# Left Ventricular Performance Monitored by Radionuclide Cardiography during Induction of Anesthesia 

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#### Abstract

Radionuclide cardiography with ${ }^{99 m}$ Tc-labeled erythrocytes was carried out in three different studies comprising 20 female patients without heart or lung diseases. Left ventricular ejection fraction (LVEF) and other hemodynamic variables were measured immediately before and during induction of anesthesia (thiopental, $\mathrm{N}_{2} \mathrm{O} / \mathrm{O}_{2}$, succinylcholine, laryngoscopy + oral intubation, halothane). In study 1 , serial measurements of LVEF, left ventricular volume, and derived variables were obtained by gamma camera in seven patients using $3-\mathrm{min}$ sampling periods. In Studies 2 and 3, LVEF was monitored serially in seven and six patients, respectively, by a portable, nonimaging probe (nuclear stethoscope) at $1-\mathrm{min}$ intervals or less. The induction period was prolonged to last 24 $\min$ in studies 1 and 2 , against 9 min in study 3 .

In studies 1 and 2 there was an increase in blood pressure and heart rate after thiopental and after laryngoscopy and intubation. In study 3 a similar increase was observed after intubation. In the gamma camera study LVEF decreased from 0.72 to 0.53 after thiopental, with no further decrease during intubation. This decrease was accompanied by an increase in end-systolic volume and a decrease in the ratio: systolic cuff pressure/end systolic volume, whereas end-diastolic volume and cardiac index remained unchanged. In the nuclear stethoscope studies, LVEF decreased both after thiopental and after intubation, in study 2 from 0.68 to 0.38 and from 0.53 to 0.41 , respectively; in study 3 from 0.69 to 0.53 and from 0.57 to 0.44 , respectively.

Our observation, in healthy, female individuals, provide an impetus for further noninvasive radionuclide studies during anesthesia in patients with cardiovascular disease. (Key words: Anesthetics, intravenous: thiopental. Heart: myocardial function. Induction: anesthesia. Measurement techniques: radionuclide cardiography.)


IN RECENT YEARS, noninvasive methods employing radionuclide technique for assessment of cardiac performance have found increasing clinical use. ${ }^{1-3}$ Radionuclide

[^0]studies of cardiac function can be performed with both stationary and mobile gamma cameras or with more simple, nonimaging equipment, offering bedside beat-to-beat measurement of left ventricular ejection fraction (LVEF).

The aims of the present study were as follows: 1) to compare the capability of gamma camera and a computerized nonimaging nuclear probe§ in monitoring left ventricular function during induction of anesthesia; and 2) to investigate-using radionuclide technique-the hemodynamic consequences of a standardized anesthetic induction and intubation in healthy female patients.

## Materials and Methods

A total of 20 female patients ( $30-61$ years of age) scheduled for elective hysterectomy were investigated in three different studies. The protocol was approved by the Copenhagen County Human Investigation Committee, and informed consent from each patient was obtained. All had a history without heart and lung diseases and normal findings on physical examination, ECG, and chest x-rays. Besides premedication, none of the patients were receiving any preoperative medical treatment. All investigations were performed with the patients in the supine position.

## STUDY I

Seven patients (mean age 38 yr , range $31-48 \mathrm{yr}$ ) were investigated by a stationary gamma camera in the Department of Clinical Physiology and Nuclear Medicine immediately before and during induction of anesthesia and intubation. The induction period was prolonged to last 24 min to allow for multiple $3-\mathrm{min}$ data-acquisition periods starting 1 min after each intervention. This was necessary in order to obtain sufficiently reliable counting statistics during the gamma camera studies.

## Study 2

Seven patients (mean age 39 yr , range $30-48 \mathrm{yr}$ ) were investigated following the same protocol as in

[^1]study 1 , i.e., with the induction period lasting 24 min . LVEF was measured in the anesthesia preparation room at the operating theater at intervals of 1 min or less by means of the nuclear stethoscope. ${ }^{3-6}$

## Study 3

In order to expose possible changes in circulation due to the prolonged induction in studies 1 and 2 , six other patients (mean age 42 yr , range $35-61 \mathrm{yr}$ ) were investigated in the anesthesia preparation room by the nuclear stethoscope, but now following a more realistic protocol with the induction period lasting 9 min and with more frequent measurements of LVEF.

## Anesthetic Technique

All the patients were premedicated with diazepam $0.3 \mathrm{mg} / \mathrm{kg}$ orally 2 h before surgery. Pancuronium $0.015 \mathrm{mg} / \mathrm{kg}$ was administered for precurarization, followed by thiopental $5 \mathrm{mg} / \mathrm{kg}$ over 15 s to induce sleep. When the eyelash reflex had disappeared, ventilation was controlled manually by mask with nitrous oxideoxygen 7:3 I using a Bain system. Muscle relaxation for laryngoscopy and intubation was achieved with succinylcholine $1.5 \mathrm{mg} / \mathrm{kg}$. Laryngoscopy and endotracheal intubation were performed with a MacIntosh blade laryngoscope and a $7.0-\mathrm{mm}$ tube. All patients received halothane $1 \%$ inspired concentration (and $\mathrm{N}_{2} \mathrm{O} / \mathrm{O}_{2} 7: 3$ ) after intubation. Relaxation was maintained with pancuronium $0.1 \mathrm{mg} / \mathrm{kg}$. In studies 1 and $2,4 \mathrm{~min}$ passed between each intervention in contrast to 1 min between interventions in study 3 (apart from precurarization 3 min before induction of sleep).

## Radionuclide Investigations

Gamma Camera Imaging (Study 1). Left ventricular performance was assessed by gated equilibrium radionuclide blood pool imaging, using red blood cells labeled in vitro with stanno-pyrophosphate (Techephos®, Hoechst) and 20 mCi of ${ }^{99 \mathrm{~mm}}$ technetium pertechnetate. ${ }^{7}$ Images were obtained with the patient in the supine position using a modified left anterior oblique view. Counts were collected into 24 frames per R-R interval during data acquisition periods of exactly 3 min using a dedicated medical computer system (Gamma-11®, Digital Equipment Corporation). LVEF was calculated as (EDCESC)/EDC, where EDC and ESC represent the background corrected end-diastolic and end-systolic counts, respectively. The accuracy and reproducibility of this method in determining LVEF has been described elsewhere. ${ }^{8}$
Left ventricular volumes and cardiac output were calculated using a nongeometric count-based principle ${ }^{9}$ (see Appendix 1).


FIG. 1. A polaroid photo of the continuous radionuclide left ventricular time-activity curve (TAC) recorded by the nuclear stethoscope. The dotted horizontal line indicates the background (BKG) activity level that is coded into the microcomputer and can be subtracted from the time-activity curve. Probe position is guided by the length of the broad horizontal bar seen below the abscissa axis. ${ }^{6}$ Left ventricular ejection fraction is determined as the average value of all beats lying between the two adjustable vertical cursors (VC). The amalog time-activity curve also may be recorded continuously together with other variables on a strip chart recorder.

Nuclear Stethoscope Measurements (Studies 2 and 3). Red blood cells were labeled in vivo with stanno-pyrophosphate and $15-20 \mathrm{mCi}{ }^{99}{ }^{991}$ technetium pertechnetate. ${ }^{7}$ The probe was placed over the chest in a 30 degree left anterior oblique position with 10 degree caudal tilt. For procedures and problems concerning probe positioning over the left ventricle, recording of background activity, and the different modes of measuring LVEF, the reader is referred to previous descriptions. ${ }^{5,6}$ In the present investigation LVEF was determined using the so-called beat-to-beat mode, i.e., from a continuously recorded left ventricular time-activity curve (fig. 1). From this curve LVEF can be calculated on the basis of a single or several successive beats by moving the two adjustable vertical cursors (fig. 1) to include only a single or several beats between them. We used a constant interval between the cursors of about 10 s . In our laboratory we have found satisfactory ( $\mathrm{r}=0.90$ ) agreement between values of LVEF obtained by the nuclear stethoscope beat-tobeat mode compared with corresponding values determined by gamma camera. ${ }^{6}$

Other Measurements. ECG (lead II) was monitored continuously. Heart rate was calculated as the average number of beats per minute during the gamma camera studies or recorded by the nuclear stethoscope during LVEF measurements. Blood pressure was measured indirectly by an automatic recording device (Arteriosonde ${ }^{\circledR}$, Roche). All control values in the three studies were obtained after $15-20 \mathrm{~min}$ of supine rest. Variables measured by gamma camera represented ipso facto the mean values of the 3 -min acquisition periods. All other control values were the mean of four to five single


FIG. 2. Relationship between mean arterial blood pressure (MABP), heart rate, and left ventricular ejection fration (LVEF) recorded in study 1 (gamma camera) (solid lines) and study 2 (nuclear probe) (dotted lines). Stars and cubes denote values diverging significantly from control value (C). + denote significant change compared with preceding value.
measurements recorded-regardless of the respiratory phase-during a $5-\mathrm{min}$ period before the start of induction. Following intubation, end-tidal $\mathrm{CO}_{2}$ was monitored with a Gould Godart Capnograph MK-II®, keeping the $\mathrm{CO}_{2}$ in all patients between 4.5 and $5.5 \%$.
Statistical Analysis. A nonparametric test for paired data (Pratt's test)! was used within each group to compare data obtained after each intervention with control data.
§Rahe AJ: Tables of critical values for the Pratt matched pair signed rank statistic. Journal of the American Statistical Association 69:368-373, 1974.

The Mann-Whitney U-test was used for comparisons between groups. The level of significance was $2 \alpha<0.05$. All data are given as mean $\pm$ SEM.

## Results

Study 1 (figs. 2, 3, AND 4)
Following thiopental and the beginning of manual ventilation with nitrous oxide-oxygen, mean arterial blood pressure increased, accompanied by a further increase after succinylcholine, laryngoscopy, and tracheal intubation, reaching a peak value $21 / 2 \mathrm{~min}$ after intubation. Control values were reached at the final measurement. Heart rate increased slightly following precurarization and markedly after thiopental, remaining at this level throughout the study. The injection of thiopental


Fig. 3. Relationship between left ventricular end diastolic volume (LVEDV), stroke volume (LVSV), end-systolic volume (LVESV), and cardiac index (CI) recorded by gamma camera in study 1. Stars denote values diverging significantly from control value (C).
and manual ventilation resulted in a decrease in LVEF from $0.72 \pm 0.03$ to $0.53 \pm 0.05$, followed by a gradual increase toward control values at the end of the study period.

Left ventricular end-diastolic volume did not change significantly throughout the study (fig. 3). Left ventricular stroke volume decreased after thiopental, increased following laryngoscopy and intubation, and decreased again after halothane. After thiopental there was an increase in left ventricular end systolic volume, succeeded by a steady decrease towards control values at the end of the study. Except for a small increase after laryngoscopy and intubation, cardiac index did not change. There was an increase in total peripheral resistance after thiopental, whereas the ratio of systolic cuff pressure to end-systolic volume decreased by $33 \%$ and remained depressed almost to the end of the study period (fig. 4).

## Study 2 (fig. 2)

Following the same time schedule as in study 1 , the same main tendencies were observed. Differences were recorded due to the higher temporal resolution of the nuclear stethoscope but at the expense of volume determinations. There was a two-step increase in mean arterial blood pressure and heart rate, one after thiopental and manual ventilation and another after intubation. The increase in blood pressure seen after thiopental was


FIc. 4. Changes in total peripheral resistance (TPR) and the ratio: systolic cuff pressure/end-systolic-volume (SP/V) recorded in study 1. Stars denote values diverging significantly from control value (C).


Fig. 5. Relationship between mean arterial blood pressure (MABP), heart rate, and left ventricular ejection fraction (LVEF) recorded in study 3 (nuclear probe). Stars denote values diverging significantly from control value ( C ). + denote significant change compared with preceding value.
preceded by a short-lasting decrease. Following halothane, the blood pressure decreased below the control value. A modest increase in LVEF followed precurarization and was succeeded by a steep decrease from 0.68 $\pm 0.03$ to $0.38 \pm 0.03$ after thiopental. After partial recovery, another decrease was seen following laryngoscopy and intubation, this time from $0.53 \pm 0.03$ to 0.41 $\pm 0.02$. Toward the end of the study period, LVEF differed insignificantly from the control value.

Study 3 (fig. 5)
During the nuclear stethoscope study with the shortlasting induction, we saw a small decrease in mean
arterial blood pressure following thiopental, succeeded by an increase reaching a peak value after intubation. Mean arterial blood pressure returned to control value within $21 / 2 \mathrm{~min}$. Heart rate increased after thiopental, with a further increase following intubation. Thiopental was followed by a decrease in LVEF from $0.69 \pm 0.04$ to $0.53 \pm 0.04$. After a short recovery to $0.61 \pm 0.07$, there was a further decrease to $0.44 \pm 0.05$ after laryngoscopy and tracheal intubation. Two minutes after intubation, LVEF had approached baseline level.

## Comparison of the Three Studies

In all three studies, the most pronounced changes in mean arterial blood pressure, heart rate, and LVEF occurred at about $21 / 2 \mathrm{~min}$ after thiopental (figs. 2 and 5). Common to the three studies was that peak mean arterial blood pressure was reached after laryngoscopy and intubation with a return to baseline level toward the end of the study period. Further, the increase in heart rate was of similar size in all studies, with tachycardia persisting throughout the induction period. Different was the recording in study 1 of only a single minimum value for LVEF compared with the diphasic course observed in the other two studies, with the lower value occurring after thiopental in study 2 and following intubation in study 3.

## Discussion

Radionuclide cardiography offers an opportunity to monitor noninvasively global left ventricular function during anesthesia. A brief description is given in Appendix 2 of the possible radionuclide techniques, the necessary equipment, and some problems concerning radiation safety.

## Radionuclide Monitoring during Anesthesia

The different time schedules for the induction period were chosen to compensate for inherent technical limitations of the radionuclide equipment.Ideally, radionuclide monitoring should not interfere with the anesthetic procedure. In this respect, the nuclear stethoscope is best suited. If volume data are wanted, a mobile gamma camera should be applied.

In the present investigation, the circulatory effects following thiopental probably were only observed, because the induction period had to be prolonged in study 1 due to the low sampling rate of the gamma camera. The unwanted effect of this was damping of the LVEF curve recorded by gamma camera compared with that registered with the nuclear stethoscope (fig. 2, lower panel).

If the position of the heart or the activity in the pulmonary blood pool is altered during interventions,
the nonimaging probe must be repositioned and the background readjusted accordingly to secure reliable measurements. We found that this was almost always necessary after relaxation and manual ventilation. Also, changes in background activity often were noted after halothane. Rapid probe reorientation requires operator skill. With the gamma camera reorientation is seldom necessary, because corrections can be made visually on the image screen, as long as movements of the heart take place within the large field of view of the camera.

## Hemodynamic Changes

With our investigation we did not intend to expose the characteristic, inherent pharmacologic effects of each single intervention. Rather, with the radionuclide methods we wanted to monitor the course of events caused by the more or less cumulative effects of the different procedures used during a standardized type of anesthesia induction. Still, the circulatory response to thiopental was truly remarkable, with a substantial increase in systemic vascular resistance and mean arterial blood pressure recorded in studies 1 and 2 (fig. 2). However, the increase in blood pressure in study 2with the higher temporal resolution-was preceded by a shortlasting decrease. A similar small, but significant, decrease also was noted in study 3 immediately before the steep increase in blood pressure (fig. 5). In both instances, the decrease in blood pressure occurred at the same time as the onset of LVEF depression (figs. 2 and 5). The literature on the circulatory effects of thiopental ${ }^{10-19}$ seems rather contradictory and is difficult to use for comparison because of heterogeneity in investigative design (animal or human experiments, pure pharmacologic studies or trials during anesthesia, different types of induction, of barbiturates, of administered doses, etc.). It is well known that thiopental causes an increase in heart rate, possibly with a "resetting" of the baroreceptor reflex, i.e., with a higher heart rate for a given blood pressure and less change in heart rate for a certain change in blood pressure. ${ }^{13}$ In theory, this mechanism also might contribute to the increase in blood pressure. Most investigators have found no change or an increase in systemic vascular resistance following thiopental ${ }^{11,12,16,19}$ but with the frequent observation of a decrease in blood pressure. ${ }^{11,12,14,16,19}$ Some have found an increase in central venous pressure, ${ }^{12,19}$ while others observed no change, ${ }^{12}$ and still others a decrease with signs of marked venous pooling of blood, impaired venous return, and resulting decrease in cardiac output. ${ }^{11,12}$ In the normal heart, the latter phenomena should provoke an increase in ejection fraction to keep up stroke volume, but we found the opposite. In only a single report, we have found an increase in blood pressure comparable to our observations (Takki et al.,
fig. 1). ${ }^{15}$ Interestingly, this increase also started shortly before intubation, which was not carried out until 3 $\min$ after the administration of thiopental. One may ask whether the recorded effects of thiopental in our investigation were a result of an insufficient degree of anesthesia during the artificially prolonged induction period or if the rather large premedication dose of diazepam was a contributive cause. We cannot exclude the former possibility, although it does not seem very likely, considering the administered doses of diazepam, thiopental, and $\mathrm{N}_{2} \mathrm{O}$. As for diazepam, if this drug has any effect on blood pressure at all, we would rather expect a decrease. ${ }^{11}$
Whether the decrease in LVEF after thiopental was due to a direct myocardial depressant action of the drug is difficult to say. Previous work has claimed such an effect, ${ }^{11,12}$ but this was not confirmed in fairly recent experiments in canine preparations ${ }^{17}$ nor in patients during anesthetic induction with thiopental, 2-2.5 $\mathrm{mg} / \mathrm{kg}$, intravenously. ${ }^{18}$ However, the response in the latter work by Becker et al. may have been somewhat blunted by premedication with atropine. An increase in aortic impedance may lower LVEF ${ }^{20,21}$ but still the decrease in LVEF in study 2 and 3 (with high temporal resolution) was initiated simultaneously with the shortlasting decrease in blood pressure (figs. 2 and 5), i.e., about $11 / 2 \mathrm{~min}$ before the increase in blood pressure took place. The increase in heart rate also might influence LVEF, but because of the relatively small effect of heart rate on LVEF, ${ }^{22-24}$ the increases observed in our studies could not nearly account for the decreases in LVEF.

The decrease in LVEF following instrumentation and intubation was hardly due to coronary artery disease in this young female population. At least none of the patients examined with gamma camera had segmental wall motion abnormalities. It is more likely that the reflex tachycardia/hypertension evoked by intubation was responsible for the decrease in LVEF, as also reported by Giles et al. ${ }^{25}$
With the possibility of measuring left ventricular end systolic volume by radionuclide imaging, we found it interesting to see whether changes in the ratio of systolic cuff blood pressure to end-systolic volume followed the course of changes in LVEF. In animal experiments, the end-systolic pressure-volume relation is relatively insensitive to changes in loading conditions. ${ }^{26,27}$ The slope of this relation is determined by the myocardial contractile state and is increased by positive inotropic interventions. ${ }^{26-28}$ Clinical studies using invasive techniques have demonstrated a linear relation between end-systolic pressure and volume in the physiologic range of the human left ventricle. ${ }^{28,29}$ Peak pressure has been used ${ }^{28,30,31}$ instead of end-systolic pressure, because there is close correlation between these two variables. ${ }^{30,31}$

Recently, the pressure-volume relation was applied in radionuclide studies. ${ }^{31-93}$ It remains, of course, to be demonstrated if the noninvasively obtainable ratio of systolic cuff pressure to end-systolic volume is also an index of contractility, especially in the intact human left ventricle. Nevertheless, with our method of measuring left ventricular volume we found it reasonable to report these data and suggestive that the changes in LVEF in our study 1 was paralleled by the changes in the systolic cuff pressure-end systolic volume ratio (figs. 2 and 4).
We found that the increases in afterload were due solely to increases in mean arterial blood pressure without concomittant increases in left ventricular end diastolic volume, as demonstrated by the insignificant changes in this variable in study 1 (fig. 3). This is in agreement with Giles et al., ${ }^{25}$ who did not with the nuclear stethoscope detect any significant changes in left ventricular end-diastolic counts or the relative cardiac output. Combined, these findings seem to indicate that the reaction to an acute depression of left ventricular performance is not an increase in end-diastolic volume but an enlargement of exclusively the end-systolic volume. Apparently, this is the case not only in the presence of coronary artery disease but also in the normal female heart.

## Clinical Implications

The significance of LVEF as a "gross" indicator of global left ventricular function has been demonstrated in several clinical studies. The noninvasive nature of the radionuclide techniques make them suited for repeat determination of LVEF in the operating room setting and in the intensive care unit. Our recording of substantial changes in LVEF in healthy female patients during a common type of anesthesia induction seems to indicate that monitoring of LVEF in high-risk patients might be clinically relevant. Thus, Giles et al. ${ }^{25}$ observed with the nuclear stethoscope a persistent depression of left ventricular function after intubation in some patients with coronary artery disease, although these patients were otherwise indistinguishable from other investigated patients with coronary artery disease. Preoperative radionuclide cardiography may prove useful in the selection of patients needing intensive peroperative monitoring. Measurement of ventricular volume is physiologically attractive, but further studies are needed to reveal the possible clinical yield of this parameter. Clearly, several problems should be addressed and solved before we know whether the radionuclide techniques in anesthesia may develop beyond their present state as a mere research tool.

## Appendix 1

Absolute left ventricular volume can be determined from the externally registered, attenuation-corrected activity in the
left ventricular blood pool and the measured concentration of activity in the circulating blood. The left ventricular enddiastolic count rate (EDCR) was calculated as the backgroundcorrected activity (counts) within the left ventricular region of interest in the end-diastolic frame, divided by the frame duration (s) and the number of accepted heart beats. The correction for the individual degree of radiation attenuation was based on echocardiographic measurements of left ventricular depth in each patient and previous laboratory experiments relating radiation attenuation to the depths of different-sized ${ }^{99}{ }^{\prime \prime \prime} \mathrm{Tc}$-filled left ventricular phantoms immersed in ${ }^{99}{ }^{\prime \prime \prime} \mathrm{Tc}$ containing water. ${ }^{9}$ The radioactivity in peripheral blood was determined from blood samples drawn during the middle of each acquisition period. Finally, left ventricular end diastolic volume (LVEDV) was calculated as EDCR times the individual attenuation correction factor (ACF) divided by blood activity (BA):

$$
\operatorname{LVEDV}(\mathrm{ml})=\frac{\operatorname{EDCR}(\mathrm{cps}) \times \mathrm{ACF}}{\mathrm{BA}(\mathrm{cps} / \mathrm{ml})}
$$

Left ventricular stroke volume was derived as end-diastolic volume times LVEF, left ventricular end systolic volume as end-diastolic minus stroke volume, cardiac output as stroke volume times heart rate, and cardiac index as cardiac output divided by body surface. Further, the ratio between systolic pressure and end-systolic volume was determined as the mean of three cuff measurements of systolic arm blood pressure made during each radionuclide study divided by end-systolic volume. The total peripheral resistance was calculated as the mean arterial blood pressure divided by cardiac output. In our laboratory we have found a good agreement between volumes determined simultaneously by radionuclide imaging and thermodilution ( $r$ values were for cardiac output, 0.95 , for stroke volume, 0.90 , for end-diastolic volume, 0.96 , and for endsystolic volume, 0.98 ). ${ }^{9}$

## Appendix 2

## Radionuclide Principles

First Pass Technique. A bolus of radioisotope is injected intravenously. During its first passage through the chambers of the heart, time-activity curves from both ventricles are recorded externally over the precordium. Alterations in activity during ventricular ejection are proportional to volume changes, allowing calculation of the ejection fraction from a few successive beats during the passage of the bolus through the ventricle. ${ }^{1,2,34}$ The method is quick and easy to perform. Like x-ray angiography, it gives a snapshot of ventricular function encompassing only a few seconds. Repeat determination of ejection fraction within the same hour or day requires serial injections of radioisotope with consequent increase in blood-background activity, eventually rendering the measurements unreliable. Determination of cardiac output after single injections according to the indicator dilution principle has been reported by this method. ${ }^{35,36}$

Gated Equilibrium Technique. With this technique, the red blood cells in a venous sample of blood is labeled with ${ }^{99 \mathrm{~m}} \mathrm{Tc}$.

Within a few minutes after reinjection, these cells are distributed in the circulating blood volume ("equilibrium"). By means of a gamma camera with a dedicated computer, the radiation from the left ventricular blood pool-in any particular phase of the heart cycle-can be recorded externally and averaged over several hundred successive heart beats. This process is governed by the R-wave of the patient's ECG ("multigated acquisiton'") to accomplish correct synchronization. Dependent on heart rate, the dose of radioactive tracer injected and the counting statistics wanted in the study, data collection typically may last from 3 to 8 min . From the resulting, composite timeactivity curve, an average LVEF can be calculated using automatic computer programs. ${ }^{2,34}$ The method allows multiple measurements throughout the same day without relabeling of the red blood cells.

Determination of Volume. Various principles for determination of left ventricular volume and cardiac output by the gated equilibrium technique have been described. Most of these are dependent on the same geometric assumptions as used in angiography ${ }^{37,38}$ or they require correction by means of a regression equation obtained by previous comparison with angiographic volume. ${ }^{39-41}$ Recently, methods have been elaborated, based exclusively on data obtained by radionuclide imaging, ${ }^{9,42,43}$ i.e., without the use of multiple imaging or regression equations to convert a radionuclide index of volume to actual volume. The basic principle is that the radioactivity recorded from the left ventricle in a left anterior oblique view is proportional to left ventricular volume. Correction for absorption of radiation in the myocardium and the thoracic wall can be made if the depth of the left ventricle in the chest is known. The individual depth can be measured by either echocardiography or radionuclide methods. After measurement of the concentration of activity in peripheral blood, absolute volumes can be determined. A detailed description of this method, including an explanation of theory, methods, and accuracy has been given elsewhere. ${ }^{9}$

Gamma Camera. Stationary gamma cameras obviously are unpractical for monitoring purposes during anesthesia and surgery or in the intensive care unit. Better suited are the mobile-type of cameras with smaller camera head. Many of these are designed specially for radionuclide heart studies and equipped with the necessary data processing facilities.

The gamma camera/computer system can produce a picture containing quantitative information about the distribution of radioactivity (i.e., blood) in the body. With this system it is possible to measure absolute left ventricular volume and cardiac output noninvasively. ${ }^{9,42,43}$ Inherent technical limitations make sampling times of at least some minutes necessary in order to obtain sufficiently reliable counting statistics.

Nuclear Stethoscope. Nonimaging devices for radionuclide assessment of left ventricular function also have been described. ${ }^{3-5,44}$ Their smaller size and true mobility is an obvious advantage for bedside use. Due to a higher counting efficiency than can be obtained with the gamma camera, the real-time left ventricular time-activity curve can be recorded reliably by the nuclear stethoscope (fig. 1), so that LVEF can be measured from beat-to-beat. ${ }^{4-6}$ Average left ventricular time-activity curves also can be obtained during preset time intervals of 30 , 60,120 , or 240 s and displayed with a time resolution sufficient
for calculation of peak ejection and peak filling rates. ${ }^{45,46}$ Measurements of left ventricular volume are difficult to obtain with this instrument due to the fixed field of view of the detector and to problems in the selection of the background activity level.

Radiation Safety. The total radiation dose to patients investigated by gated equilibrium imaging with ${ }^{99 m} \mathrm{Tc}$-labeled red blood cells is about $26 \mathrm{mrem} / \mathrm{mCi}$. ${ }^{47}$ The dose is comparable to the doses involved in many common radiologic investigations and may be considered fully acceptable, as long as imaging is carried out for diagnostic and/or therapeutic purposes.

Radiation doses to the health personnel depends upon the proximity to the patient and the time of exposure. In the operating room some staff members may be very close to the patient, often for several hours, whereas personnel in the intensive care unit seldom come that close for a longer time. Their radiation exposure will increase with the number of labeled patients needing radionuclide monitoring in the same room. Obviously this problem has to be considered in detail if peroperative radionuclide monitoring of cardiac performance is going to be used in the daily clinical routine. The Danish National Institute of Radiation Hygiene has determined the radiation dose to staff members, who are nursing labeled patients in the intensive care unit, to be less than $10 \mathrm{mrem} /$ 30 mCi per patient (measured within the first 24 h after injection, unpublished data). In the nuclear medicine departments, where the majority of patients are investigated using ${ }^{99 n} \mathrm{Tc}$-radiopharmaceuticals, the total dose to the personnel is also very low, on an average $220 \mathrm{mrem} / \mathrm{yr} .{ }^{48}$ For "radiation workers' the maximum permissible level of irradiation of the whole body (recommended by the International Commission on Radiological Protection) is $5 \mathrm{rem} / \mathrm{yr}$.

## References

1. Berger HJ, Matiliay RA, Pytlik LM, Gottschalck. A, Zaret BL: First-pass radionuclide assessment of right and left ventricular performance in patients with cardiac and pulmonary disease. Semin Nucl Med 9:275-295, 1979
2. Bodenheimer MM, Banka VS, Helfant RH: Nuclear cardiology. I. Radionuclide angiographic assessment of left ventricular contractions: Uses, limitations and future directions. Am J Cardiol 45:661-673, 1980
3. Wexler JP, Blaufox MD: Radionuclide evaluation of left ventricular function with nonimaging probes. Semin Nucl Med 9:310-319, 1979
4. Wagner HN, Rigo P, Baxter RH, Alderson PO, Douglass KH, Housholder DF: Monitoring ventricular function at rest and during exercise with a nonimaging nuclear detector. Am J Cardiol 43:975-979, 1979
5. Berger HJ, Davies RA, Batsford WP, Hoffer PB, Gottschalck A, Zaret BL: Beat-to-beat left ventricular performance assessed from the equilibrium cardiac blood pool using a computerized nuclear probe. Circulation 63:133-141, 1981
6. Høilund-Carlsen PF, Marving J, Jensen G: Accuracy of left ventricular ejection fraction determined by the nuclear stethoscope. Int J Cardiol 2:237-246, 1982
7. Bauer R, Haluszczynski I, Langhammer $H$, Bachmann $W$ : In vivo/in vitro labelling of red blood cells with ${ }^{99 n}$ Tc. Eur J Nucl Med 8:218-222, 1983
8. Høilund-Carlsen PF, Rasmussen S, Hesse $\dot{B}$, Dige-Petersen $H$, Folke K, Godtfredsen J, Jensen G, Fabricius J: Determination
of left ventricular ejection fraction by radionuclide angiocardiography. Ugeskr Laeger 144:3234-3239, 1982
9. Høilund-Carlsen PF, Marving J, Rasmussen S, Haunsø S, Pedersen JF: Accuracy of absolute left ventricular volumes and cardiac output determined by radionuclide cardiography. Int J Cardiol 6:505-527, 1984
10. Marshall BE, Wollmann H: General anesthetics, The Pharmacological Basis of Therapeutics, 6th edition. Edited by Goodman LS, Gilman A. New York, Macmillan, 1980, pp 292295
11. Stanley TH: Pharmacology of intravenous non-narcotic anesthetics, Anesthesia. Edited by Miller RD. New York, Churchill Livingstone, 1981, pp 453-458, 458-461
12. Conway CM, Ellis DB: The hemodynamic effects of shortacting barbiturates. A review. Br J Anaesth 41:534-542, 1969
13. Bristow JD, Prys-Roberts C, Fisker A, Pickering TG, Sleight P: Effects of anesthesia on baroreflex control of heart rate in man. Anesthesiology 31:422-428, 1969
14. Millar Forbes A, Dally FG: Acute hypertension during induction of anesthesia and endotracheal intubation in normotensive man. Br J Anaesth 42:618-624, 1970
15. Takki S, Tammisto T, Nikki P, Jäättelä A: Effect of laryngoscopy and intubation on plasma cathecholamine levels during intravenous induction of anaesthesia. Br J Anaesth 44:13231328, 1972
16. Sonntag H, Hellberg K, Schenk H-D, Donath U, Regensburger D, Kettler D, Duchanova H, Larsen R: Effects of thiopental (Trapanol) on coronary blood flow and myocardial metabolism in man. Acta Anaesthesiol Scand 19:69-78, 1975
17. Chamberlain JH, Seed RGFL, Chung DCW: Effect of thiopentone on myocardial function. Br J Anaesth 49:865-870, 1977
18. Becker KE, Jr, Tonnesen AS: Cardiovascular effects of plasma levels of thiopental necessary for anesthesia. ANESTHESIOLOGY 49:197-200, 1978
19. Lebowitz PW, Cote ME, Daniels AL, Remsey FM, Martyn JAJ, Teplick RS, Davison JK: Comparative cardiovascular effects of midazolam and thiopental in healthy patients. Anesth Analg 61:771-775, 1982
20. Ross J Jr: Afterload mismatch and preload reserve: a conceptual framework for the analysis of ventricular function. Progr Cardiovasc Dis 18:255-265, 1976
21. Prewitt RM, Wood LDH: Effect of altered resistive load of left ventricular systolic mechanics in dogs. Anesthesiology 56:195-202, 1982
22. Ricci DR, Orlick AE, Alderman EL, Ingels NB, Daugters GT, Stinson EB: Influence of heart rate on left ventricular ejection fraction in man. Am J Cardiol 44:447-451, 1979
23. Narahara KA, Blettel ML: Effect of rate on left ventricular volumes and ejection fraction during chronic ventricular pacing. Circulation 67:323-329, 1983
24. Rozenman Y, Weiss AT, Atlan H, Gotsman MS: Left ventricular volumes and function during atrial pacing in coronary artery disease: A radionuclide angiographic study. Am J Cardiol 53:497-502, 1984
25. Giles RW, Berger HJ, Barash PG, Tarbadkar S, Marx PG, Hammond GL, Geha AS, Laks H, Zaret BL: Continuous monitoring of left ventricular performance with the computerized nuclear probe during laryngoscopy and intubation before coronary artery bypass surgery. Am J Cardiol 50:735741, 1982
26. Suga H, Sagawa K, Shoukas AA: Load independence of the instantaneous pressure-volume ratio of canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res 32:314-322, 1973
27. Sagawa K: The end-systolic pressure-volume relation of the
ventricle: Definition, modifications and clinical use. Circulation 63:1223-1227, 1981
28. Marsh JD, Green LH, Wynne J, Cohn PF, Grossman W: Left ventricular end-systolic pressure-dimension and stress-length relations in normal human subjects. Am J Cardiol 44:13111317, 1979
29. Mehmel HC, Stockins B, Ruffmann K, v. Olshausen K, Schuler $G$, Kübler $W$ : The linearity of the end-systolic pressurevolume relationship in man and its sensitivity for assessment of left ventricular function. Circulation 63:1216-1222, 1981
30. Nivatpumin T, Katz S, Scheuer J: Peak left ventricular systolic-pressure/end-systolic volume ratio: A sensitive detector of left ventricular disease. Am J Cardiol 43:969-974, 1979
31. Iskandrian AS, Hakki AH, Bemis CE, Kane SA, Boston B, Amenta A: Left ventricular end-systolic pressure-volume relation: A combined radionuclide and hemodynamic study. Am J Cardiol 51:1057-1061, 1983
32. Slutsky R, Karliner J, Gerber K, Batter A, Froelicher V, Gregoratos G, Peterson K, Ashburn W: Peak systolic blood pressure/end-systolic volume ratio: Assessment at rest and during exercise in normal subjects and patients with coronary heart disease. Am J Cardiol 46:813-820, 1980
33. Dehmer GJ, Lewis SE, Hillis LD, Corbett J, Parkey RW, Willerson JT: Exercise-induced alterations in left ventricular volumes and the pressure-volume relationship: A sensitive indicator of left ventricular dysfunction in patients with coronary artery disease. Circulation 63:1008-1018, 1981
34. Wexler LF, Pohost GM: Hemodynamic monitoring: Non-invasive techniques. ANesthesiology 45:156-183, 1976
35. Steele PP, Van Dyke D, Trow RS, Anger HO, Davies H: Simple and safe bedside method for serial measurement of left ventricular ejection fraction, cardiac output, and pulmonary blood volume. Br Heart J 36:122-127, 1974
36. Harpen MD, Dubuisson RL, Head GB, Parmley LF, Jones TP, Robindon HE: Determination of left ventricular volume from first pass kinetics of labelled red cells. J Nucl Med 24:98103, 1983
37. Strauss HW, Zaret BL, Hurley PJ, Natarajan TK, Pitt B: A scintiphotographic method for measuring left ventricular ejection fraction in man without cardiac catheterization. Am J Cardiol 28:575-580, 1971
38. Ashburn WL, Kostuk WJ, Karliner JS, Petersen KL, Sobel BE: Left ventricular volume and ejection fraction determination by radionuclide angiography. Semin Nucl Med 3:165-176, 1973
39. Slutsky R, Karliner J, Ricci D, Kaiser R, Pfisterer M, Gordon D, Petersen K, Ashburn W: Left ventricular volumes by gated equilibrium radionuclide angiography: A new method. Circulation 60:556-564, 1979
40. Dehmer GJ, Lewis SE, Hillis LD, Twieg D, Falkoff M, Parkey RW, Willerson JT: Nongeometric determination of left ventricular volumes from equilibrium blood pool scans. Am J Cardiol 45:293-300, 1980
41. Konstam MA, Wynne J, Holman BL, Brown EJ, Neill JM, Kozlowski J: Use of equilibrium (gated) radionuclide ventriculography to quantitate left ventricular output in patients with and without left-sided valvular regurgitation. Circulation 64:578-585, 1981
42. Links JM, Becker LC, Shindledecker JG, Guzman P, Burow RD, Nickoloff EL, Alderson PO, Wagner HN: Measurement of absolute left ventricular volume from gated blood pool studies. Circulation 65:82-91, 1982
43. Burow RD, Wilson MF, Heath PW, Corn CR, Amil A, Thadani U : Influence of attenuation on radionuclide stroke volume determinations. J Nucl Med 23:781-785, 1982
44. Bacharach SL, Green MV, Borer JS, Ostrow HG, Redwood DR, Johnston GS: ECG-gated scintillation probe measurement of left ventricular function. J Nucl Med 18:1176-1183, 1977.
45. Bonow RO, Bacharach SL, Green MV, Kent KM, Rosing DR, Lipson LC, Leon MB, Epstein SE: Impaired left ventricular diastolic filling in patients with coronary artery disease: Assessment with radionuclide angiography. Circulation 64:315-323, 1981
46. Strashun A, Horowitz SF, Goldsmith SJ, Teichholz LE, Dicker A, Miceli K, Gorlin R: Noninvasive detection of left ventricular dysfunction with a portable electrocardiographic gated scintillation probe device. Am J Cardiol 47:610-6I7, 1981
47. Radiation Doses from Radiopharmaceuticals, 2nd edition. Edited by the Swedish National Institute of Radiation Protection, Stockholm, 1981
48. Report on the Activities during the Time 1981-83. Edited by the Danish National Institute of Radiation Hygiene, Copenhagen (In press)

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