Cardiac Output and Index in Obese and Non-obese Patients using Gated Single Photon Emission Computed Tomography Sestamibi Perfusion Imaging

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ABSTRACT

Objective: To assess prospectively the overall prevalence of abnormal cardiac index values in a symptomatic group of patients from gated single photon emission computed tomography perfusion studies and to compare cardiac index of patients with body mass index <30 and obese patients (body mass index >30).

Patients and Methods: 112 patients (62 females) aged 37 to 81 years (mean, 57 years) referred for evaluation of chest pain, dyspnoea or inconclusive exercise electrocardiogram, underwent gated single photon emission computed tomography perfusion imaging with technetium 99m sestamibi intravenously following Bruce exercise protocol (102 patients) or dobutamine stressing (10 patients). Cardiac output was calculated as the product of resting heart rate and stroke volume and cardiac index determined using the body mass index. Left ventricular ejection fraction, stroke volume, and end-systolic volume were determined for each patient.

Results: Seventy three patients (65%) had an abnormal cardiac index (<2.5 L/min/m²). The mean cardiac index overall was 2.19 L/min/m². Twelve patients had left ventricular ejection fraction less than 50%, and the mean left ventricular ejection fraction overall was 61%. Thirty two patients with body mass index >30 had mean cardiac index of 2.28 L/min/m², which was not significantly different from an age-matched group of 32 non-obese controls (body mass index <30; mean cardiac index, 2.24 L/min/m²). Left ventricular ejection fraction was elevated in the obese group compared with the non-obese group (mean, 65.2% versus 58%; p < 0.03).

Conclusions: A high prevalence of abnormally low cardiac index was observed in symptomatic patients. Obese patients had similar cardiac index to non-obese control patients, but had an elevated left ventricular ejection fraction suggesting hypersystolic function.

Key Words: Obesity, Cardiac output, Technetium Tc99m sestamibi, Tomography, emission-computed, single-photon, Tomography, X-ray computed, Ventricular dysfunction, left

INTRODUCTION

Cardiac output (CO) has been recognised as the most important measurement in the assessment of cardiac pump function and overall haemodynamic function. CO normalised to body surface area (BSA) as cardiac index (CI) readily enables comparison of haemodynamic function, independently of body mass, between patients.

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Gated single photon emission computed tomography (SPECT) imaging permits automated calculation of end-diastolic volume, end-systolic volume, stroke volume (SV) and left ventricular ejection fraction (LVEF). Strong correlations between the values of volumetric data acquired by this imaging modality and those from echocardiography, gated blood pool scanning and magnetic resonance imaging have been consistently reported in the literature, with overall correlation coefficients ranging up to 0.9. To date, the use of gated SPECT perfusion imaging has not been reported in the measurement of CO/CI in the clinical setting with differing patient groups.

Obesity is well-recognised as an influence on cardiovascular morbidity and mortality; clinical and autopsy
studies have confirmed the pathological entity of obese cardiomyopathy, characterised by volume overload and hyperdynamic circulation, leading frequently to congestive cardiac failure. Relations between structural cardiac anomalies, systolic function and morbid obesity have been confirmed by echocardiography, cardiac catheterisation and necropsy.\textsuperscript{7-9} These correlations are also evident even in mild obesity.\textsuperscript{10,11} Obesity is associated with haemodynamic overload with increased blood volume, elevated SV\textsuperscript{12} and increased CO, owing in part to increased lean body mass.\textsuperscript{13,14} Hypersystolic function at rest has been reported in obesity,\textsuperscript{7} but in response to exercise, the expected LVEF increase is impaired in obese patients.\textsuperscript{15}

Gated SPECT perfusion imaging of left ventricular function of obese patients is less operator-dependent and volumetric data acquisition is likely to be less restricted by patient body habitus than with echocardiography.

This two-part observational study firstly evaluated, prospectively, the overall prevalence of reduced CO and CI in a cohort of symptomatic patients referred in an outpatient setting for technetium 99m sestamibi (MIBI) SPECT cardiac perfusion imaging. The second part of the study compared CI of obese patients with an age-matched group of non-obese patients, thereby assessing the relative haemodynamic function of both of the groups.

**PATIENTS AND METHODS**

112 patients (62 females), aged 37 to 81 years (mean, 57 years) referred for evaluation of symptoms (dyspnoea, reduced exercise tolerance, chest pain whether typical or atypical of cardiac origin) by myocardial stress perfusion imaging were studied prospectively in an outpatient setting. Body mass index (BMI) was calculated for each patient and BSA determined using the Mosteller (modified Dubois) method. 450 MBq of technetium 99m MIBI was injected intravenously following exercise using the Bruce treadmill protocol. 10 patients underwent pharmacological stressing using dobutamine. Beta-blocker therapy was stopped at least 24 hours before the stress testing. Gated SPECT perfusion imaging was performed 45 minutes later using 64 x 64 matrix, cardiac cycle divided into 8 equal intervals, filtered backprojection and data sets reconstructed using Quantitative Gated SPECT (QGS; Cedars Sinai, Los Angeles, CA, USA) software. Satisfactory time volumetric curves for ventricular filling were obtained for each patient together with readings for LVEF, SV, end-diastolic volume and end-systolic volume. Three values for resting heart rate (HR) were taken and the mean recorded, with the patient supine during the scanning interval of typically 20 to 30 minutes. CO was calculated as the product of HR and SV and the CI determined accordingly.

In our institution, in accordance with accepted practice for limiting administered radiation dose, only those patients with perfusion anomalies identified on the initial post-stress study receive a resting gated MIBI scan for corroboration. Consequently, in order to eliminate a selection bias against patients with normal post-stress perfusion images, only the post-stress gated images, which were acquired for all patients, were used in this volumetric study. Prognostic information incremental to that obtained perfusion and pretest data is also supplied by LVEF and systolic volumetric measurements from post-stress gated SPECT imaging.\textsuperscript{16}

SV, LVEF and CO values from both post-stress and later resting gated studies were, however, compared in 32 patients who had perfusion anomalies identified on the initial post-stress scan. This was done to preclude any possibility of myocardial stunning influencing the volumetric and CO readings of the post-stress studies.

**RESULTS**

Seventy three patients (65%) had an abnormal CI, defined as <2.5 L/min/m\textsuperscript{2} (mean ± standard deviation [SD] CI, 2.19 ± 0.51) with only 12 patients having LVEF less than 50% (mean ± SD LVEF, 61 ± 15.4). Thirty two patients (28%) had perfusion abnormalities of 1 to 5 cardiac segments and/or 1 to 3 fixed perfusion defects consistent with possible infarcted segments. Of this group, 25 patients had an abnormal CI (<2.5 L/min/m\textsuperscript{2}). However, angiographic correlation of the perfusion anomalies was not available and as a result the clinical significance of these perfusion anomalies is uncertain. These 32 patients underwent further imaging with a resting MIBI gated SPECT study. t-tests (two sample test of means) revealed no significant differences between resting and post-stress SV and LVEF in this group. A typical volumetric data screen is shown in Figure 1.

Thirty two patients with BMI >30 kg/m\textsuperscript{2} (mean BMI, 35.7) had a mean CI of 2.28 L/min/m\textsuperscript{2} and were compared with an age-matched group of 32 patients with BMI <30 (mean, 26) with mean CI of 2.24 L/min/m\textsuperscript{2}. Similarly, CO was significantly increased in the obese...
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group compared with the non-obese group (mean, 4.8 L/min and 4.2 L/min, respectively; p < 0.01) [Figure 2]. LVEF was significantly increased in the obese group (mean, 65.2% vs 58%; p < 0.03) [Figure 3]. Figure 4 shows a box plot of SV in the 2 groups.

Despite the significant increases in CO and LVEF associated with obesity, t-tests revealed no difference between the obese and non-obese groups with respect to mean CI (p = 0.92). Figure 5 shows regression plots of BMI versus CI in the obese and non-obese groups.

DISCUSSION
Abnormal haemodynamic parameters are primary indicators of cardiovascular disease and can be used to assess cardiovascular pathophysiology in the clinical setting. CO has been described as the ultimate expression of cardiovascular performance. In mammalian tissue, CO at rest is 0.1 L/min/kg and is therefore linearly related to body weight. By indexation to BSA, CI allows appropriate comparison between individuals of differing body weight and permits satisfactory determination of normal ranges for overall cardiac pump function within a population. Determination of the CI for the individual patient in the outpatient setting is seldom performed but may provide insight into individual haemodynamics and by extension, into the patient’s symptoms and treatment.

The most popular methods for measuring CO in current clinical use are thermodilution techniques in the ITU setting, which exploit the principle of the Stewart-Hamilton equation and appear to be more practical than the earlier Fick principle or dye dilution method. The Stewart-Hamilton Equation can be expressed as:

\[ CO = \frac{Q}{\int P(t)/dt} \]

where \( Q \) = injected dose and \( \int P(t)/dt \) = integral of tracer concentration from 0 to \( \infty \). However, this method has
drawbacks, in that flow rate theoretically should be constant; anatomical abnormalities and irregular respiration can introduce inaccuracies and the injection must be made at a constant rate over a brief interval.\textsuperscript{17-19} Readings for CO by this method can still vary in the individual patient, but it appears to be more accurate and less operator-dependent than CO measurement using echocardiography.\textsuperscript{20}

Cardiac volumetric determination by gated SPECT MIBI imaging has the advantage of being largely operator-independent and of being non-invasive. Satisfactory correlation is reported in the literature between volumetric measurements by this method and echocardiography and magnetic resonance imaging.\textsuperscript{3-6} To date, its use for CO evaluation has not been reported in the literature despite the potential advantages of the technique.

An association between obesity and elevated CO has long been observed and increased vascular volume, enlarged vascular tree and elevated CO were thought essential to supply the metabolic demands of the expanded adipose tissue volume.\textsuperscript{21} Fat-free mass is also increased in obesity and its higher metabolic requirements may be a greater determinant of changes in CO and SV in obesity.\textsuperscript{13} Obesity has been implicated in the deaths of 300,000 adults annually in the USA and over 20\% of the adult American population are classified as clinically obese. An elevated two-fold risk of coronary artery disease has been observed in obese women\textsuperscript{22-24} and the Framingham study has revealed an increased risk for coronary artery disease by a factor of 2.4 in obese women and of 2 in obese men under age 50.\textsuperscript{25} Obesity is prominently associated with congestive cardiac failure and appears to be an important risk factor for this disorder. Risk of heart failure increases proportionally with BMI\textsuperscript{26-29} and of all the cardiac complications of obesity, obese cardiomyopathy appears the most serious with left ventricular dilatation, cardiomegaly and myocyte hypertrophy predisposing to ventricular arrhythmias and altered myocardial contractility.
Pascual et al\(^8\) have observed alterations in diastolic function in slightly and moderately obese patients as well as the severely obese. These alterations of diastolic function were correlated strongly with BMI. Cardiac adaptations to volume overload in obesity are manifest as eccentric hypertrophy and anomalies of diastolic function from the initial stages of obesity, suggesting that features of obese cardiomyopathy arise in all obese patients.\(^{30,31}\)

To date CI, despite being an important overall haemodynamic parameter, has not been systematically compared between a non-obese and obese group of patients in a clinical setting. Our findings indicated a clinically significant increase in CO for the obese group (consistent with previous literature) but no significant alteration in CI. This suggests that obese patients have a similar haemodynamic status with respect to overall tissue perfusion as their non-obese counterparts. Increased myocardial contractility or hypersystolic function in the form of increased ejection fraction appears to account for this, in part, in our patient group.

Of interest is the finding of a low CI in both groups, with a mean value of 2.19 L/min/m\(^2\) overall for a population with an overall mean age of 57 years. This appeared to be independent of the presence of perfusion anomalies on the initial post-stress study. The finding suggests that global impairment of haemodynamic function in the form of reduced CI may contribute to patients’ symptoms in the absence of obvious myocardial perfusion defects.

CI and haemodynamic status are dependent on three principal variables: HR (chronotropic input), SV (inotropic input) and mean arterial pressure. These variables may alter over short intervals; therefore, assessing haemodynamics over a 20-minute interval scanning time necessarily represents a simplification of the true global perfusion status. Another limitation of the study is the known overestimation of LVEF and SV with small left ventricular capacity at end-diastole in gated SPECT perfusion imaging. This source of error could lead to underestimation of true prevalence of reduced CO and CI in this patient subgroup.\(^{32-34}\) Use of a standard division of the cardiac cycle into eight intervals can lead conversely to underestimation of the LVEF in some cases.\(^{35}\) A further limitation of the study is the exclusive use of BMI in categorising obesity with no assessment of distribution of body fat. Correlation of abdominal fat, particularly in males, with CI might have produced a stronger relationship. However, despite this, the gender distribution of the two groups (51% female) does not necessarily preclude extrapolation of results to the general population of symptomatic patients.

Many factors, such as heart size, perfusion defects and subdiaphragmatic activity of tracer together with quantitative software, reconstruction algorithm and filter parameters may affect EF calculation and volumetric analysis. However, in a study population of 112 patients, these factors may reasonably be expected to apply uniformly across the entire group. No obvious bias was present to account specifically for differences between groups. While bias cannot be discounted, it appears...
unreasonable to dismiss obesity as a factor in inter-group disparity in EF.

Soft-tissue attenuation can affect the accuracy of scintigraphic quantitative measurements, particularly in obese subjects with production of artefactual perfusion defects. This could, on occasion, lead to spurious perfusion defects with possible consequent underestimation of volumetric data.

In this study, only the post-stress gated data were used in calculating CO and CI and some degree of myocardial stunning might account for the low readings for CI in some cases. This concern would appear to be small, however, in view of the fact that overall LVEF readings were high with only 12 patients (10%) having abnormally low LVEF. In addition, comparison of the post-stress and resting volumetric data acquired for 32 patients with suspected perfusion anomalies showed no statistically significant differences between the two sets of volumetric data.

In conclusion, this study supports the use of volumetric data from myocardial SPECT MIBI perfusion imaging in calculating CO and CI in an outpatient clinical setting. The prevalence of abnormally reduced CI was found to be unexpectedly high in both obese and non-obese patients, suggesting that this should be taken into account in assessment and treatment of symptoms. Obese patients had a similar haemodynamic status to non-obese patients, despite overall elevated CO and ejection fraction.

REFERENCES


