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Letter to the Editor

Detection of left ventricular systolic dysfunction using a newly developed, laptop based, impedance cardiographic index

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Congestive heart failure (CHF) is a major cause of morbidity and mortality worldwide [1]. The development of left ventricular systolic dysfunction (LVSD) is a marker of poor prognosis. Mild reduction in EF progresses with time and when EF gets to <40%, most patients develop CHF and their prognosis is dismal [2,3]. Simple, cheap techniques that will reliably detect mild reduction of the EF, typical for ALVSD, will thus be of enormous value to reduce the occurrence of CHF and cardiac mortality [3–7].

Impedance Cardiography (ICG) is a noninvasive method of determining hemodynamic status and reliable estimates of myocardial contractility (and EF) can be obtained using indices based on systolic time intervals [8–10]. We have recently developed an index—Granov Goor Index (GGI)—that combines time interval and impedance parameters in order to identify subjects with LVSD. The GGI is obtained from a regional ICG signal—measured using wrist and ankle electrodes [10–13].

In this manuscript we determined the accuracy of GGI in identifying subjects with LVSD (in a "training" cohort of 100 individuals) and validated the findings in an additional cohort of 201 subjects.

The regional ICG signal is obtained from 2 pairs of tetra-polar electrodes: one on the wrist, above the radial artery, and the other on the contra-lateral ankle above the posterior tibial artery. The detailed description of the system and measured parameters can be reviewed in previous publications [10–13]. The GGI is designed to assess the systolic contractile function of the LV and is obtained from the following formula:

$$GGI = \Delta R/R \times \alpha \times HR(\text{corrected})$$

where R is the basal impedance and ΔR is the change in impedance, α is the time to peak ΔR and HR is the heart rate. The GGI takes into account both ΔR as an estimate of stroke volume and α as a time interval parameter. HR and R are used as normalization factors so that the result is a dimensionless index that reflects the systolic function of the LV.

The entire system (electrode, signal analysis and calculations) can replace the CD ROM in a regular computer, transforming any laptop into a simple diagnostic device—ideal for screening.

Echocardiography was performed using GE Vivid 7 (GE Vingmed Ultrasound A/S, Norway). EF was calculated using the biplane Simpson's technique [14]. Echocardiography and ICG were performed on the same day.

Patients who were referred for screening echocardiography at the outpatient clinic of the E. Wolfson Medical Center were considered for this trial.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institution's human research committee.

Optimal cutoff value for the GGI for detection of LVSD was determined from the Receiver Operating Characteristic (ROC) curve of the training set. Sensitivity specificity and predictive accuracy of GGI to detect LVSD were determined using standard technique. Statistical analysis was performed using MedCalc® software (Broekstraat, Belgium version 9.5.2.0).

Tables 1 and 2 describe the demographic echocardiographic and ICG results. The superiority of GGI in detecting LVSD is confirmed using ROC curve analysis (Fig. 1). The area under curve (AUC) of ROC curves of ΔR/R and α as predictors of LVSD were 0.84 and 0.75 respectively, significantly lower ($p<0.001$) than the value for GGI (0.97 CI 0.92 to 0.99). For a GGI cutoff value of 10 the sensitivity, specificity positive and negative predictive values are 86%, 100%, 100% and 96% respectively.

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Patients in the validation set were slightly older with a tendency for lower prevalence of smoking. Echocardiographic and ICG values were similar in these two sets of patients (Tables 1 and 2). A GGI cutoff of 10 was 89% sensitive and 96% specific for detection of LVSD, confirming the excellent results of the training set. Positive and negative predictive values were 78% and 98% respectively.

False positives and false negatives of GGI as a predictor of EF are extremely rare (Fig. 2) reflecting the accuracy of GGI to detect LVSD. Careful observation of the data points suggests that rather than a simple correlation, the relation between EF and GGI is more like a step function with a GGI<10 corresponding to a wide range of EF<55% while a GGI≥10 corresponds to varying levels of EF≥55%.

In this study we were able to demonstrate that a simple regional impedance based technology can reliably detect LVSD. Regional (as compared to thoracic) ICG enables more accurate determination of stroke volume and cardiac output [10–12]. The addition of α, a time interval parameter, with the resulting GGI adds significantly to accuracy of this method to identify subjects with LVSD (increasing the AUC from 0.84 to 0.97). Most importantly, also those at the asymptomatic stage of mild LVSD are accurately detected.

Some of the energy of the LV contraction produces forward blood flow during systole, while a significant amount is briefly stored as potential energy in the distended arteries—maintaining the forward flow during diastole [15]. The information provided by α relates to this stored energy while the ΔR is related to the stroke volume. The incorporation of both these parameters into the GGI makes the GGI a more reliable index of the energy generated by the contraction of the LV. Time interval parameters were used in the past from the ICG curve (or its derivative) to try to estimate the EF. Despite significant correlation [9] the coefficient values (typically approximately 0.5) are not high enough for clinical purpose. Thus accurate estimation of the value of EF is limited but, as we have showed, the GGI very accurately determines whether the LVEF is normal or abnormal (step function rather than simple correlation).

The natural history of patients with ALVSD is dismal [4]. Compared with those with normal LV, patients with ALVSD had 4–5-fold increase risk of CHF and death. Early detection of ALVSD requires a search for CAD as a possible etiology. When CAD is causing reversible dysfunction prompt revascularization is essential to improve outcome; preventing CHF and early arrhythmic death [16–19]. In those with irreversible ALVSD; further deterioration can be attenuated by the use of appropriate drug therapy [3].

Since early intervention in subjects with ALVSD is beneficial, screening programs need to be implemented to identify these individuals. Echocardiography—the "gold standard" in the assessment of LVSD—is impractical for general screening since it is very expensive. Thus an effective screening program should use an inexpensive diagnostic test (such as GGI) to identify those who are likely to have ALVSD.

Table 1
Clinical characteristics of subjects in the training and validation cohorts.

	All	Training cohort	Validation cohort	p
Number	301	100	201	
Male (%)	56	65	52	NS
Age (mean ± SD)	63 ± 9	60 ± 10	64 ± 11	P = 0.0027
BMI (kg/m^2), (mean ± SD)	28.2 ± 3.5	28 ± 4.5	28 ± 4.4	NS
Hypertension (%)	44	41	44	NS
Diabetes (%)	20	27	17	NS
Dyslipidemia (%)	51	57	48	NS
Smoke (%)	20	28	16	P<0.055
Family history of CAD (%)	52	58	49	NS
Asymptomatic CAD (%)	29	28	29	NS

BMI—body mass index.

Table 2
Echocardiographic findings of subjects in the training and validation cohorts.

	All	Training cohort	Validation cohort	p
Echocardiography				
LVEF (%)	56 ± 9	55 ± 9.6	57 ± 9.2	NS
LVEDD (cm)	4.8 ± 0.6	4.9 ± 0.6	4.8 ± 0.6	NS
LVESD (cm)	3.0 ± 0.8	2.9 ± 0.7	3.0 ± 0.8	NS
IVS (cm)	1.0 ± 0.1	1.0 ± 0.16	1.0 ± 0.16	NS
LVPW (cm)	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.8	NS
LA diameter (cm)	3.8 ± 0.6	3.8 ± 0.55	3.8 ± 0.6	NS
MR (%)	27	27	26	NS
LVH (%)	22	26	19	NS
LA area (cm^2)	18.9 ± 5	18.5 ± 4.9	19.0 ± 5.0	NS
Diastolic dysfunction (%)	19	14	20	NS
ICG				
Cardiac index (l/m^2)	3.5 ± 0.8	3.5 ± 0.9	3.6 ± 0.75	NS
Stroke index (cc/m^2)	50 ± 9.3	50 ± 9.5	49 ± 9.2	NS
TPR(dynes-sec-cm^{-5})	1299 ± 341	1280 ± 350	1308 ± 337	NS
GGI	11.6 ± 2.3	11.6 ± 2.6	11.6 ± 2.1	NS
GGI <10 (%)	17	18	16	NS

LVEDD and LVESD are left ventricular end diastolic and end systolic diameters. IVS and LVPW are LV septal and posterior wall thicknesses. MR—mitral regurgitation (minimal or mild), LVH—left ventricular hypertrophy, LA—left atrium and TPR—total peripheral resistance.

Even though we excluded patients with symptoms of suggestive of heart disease the decision to refer patients for echocardiography biases the population so that data was not collected from the true target population—asymptomatic individuals with no prior history of heart disease. However the likelihood that this will change the observed relation between GGI and EF is small.

The GGI can accurately detect LVSD in subjects at risk (referred for echocardiography). The GGI can be easily obtained from regional ICG signal using any laptop by replacing the CD ROM with the measuring hardware and software. This laptop based device is cheap and easy to operate making it an attractive tool to screen for LVSD. Additional trials are required to prove the efficacy of this device in the target population of asymptomatic patients at risk.

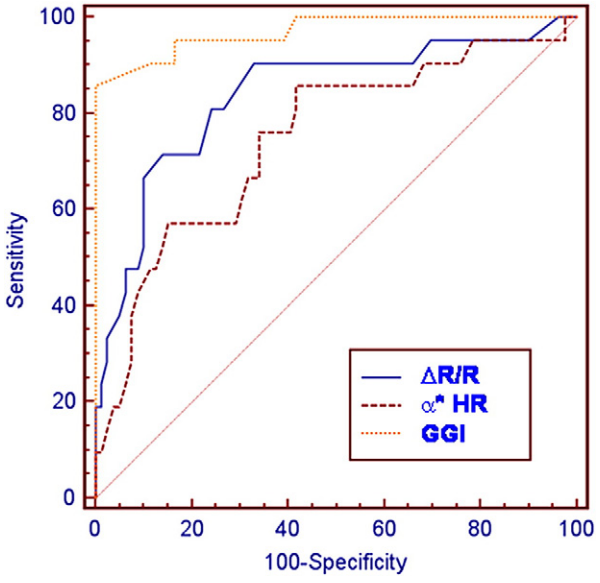

Fig. 1. Receiver operating characteristic (ROC) curve of ΔR/R, α×HR and GGI as diagnostic tests for LVSD (EF<55%).

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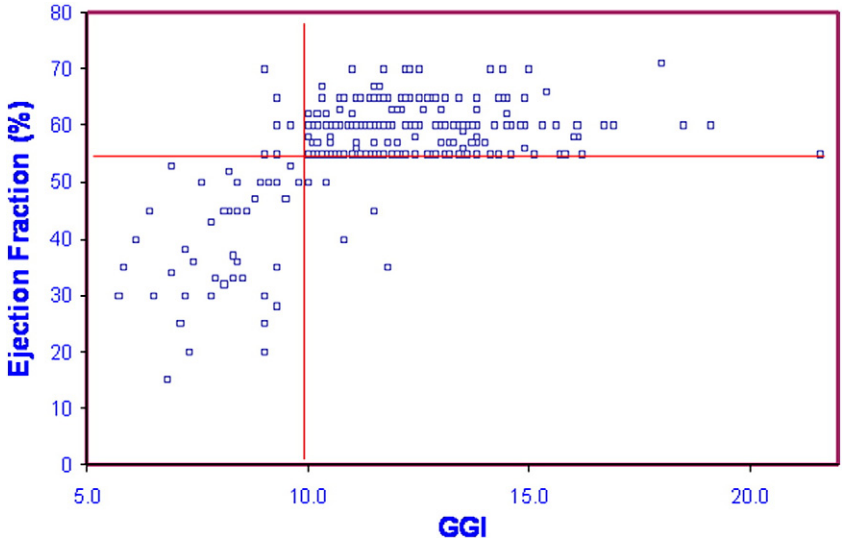

Fig. 2. Scatter plot of EF vs. GGI demonstrating the diagnostic power GGI (with cutoff value of 10) to detect LVSD (EF<55%) (data from the entire cohort, n = 301).

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [20].

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