Pre-chemotherapy values for left and right ventricular volumes and ejection fraction by gated tomographic radionuclide angiography using a cadmium-zinc-telluride detector gamma camera

Christian Haarmark, MD, PhD,[a,b] Christine Haase, MD,[a] Maria Maj Jensen, MD,[a] and Bo Zerahn, MD[a]

[a] Department of Clinical Physiology and Nuclear Medicine, Herlev Hospital, Herlev, Denmark
[b] Department of Clinical Physiology and Nuclear Medicine, Bispebjerg Hospital, Copenhagen, Denmark

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Background. **Estimation of left ventricular ejection fraction (LVEF) using equilibrium radionuclide angiography is an established method for assessment of left ventricular function. The purpose of this study was to establish normative data on left and right ventricular volumes and ejection fraction, using cadmium-zinc-telluride SPECT camera.**

Methods and results. **From routine assessments of left ventricular function in 1172 patients, we included 463 subjects (194 men and 269 women) without diabetes, previous potentially cardiotoxic chemotherapy, known cardiovascular or pulmonary disease. The lower limits defined as mean value minus two standard deviations for ventricular ejection fraction and end diastolic volume were LVEF (men: 50%, women: 50%), LEDV (men: 45 mL, women: 40 mL), RVEF (men: 29%, women: 28%), and REDV (men: 73 mL, women: 57 mL).There was a significant negative correlation between age and both left and right ventricular volumes in women ($r = -0.4$, $P < .001$) but only for right end systolic ventricular volume in men ($r = -0.3$, $P = .001$).**

Conclusion. **A set of reference values for cardiac evaluation prior to chemotherapy in cancer patients without other known cardiopulmonary disease is presented. There are age-related changes in cardiac dimensions with age depending on gender, although with only limited influence on LVEF or RVEF. (J Nucl Cardiol 2016;23:87–97.)**

Key Words: LVEF • CZT-SPECT camera • chemotherapy • radionuclide angiography • multigated acquisition scan

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Reprint requests: Christian Haarmark, MD, PhD, Department of Clinical Physiology & Nuclear Medicine, Bispebjerg Hospital, Bispebjerg Bakke 23, Building 60, Floor A, 2400 Copenhagen NV, Denmark; *Haarmark@dadlnet.dk*

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Abbreviations

CZT	Cadmium-zinc-telluride
MRI	Magnetic resonance imaging
MPI	Myocardial perfusion imaging
MUGA	Multigated acquisition scans
R/LVEF	Right/left ventricular ejection fraction
R/LEDV	Right/left ventricular end diastolic volume
R/LESV	Right/left ventricular end systolic volume
SPECT	Single photon emission computer tomography

INTRODUCTION

The continuous development of more efficient cancer therapies and effective screening has led to an impressive rise in long-term cancer survivors.[1] Thus, focus is increasingly being directed on the management of potentially long-term side effects, i.e., cardiotoxicity and chronic heart failure.[1,2] There is an increasing need for more precise evaluation of cardiac function in order to navigate between the risk of cardiotoxicity and otherwise potentially lifesaving therapy.[3]

Cardiotoxicity especially with anthracyclines and trastuzumab is often monitored via measuring left ventricular volumes and function,[2,3] primarily focusing on left ventricular ejection fraction (LVEF). This is traditionally performed non-invasively with echocardiography, magnetic resonance imaging (MRI) or radionuclide angiography with either planar acquisition or single photon emission computer tomography (SPECT).

The use of serial MUGA to prevent heart failure in patients receiving cardiotoxic drugs is well established and was originally proposed in 1979 by Alexander et al in 55 patients receiving doxorubicin for treatment of cancer.[4] Later Schwartz el al[5] suggested guidelines for serial MUGA's and when to stop therapy. They showed adhering to these guidelines could reduce incidence of heart failure. A finding that still holds in the modern era.[6] Evidence also suggest that long-term (>3 months post dosing) monitoring is also warranted at least in patients receiving epirubicin.[7] The importance of the radionuclide angiography in evaluating LVEF is also highlighted by the use of this technique in large clinical oncological trials—i.e., in the evaluation of trastuzumab (Herceptin Adjuvant Trial).[8]

There are no current evidence-based guidelines stipulating how and when to monitor cardiac function. The most resent multicenter studies have used multigated acquisition scans (MUGA) or echocardiography.[1,3] MUGA is often regarded as a non-invasive gold standard for the evaluation of cardiotoxicity, due to higher reproducibility and lower interobserver variability than echocardiography.[3,9]

Advances in radionuclide angiography include SPECT, which allows for calculation of additional variables on end systolic (ESV) and end diastolic volumes (EDV) for both ventricles.[3,9,10] Since 2005, new dedicated cardiac gamma camera types equipped with cadmium-zinc-telluride (CZT) detectors have been commercially available, with improved spatial resolution, faster acquisition times and potentially lower radiation doses as well as improved reproducibility.[11-13] This calls for establishing normative data for this new camera type given the fact that its increased spatial resolution might give rise to adjustments of previously established limits for normalcy as well as establishing normative data for right ventricular variables.

The primary aim of this study is to establish normative data on patients with cancer referred for measurement of baseline data of LVEF prior to potentially cardiotoxic chemotherapy. The secondary objective was to test for gender and age-specific changes or differences related to blood pressure and heart rate at rest.

METHODS

From October 1st 2012 to September 30th 2014, we performed 2691 consecutive routine assessments of left ventricular function in 1172 patients after informed consent was given. Patients were excluded from this study if they had diabetes, pleural effusions, prior lung resection, previous cancer-related chemotherapy and known cardiovascular disease including cardiac insufficiency, valvular disease, myocardial infarction, coronary revascularization, and cardiac arrhythmias treated medically or with pacemaker. In all 463 patients (194 men and 269 women) were included (Figure 1). The study was approved by the Danish data protection Agency.

Information on hypertension was also recorded. The data were retrieved from patient files. Patients with large thoracic circumferences and patients unable to rest with their left arm above the head were scanned on other cameras and could subsequently not be included (Figure 1).

Image Processing

All acquisitions were performed at the Department of Clinical Physiology and Nuclear Medicine at Herlev Hospital. After a 9-month test period from January through September 2012 the CZT-cardiac SPECT gamma camera, GE Discovery 530c (GE Healthcare, Milwaukee, WI, USA) (DNM) was adapted for routine measurements of left ventricular function as previously described.[11,12] In brief, a dose of 550-600 MBq (15-16 mCi) 99mTc-labeled human serum albumin (HSA) was administered intravenously to each patient. An acquisition protocol for multigated acquisition, using 16 bins and requesting 600 accepted beats was adapted and a 20% energy window

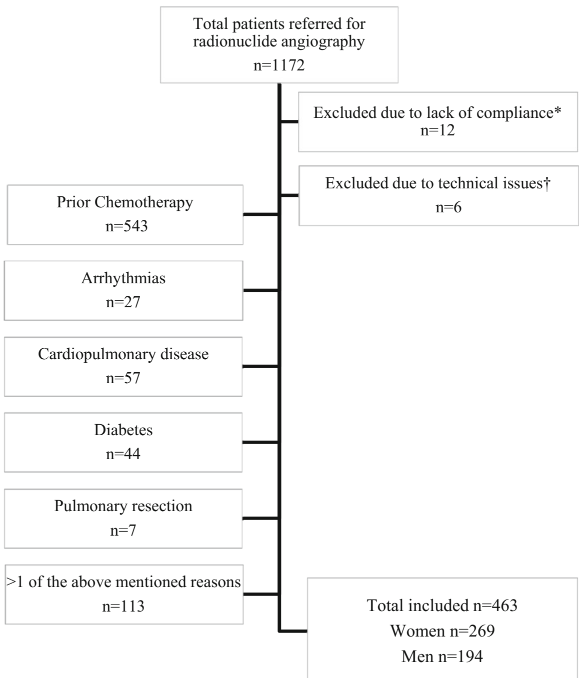

Figure 1. Flow chart illustrating the in- and exclusion of patients. *Inability to focus on heart, unable to raise left arm above head, claustrophobia, metastasis close to the heart. † Camera break down, trigger problems, LVEF determined by MPI instead.

centered on 140 keV was performed in all cases. A Xeleris 3 Imaging workstation (GE Wauwatosa, WI, US) equipped with software version no. 3.0562 was used for reorientation of the heart after applying a generic reconstruction algorithm and filtering. The matrix was resized from 74 × 74 to 64 × 64. Assessment of the left and right ventricular ejection fraction as well as estimations of end diastolic and end systolic volumes was carried out with the Cedars-Sinai QBS processing software (Cedars-Sinai, Ca, USA—revision 2009.0).

Each acquisition was analyzed twice by two experienced technologists. If LVEF differed more than 2% points between the two analyses, repeated processing was performed until sufficient agreement was obtained. All results were revised to ensure that the region of interest (ROI) automatically drawn by the software around the ventricles, were in accordance with visually estimated ventricular borders

Statistical Analysis

A paired two-tailed *t* test was applied to both datasets and used to compare differences between groups with normally distributed variables. One-way ANOVA was used to compare variations between more than two groups and changes in cardiac variables with age.

Pearson correlation was performed to evaluate relationship between continuous variables. A probability of less than .05 was regarded as significant.

RESULTS

Demographic data, selected cardiovascular variables, smoking status, and prior medical history regarding hypertension and hypercholesterolemia are presented in Table 1 divided by gender. Men were older, taller, and had higher blood pressure than women. The majority of patients with hypertension on the day of investigation had only mild hypertension (81/114 patients) and 9 patients had severe grade 3 hypertension. There were no differences in ventricular volumes or ejection fraction (EDV, ESV, and LVEF) between age,

Table 1. Study population characteristics

	Total	Men	Women	*P* value‡
N	463	194	269	
Age* (years)	59.9 ± 15.5	62.6 ± 14.4	58.0 ± 16.0	.002
Height* (cm)	170.8 ± 9.1	177.6 ± 7.8	165.8 ± 6.4	<.0001
Weight* (kg)	74.6 ± 15.2	82.4 ± 13.5	69.0 ± 13.8	<.0001
BSA* (m^2)	1.87 ± 0.22	2.00 ± 0.19	1.77 ± 0.19	<.0001
Systolic BP* (mmHg)	129.9 ± 19.7	134.1 ± 19.5	126.8 ± 19.2	<.0001
Diastolic BP* (mmHg)	76.7 ± 11.1	79.1 ± 10.8	75.0 ± 11.0	<.0001
Heart rate* (bpm)	74.9 ± 13.1	75.7 ± 13.5	74.4 ± 12.8	n.s.
Smokers†	45%	56%	37%	<.0001#
Hypertension†	28%	35%	23%	.005#
Hypercholesterolemia†	12%	14%	10%	n.s.

* Mean ± SD
† Percent of population
‡ *P* value for gender difference
# Mantel Heanszel χ^2

gender, height, and weight matched hypertensive and normotensive patients ($P = .42$, .70, and .23).

Left and right ventricular volumes and ejection fraction on the included patients are presented in Tables 2 (women) and 3 (men). Overall differences between age groups as calculated by one-way ANOVA are presented by an overall P value in the far right column of each Table.

Figures 2A and 3A depict normal ranges for LVEF, LESV, and LEDV with 10 years intervals for men (men aged <45 were pooled into one age group because of low numbers) and women, respectively. Similar figures for right ventricular variables are given in Figures 2B and 3B.

Both right and left ventricular volumes declined significantly with increasing age for women along with a significant increase in LVEF and a trend toward an increase in RVEF. There was no significant development in left ventricular volumes or ejection fraction with increasing age for men, whereas there was a decline in right ventricular end systolic volume and an increase in RVEF with increasing age ($r = -0.25$, $P = .001$, and $r = 0.29$, $P < .001$, respectively). Correlation matrices are presented for each gender in Tables 4 and 5.

A high heart frequency was associated with low right and left ventricular volumes and higher ejection fractions. A high systolic blood pressure was associated with lower right ventricular volumes and higher ejection

Table 2. Ventricular volumes, ejection fractions, and cardiac output for women

	Mean	SD	Mean − 2 SD	Minimum	Maximum	Age group ANOVA
LEDV	83.6	21.9	39.8	30.5	154.0	0.001
LESV	26.5	12.3	2.0	2.0	62.0	0.001
LVSV	57.1	14.0	29.1	22.0	123.0	0.001
LVEF	69.3	9.8	49.7	38.9	95.8	0.001
COLV	4196	1093	2011	1650	7728	0.001
REDV	116.5	29.7	57.2	50.0	230.0	0.001
RESV	63.2	19.0	25.2	18.5	115.5	0.001
RVSV	53.2	17.1	19.0	12.0	134.0	0.005
RVEF	45.8	9.0	27.7	17.0	75.3	n.s.
CORV	3945	1424	1097	864	9960	0.004

All volumes are depicted as mL and ejection fractions in percent
L, left ventricular; *R*, right ventricular; *xEDV*, end diastolic volume; *xESV*, end systolic volume; *xVSV*, ventricular stroke volume; *xVEF*, ventricular ejection fraction; *COLV*, left ventricular cardiac output; *CORV*, right ventricular cardiac output
* Lower normal limit defined as 2 SD below mean value

Table 3. Ventricular volumes, ejection fractions, and cardiac output for men

	Mean	SD	Mean − 2 SD*	Minimum	Maximum	Age group ANOVA
LEDV	94.4	24.9	44.7	34	189	0.020
LESV	30.9	14.5	1.8	4.5	108.5	n.s.
LVSV	63.5	15.1	33.4	26.0	115.5	n.s.
LVEF	68.3	9.2	50.0	42.6	89.2	n.s.
COLV	4758	1287	2184	2184	8817	0.004
REDV	139.1	33.2	72.7	64.5	256.5	n.s.
RESV	73.8	21.8	30.2	12.0	151.0	n.s.
RVSV	65.2	19.0	27.2	20.5	122.0	n.s.
RVEF	47.1	9.0	29.0	17.6	87.2	n.s.
CORV	4874	1540	1795	1784	9394	n.s.

Abbreviations as in Table 2
* Lower normal limit defined as 2 SD below mean value

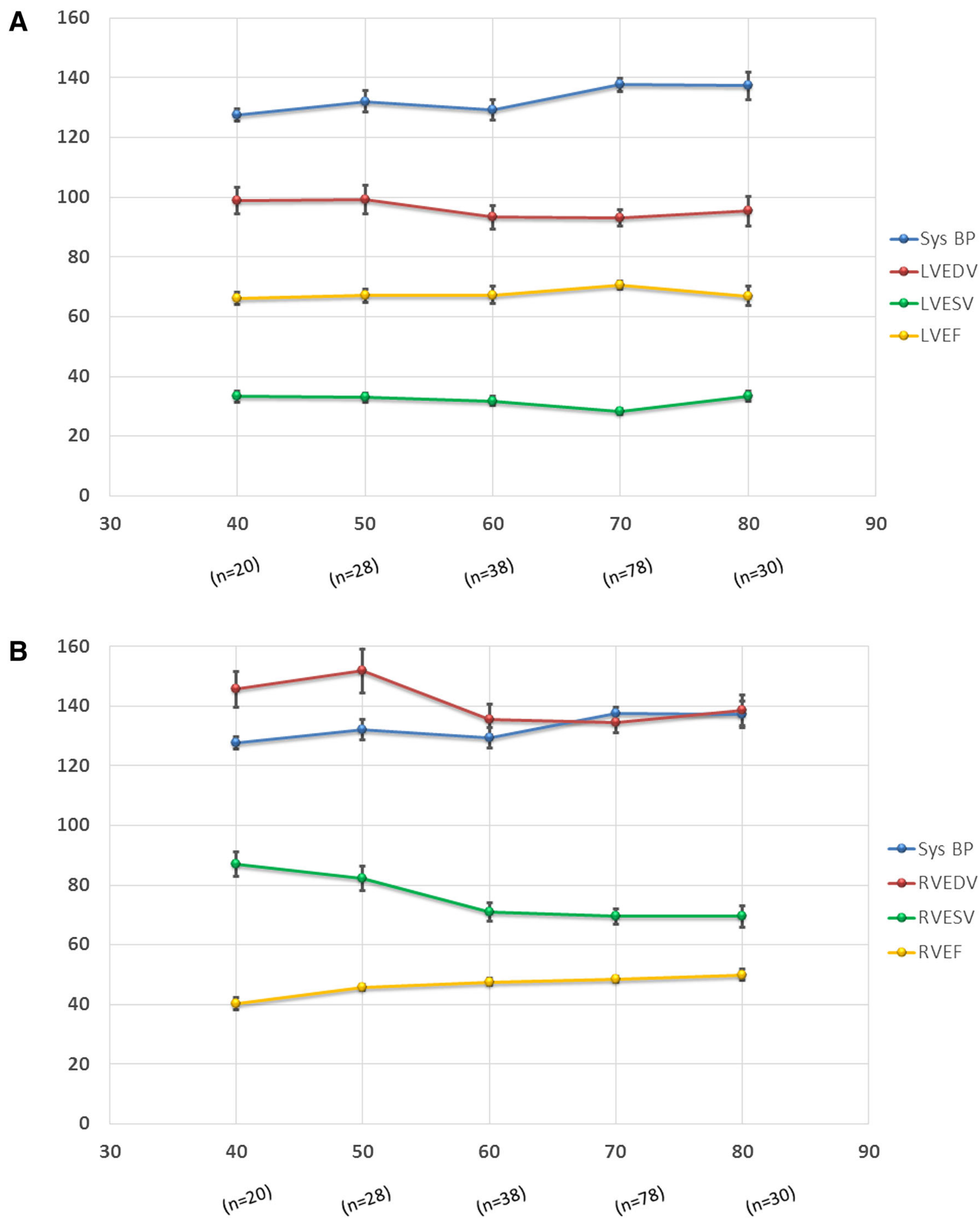

Figure 2. **A** Systolic blood pressure (Sys BP) and left ventricular volumes and ejection fraction divided in age groups (*horizontal axis*) for men. **B** Systolic blood pressure (Sys BP) and right ventricular volumes and ejection fraction divided in age groups (*horizontal axis*) for men. *Error bars* indicate standard error of mean. *Numbers in parentheses* indicates number of patients in each age group.

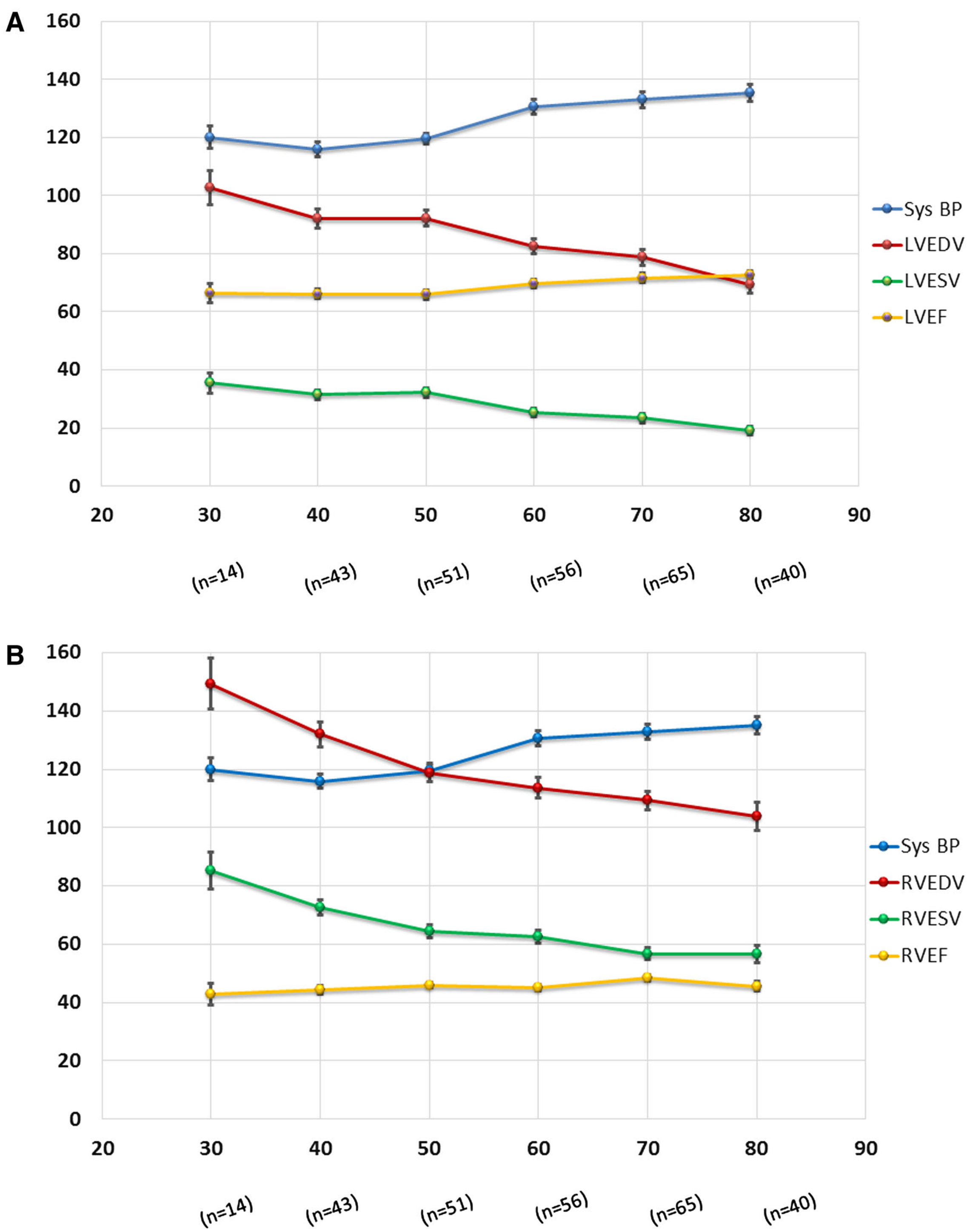

Figure 3. **A** Systolic blood pressure (Sys BP) and left ventricular volumes and ejection fraction divided in age groups (*horizontal axis*) for women. **B** Systolic blood pressure (Sys BP) and right ventricular volumes and ejection fraction divided in age groups (*horizontal axis*) for women. *Error bars* indicate standard error of mean. *Numbers in parentheses* indicates number of patients in each age group.

Table 4. Correlation matrix between cardiac variables and patient characteristics for men

		LVEDV	LVESV	LVEF	RVEDV	RVESV	RVEF	COLV	CORV
Age	*R* value	−0.050	−0.055	0.100	−0.105	−0.245	0.288	−0.045	0.080
	P value	n.s.	n.s.	n.s.	n.s.	.001	<.001	n.s.	n.s.
Height	*R* value	0.312	0.174	−0.019	0.300	0.286	−0.063	0.248	0.143
	P value	<.001	.015	n.s.	<.001	<.001	n.s.	<.001	.046
Weight	*R* value	0.095	−0.038	0.126	0.250	0.208	−0.042	0.140	0.152
	P value	n.s.	n.s.	n.s.	<.001	.004	n.s.	n.s.	.034
BSA	*R* value	0.193	0.038	0.089	0.311	0.274	−0.059	0.202	0.172
	P value	.007	n.s.	n.s.	<.001	<.001	n.s.	.005	.016
SysBP	*R* value	−0.069	−0.059	0.067	−0.197	−0.259	0.176	−0.020	−0.016
	P value	n.s.	n.s.	n.s.	.006	<.001	n.s.	n.s.	n.s.
DiaBP	*R* value	−0.167	−0.060	−0.058	−0.247	−0.238	0.059	−0.061	−0.031
	P value	.020	n.s.	n.s.	.001	.001	n.s.	n.s.	n.s.
HR	*R* value	−0.237	−0.198	0.147	−0.351	−0.375	0.164	0.462	0.401
	P value	.001	.006	.041	<.001	<.001	.022	<.001	<.001

BSA, body surface area (m^2); *SysBP*, systolic blood pressure (mmHg); *DiaBP*, diastolic blood pressure (mmHg); *HR*, heart rate (bpm)
Other abbreviations as in Table 2

fractions in both genders. For women this relationship was also found for left ventricular variables. The distribution of patients in overall cancer groups is given in Table 6.

DISCUSSION

With the data presented above it is our intention to provide reference values for chemotherapy naïve cancer patients over a wide range of age and for both genders using a new and very reproducible technique.

We have not directly compared our values with MRI or echocardiography. Instead, we must relate our findings to previous studies using either CZT-camera technology, radionuclide angiography SPECT, or estimates of left ventricular function based on gated myocardial perfusion scintigraphy (MPI).

Cadmium-Zinc-Telluride-Cameras

To our knowledge, this is the first attempt to produce reference values for gated tomographic radionuclide angiography using a CZT-detector gamma camera. Previously, only re-projecting gated blood-pool SPECT from CZT-camera to standard 2D-planar radionuclide angiography have been described.[14] Absolute values were not given, but the authors found excellent correlation with the reprojected data compared to traditional imaging with sodium-iodine-cameras (NaI-cameras). It has also been shown that the CZT-camera is superior to both planar and SPECT radionuclide angiography obtained with traditional NaI-cameras regarding intra- and interobserver variation.[12] Both SPECT systems tended to produce higher LVEF than the planar acquisition, and NaI-SPECT marginally higher values than CZT-SPECT. It has been also demonstrated that radionuclide angiography using CZT-cameras has excellent reproducibility when estimating left ventricular volumes and ejection fraction from repeated scans comparable to the gold standard MRI.[11]

CZT-camera technology has foremost been developed and used for myocardial perfusion imaging. The higher sensitivity, better energy resolution and improved spatial resolution allows for faster acquisition times,[15] lower radiation doses and fewer equivocal results.[16] Left ventricular volumes and ejection fraction estimated from perfusion imaging using CZT-cameras has been shown be highly correlated with standard NaI-SPECT[15] and cardiac MRI.[17-19] However, CZT tends to underestimate the EDV and ESV compared to MRI (i.e., 10-30 mL for EDV). This could be due to incomplete segmentation of base and outflow tract on SPECT as these structures contain fewer myocytes.[19] Still, LVEF did not differ between CZT-SPECT and MRI.[17-19]

Comparing absolute values for the left ventricle, our findings are in agreement with those found on perfusion

Table 5. Correlation matrix between cardiac variables and patient characteristics for women

		LVEDV	LVESV	LVEF	RVEDV	RVESV	RVEF	COLV	CORV
Age	*R* value	−0.388	−0.386	0.271	−0.371	−0.363	0.105	−0.245	−0.215
	P value	<.001	<.001	<.001	<.001	<.001	n.s.	<.001	<.001
Height	*R* value	0.396	0.345	−0.202	0.277	0.206	0.001	0.261	0.191
	P value	<.001	<.001	.001	<.001	.001	n.s.	<.001	.002
Weight	*R* value	−0.014	−0.128	0.178	0.277	0.202	0.052	0.152	0.289
	P value	n.s.	.036	.003	<.001	.001	n.s.	.012	<.001
BSA	*R* value	0.109	−0.005	0.092	0.330	0.241	0.047	0.212	0.312
	P value	n.s.	n.s.	n.s.	<.001	<.001	n.s.	<.001	<.001
SysBP	*R* value	−0.226	−0.292	0.271	−0.166	−0.249	0.216	0.058	0.102
	P value	<.001	<.001	<.001	.006	<.001	<.001	n.s.	n.s.
DiaBP	*R* value	−0.215	−0.155	0.085	−0.134	−0.203	0.178	0.030	0.168
	P value	<.001	.011	n.s.	.028	.001	.003	n.s.	.006
HR	*R* value	−0.339	−0.306	0.223	−0.190	−0.268	0.216	0.401	0.462
	P value	<.001	<.001	<.001	.002	<.001	<.001	<.001	<.001

BSA, body surface area (m^2); *SysBP*, systolic blood pressure (mmHg); *DiaBP*, diastolic blood pressure (mmHg); *HR*, heart rate (bpm)
Other abbreviations as in Table 2

CZT-SPECT and MRI by Cochet et al[19] but lower than Giorgetti et al[18] and Baillez et al.[17] However, in Baillez et al more than half of the patients had known LV hypertrophy, dilated, or ischemic cardiomyopathy and the majority of Giorgetti et al's patients had known ischemic heart disease and were older, thus not comparable to our population.

Gated Radionuclide Angiography SPECT Using NaI-Cameras

First and foremost the presented data are in good accordance with results from De Bondt et al[20] who used normal volunteers for assessment of gender-specific data on right and left ventricular volumes also using gated tomographic radionuclide angiography on NaI-cameras. RVEF, RVEDV, RVESV, and LVEF are all similar to those measured by De Bondt et al, whereas we found slightly smaller left ventricular volumes.

In 55 patients referred for routine LVEF assessment Harel et al[21] conducted both gated radionuclide angiography SPECT, planar radionuclide angiography and cardiac MRI. Overall there was excellent correlation between LVEF, LESV, and LEDV between the different modalities. However, the radionuclide angiography tended to underestimate volumes and overestimate LVEF compared to cardiac MRI. The absolute values for ventricular volumes were higher and LVEF lower than our findings. However, their population had a high proportion of patients with ischemic cardiomyopathy (49%) and previous CABG or PCI (59%).

Table 6. Distribution of cancer forms

Cancer form	n	%
Women		
Breast	135	50
Leukemia	11	4
Lymphoma	30	11
Sarcomas	40	15
Carcinoma	33	12
Other	20	7
Men		
Prostate	7	4
Leukemia	15	8
Lymphoma	38	20
Sarcoma	50	26
Carcinoma	66	34
Other	18	9

Gated Perfusion SPECT (MPI)

Ababneh et al investigated ejection fraction and left ventricular volumes in 1513 patients undergoing MPI SPECT with either technetium-99m or thalium-201.

They found no difference between tracers or acquisition cameras, but did find a significant difference in LVEF and volumes amongst genders with women having smaller ventricles and larger LVEF. They found lower limits for LVEF to be 50% for women and 43% for men, and higher ventricular volume in men.[22] Our lower limit for LVEF is a bit higher for men (50%) and similar for women (50%). Both mean values and upper limit of normal of left ventricular volumes are higher in our material for both genders. The discrepancy can be due to different imaging techniques (perfusion SPECT vs blood-pool SPECT) and difference in population. Ababneh used normal MPI in patients referred for angina or dyspnoea as inclusion.

When comparing gated myocardial perfusion tomography with gated blood-pool tomography there is overall a very good correlation between the measured left ventricular volumes and ejection fractions. Whereas the systematic error for LVEF measurement looks to be linear for the whole spectrum of LVEF, the difference in volume estimation is not with a tendency toward larger differences with larger volumes.[23,24] Right ventricular estimation is even more troublesome with relatively large biases between the two methods.[24]

Different processing algorithms have shown, despite being well correlated, to produce varying ventricular volumes and ejection fractions.[20,21,25] Often the bias between imaging techniques or software is linear with over- or underestimating ''true'' volumes, but this is not always the case.[21,23,25] Therefore, in optimal circumstances individual patients should only be evaluated using same equipment regarding both hardware and software.

Right Ventricle

In a series of 58 patients[26] referred for evaluation of ventricular function both gated radionuclide angiography SPECT, echocardiography and MRI was done, with the latter as the reference standard. Radionuclide angiography showed high correlation with MRI for right ventricular volumes (r values 0.67-0.84), whereas echocardiographic derived indices of volumes and function performed less well. Our absolute values for right ventricular volumes and RVEF was comparable to the SPECT findings in the above series, and especially similar to the MRI findings, although not stratified by gender, confirming the ability of gated radionuclide angiography SPECT to asses right ventricular size and function.

In a selection of healthy volunteers (29% female), however, Kjær et al[27] found higher RVEF both on MRI and SPECT and somewhat lower volumes (when presuming BSA of 1.73 m^2 on average) than our results. In their experience there was agreement between MRI and radionuclide angiography SPECT for absolute volumes, however, with wide limits of agreement.

Age-Related Changes in Cardiac Variables

In concordance with the findings of De Bondt et al,[28] we found a significant negative correlation between age and left ventricular volumes, and positive correlation with LVEF. Both in our study and in that of De Bondt the correlation was only seen in women.

Cardiac MRI have demonstrated similar results with decreases in ESV and EDV for both ventricles together with a significant increase in ejection fraction with advancing age.[29-31]

Important cardiovascular changes occur with advancing age. Increased vascular intimal thickness and vascular stiffness lead to increased afterload and hypertension. In the heart, the number of myocytes decreases, while the remaining myocyte hypertrophies, thus myocardial mass, remain relatively stable. Left ventricular wall is thickened leading to changes in diastolic filling. Other changes included reduced heart rate variability and reduced SA-node cells and beta-adrenergic modulation.[32,33]

The changes in left ventricular wall size, compliance and ventricular filling leads to decreased left ventricular volumes but increased ejection fraction, the later perhaps due to changes in diastolic filling behavior and to more twisting and torsion of the left ventricle in the elderly. Another explanation could be reduced physical activity.[30-32]

In our study, we did not see any age-related change in left ventricular volumes or ejection fraction in men. Perhaps the smaller sample size and more skewed age distribution in our male group could account for this discrepancy.

Gender-Specific Differences

To our knowledge, our study is the first to address any gender difference in ventricular volumes and ejection fraction using CZT-cameras in a large sample of patients. We found that although there was a difference in absolute volumes the lower limit of ejection fraction did not differ between genders.

Giorgetti et al[18] reported no gender difference in ventricular volumes in a smaller sample of 55 patients (50% women), however, their population might be too small to identify minor differences. Ababneh et al[22] and Sharir et al[34] found significant differences in both left ventricular volumes and ejection fraction between men and women, with men having higher volumes and a lower ejection fraction. We did find a similar difference regarding volumes, but identified equal lower limits for LVEF between genders. This could be attributed to differences in population (patients referred for MPI) and method (perfusion vs blood pool).

In a smaller samples of 36 healthy volunteers cardiac MRI have shown that men had larger volumes and ventricular mass than women.[35] However, the LVEF was only slightly different and in the authors view relatively independent of gender. Again the small sample size might influence the finding, but overall the finding is in agreement with the presented data above.

In summary, our population is neither normal (cancer diagnosed) nor are they suspected of ischemic heart disease. Some of the large SPECT ''normal'' materials are patients referred for MPI with an intermediate risk of IHD—with a normal MPI. Thus, they do not have diagnosed IHD, but still are not normal as they where referred for MPI. In theory they could have other cardiac or pulmonary disease or false negative MPI.

The much larger Dallas Heart Study[36] conducted cardiac MRI on 1435 women and 1183 men without self-reported valvular abnormalities or congenital defects. They found lower limits for LVEF to be 61% in women and 55% in men, thus higher than our results and with a gender difference. Their populations were at mean younger than ours and much more ethnical diverse. A recent MR-study evaluating a population more similar to ours (Framingham Heart Study, n = 852)—found only small difference in lower limit LVEF between genders (men 59% and women 61%).[29]

Thus, our results regarding modest gender difference in lower limits of LVEF are conflicting with SPECT studies and to a lesser extend MRI-data. However, the gender difference in lower limits in LVEF seems to be smaller in MR-studies (3-6%) than SPECT studies. As previously discussed CZT offers increased resolution and reproducibility compared to SPECT and accordingly our results with little/no difference in LVEF is closer to the findings from large MRI studies. Other reasons for some of this discrepancy could, as discussed, be difference in techniques and difference in populations. As a consequence, we are currently in the process of setting up a comparison of CZT and MRI.

Limitations

The included patients are without diabetes, arrhythmia, or known cardiovascular or valvular disease. Still, they do not reflect a random sample and the underlying angiographic data cannot be considered complete in order to represent normal values in the traditional sense. However, the presented data still provide reference values for patients as they present themselves to the clinical oncologist before potentially cardiotoxic chemotherapy.

CONCLUSION

Reference values in a large sample of patients with no known cardiovascular or pulmonary disease is now provided. Despite gender-related differences in ventricular volumes, the lower limit of LVEF and RVEF is similar in the two groups. Finally, there is a decrease in ventricular volumes and a slight increase in LVEF in women with advancing age.

NEW KNOWLEDGE GAINED

Cardiac-dedicated CZT-detector cameras offer improved resolution and improved reproducibility. Although primarily intended for MPI, we here report normal values for gated radionuclide angiography using CZT-detector technique in chemotherapy naïve patients. Overall these values are in accordance with previous reporting's of gated blood-pool SPECT.

Disclosure

The authors declare that they have no conflict of interest.

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