.1 (6, 23)	13 ± 3.0 (7, 19)
Septal AVPD/long length (%)	17 ± 4.2 (9, 25)	17 ± 4.5 (8, 26)	17 ± 3.9 (9, 25)
Lateral AVPD (mm)	21 ± 3.9 (13, 29)	22 ± 4.4 (13, 30)	21 ± 3.5 (14, 27)
Lateral AVPD/long length (%)	23 ± 4.0 (15, 31)	23 ± 4.1 (15, 31)	24 ± 4.0 (16, 32)

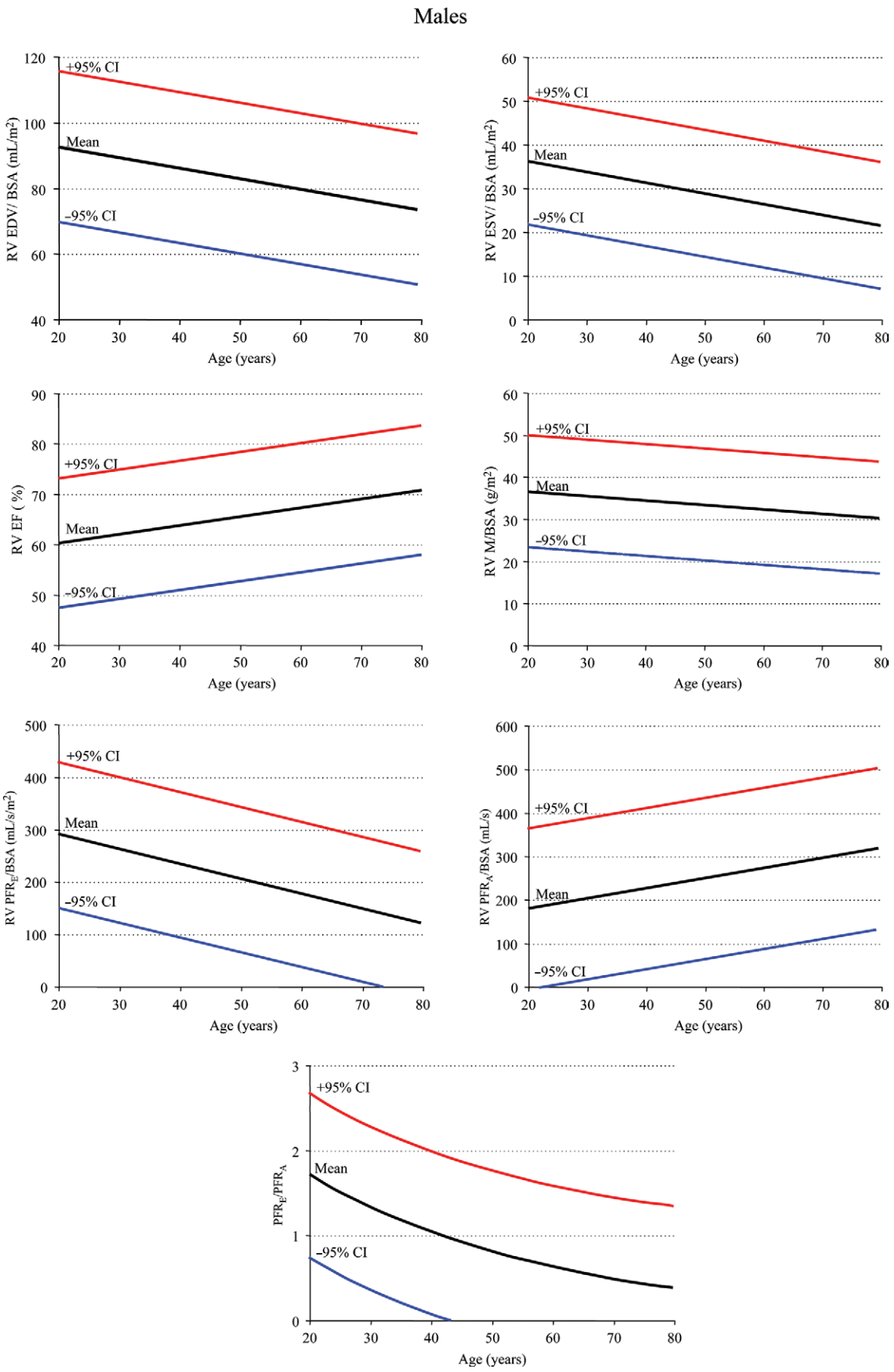

Figure 3 Males: RV volumes, mass, diastoilc function (normalized to BSA) and systolic function (absolute) by age decile (mean, 95% confidence interval).

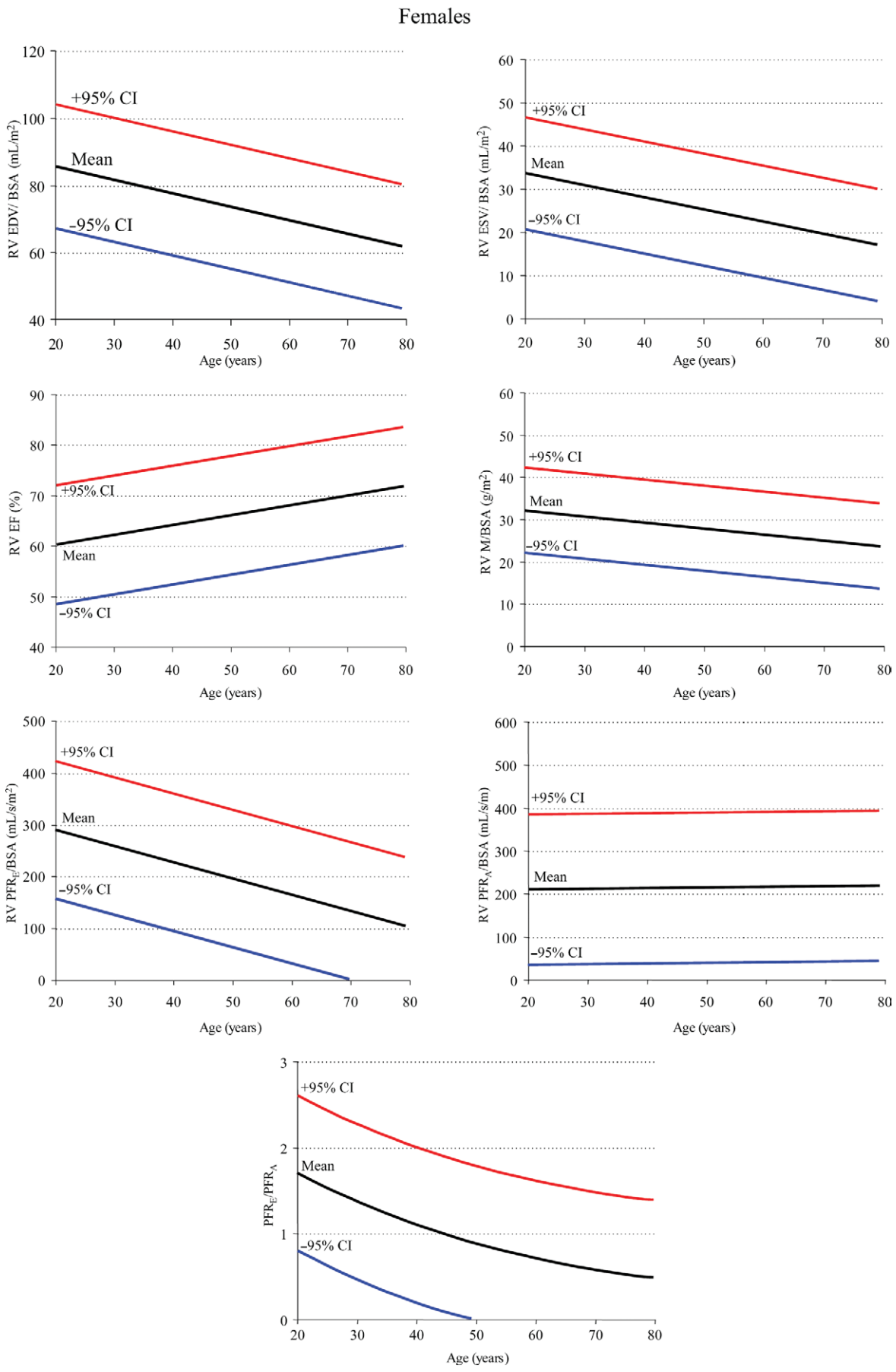

Figure 4 Females: RV volumes, mass, diastolic function (normalized to BSA) and systolic function (absolute) by age decile (mean, 95% confidence interval).

Discussion

These data show that many clinical parameters of RV volume and systolic/diastolic function are significantly dependent on gender, age, and BSA. This study brings previous data up to date using state-of-the-art CMR techniques and analysis, in a moderately large healthy population, well characterized for the absence of significant coronary disease and heart failure. We are unaware of any previously published normal values for RV diastolic function by CMR. The findings suggest that the interpretation of RV parameters in borderline clinical cases, especially in arrhythmogenic RV cardiomyopathy, cardiovascular shunting, and adult congenital heart disease should be referred to age, gender, and BSA-normalized values in order to determine normality, or severity of abnormality. This is also of special interest because the functional capacity of the RV is an important prognostic determinant in several pathologies.

In general there has been a lack of techniques that give a reliable measurement of RV mass and volumes. Echocardiography plays an important role in the evaluation of patients with suspected RV pathology, but it has many limitations and there is still no generally recommended echocardiography method for quantifying RV function.[15] As CMR is now considered a gold standard clinical technique to measure RV volumes and function, these new data have important current and future clinical and research utility.

Previous CMR studies with other techniques accord with some of the results presented in the current study, but there are differences. The decrease in RV volumes with age with no effect on RVM is in agreement with a previous CMR study of 36 subjects using FLASH cines,[16] although we found in addition a decrease in normalized RVM with age. This may be because we controlled carefully for cardiovascular abnormality in all age groups. Sanstede's study also found that females have lower RV mass and volumes, and these differences persisted when normalized by BSA and this accords with our study.

RV diastolic parameters have not been extensively studied in the past. Echocardiographic tissue Doppler of the tricuspid annulus,[17] and conventional pulsed Doppler of tricuspid and vena cava flows have been used. RV diastolic function has been shown to vary by age,[18] which is in agreement with our findings. Ageing causes a decrease in RV distensibility that increases both the early diastolic filling time, allowing the ventricle more time to fill, and the contribution of the atrial kick to RV filling. There are differences between CMR and echocardiography however. Whereas echocardiography provides peak velocities, CMR provides absolute PFRs from the volume/time curves. These are available from radionuclide ventriculography, but CMR has significantly higher spatial and temporal resolution.

Lorenz *et al.*[8] published the first normal ranges for CMR-derived LV and RV mass and volumes utilizing FLASH cines with free breathing. This study included 75 subjects (age range 8–55, mean 28 years) and all parameters were found to be significantly different between males and females except EF. Other normal ranges with FLASH cines and breath-holding have been published. Sandstede *et al.*[16] included 36 healthy volunteers subdivided in four groups of nine subjects each, according to gender and age (greater or less than 45 years). These ranges are now not ideal, because of differences between spoiled gradient echo and SSFP results and higher reproducibility of SSFP measurements.[10] Thus, new normal ranges with SSFP are needed. Some SSFP normal ranges for RV parameters have been performed. Alfakih *et al.*[19] studied 60 subjects with an age range of 20–65 years, but subdivided only into two subgroups (>40 years, $n = 34$; <40 years, $n = 26$). The subjects had a normal examination and ECG, with no history of heart disease but the 10-year risk and BNP was not measured. The data were analysed manually without AV plane correction, and the results were not divided into age deciles for regression modelling. Therefore, the capacity to compare the results with our current data is limited.

The question has been raised as to whether RV parameters should be measured in the axial orientation. Alfakih *et al.*[20] studied 20 normal subjects in whom he measured RV volumes with the axial and short-axis orientations, and found significant differences between volumes measured with the two different orientations. The axial orientation appeared to have better inter and intraobserver reproducibilities. Grothues *et al.*[7] used the short-axis orientation for assessing the interstudy reproducibility of measurements of RV volumes, function, and mass with a FLASH sequence and obtained a good interstudy reproducibility for RV function parameters in healthy subjects, patients with heart failure, and patients with hypertrophy. We used the short-axis orientation because, in practice, it allows both the left and RV dimensions to be measured simultaneously.

In conclusion, RV volumes and function (systolic and diastolic) vary with gender, age, and BSA. Identification particularly of early abnormality requires reference ranges, which normalize for all three variables. These ranges are supplied with this report in both tabular and graphical form and are of significant clinical and research utility for the interpretation of CMR studies.

Supplementary material

Supplementary material is available at European Heart Journal online.

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Conflict of interest: D.J.P. is a consultant to Siemens and a director of Cardiovascular Imaging Solutions. The other authors declare no conflicts.

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