The normal cardiac index in older healthy individuals: a scoping review

Luca Cioccari, Nora Luethi, Neil J Glassford and Rinaldo Bellomo

ABSTRACT

Objective: Despite the growing number of older patients having major surgery, the normal resting values for the cardiac index of older patients remain unclear. We aim to derive a normative value for such patients.
Design: Scoping review.
Data sources: We searched MEDLINE, EMBASE and CENTRAL for studies reporting measured values of cardiac output or cardiac index in healthy, older humans at rest.
Results: We retrieved 5340 citations and assessed 412 full-text articles for eligibility. Twenty-nine studies, published between 1964 and 2017, met our inclusion criteria. Overall, the mean cardiac index in healthy volunteers over 60 years of age was reported between 2.1 and 3.2 L/min/m^2 and the mean cardiac output was between 3.1 and 6.4 L/min. A yearly decline in cardiac index (between 3.5 and 8 mL/min/m^2 per year) was reported in some but not all studies. Only one study measured the cardiac index in nine people over 80 years of age.
Conclusions: The normal range of the cardiac index in older patients may be lower than previously reported. Its rate of decline with age is uncertain, but likely between 3.5 and 8 mL/min/m^2 per year. Data on the normal cardiac index in people older than 80 years are scant.

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The adequacy of the cardiac index is commonly assessed in the context of surrogate measures of oxygen delivery, such as mixed venous oxygen saturation, blood lactate levels, peripheral perfusion and urine output. Cardiac index is commonly measured as a part of such an assessment, and numeric thresholds have been proposed to differentiate between impaired oxygen delivery and utilisation, and to guide fluid management.[1] In addition, reference values are also used to define clinical states requiring intervention, such as the low cardiac output syndrome.[2,3]

The normal reference range of the cardiac index is typically reported as to be between 2.5 and 4.2 L/min/m^2.[4] However, these figures are mainly derived from studies conducted before 1980, using various methods of measurement, including poorly validated techniques,[5-13] and do not consider modern methods such as echocardiography or cardiac magnetic resonance imaging (CMR).[14,15] Moreover, some of these studies do not provide information on factors that might influence reference values, such as age, gender and ethnicity.

As older patients account for an increasing proportion of intensive care unit admissions,[16,17] clinicians need to be able to discern the impact of disease from that of ageing itself. Although the effect of age on haemodynamic parameters has been the subject of many investigations, most studies included only a small sample of older patients, or included patients with significant comorbidities or symptoms of cardiac dysfunction.[5,11,18-21] This limits the interpretation of reference values provided by such studies when assessing the impact of age alone.

Therefore, we sought to obtain information on the reference values for the normal cardiac index for healthy, older individuals.

Methods

Study design

We performed a scoping review using the framework described by Levac,[22] and followed the methodology and guidance outlined by Peters and colleagues.[23] Scoping reviews provide a preliminary appraisal of the magnitude and scope of published literature, aiming to identify the nature and extent of research evidence.[24] In doing so, they share several characteristics of systematic reviews,[23] but typically do not include a process of quality assessment as they focus on the research findings themselves, as opposed to the means used to obtain them.[25]

Search strategy

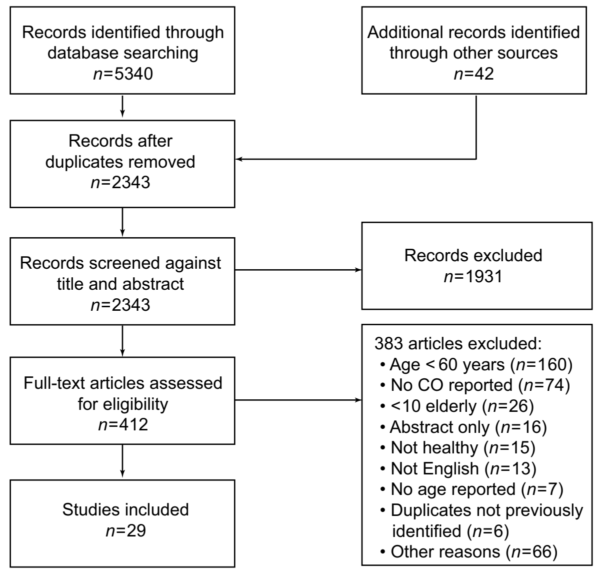
The search strategy was developed with the assistance of a clinical librarian. We searched the following databases in September 2017 without time limits: MEDLINE (Ovid), EMBASE (Ovid) and CENTRAL (the Cochrane Library). The search syntax included a comprehensive list of keywords, medical subject heading (MeSH), Boolean operators and truncations to accommodate variations in terminology and indexing terms across databases (see Appendix for full search strategy, online at cicm.org.au/journal.php). The reference lists of all included articles and the authors' personal archives were also screened for relevance.

Study inclusion and exclusion criteria

The inclusion criteria were original research articles reporting the cardiac output or cardiac index in healthy, older humans at rest. We defined "older" as the mean age of participants (or the reported subgroup of participants) being older than 60 years of age. If no mean age was reported, the age band > 60 years was used to define "older". This cut-off value was chosen because, although there is no universal definition of "older" people, an age > 60 years is frequently used as a cut-off.[26] We defined "healthy" as participants without cardiovascular disease and free of cardiac symptoms. Only publications in English language were included.[27]

In order to obtain representative reference values for healthy older people, we excluded studies including athletes, post-operative and anesthetised patients or patients with known cardiovascular disease, diabetes, hypertension, renal disease or any condition known to affect cardiac performance. Intervention studies or studies of mixed populations (fulfilling both inclusion and exclusion criteria) were included only if the cardiac output or the cardiac index value before the intervention and/or in the eligible subgroup were reported separately. We excluded studies of symptomatic patients who were later judged to have been free of cardiovascular disease, because the referral may have been due to cardiac symptoms even if no disease was detected. We did not include studies with less than the minimally suggested sample size of ten healthy older participants to determine reference values.[28] Finally, we did not consider case reports, conference abstracts and reviews.

Figure 1. Flow diagram illustrating the selection process for published reports



CO = cardiac output. Other reasons for exclusion included wrong population (athletes, pregnant women, children), animal studies, reviews and case reports.

Data collection

Two reviewers (LC and NL) independently assessed abstracts for potential relevance. The full text of potentially relevant articles was then examined. Any discrepancy between reviewers was resolved by agreement. For each study, we collected publication information including year of publication and country of origin, participant and study characteristics and measurement method. We extracted the cardiac output or cardiac index values and reference ranges as reported in the individual studies. For studies reporting the sample mean and standard deviation (SD), we calculated the 95% confidence interval (CI) (95% CI = mean ± 1.96 × standard error of the mean [SEM]). SEM was converted to standard deviation (SD) according to $SEM = \frac{SD}{\sqrt{n}}$.

Results

Search results

Database searches retrieved 5340 citations. Of these, 412 full-text articles were assessed for eligibility and 29 studies, published between 1964 and 2017, met our inclusion criteria. The study selection process and reasons for exclusion are summarised in Figure 1. The characteristics of the included studies[29-57] are summarised in Table 1. In total, 924 participants were studied. The sample size of the individual studies ranged between ten and 155 participants. Only two studies included more than 100 participants over 60 years of age.[37,54] Methods used to measure the cardiac index included transthoracic echocardiography (n = 7 studies), impedance cardiography (n = 6), CMR (n = 5), pulmonary artery catheterisation (PAC) (n = 5), rebreathing techniques or Fick principle (n = 3), radionuclide ventriculography (n = 2), and Doppler measurement of blood flow velocity (n = 1).

Fifteen studies (508 participants) reported the cardiac index and 22 studies (789 participants) reported the cardiac output. Overall, the mean cardiac index in healthy volunteers over 60 years of age was reported between 2.1 and 3.2 L/min/m^2 and the mean cardiac output was between 3.1 and 6.4 L/min (Table 2 and Table 3).

The determination of normal reference values in healthy individuals was the primary objective in seven studies (including 347 participants). In these studies, the reported mean cardiac index for people over 60 years of age was between 2.11 ± 0.46 and 2.95 ± 0.71 L/min/m^2, using transthoracic echocardiography;[45,54] 2.6 ± 0.5 L/min/m^2, using PAC thermodilution;[57] 3.2 L/min/m^2, using Doppler ultrasound;[34] 3.19 ± 0.87 L/min/m^2, using impedance cardiography;[51] 3.06 ± 0.57 L/min/m^2, using the Fick principle;[40] and between

Table 1. Characteristics of included studies

First author	Year	Country	Total participants	Participants > 60 years*	Study population	Ethnic group	Aim of study/context
Ahn[29]	2016	Korea	137	20	Healthy control	Asian	Adenosine stress CMR in severe AS
Arbab-Zadeh[30]	2004	USA	38	12	Healthy volunteers	Caucasian	Effect of ageing on LV compliance
Beere[31]	1999	USA	20	10	Healthy volunteers	na	Effect of exercise on age-related circulatory changes
Beitzke[32]	2002	Austria	51	21	Healthy control	na	Autonomic dysfunction in vitamin B12 deficiency
Carlsson[33]	2012	Sweden	361	17	Healthy volunteers	na	Cardiac index decline in age and congestive heart failure
Chan[34]	2014	China	165	78	Healthy patients	Asian	Reference values for non-invasive CO values in older Chinese adults
Chang[35]	2012	Korea	124	23	Healthy volunteers	Asian	Reference values for cardiac size and function in healthy Korean adults
Dinenno[36]	1999	USA	31	13	Healthy volunteers	na	Vascular conduction changes with age
Farinatti[37]	2009	Belgium	131	131	Healthy volunteers	Caucasian	CO in older people
Fujimoto[38]	2013	USA	71	34	Healthy volunteers	Caucasian	Haemodynamic responses to rapid intravenous saline loading
Gentilini[39]	1999	Italy	44	20	Healthy control	na	Cardiovascular response to change in posture in patients with compensated cirrhosis
Granath[40]	1964	Sweden	17	17	Healthy volunteers	na	CO in heathy older men
Guo[41]	2005	USA	22	11	Healthy volunteers	na	Arterial baroreflex study in older people
Hainsworth[42]	1988	UK	64	10	Healthy volunteers	na	Cardiovascular response to tilting
Henein[43]	2013	Sweden	31	14	Healthy control	na	Systolic function reserve in HFpEF
Hundley[44]	2007	USA	30	10	Healthy control	na	Leg flow-mediated arterial dilation in heart failure
Knutsen[45]	1989	Norway	92	15	Healthy volunteers	Caucasian	Reference values for CO in men by Doppler echocardiography
Konishi[46]	1990	Japan	78	53	Healthy volunteers	Asian	Influence of age on left ventricular performance in Japanese adults
Malayeri[47]	2008	USA	50	50	Survey cohort	Multi-ethnic	Comparing two CMR techniques for determination of myocardial mass and volumes
Pasierski[48]	1991	USA	118	38	Healthy control	na	Echocardiography in isolated systolic hypertension in older patients
Remmen (2)[49]	2002	Netherlands	28	28	Healthy volunteers	na	Finapres arterial pulse wave analysis *v* PAC for CO measurements
Remmen (1)[50]	2005	Netherlands	20	18	Healthy volunteers	na	Application of lower body positive pressure in healthy older subjects
Sathyaprabha[51]	2008	India	397	42	Healthy volunteers	na	Influence of age and gender on normal CO values
Saur[52]	2010	Germany	68	34	Healthy volunteers	na	CMR *v* gas rebreathing for CO measurement during atrial fibrillation
Schulman[53]	1996	USA	18	10	Healthy volunteers	na	Cardiovascular performance in healthy older men
Slotwiner[54]	1998	USA and Italy	464	155	Healthy volunteers	Multi-ethnic	Relation of age and cardiac index decline in healthy adults
Taylor[55]	1992	USA	27	13	Healthy volunteers	na	Orthostatic stress response
Vasilopoulou[56]	2012	Greece	90	10	Healthy control	na	CO response to exercise in COPD
Wolsk[57]	2017	Denmark	62	20	Healthy volunteers	na	Influence of age on haemodynamic parameters

AS = aortic stenosis. CO = cardiac output. CMR = cardiac magnetic resonance. COPD = chronic obstructive pulmonary disease. HFpEF = heart failure with preserved ejection fraction. LV = left ventricle. na = not applicable. PAC = pulmonary artery catheter. USA = United States of America. * Or: number of patients with mean age > 60 years, if age range not reported.

Table 2. Studies reporting the normal cardiac index

First author	Number of participants (% male)	Mean age (SD)	Age group (years)	Mean cardiac index (SD)	Cardiac index (95% CI)
CMR					
Ahn[29]	20 (40%)	65.3 (6.4)	na	3.2 (0.4)	3.0–3.4
Carlsson[33]	17 (59%)	na	60–81	3.0 (0.4)	2.8–3.2
Chang[35]	23 (57%)	na	60–69	3.2 (0.6)*	na
Pulmonary artery catheter					
Fujimoto[38]	27 (37%)	64.0 (6.0)	na	3.0 (0.4)	2.8–3.2
Wolsk[57]	20 (50%)	69.0 (nd)	60–80	2.6 (0.5)*	2.4–2.8
Transthoracic echocardiography					
Gentilini[39]	20 (50%)	60.0 (7.0)	47–73	3.1 (0.8)	2.7–3.5
Knutsen[45]	15 (100%)	na	60–69	3.0 (0.7)	2.6–3.3
Pasierski[48]	38 (50%)	69.0 (5.0)	na	2.2 (0.6)	2.0–2.4
Slotwiner[54]	155 (68%)	62.0 (7.0)	54–88	2.1 (0.5)	2.0–2.2
Blood flow velocity (USCOM)					
Chan[34]	78 (55%)	69.0 (nd)	All	3.2 (nd)†	na
	41 (59%)	65.0 (nd)	61–70	3.2 (nd)†	na
	28 (43%)	73.0 (nd)	71–80	3.3 (nd)†	na
	9 (78%)	82.0 (nd)	> 80	3.4 (nd)†	na
Impedance cardiography					
Beitzke[32]	21 (62%)	66.1 (10.4)	46–83	2.6 (1.1)	2.1–3.1
Sathyaprabha[51]	42 (48%)	67.5 (5.5)	> 60	3.2 (0.9)	2.9–3.5
	20 (100%)	na	> 60	3.4 (0.7)	3.0–3.7
	22 (0%)	na	> 60	3.1 (1.0)	2.6–3.5
Rebreathing techniques/Fick principle					
Arbab-Zadeh[30]	12 (50%)	69.8 (3.0)	na	2.6 (0.3)‡	2.5–2.8
Granath[40]	17 (100%)	71.0 (6.0)	61–83	3.1 (0.6)	3.0–3.3
Hainsworth[42]	10 (70%)	na	66–80	2.2 (0.3)*	2.0–2.3
Radionuclide ventriculography					
Schulman[53]	10 (100%)	60.0 (5.1)	na	3.2 (0.9)*	2.60–3.80

CMR = cardiac magnetic resonance. na = not applicable. nd = not determined. SD = standard deviation. USCOM = ultrasonic cardiac output monitor. Studies highlighted in bold letters were explicitly designed to derive normal values for the cardiac output. * Standard error of the mean reported (SD calculated). † Median values. ‡ Sitting position for cardiac output measurement.

3.0 ± 0.4 and 3.2 ± 0.7 L/min/m², using CMR.[33,35] Thus, the pooled mean cardiac index in older, healthy individuals over 60 years of age was 2.7 L/min/m².

Differences in cardiac index with increasing age

A decrease in cardiac index with age was described by four investigators.[30,33,40,54] Carlsson and colleagues[33] quantified the decline in the cardiac index as –8 mL/min/m² per year. In a large echocardiography study by Slotwiner et al,[54] the decline was slightly smaller (–3.5 mL/min/m² per year). However, other authors[34-36,46,57] found no difference in cardiac output with age, and one study reported higher values in older subjects.[45] Data on the cardiac function in very old individuals (over 80 years of age) were reported separately in only two studies, with a small number of participants in this age group[34,46] (Table 2 and Table 3).

Discussion

Key findings

We identified 29 articles measuring the resting cardiac output or cardiac index in healthy, older individuals. Our results suggest that the normal range of the cardiac index in the older population may be slightly lower than previously published reference values, with an overall mean cardiac index between 2.1 and 3.2 L/min/m², depending on the method used. The pooled mean cardiac index was 2.7 L/min/m². However, the association between increasing age and change in cardiac index is inconsistent across studies. Data on the normal cardiac index in people older than 80 years are scant.

Relationship to previous literature

To our knowledge, we are the first to systematically address the question of what constitutes a normal cardiac index for older individuals. Our findings that this number may be lower than the commonly reported reference range in textbooks are in accordance with the results of other studies that were not included in our review, because they fulfilled our exclusion criteria such as inclusion of individuals younger than 60 years and patients with relevant comorbidities.

Table 3. Studies reporting the normal cardiac output

First author	Number of participants (% male)	Mean age (SD)	Age group (years)	Mean cardiac output (SD)	Cardiac output (95% CI)
CMR					
Chang[35]	23 (57%)	na	60-69	5.3 (1.2)*	4.8–5.7
Malayeri[47]	50 (30%)	64.1 (9.1)	48-83	5.4 (1.0)	5.1–5.7
Saur[52]	34 (71%)	65.0 (5.1)	na	4.9 (1.3)	4.5–5.3
Pulmonary artery catheter					
Beere[31]	10 (100%)	66.0 (4.4)	na	3.9 (0.8)†	3.4–4.4
Remmen (1)[50]	20 (85%)	70.0 (4.0)	na	5.9 (1.4)	5.3–6.6
Remmen (2)[49]	28 (76%)	70.0 (4.0)	na	6.4 (1.1)	6.0–6.8
Transthoracic echocardiography					
Dinenno[36]	15 (100%)	63.0 (3.9)	na	5.1 (1.2)	4.5–5.7
Henein[43]	14 (50%)	65.0 (10.0)	na	4.8 (0.7)	4.4–5.2
Hundley[44]	10 (50%)	71.0 (22.1)	na	3.1 (0.9)	2.5–3.7
Knutsen[45]	15 (100%	na	60–69	5.7 (1.4)	5.0–6.4
Pasierski[48]	38 (50%)	69.0 (5.0)	na	3.9 (1.1)	3.6–4.3
Slotwiner[54]	155 (68%)	62.0 (7.0)	54–88	3.9 (1.1)	3.7–4.1
Blood flow velocity (USCOM)					
Chan[34]	78 (55%)	69.0 (nd)	All	5.2 (nd)‡	na
	41 (59%)	65.0 (nd)	61–70	5.3 (nd)‡	na
	28 (43%)	73.0 (nd)	71–80	5.1 (nd)‡	na
	9 (78%)	82.0 (nd)	> 80	5.2 (nd)‡	na
Impedance cardiography					
Farinatti[37]	54 (100%)	69.0 (4.0)	60–86	4.9 (0.8)†	4.7–5.1
	77 (0%)	69.0 (7.0)	61–93	4.5 (0.9)	4.3–4.7
Guo[41]	11 (64%)	69.8 (5.0)	na	3.3 (1.0)	2.7–3.9
Sathyaprabha[51]	42 (48%)	67.5 (5.5)	All	5.2 (1.5)	5.2–6.1
	20 (100%)	na	> 60	5.7 (1.2)	5.1–6.2
	22 (0%)	na	> 60	4.7 (1.6)	4.0–5.4
Taylor[55]	13 (100%)	64.3 (2.5)	61–72	6.3 (2.5)	4.9–7.7
Vasilopoulou[56]	10 (60%)	60.0 (6.3)	na	4.8 (0.6)§	4.4–5.2
Rebreathing techniques/Fick principle					
Arbab-Zadeh[30]	12 (50%)	69.8 (3.0)	na	4.9 (0.6)†	4.5–5.2
Granath[40]	17 (100%)	71.0 (6.0)	na	5.8 (1.2)	5.2–6.3
Hainsworth[42]	10 (70%)	na	66–80	3.8 (0.3)*	3.6–4.1
Radionuclide ventriculography					
Konishi[46]	45 (nd)	na	60–79	6.0 (1.3)	5.6–6.4
	8 (nd)	na	> 80	5.6 (1.7)	4.4–6.8

CMR = cardiac magnetic resonance. na = not applicable. nd = not determined. SD = standard deviation. USCOM = ultrasonic cardiac output monitor. Studies highlighted in bold letters were explicitly designed to derive normal values for the cardiac output. * Standard error of the mean reported (SD calculated). † Sitting position for cardiac output measurement. ‡ Median values reported. § Body position not reported.

Foppa and colleagues[58] studied 1336 older individuals (age 64 ± 9 years) with CMR and reported the normal values for right ventricular volumes and function. The mean cardiac index was 2.8 ± 0.6 L/min/m^2 in men and 2.6 ± 0.5 L/min/m^2 in women, and the calculated reference range was 1.5–3.5 and 1.4–3.8 L/min/m^2, respectively. In the subgroup of those older than 75 years (n = 172), the mean cardiac index was 2.6 ± 0.6 L/min/m^2 in men and 2.5 ± 0.5 L/min/m^2 in women. The study did, however, include a significant proportion of patients with hypertension and diabetes.

In a cohort of 172 Korean individuals (mean age 58 ± 10.9 years), the cardiac index was measured with coronary computed tomography angiography and reported as 2.5 ± 0.5 L/min/m^2.[59] A similar figure (2.8 ± 0.7 L/min/m^2) was reported by Sandstede[60] using CMR in a smaller group of 18 subjects aged 45–74 years, and by Andrén (2.7 ± 0.6 L/min/m^2), who used Doppler echocardiography in a mixed population of 584 healthy volunteers and patients (all aged 70 years).[61]

Contrary to previous research,[8,62-65] the association between increasing age and decline in cardiac index was inconsistent across the studies included in our review.[34-36,46] This underlines the importance of sample size, age stratification and statistical techniques used when addressing this question. A comparison of values among discrete age groups of small size[36] may not be as sensitive as a regression analysis in a large cohort study.[33,54,65] Interestingly, in three large Asian studies the cardiac index did not decline with age.[34,35,46] This raises the question whether such an age-related decline may vary among different ethnic groups.

The EchoNoRMAL study sought to derive age-, sex- and ethnic-appropriate adult reference values for echocardiographic measurements using population-based datasets from 22 404 healthy adults.[66] Although the study did not report the cardiac index, the lower reference limits for ejection fraction differed by ethnicity, with significantly lower values for Europeans compared with East Asians. By demonstrating important differences by sex, ethnicity and age, this study supports the need for more comprehensive reference values for patients undergoing haemodynamic monitoring.

Finally, the Multi-Ethnic Study of Atherosclerosis (MESA) included 400 men and 400 women across four age strata ranging from 45 to 84 years to determine normal values of left ventricular (LV) function and mass using CMR.[65] The mean cardiac index was 2.9 ± 0.6 L/min/m^2 for both men and women. LV volumes were inversely associated with age for both sexes, except for the LV end-systolic volume index. The cardiac index was similar in most ethnic groups, with the exception of Asian women, who had higher values. However, the cardiac index of participants over 60 years of age was not reported separately.

Implications of study findings

Our results suggest that the normal cardiac index in older individuals may be lower than the commonly suggested reference limits. Therefore, they emphasise that the patient's age is an important factor to consider when defining haemodynamic goals and when interpreting a lower cardiac index. Our results also imply that reference values vary across different techniques, and that such differences may be even more important among older patients. Finally, the paucity of data on the normal cardiac index in very old individuals highlights our lack of knowledge of normative values in such patients.

Strengths and limitations

Our review has several strengths. First, to our knowledge, no other investigators have systematically reviewed the literature on what constitutes a normal cardiac index in healthy, older humans. Second, by using a comprehensive, iterative search strategy, we explored datasets across a wide time span, making it unlikely that any relevant data were missed. Third, we used three electronic databases with additional hand searching, allowing us to assess a large body of literature.

Our study has some limitations. First, we focused on the normal cardiac index in healthy individuals and did, therefore, not analyse studies including patients with potentially compromised cardiovascular function. However, our aim was to investigate the normal cardiac index, and including such studies would have biased our results.[67] Our goal was to select studies of individuals without health issues that potentially could attenuate cardiac function, in order to assess the effects of age alone. Therefore, we have chosen similar exclusion criteria as in other studies on the subject.[68] Of note, our results are comparable to those of several large studies with less stringent exclusion criteria[58-61] and may, therefore, be applicable to most older patients. Second, we conducted a scoping review instead of a meta-analysis and cannot provide reliable pooled estimates of normal reference ranges in light of the disparate techniques used and the lack of quality assessment of the individual studies. Reference values are derived from the upper and lower margins of the normal distribution. As such, they are sensitive to variability, and for age-dependent values, they require sufficient data at each age to be representative. Therefore, our pooled estimate of the mean cardiac index should be interpreted with significant caution. Moreover, many of the studies included a majority of male subjects and were not specifically designed to measure the normal cardiac output. Finally, excluding studies published in a language other than English is a weakness, although there is no evidence of a systematic bias from the use of such language restrictions in systematic reviews and meta-analyses.[27]

Conclusion

This scoping review identified 29 articles reporting the normal cardiac index in healthy, older individuals. Our results suggest that the normal cardiac index in this population may be lower than the commonly suggested general reference limits. Therefore, our results imply that the patient's age is an important factor to consider when defining haemodynamic "normality". Finally, there are essentially no data on what constitutes a normal cardiac index in patients older than 80 years. As these patients now make up a significant proportion of surgical patients, such a knowledge gap needs to be addressed in future studies.

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Competing interests

None declared.

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