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USEFULNESS OF THORACIC ELECTRICAL BIOIMPEDANCE IN DETECTION OF EJECTION FRACTION CHANGES

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The aim of this study was to evaluate a usefulness of thoracic electrical bioimpedance (TEB) in following adaptive haemodynamic adjustments to postural change and isometric exercise. Sixteen subjects with intact cardiovascular system took part in this study. Haemodynamic parameters were obtained in recumbency and after taking up erect posture. Besides, TEB was performed during handgrip test and the results were compared with baseline resting data. Each time the radionuclide ventriculography (RV) was performed concurrently with TEB to obtain an independent measurement of ejection fraction (EF). Active orthostasis was associated with a change in stroke volume, cardiac output and total vascular resistance by -29.7%, -3.4%, $+3.9\%$, respectively. The handgrip produced a significant increase in cardiac output by 16.3%, however it was not associated with an enhancement of stroke volume. Although there was a moderate correlation between EF calculated by TEB and RV in supine position ($r = 0.66$; $p < 0.001$), TEB failed to reflect changes of EF in orthostasis and isometric exercise. In conclusion, our results suggest that TEB offers in subjects with normal cardiovascular function a valuable alternative to cardiovascular monitoring of stroke volume and cardiac output, but calculation of EF is associated with a risk of serious error.

K e y   w o r d s: *thoracic electrical bioimpedance, radionuclide ventriculography, postural change, orthostasis, handgrip*

INTRODUCTION

Continuous and non-invasive monitoring of cardiac performance and peripheral vascular resistance is required in clinical practice and in research studies. Thoracic electrical bioimpedance (TEB) has gained interest as an instrument of measurement of ejection fraction (EF), stroke volume and cardiac output (1, 2). Opinions on accuracy of TEB measurements are inconclusive as only certain authors demonstrated close correlation with thermodilution, doppler echocardiography or radionuclide ventriculography (3—7). It should be emphasized that in majority of studies TEB was performed at rest with

stabilized cardiovascular function, while its recordings which are based on detection of pulsatile change in aortic blood volume may be sensitive to redistributions of circulating blood accompanied by orthostasis or exercise stress.

In the present study we attempted to evaluate a usefulness of TEB in recognition of well recognized haemodynamic adjustments to postural change and isometric exercise. For this purpose we investigated in healthy individuals the cardiovascular effects of active orthostasis and handgrip test. Furthemore, we looked at relationship between EF measured simultaneously with TEB and radionuclide ventriculography.

MATERIAL AND METHODS

Subjects

Subjects were informed of the purpose and characteristics of the study and all consented to participate. The protocol was approved by the local Ethical Committee.

Criteria for exclusion were conductance defect, arrhythmia, valvular or myocardial abnormalities, diabetes mellitus, any pulmonary disease, use of cardiovasoactive drugs and age over 65 years. The haemodynamic studies were performed in the morning, with patients fasting and having stopped drinking 8 hours before. Subjects were weighed to the nearest 0.5 kg and height was measured to the nearest 1 cm. Ejection fraction measurements were performed simultaneously with TEB and radionuclide ventriculography. The arterial pressure was measured with automatic sphygmomanometry and the heart rate from mean R-R interval during continuous ECG recording. The arterial pressure was registered every minute.

Sixteen subjects (9 males, 7 females), mean age of 48.3 years, range 19—64 years participated in the study. In all patients haemodynamic measurements were carried out in supine and upright posture. Study in the supine position was started after 30 minutes rest and in the upright posture after being erect for 5—10 minutes. The mean values of TEB-derived parameters collected in each position over consecutive 8 minutes were taken to calculations.

The exercise test was performed in supine position (after 30 minutes of haemodynamic stabilization) by squeezing a standard handgrip device. During the study, subjects were working at 30% of their previously determined maximal level. TEB recordings were obtained continuously between 3 and 4 minute of the test (three measurements of arterial pressure) and mean values of haemodynamic parameters were subsequently calculated. The reference data were the results of the resting supine study.

Thoracic Electrical Bioimpedance

We used a commercially available TEB device — AVL 2001 HDM impedance analyzer (AVL LIST GmbH Medical Instruments, Graz, Austria). Briefly, four pairs of ECG electrodes were attached bilaterally to the skin surface at the base of the neck and to the torso at the diaphragm level. The electrodes were then connected to a Hewlett-Packard computer analyzer. The outer pairs of electrodes injected a 70 kHz, 2.5 mA current into the thoracic tissue and the inner electrodes sensed the high frequency voltage, proportional to the overall thoracic impedance. The monitor system recognized and eliminated the impedance changes arising from ventilation and body movements. Each set of data was a mean of 16 consecutive cardiac cycles where good quality signals were recorded.

Stroke volume (SV; ml) was calculated according to the modified Sramek-Bernstein formula (8):

$$SV = VEPT \times VET \times (dZ/dt)_{max}/Z_0$$

where VEPT is thorax capacity (ml) obtained from the software — inserted nomogram based on sex, height and weight; VET, ventricular ejection time (s); dZ/dt_{max} maximum rate of impedance change (Ω/sec); Z_0, baseline impedance (Ω). Cardiac output was calculated as product of SV and the heart rate, and EF (%) as (0.84—0.64 *STR)* 100, where STR is systolic time ratio i.e., PEP/VET (PEP; pre-ejection period). Total vascular resistance (dyn*sec*cm^{-5}) was calculated as mean arterial pressure reduced by 5 mmHg and divided by the cardiac index.

Gated Equilibrium Radionuclide Ventriculography

Studies were performed with a gamma camera DIACAM-Siemens linked to an ICON computer system. The red cells were labelled *in vivo* with an intravenous injection of 3 mg/60 kg stannous pyrophosphate, followed 20 minutes later by injection of 740 MBq/60 kg (20 mCi/60 kg) Tc-99m-pertechnetate (TcO_4^-). Imaging was then performed at least 5 minutes following the TcO_4^- injection. The detector was placed in the left anterior oblique position (LAO 40°—50°) with a 5° to 15° caudal tilt for separation the left from right ventricle. Low energy all-purpose collimator was used and the photopeak of the camera was set at 140 keV with a 15% window. The data were formatted in frame mode on a 64×64 matrix with the aid of an ECG gate, allowing production of the composite 20-frames from 100 cardiac cycles. The scan frames were frequency filtered, using temporal filter. Cardiac cycles that fell outside a 15% range of R-R interval were excluded.

The end-diastole and end-systole frames were defined by the volume curve from a box region of interest (ROI) over the left ventricle. Final selection of ROIs over the left ventricle was made by manual delineation, using the threshold and functional image techniques. Background was assigned laterally to the left ventricle at the end-systole. EF was calculated as 100*(EDC-ESC)/EDC, where EDC and ESC are counts in the end-diastole and the end-systole, respectively. In addition, to compare the end-diastolic volume in supine and erect posture in a single subject we analyzed EDC corrected for the heart rate and the number of cardiac cycles.

In both the supine and erect position the images were acquired 3 times while during handgrip only once and data acquisition lasted 1—2 minutes starting from 150 second of the exercise.

Data analysis

Data are given as the mean ± standard deviation. Intragroup and intergroup comparisons were performed as appropriate by the paired or unpaired Student'st test. A p value less than 0.05 was considered to indicate a significant difference between groups. Relationships between EF values obtained in TEB and ventriculography were analyzed by linear regression function.

RESULTS

Response to orthostasis and handgrip

Assumption of the upright position was associated with a significant decrease of stroke volume. The heart rate significantly increased, but the cardiac index, mean arterial pressure and total vascular resistance remained unchanged. Haemodynamic parameters measured by TEB in supine and erect positions are shown in *Table 1*. The handgrip test produced a significant increase in the heart rate, cardiac index, mean arterial pressure and TVR (*Table 1*).

Comparison of simultaneous measurement of EF with radionuclide ventriculography and TEB

In supine position the absolute values of EF calculated from TEB and radionuclide ventriculography provided comparable results ($59.4 \pm 7.1\%$ vs $61.8 \pm 7.5\%$). The slope of regression line was 0.63 and Y intercept was 20.7 (*Fig. 1*). After 10 minutes of erect posture EF detected by TEB decreased to $52.0 \pm 7.4\%$ ($p < 0.001$), while that measured with radionuclide ventriculography increased to $65.9 \pm 9.3\%$ ($p < 0.05$). Individual changes of EF are depicted in *figure 2*. In upright subjects there was remarkable difference between EF measured with both methods ($p < 0.0001$) and the regression line was shifted in comparison with supine subjects — slope of regression line was 0.51 and Y intercept was 18.2 (*fig. 1*). Assumption of erect posture was associated with a decline of EDC by 17.7% ($p < 0.006$). The handgrip test had no significant influence on EF measured with TEB, while the radionuclide ventriculography demonstrated a significant rise of EF from $61.8 \pm 7.5\%$; to $65.3 \pm 6.7\%$; $p < 0.05$ (individual changes are shown in *Fig. 2*) with no change of EDC. There was no relationship between EF measured with both methods during the handgrip test (*Fig. 1*). Figure 1 (lower panel) demonstrates an agreement analysis, i.e., a plot
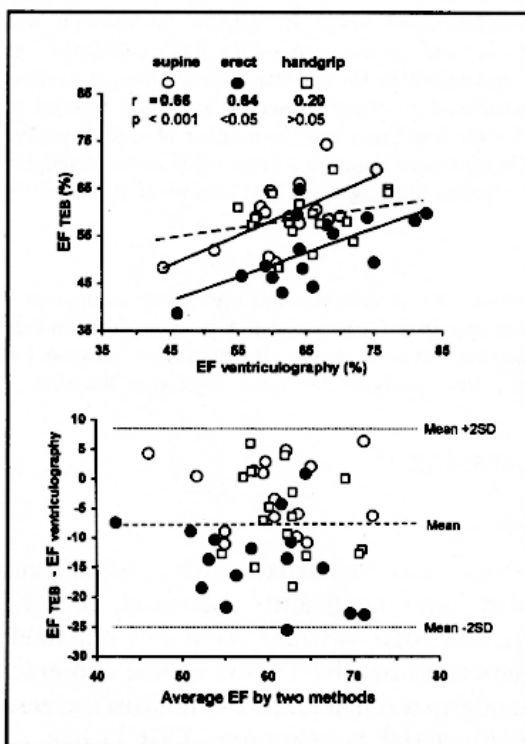

Fig. 1. EF measured with radionuclide ventriculography and TEB. Regression line for handgrip test is marked with dashed line.
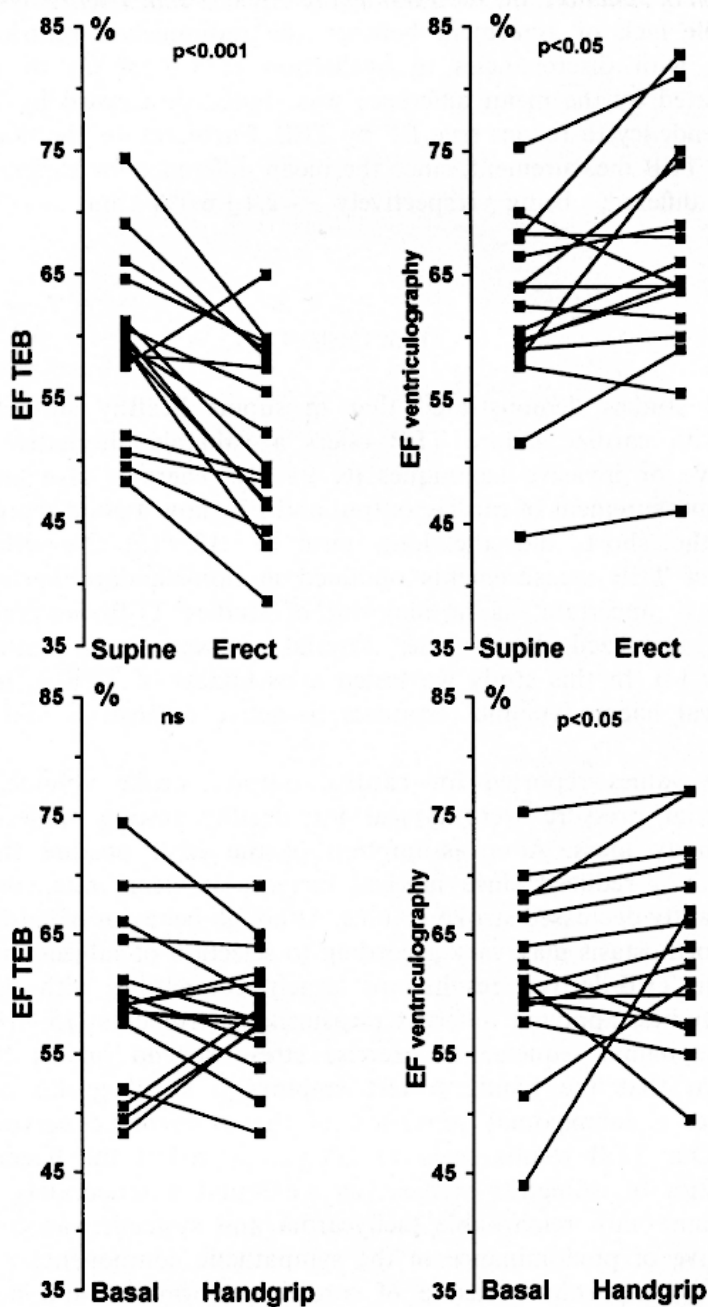
Fig. 2. Change in EF measured with TEB and radionuclide ventriculography after taking up erect posture and during isometric exercise (handgrip).

of the difference between the methods against their mean. This analysis displays considerable lack of agreement between the radionuclide ventriculography and TEB, with discrepancies in evaluation of EF of up to 16%. The bias estimated by the mean difference was shifted downward by 7.6%, that means a tendency to reduce true EF by TEB. Furthermore, the body posture influenced TEB measurement, since the mean difference for supine and erect positions differed, being respectively $-2.4 \pm 6.0\%$ and $-13.9 \pm 7.3\%$; $p < 0.0005$.

DISCUSSION

Several studies demonstrated that in supine healthy subjects and in patients with cardiac failure TEB offers a valuable alternative to other non-invasive or invasive techniques (6, 9—11). There is also an evidence that TEB measurement of cardiac output and EF show a good reproducibility at both the short and the long term (7, 12, 13). Nevertheless, the relevance of TEB measurements obtained in non-standard haemodynamic conditions is uncertain, as in majority of studies TEB was validated at rest with stabilized heart rate, arterial pressure and central blood volume (1, 14). In this study we tested a usefulness of TEB in monitoring physiological haemodynamic responses to active orthostasis and isometric exercise.

Present values reported for cardiac output, stroke volume, EF and mean arterial pressure were typical for healthy resting subjects of this age and body mass. After assumption of the erect posture the cardiac index was not reduced since marked increase in heart rate compensated for significantly decreased stroke volume. Although behavior of cardiovascular system in orthostasis may vary according to selection of subjects or protocol design, our TEB-derived results are largely compatible with data found in other studies, applying different measuring instruments (15—18).

Haemodynamic sequelae of exercise stress depend on its type. It is well known that the handgrip test employs a small group of muscles and induces a submaximal activation of the sympathetic nervous system (19—20). Our TEB results seem to adequately reflect the haemodynamic characteristics of isometric exercise, as we found a moderately decreased stroke volume with remarkable tachycardia and systemic vasoconstriction, all suggestive of predominance of the sympathetic component.

EF is an important measure of cardiac performance and normally is determined from the ratio of stroke volume to end-diastolic volume. The radionuclide ventriculography in either first-pass or gated pooled model is a well validated instrument to directly determine EF (21, 22). In comparison

with echocardiography the measurement of EF by radionuclide ventriculography is not influenced by the shape of heart chambers and is less operator-dependent (23). Unlike the radionuclide ventriculography, TEB calculates indirectly EF from the ratio of pre-ejection period (PEP) to ejection time (ET). In normal subjects this ratio shows large variation and seems to be more dependent on cardiac volaemia than myocardial contractility (23). In fact, PEP/ET is highly sensitive to changes of the arterial pressure, body posture, heart rate, age, sex or body mass (24—26). Although overall correlation of PEP/ET with EF is rather poor, an inverse relationship between these two parameters was found in patients with reduced ventricular function (27, 28). It is, however, unknown if this paradigm keeps true for such physiological tests as orthostasis or isometric exercise.

In our study EF derived from the impedance formula showed in both the recumbency and erect posture a moderate strenght of relation with EF simultaneously measured with the radionuclide ventriculography (r = 0.66 and 0.64), although Y intercepts of 20.7 and 18.2 are indicative of a serious systematic error in calculation of EF by TEB. In accordance, plotting of the EF difference between two methods against their mean disclosed considerable lack of agreement between two instruments. Previous studies examining relationships between TEB-calculated PEP/ET and radionuclear measurements of EF provided inconclusive results (9, 29—31). Besides, certain studies demonstrated that TEB either overestimates of low EF in critically ill patients (1, 32) or underestimates of normal EF (12, 33). In our study there was a tendency to supress by TEB higher ranges of EF, and orthostasis was associated with a significant decrease in EF. A similar decline of EF was recorded by this method during active and passive orthostasis in the study by Ng et al. (12). Nevertheless, these findings are in conflict with the evidence that orthostasis and isometric exercise rather enhance EF of the intact heart (20), like it was found in our radionuclear measurements. Although we cannot assert if this disagreement in measurement of EF in non-resting conditions should be attributed to actual loss of correlation between EF and PEP/ET or exclusively to modification of impedance phenomena beyond thoracic aorta, it clearly precludes TEB from reliable measurement of EF.

In summary, our findings are consistent with the opinion that TEB is a relevant method to pursue haemodynamic trends in terms of stroke volume and cardiac output. On the other hand, TEB introduces a systematic error to calculation of EF. In consequence, TEB is an unreliable instrument for calculation of EF and the parameters directly determined from EF i.e., end-diastolic and end-systolic volumes, that is particularly apparent for non-resting haemodynamic conditions.

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