Age-specific non-invasive transcutaneous Doppler ultrasound derived haemodynamic reference ranges in elderly Chinese adults

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ABSTRACT

Background: Whilst there is a presumption in medicine that ageing adversely affects cardiovascular function, it is unknown if resting haemodynamics are compromised in the elderly, and if so, to what degree. This study was intended to answer several questions; whether age-related changes in haemodynamics occur; whether there was a difference between the haemodynamics of ageing subjects with and without mild chronic disease; whether there was a difference in haemodynamics as measured from either the aortic or the pulmonary valve; and to establish reference ranges for this population.

Methods: Chinese adults aged over 60 years were divided into three age bands of 61–70, 71–80 and over 80 years. The haemodynamic parameters were measured using a non-invasive Doppler ultrasound-based instrument, the Ultrasonic Cardiac Output Monitor (USCOM).

Results: One hundred and sixty-five subjects (48.5% males) were recruited. 78 (47.3%) had no known disease whilst 87 (52.7%) had mild chronic illness. A total of 21 individual haemodynamic parameters were measured or calculated for each subject. There were no significant differences in stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR) or in body surface area (BSA)-indexed parameters, SV index (SVI), cardiac index (CI) and SVR index (SVRI) across age groups, or in other indexed haemodynamic parameters. No significant differences in indexed haemodynamics were found between those subjects with and those without mild chronic disease. Small, statistically significant, but clinically insignificant, differences (<5%) were found between the aortic and pulmonary valve measurements for SV, SVI and heart rate.

Conclusions: Ageing does not have any significant effect on resting haemodynamics in the elderly population studied. Mild chronic disease does not adversely affect resting haemodynamics in this population.

General Significance: Reference ranges were established for 21 haemodynamic parameters, as measured by USCOM, for an elderly Chinese population but not for non-Chinese populations.

1. Introduction

Population ageing is widespread around the world. The ageing trend began in developed countries and is now accelerating, not only in the first world, but also in developing countries. The major drivers of population ageing are increasing longevity and declining fertility [5]. The Chinese population is ageing particularly rapidly due to a falling mortality rate and the one child policy. By 2050 more than one quarter of the population will be over 65 years old [1]. Whilst ageing is known to affect the cardiovascular system both structurally and functionally [21,25], it is still unclear how, or if, ageing affects the resting haemodynamic profiles of the elderly.

The Ultrasonic Cardiac Output Monitor (USCOM) is a non-invasive continuous wave Doppler ultrasound device derived from echocardiography, which measures haemodynamic parameters, accurately and reliably [8,10,23,27,32,37]. It allows the measurement of haemodynamics in normal conscious subjects in a totally non-invasive manner, by measuring transvalvular flow across either the aortic or the pulmonary valve. It has been shown to be more accurate and more sensitive to change than the pulmonary artery catheter [32], and at least as accurate as research quality echocardiography [16,30], with a much shorter learning curve than echocardiography [15,26,27]. As with all quantitative tests, it is essential to have a reference range to compare any given reading against. By definition,

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values beyond the normal reference range are regarded as abnormal clinically. Equally, from a prognostic viewpoint, knowledge of the normal range is required to establish goals of therapy. Reference ranges for haemodynamic parameters as measured by USCOM have been established for Chinese full-term neonates [16,17], Chinese children aged 1 month–12 years [8], Chinese and Caucasian adolescents aged between 12 and 18 years [18], and Chinese and Caucasian adults aged between 18 and 60 years (unpublished data). However, there are no reference ranges for the elderly, despite the increasing use of point of care haemodynamics in general, and the USCOM in particular, in clinical practice. It is also unknown to what degree mild chronic disease, prevalent in the elderly population, affects resting haemodynamics.

This study was undertaken to establish whether age-related changes in haemodynamics occur; to what degree the haemodynamics of ageing subjects are affected by mild chronic disease; whether there is any discrepancy in measurements between the aortic valve and the pulmonary valve in this age group; and to establish reference ranges for this population.

2. Methods

2.1. Study design

This was a prospective cross-sectional study conducted between February and October 2012 in the Emergency Department of the Prince of Wales Hospital, Hong Kong. All aspects of the study were approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (reference number CRE-2009.482). Chinese adults aged over 60 years were recruited through Ma On Shan Neighbourhood Elderly Centre, the Department of Otorhinolaryngology, Head and Neck Surgery of Prince of Wales Hospital, and volunteers' referrals from other districts in Hong Kong. Exclusion criteria included age under 61 years, lack of consent, non-Chinese adults, and acute illness within the past four weeks. Following a detailed explanation of the study, written consent was obtained from all recruited subjects. Each subject was requested to complete a health questionnaire to identify current and past health status, and current medication use. Clinical management systems were also used to cross reference data from the subjects' medical records, where available.

Subjects were divided into two groups. Group 1 included those with no known acute or chronic illness, and who had taken no medication in the previous four weeks, and would be classed as ASA 1 (a normal healthy subject) according to the classification of the American Society of Anesthesiology [2]. Group 2 included subjects categorized as ASA 2, a patient with mild systemic disease. Subjects with more severe chronic disease, corresponding to ASA 3 and above, were excluded.

Physical characteristics of all subjects were recorded. Standing height was measured barefoot to the nearest 0.1 cm using a measuring tape. Body weight was measured to the nearest 0.1 kg using an electronic scale (Compact Precision Scale C200H, Conair Far East Ltd., Hong Kong). Arterial pressure was measured in the right arm in the supine position with an appropriately sized cuff using an oscillometric device (Omron HEM-7200 Automatic Blood Pressure Monitor, Omron Healthcare Co., Ltd, Japan), followed immediately by the USCOM measurement. Haemoglobin concentration was measured with a capillary blood sample collected by finger prick using HemoCue® B-Hemoglobin system (HemoCue® AB, Ängelholm, Sweden).

2.2. USCOM measurements

The USCOM device (USCOM Ltd, Sydney, Australia) calculates stroke volume (SV) by measuring the ejection velocity of blood flow across the aortic or pulmonary valves and multiplying the velocity time integral (VTI) of the trace of the Doppler flow profile by the cross-sectional area (CSA) of the minimum outflow tract diameter (OTD), which is derived from the subject's weight and height using a proprietary algorithm. Heart rate (HR) is also measured from the periodicity of the Doppler waveform, and cardiac output calculated as $CO = SV \times HR$. The mean arterial pressure (MAP) is calculated from the inputted systolic and diastolic blood pressures as $MAP = DBP + [(SBP - DBP) / 3]$ and systemic vascular resistance (SVR) from CO, MAP and central venous pressure (CVP) as $SVR = (MAP - CVP) \times 80 / CO$. CVP was assumed to be zero [20].

The USCOM uses measured oxygen saturation (SpO_2) from an integral pulse oximeter probe and inputted haemoglobin concentration [Hb] to calculate oxygen delivery (DO_2). Smith–Madigan inotropy index (SMII) and potential to kinetic energy ratio (PKR) are calculated using the method of Smith and Madigan [35]. The 21 haemodynamic parameters are explained further in Appendix 1 [19,35].

All USCOM measurements were performed by a senior researcher with experience of over 1000 USCOM examinations in a wide variety of patients and research subjects. To achieve acceptable proficiency in the use of the USCOM, trainees must achieve a level of inter- and intra-observer variability which is within the limits of physiological variation of patients, i.e. less than 10%, and typically the values are around 5–8% [9,14,16]. Measurements were performed with the subject in the supine position, following a period of rest of at least 5 min, and immediately following blood pressure measurement. The suprasternal insonation window was used for aortic measurements, which was performed first, whilst the left parasternal insonation window was used for pulmonary valve measurements. A minimum of three consecutive diagnostic quality Doppler ejection profiles were required for each measurement, and three measurements were made for each subject on each of the two valves. This generated a minimum of 18 diagnostic quality ejection waveforms for each subject, nine for each valve. This leads to a threefold improvement in measurement accuracy, as the standard error of the measurement is directly proportional to the standard deviation of SV and inversely proportional to the square root of the number of measurements, in this case $\sqrt{9} = 3$. This provides a greater degree of measurement accuracy than the single waveform examination often employed in echocardiography.

2.3. Sample size calculation

Based on published values [6], the mean SV for subjects aged 65 and 73 years were 69.5 ± 4.9 mL and 63.0 ± 4.7 mL respectively. Therefore, a minimum sample size of 9 subjects in each group would be required to achieve a power of 80% with a 2-sided significance level of $\alpha = 0.05$. In order to investigate the difference in haemodynamic parameters between the three age groups, the two ASA groups and the two aortic and pulmonary windows, the minimum sample size required for this study is 108 subjects (9×3 age groups $\times 2$ ASA groups $\times 2$ valves $= 108$). From previous experience with this population, we estimated that up to 25% of subjects might yield sub-optimal quality images. The minimum sample size was therefore set at 135.

2.4. Statistical analysis

Continuous variables were analyzed using the Mann–Whitney U test or Wilcoxon Rank Sum test. Multiple comparisons of different age groups were performed using the Kruskal–Wallis test. Categorical variables were analyzed using the Chi-square test or Fisher's exact test. As the data showed a normal distribution, the

reference ranges were defined using 2.5th and 97.5th percentiles to include the central 95% of the population. The data were analysed using PASW Statistics v18.0 (SPSS Inc., IBM Corporation, Chicago, IL) and MedCalc version 11.5.1.0 (MedCalc Software, Mariakerke, Belgium). A P value of <0.05 was regarded as statistically significant. Data are presented as median, 2.5th and 97.5th percentiles, 95% confidence intervals, and mean with standard deviations as appropriate. Frequencies are expressed as counts and percentages.

3. Results

One hundred and sixty five subjects (48.5% males) were enrolled in the study. 77 subjects (46.4%) were able to be checked through clinical management systems to cross reference data. 78 subjects (47.3%) had no known disease, the ASA 1 group, whilst 87 (52.7%) had mild chronic illness, the ASA 2 group. This group included one subject (1.1%) with an irregular heartbeat, 65 (74.8%) with hypertension, 18 (20.6%) with diabetes, 30 (34.4%) with hypercholesterolemia, and 14 (16.1%) with a history of cancer but no recurrence or need for treatment within the last 10 years, but who could be expected to have mild systemic disturbance caused by this or another pathological process [2].

The demographic data for all subjects are shown in Table 1. For healthy subjects (ASA 1), the 71–80 years group had significantly lower body weight (P = 0.029) and body surface area (BSA) (P = 0.015) than for subjects of <71 years and >80 years. Compared to the ASA 2 group, ASA 1 subjects aged 61–70 years had significantly lower SBP (P = 0.045), and those aged 71–80 years had significantly lower body weight (P = 0.003), BSA (P = 0.008) and body mass index (BMI) (P < 0.001). ASA 1 subjects aged over 80 years were significantly taller than their ASA 2 counterparts (P = 0.007), and had higher BSA (P = 0.019).

Table 2 shows the SV, CO, SVR and respective index values for all subjects by age groups. ASA 1 patients aged 61–70 showed a slightly higher SV in comparison to their ASA 2 counterparts at 84.8 (80.8–89.7) mL vs. 79.0 (77.2–85.0) mL (P = 0.047). Otherwise, there were no significant differences in any of the parameters between the ASA 1 and ASA 2 groups, or between any age groups within or between ASA groupings.

The data for both the aortic and pulmonary valve-derived values for ASA 1 subjects are shown in Table 3. HR, VTI, peak ejection velocity (Vpk), the mean pressure gradient (Pmn) and minute distance (MD) were significantly higher in aortic measurements whilst SMII, PKR, SV, SVI and stroke work (SW) were significantly higher in pulmonary measurements.

The comparison data for both ASA 1 female and male patients is shown in Table 4. CI, Pmn, MD, Vpk, SVI and VTI were all significantly higher in females, whilst PKR and SVRI were significantly higher in males.

4. Discussion

Echocardiography is a standard technique which has been used for many years to provide data on both cardiac morphology and haemodynamics. It has come to be regarded as a clinical gold standard for anatomical evaluation and is often used to evaluate haemodynamics clinically. However, echocardiography requires extensive training, particularly for accurate haemodynamic measurements [34]. The largest source of error in haemodynamic measurements with echocardiography stems from difficulty in measuring the aortic and pulmonary outflow diameters. The American Society of Echocardiography recommends that the average of a minimum of three measurements should be used for the aortic diameter, and more than this for the pulmonary diameter. In addition, conventional echocardiography generally uses

pulsed-wave Doppler (PWD) to measure the flow velocity and calculate VTI. Evidence suggests that this is less accurate than using continuous-wave Doppler (CWD). The current standard of care recommends the use of a non-imaging probe and the use of CWD [31,34]. The USCOM predicts the diameter of the aortic and pulmonary valves based on a proprietary algorithm which is similar to the equations described by Nidorf et al. [28]. Measurement of VTI is largely automated that enables several ejection waveforms to be measured in real time and can then be averaged. A typical examination takes less than 3 min. As a result, USCOM is simpler and more practical to use, yet provides high quality beat-to-beat haemodynamic measurements that are at least comparable if not better than echocardiography [16,22,30]. Interobserver variability is significantly lower than echocardiography, ranging from 5.1 to 17%, [8,9,23] indicating minimal user dependency. As with echocardiography, SV is calculated from VTI and CSA. Multiplying this by HR yields CO, and further calculations based on MAP, [Hb], ejection velocities and time measurements yield further derived parameters. BSA is calculated from input height and weight data and this is used to calculate index values for each parameter [19].

As the data was normally distributed, normal ranges can be defined for the population (Tables 3 and 4). Reference ranges for haemodynamic parameters are essential for both diagnosis and guidance of therapy. Haemodynamic parameters outside the reference range indicate an increased probability of illness, whilst treatment should logically aim to bring those parameters back towards the reference ranges. The paediatric advanced life support (PALS) guidelines for example, now specify a target CI value of 3.3 to 6.0 L/min/m^2 as a resuscitation goal [7].

In this study, we found that there was no significant change in resting haemodynamic parameters with increasing age in subjects both with and without known chronic disease. Similar findings have been reported previously [11,33]. Left ventricular systolic function remains relatively well preserved and left ventricular ejection fraction, SV and CO at rest did not change significantly with ageing [11,33]. Although the ASA 1 subjects aged 61–70 years had slightly higher SV than ASA 2, the difference, after indexing to body surface area (SVI), was not significant.

In our study the mean CI was 3.3 L·min^{-1}.m^{-2}, which was higher than those of the elderly subjects reported by Australian (3.0 L·min^{-1}·m^{-2}) [36], Swedish (2.4 L·min^{-1}·m^{-2}) [3,4] and American (2.0 L·min^{-1}·m^{-2}) [24] studies. This may be due to methodological differences or may reflect different levels of adiposity between differing populations. Studies have shown that the United States has the highest obesity rate amongst adults (33.8%), followed by Australia (24.6%) and Sweden (11.2%), whilst China has the lowest obesity rate (2.9%) amongst these countries [12,29]. Curiously, the magnitude of CI is similar to that of life expectancy across the races. Amongst these countries, CI and life expectancy is highest in Chinese and lowest in Americans. The current life expectancy at birth in Hong Kong is higher than that in Australia, Sweden and the United States [38].

In our previous studies, CI was highest in Chinese children aged 1 month–12 years (n = 1197; CI = 4.8 L·min^{-1}·m^{-2}) [8], followed by Chinese adolescents aged between 12 and 18 years (n = 362; CI = 4.2 L·min^{-1}·m^{-2}) [18], and Chinese adults aged between 18 and 60 years (n = 510; CI = 3.2 L·min^{-1}·m^{-2}) (unpublished data). The CI was similar in Chinese adults aged below 60 years and those over 60 years, with a lower SVI (43.7 mL·m^{-2}) but a higher HR (73 bpm) in those aged below 60 years. This is at variance with Australian and American studies which showed that mean CI was lower in the elderly compared with younger adults [24,36]. Whilst it may appear surprising that resting cardiovascular function in elderly Chinese is of a similar level to that of young adults, this may reflect differences in adaptive processes that occur with ageing,

Table 1
Characteristics of study participants.

Variables (median and 95% CI)	Subjects without chronic disease n = 78	P[a]	Subjects with chronic disease n = 87	P[a]	P[b]
Age (years)					
Overall	69.0 (67.0–72.0)	<0.001	72.0 (70.0–74.0)	<0.001	0.080
61–70 years	65.0 (64.0–65.0)		65.0 (64.0–66.8)		0.646
71–80 years	73.0 (72.0–75.6)		74.0 (73.0–74.3)		0.753
>80 years	82.0 (81.1–86.7)		84.5 (82.0–87.0)		0.413
Males, n (%)					
Overall	43 (55.1)	0.152	37 (42.5)	0.418	0.144
61–70 years	24/41 (58.5)		14/35 (40.0)		0.167
71–80 years	12/28 (42.8)		18/36 (50.0)		0.752
>80 years	7/9 (77.7)		5/16 (31.3)		0.069
Height (m)					
Overall	158.9 (155.5–162.5)	0.058	155.0 (152.0–159.0)	<0.001	0.038 *
61–70 years	160.0 (156.7–166.1)		157.0 (154.5–162.0)		0.100
71–80 years	154.5 (151.5–162.8)		157.5 (152.7–161.5)		0.978
>80 years	159.0 (153.1–162.6)		148.0 (144.0–151.7)		0.007 *
Weight (kg)					
Overall	55.3 (53.0–60.6)	0.029	58.0 (55.0–61.0)	0.027	0.283
61–70 years	59.9 (53.2–65.2)		58.8 (54.7–63.9)		0.972
71–80 years	51.7 (47.0–57.2)		59.4 (54.8–64.8)		0.003 *
>80 years	55.5 (54.0–65.2)		52.3 (45.2–59.2)		0.053
BSA (m^2)					
Overall	1.56 (1.50–1.65)	0.015	1.57 (1.53–1.61)	0.003	0.718
61–70 years	1.63 (1.50–1.73)		1.60 (1.53–1.70)		0.766
71–80 years	1.48 (1.42–1.60)		1.58 (1.52–1.71)		0.008 *
>80 years	1.56 (1.52–1.71)		1.45 (1.35–1.55)		0.019 *
BMI (kg/m^2)					
Overall	22.7 (21.3–23.4)	0.102	24.2 (23.5–25.2)	0.513	0.002 *
61–70 years	23.4 (21.2–23.9)		23.6 (22.9–25.3)		0.215
71–80 years	21.5 (20.5–23.1)		24.3 (23.2–26.1)		<0.001 *
>80 years	23.4 (21.7–25.3)		23.2 (21.2–26.4)		0.913
MAP (mm Hg)					
Overall	96.4 (93.8–99.3)	0.664	97.2 (95.0–100.9)	0.769	0.151
61–70 years	96.3 (88.1–100.5)		98.2 (94.2–105.3)		0.120
71–80 years	96.5 (93.9–101.9)		96.3 (93.4–101.9)		0.620
>80 years	95.3 (90.6–116.8)		94.0 (89.3–113.0)		0.874
SBP (mm Hg)					
Overall	138.0 (134.0–141.1)	0.097	141.0 (138.9–147.1)	0.146	0.004 *
61–70 years	138.0 (130.0–139.5)		141.0 (135.2–147.0)		0.045 *
71–80 years	136.5 (132.7–150.3)		143.5 (135.7–156.0)		0.127
>80 years	149.0 (134.0–177.9)		148.0 (138.3–177.7)		0.423
DBP (mm Hg)					
Overall	74.5 (71.9–79.1)	0.832	74.0 (71.0–77.0)	0.007	0.697
61–70 years	75.0 (70.8–80.5)		78.0 (77.0–80.8)		0.326
71–80 years	74.5 (71.4–80.3)		72.5 (69.7–75.3)		0.404
>80 years	73.0 (63.8–82.7)		69.0 (63.6–78.8)		0.728
Heart rate (bpm)					
Overall	63.4 (60.4–65.8)	0.115	63.3 (62.0–65.2)	0.315	0.985
61–70 years	62.9 (58.4–65.5)		63.9 (55.7–69.8)		0.540
71–80 years	66.6 (62.7–71.6)		62.4 (59.5–64.9)		0.161
>80 years	58.7 (52.9–66.1)		64.2 (60.3–71.2)		0.562

Legend to Table 1.
Variables are quoted as medians and 95% confidence intervals.
[a] Comparison between age groups.
[b] Comparison between subjects without (ASA 1) and with (ASA 2) chronic disease.
* = statistically significant.

particularly preservation of left ventricular systolic function, in this population.

4.1. Aortic versus pulmonary measurements

Heart rate was significantly higher in the aortic approach than in the pulmonary approach, whilst SV and SVI were significantly lower. As CO = SV × HR, the net result was that CO and CI were similar for both approaches. This may represent some degree of anxiety-induced tachycardia during the aortic measurements which were performed first, which settled over the following few minutes prior to the pulmonary measurements being made. As the heart rate slows, so diastolic ventricular filling and stroke volume both increase, resulting in similar cardiac outputs between the two measurements. It is striking that the percentage differences in HR, SV and SVI between the aortic and pulmonary approaches were only around 5% and that the measurements of CO and CI showed less than a 3% difference for the two approaches.

The differences between the aortic and pulmonary values for Pmn, MD, Vpk and VTI are not surprising. Aortic Pmn, MD, Vpk and VTI were also found to be higher than pulmonary values in Australians [36]. The aortic valve is a higher pressure-lower diameter structure than the pulmonary valve, with the latter having a diameter approximately 11% greater than the aortic valve, and a cross-

Table 2
Stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR) and the corresponding index values for both groups.

Parameters median (2.5th–97.5th percentiles)	Subjects without chronic disease n = 78	P[a]	Subjects with chronic disease n = 87	P[a]	P[b]
SV (mL)					
Overall	82.6 (53.9–112.9)	0.093	78.4 (56.9–112.3)	0.237	0.052
61–70 years	84.8 (58.5–112.8)		79.0 (60.9–107.6)		0.047 *
71–80 years	79.4 (51.9–105.9)		78.8 (58.5–115.0)		0.588
>80 years	78.9 (64.5–103.4)		75.7 (57.4–101.0)		0.141
SVI (mL·m^{-2})					
Overall	53.6 (35.5–70.4)	0.963	50.1 (35.5–69.5)	0.727	0.056
61–70 years	53.8 (36.7–70.3)		50.0 (37.5–64.5)		0.105
71–80 years	53.6 (36.7–70.4)		49.7 (35.8–69.4)		0.218
>80 years	53.0 (37.4–66.8)		52.2 (35.4–69.1)		0.821
CO (L·min^{-1})					
Overall	5.2 (3.6–7.3)	0.757	5.0 (3.4–7.0)	0.535	0.267
61–70 years	5.3 (3.7–7.0)		5.1 (3.4–6.5)		0.346
71–80 years	5.1 (3.7–8.0)		5.1 (3.6–7.0)		0.978
>80 years	5.2 (4.3–6.0)		4.7 (3.7–6.4)		0.365
CI (L·min^{-1}·m^{-2})					
Overall	3.2 (2.3–4.7)	0.553	3.1 (2.2–4.5)	0.512	0.164
61–70 years	3.2 (2.1–4.5)		3.1 (2.4–4.0)		0.221
71–80 years	3.3 (2.3–5.4)		3.1 (2.2–4.6)		0.163
>80 years	3.4 (2.7–3.7)		3.3 (2.5–4.2)		0.497
SVR (d·s·cm^{-5})					
Overall	1481 (980–2106)	0.545	1553 (1128–2606)	0.446	0.080
61–70 years	1438 (1103–1967)		1576 (1178–2238)		0.051
71–80 years	1590 (943–2307)		1508 (1175–2359)		0.957
>80 years	1627 (1231–1863)		1655 (1133–2454)		0.497
SVRI (d·s·cm^{-5}·m^2)					
Overall	2515 (1527–3507)	0.755	2512 (1812–4061)	0.616	0.084
61–70 years	2495 (1686–3500)		2662 (1983–3769)		0.057
71–80 years	2515 (1342–3607)		2455 (1873–4015)		0.239
>80 years	2652 (2079–3191)		2485 (1722–3653)		0.821

Legend to Table 2.
Data presented as medians (2.5th–97.5th percentiles).
[a] Comparison between age groups.
[b] Comparison between subjects without (ASA 1) and with (ASA 2) chronic disease.
* = statistically significant.

Table 3
Haemodynamic parameter values for both aortic and pulmonary valve measurements in subjects without chronic disease (ASA 1) (n = 78).

Parameter	Unit	Overall	Aortic approach	Pulmonary approach	P
Preload					
FT	ms	405 (329–456)	396 (321–462)	402 (330–449)	0.326
FTc	ms	413 (355–471)	414 (356–474)	412 (346–475)	0.627
SVV	%	17.0 (10.7–30.6)	18.0 (8.9–37.7)	16.6 (8.0–30.6)	0.148
Contractility					
HR	bpm	63.4 (48.9–88.1)	65.0 (47.3–89.4)	61.9 (47.6–85.8)	0.000 *
VTI	m	28.9 (20.5–37.8)	30.0 (22.9–41.1)	26.2 (20.8–38.3)	0.000 *
Vpk	m·s^{-1}	1.1 (0.9–1.5)	1.2 (1.0–1.7)	1.1 (0.8–1.5)	0.000 *
ET	%	42.4 (34.1–52.3)	42.5 (33.3–52.5)	41.8 (32.4–54.5)	0.093
SV	mL	82.6 (53.9–112.9)	79.7 (59.2–111.3)	83.9 (62.3–120.0)	0.001 *
SVI	mL·m^{-2}	53.6 (35.5–70.4)	50.6 (36.6–70.2)	53.5 (37.8–77.3)	0.001 *
SMII	W·m^{-2}	1.8 (1.1–2.4)	1.8 (1.2–2.5)	1.9 (1.2–2.6)	0.022 *
Pmn	mm Hg	2.3 (1.3–3.9)	2.7 (1.7–4.6)	2.0 (1.1–4.0)	0.000 *
MD	m·min^{-1}	18.0 (13.0–26.0)	19.4 (13.5–28.3)	16.2 (12.0–26.6)	0.000 *
SW	mJ	1067 (676–1622)	1031 (633–1531)	1072 (720–1758)	0.002 *
CP	W	1.1 (0.7–1.6)	1.1 (0.7–1.7)	1.1 (0.7–1.8)	0.054
Afterload					
PKR		44.7 (24.6–77.0)	35.9 (20.7–62.1)	48.2 (23.9–82.3)	0.000 *
SVR	d·s·cm^{-5}	1481 (980–2106)	1446 (1036–2301)	1486 (902–2094)	0.157
SVRI	d·s·cm^{-5} m^2	2515 (1527–3507)	2486 (1542–3498)	2390 (1321–3478)	0.124
Tissue perfusion					
CO	L·min^{-1}	5.2 (3.6–7.3)	5.2 (3.5–7.2)	5.2 (4.0–8.1)	0.070
CI	L·min^{-1}.m^{-2}	3.2 (2.3–4.7)	3.2 (2.2–4.9)	3.3 (2.4–5.6)	0.081
DO$_2$	mL·min^{-1}	786 (493–1232)	802 (422–1171)	817 (540–1316)	0.074
DO$_2$I	mL·min^{-1} m^{-2}	520 (356–856)	528 (305–817)	515 (357–920)	0.099

Legend to Table 3.
Data presented as medians (2.5th–97.5th percentiles).
* = statistically significant.

Table 4

Comparison of hemodynamic parameters in males and females without chronic disease (ASA 1) (n = 78).

Parameter	Unit	Males	Females	P
Preload				
FT	ms	396 (321–462)	410 (330–449)	0.267
FTc	ms	405 (312–458)	418 (358–447)	0.094
SVV	%	17.2 (11.4–30.0)	16.4 (8.6–29.6)	0.001*
Contractility				
HR	bpm	63.8 (46.9–89.8)	62.7 (50.2–79.7)	0.948
VTI	m	26.9 (20.9–34.2)	30.0 (20.4–38.5)	0.173
Vpk	$m \cdot s^{-1}$	1.1 (0.9–1.4)	1.2 (0.9–1.6)	0.012*
ET	%	41.7 (34.4–52.9)	43.1 (33.9–50.7)	0.308
SV	mL	82.4 (63.0–112.5)	82.8 (53.0–106.7)	0.001*
SVI	$mL \cdot m^{-2}$	48.3 (35.9–65.4)	55.8 (36.0–70.5)	0.430
SMII	$W \cdot m^{-2}$	1.7 (1.2–2.5)	1.8 (1.1–2.3)	0.379
Pmn	mm Hg	2.2 (1.4–3.6)	2.5 (1.4–4.3)	0.011*
MD	$m \cdot min^{-1}$	17.1 (13.1–27.2)	19.0 (14.1–25.3)	0.009*
SW	mJ	1083 (690–1623)	985 (674–1421)	0.736
CP	W	1.1 (0.7–1.7)	1.0 (0.7–1.5)	0.121
Afterload				
PKR		50.2 (31.0–76.7)	38.4 (22.4–86.7)	0.001*
SVR	$d.s.cm^{-5}$	1548 (989–1967)	1449 (1023–2204)	0.655
SVRI	$d.s.cm^{-5} \, m^2$	2630 (1557–3401)	2024 (1507–3661)	0.003*
Tissue perfusion				
CO	$L \cdot min^{-1}$	5.3 (4.1–7.7)	5.1 (3.6–6.8)	0.448
CI	$L \cdot min^{-1} \cdot m^{-2}$	3.0 (2.3–5.3)	3.5 (2.3–4.6)	0.004*
DO_2	$mL \cdot min^{-1}$	845 (390–1335)	751 (517–1133)	0.076
DO_2I	$mL \cdot min^{-1} \cdot m^{-2}$	520 (244–899)	524 (358–761)	0.577

Legend to Table 4.
Data presented as medians (2.5th–97.5th percentiles).
* = statistically significant.

sectional area around 21% greater than the aortic valve. As the volume flow through both is the same, then the velocity of flow will be around 18% lower through the pulmonary valve than through the aortic valve.

4.2. Sex differences

In this study, relative to males, females showed similar values for SV but lower values for BSA. Consequently, SVI and CI were higher in females. Absolute SV and CO were higher in American Indian males than females, whereas normalization for BSA eliminated the sex difference in SV and resulted in slightly higher CI in females [13]. SV and CO normalized for fat-free body mass (FFM) were considerably higher in females than males. There was no significant difference in absolute values for SVR in the current study, but females had lower SVRI values as a result of their lower BSA. Females had lower haemoglobin concentrations (P < 0.001) and, as a consequence of their smaller size, smaller valve diameters (P < 0.001) than males. They would therefore be expected to show higher ejection velocities, with higher Pmn, MD and Vpk. The increased velocity of ejection leads to a higher value for kinetic energy, which is the divisor in the PKR calculation (PKR = PE / KE) resulting in a lower value for PKR. The differences between the sexes shown in Table 4 are therefore entirely physiological and anatomical and are expected.

4.3. Study limitations

Firstly, the number of subjects aged over 80 years both with and without chronic disease was small (9 and 16 respectively). However, this number is greater than in previously reported studies [3,4,6,24]. There were only nine patients in the ASA 1 group and seven of these were male. This could explain why the average height is significantly different. Conversely, in the ASA 2 group, only five of the 16 were male could have skewed the height data in the opposite direction. The figures for the 61 to 70 group and 71 to 80 group are much more evenly balanced. Secondly, the subjects were classified as ASA 1 (a normal healthy subject) and ASA 2 (a patient with mild systemic disease) according to the American Society of Anesthesiology grading. The definition is broad. However, this system has been well validated and is universally known and accepted. The use of a health questionnaire and direct questioning of the subject is a recognised standard for ASA grading. Given the large number of potential conditions which could be present in this age group, it is simply a pragmatic way of defining them. Thirdly, as the reference ranges were defined using 2.5th and 97.5th percentiles to include 95% of the population, there is a 5% possibility that an otherwise normal subject may have an USCOM measurement that lies outside the reference ranges, but this applies to all variables. In addition, although the CVP was assumed to be zero for calculation of MAP–CVP in this study, which in turn affects cardiac power (CP), SW, SVR, SVRI, SMII and PKR, the likely effect on these variables is minimal. In percentage terms, the differences in these haemodynamic parameters would be typically 1.5%, 3.0% and 6.0% respectively for CVP values of 5, 10 and 20 mm Hg. More significantly, this study only included subjects from Hong Kong. Our results may not be generalizable to other parts of China, let alone elsewhere in the world. Nevertheless, they are the first published data for this technique in any elderly ethnic group.

We believe it would be appropriate to extend this study with a larger sample size for those aged over 80 years, particularly as so many Chinese and other races are now living to this age and beyond. A multinational study is also indicated to explore the differences between races as suggested by studies from the United States, Australia and Sweden. Only then could the true generalizability or otherwise of our results be established.

5. Conclusion

This study showed no adverse effects of ageing on resting haemodynamics. There were no significant differences in resting haemodynamics between healthy (ASA 1) and mild chronic disease (ASA 2) subjects. There were no clinically significant differences between haemodynamic measurements from the aortic valve as opposed to the pulmonary valve; the two are interchangeable in terms of indexed values. Reference ranges for 21 haemodynamic parameters measured by USCOM in Chinese adults (but not for non-Chinese populations) aged over 60 years have been established.

Conflicts of interest

None of the authors declares any conflict of interest. Specifically, none of the authors has any financial relationship with USCOM Pty Ltd, Australia, or other related commercial organization to perform or publish any aspect of this study.

Appendix 1. Haemodynamic parameters measured or calculated by USCOM [19,35].

Parameter	Unit	Definition/equation
Preload		
Flow time (FT)	ms	Systolic ejection time
Flow time corrected (FTc)	ms	FTc = FT / $\sqrt{\text{R–R interval}}$
Stroke volume variation (SVV)	%	SVV = (SV$_{max}$ − SV$_{min}$ × 100) / [(SV$_{max}$ + SV$_{min}$) / 2]
Contractility		
Heart rate (HR)	bpm	Number of cardiac cycles in beats per min
Velocity time integral (VTI)	m	TI = $\int_0^{FT} V(t)dt$
Peak ejection velocity (Vpk)	m·s^{-1}	Maximum ejection velocity through valve
Ejection time (ET)	%	ET% = (ET / cycle duration) × 100
Stroke volume (SV)	mL	SV = vti × πr^2
Stroke volume index (SVI)	mL·m^{-2}	SVI = SV / BSA
Smith–Madigan inotropy index (SMII)	W·m^{-2}	SMII = (PE + KE) / BSA
Mean pressure gradient (Pmn)	mm Hg	Pmn = 4 × Vmean^2
Minute distance (MD)	m·min^{-1}	MD = HR × vti
Stroke work (SW)	mJ	SW = (60/450) (MAP–CVP) × SV
Cardiac power (CP)	W	CP = (MAP–CVP) × CO / 450.037
Afterload		
Potential to kinetic energy ratio (PKR)		PKR = PE / KE
		PE = (ΔP × SV × 10^{-3}) / (7.5 × FT)
		KE = (SV × 10^{-6} × ρ × Vm^2) / (2 × FT)
Systemic vascular resistance (SVR)	d·s·cm^{-5}	SVR = (MAP − CVP) x 80/CO
Systemic vascular resistance index (SVRI)	d·s·cm^{-5}·m^2	SVRI = SVR × BSA
Tissue perfusion		
Cardiac output (CO)	L·min^{-1}	CO = SV × HR
Cardiac index (CI)	L·min^{-1}.m^{-2}	CI = CO / BSA
Oxygen delivery (DO$_2$)	mL·min^{-1}	DO$_2$ = 1.34 × Hb × SpO$_2$ / 100 × CO
Oxygen delivery index (DO$_2$I)	mL·min^{-1}·m^{-2}	DO$_2$I = DO$_2$ / BSA

BSA: body surface area (m^2); CVP: central venous pressure (mm Hg); Hb: haemoglobin concentration (g·L^{-1}); MAP: mean arterial pressure (mm Hg); SpO$_2$: peripheral oxygen saturation (%); R–R interval: heart beat periodicity (s); Vm: mean velocity (m·s^{-1}); ρ: density of blood (kg·m^{-3}); ΔP: MAP–CVP (mm Hg); πr^2: cross-sectional area of outflow tract (m^2).

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