Bland–Altman analysis as an alternative approach for statistical evaluation of agreement between two methods for measuring hemodynamics during acute myocardial infarction

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Key words: *acute myocardial infarction; impedance cardiography; pulmonary artery catheter; Bland–Altman analysis; linear regression.*

Summary. *Background and objective. Evaluation of hemodynamics in patients with acute myocardial infarction is crucial. In clinical practice, the comparison of a new measurement technique with an established one is often needed to see whether they agree sufficiently for the new to replace the old. Such investigations are often analyzed inappropriately, notably by using correlation coefficients. Our objective is to present an alternative approach, suggested by D. G. Altman and J. M. Bland, based on graphical techniques and simple calculations, for evaluation of the agreement of two methods – intermittent thermodilution (recognized and accepted as a "gold standard" for hemodynamic monitoring) and impedance cardiography (newly introduced method).*

Patients and methods. A total of 34 patients (20 (58.8%) men and 14 (41.2%) women) were investigated according to the study protocol at Kaunas University of Medicine Hospital.

A prospective controlled study was designed to compare two different methods – intermittent thermodilution and impedance cardiography – of cardiac output measurement simultaneously in patients with acute myocardial infarction. Statistical analysis was performed with Bland–Altman and linear regression.

Results. A total of 34 paired measurements were carried out in 34 patients at the initiation of hemodynamic monitoring and 30 paired measurements in 32 patients after subsequent improvement or stabilization of clinical status. Correlation coefficient ranged from 0.37 to 0.98.

Conclusions. Bland–Altman analysis is an alternative method for assessing the agreement between two methods of clinical measurement. According to our data, noninvasive technique – impedance cardiography – is a reliable method for hemodynamic monitoring in noncomplicated cases of acute myocardial infarction.

Introduction

In clinical practice, it is usually expected to have precise values of different parameters, for example cardiac output or stroke volume where direct measurements without adverse effects are difficult or impossible (1). Almost all direct measurements are obtained by the application of invasive techniques and procedures. Therefore, priority is given for noninvasive methods, as for more convenient and safe ones. The main problem is validation of noninvasive techniques and further legalization for clinical application. Traditionally, if a new method agrees sufficiently well with the old, the old may be replaced (1). Recently, many statistical approaches have been proposed for the evaluation of correlation between two different methods.

A new statistical approach to compare two measurement methods was suggested by D. G. Altman and J. M. Bland. The method proposed by authors was successfully introduced into practice; the authors are still active supporters of this statistical tool (2).

Bland–Altman statistical analysis was successfully used by many authors. Recently new studies were published using Bland–Altman statistical analysis for the comparison of different methods for assessment of hemodynamics (3). Despite this, there is a lack of validated studies using Bland–Altman analysis for the application of impedance cardiography (ICG) in critical care patients. If intermittent thermodilution (ITD) is accepted as a "golden standard" in hemodynamic monitoring, this cannot be said about all noninvasive

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methods for the assessment of hemodynamics (4). Many studies use "regular" regression analysis for the validation of impedance cardiography data (5, 6).

Inappropriate use of correlation coefficient

Investigators usually limit their statistical analysis by calculation of the correlation coefficient between the two methods. However, according to J. M. Bland and D. G. Altman, correlation does not mean that the two methods agree (1). Original motivation suggested by authors (1) is presented below:

- Correlation coefficient measures the strength of a relation between two variables, not the agreement between them. Perfect agreement is observed only if the points lie along the line of equality, but we will have perfect correlation if the points lie along any straight line;
- A change in scale of measurement does not affect the correlation, but it certainly affects the agreement;
- Correlation depends on the range of the true quantity in the sample. If this is wide, the correlation will be greater than if it is narrow;
- The test of significance may show that the two methods are related, but it would be amazing if two methods designed to measure the same quantity were not related. The test of significance is irrelevant to the question of agreement;
- Data which seem to be in poor agreement can produce quite high correlations (1).

The objective of this study was to analyze the possibility of the application of Bland–Altman *versus* regression analysis in order to compare two methods – intermittent thermodilution and impedance cardiography – for the assessment of hemodynamics.

Material and methods

A total of 34 patients were investigated according to the study protocol at Kaunas University of Medicine Hospital. There were 20 (58.8%) men and 14 (41.2%) women. The mean age was 70.7±9.6 years, body mass index – 26.8±3.7.

Anterior AMI was diagnosed in 23 (67.6%) patients, inferior in 10 (29.4%), and circular in 1 (29.4%) patient. Eight (23.6%) patients were in Killip class II, 6 (17.6%) in class III, and 20 (58.8%) in class IV.

Coronary angiography was performed in all the patients. One-vessel disease was diagnosed in 3 (8.8%) patients, two-vessel disease in 9 (26.5%), and three-vessel disease in 22 (64.7%).

Primary percutaneous transluminal coronary angioplasty (PTCA) was successfully performed in (52.9%) patients, 14 (41.2%) underwent cardiac surgery within the first two weeks. Primary PTCA was unsuccessful in 2 (5.9%) patients, who died within the first 18 hours. Ejection fraction on admission was 22.9±14.8%. The mean durations from onset of pain to hospitalization and to primary coronary angiography were 7.1±5.5 hours and 9.4±5.2 hours, respectively.

Series of two measurements of ITD and ICG were made to evaluate patient's hemodynamics. All measurements were carried out in Cardiac Intensive Care Unit, using the same two instruments. The data were collected to demonstrate the statistical method and provide the possibility to evaluate the comparability of these two instruments. Measurements of cardiac output (CO) by both methods are used to illustrate the comparison of methods.

The instrumentations performed included a pulmonary artery catheter (7 F, Baxter™); a software for ITD measurement was Datex® CS/3 by Datex-Engstrom®; an original recording system Heartlab™ (certificate No. LS. 08.02.1957) was used for ICG signal acquisition and primary analysis.

The sample of patients with acute myocardial infarction (AMI) of Killip class II–IV was chosen to give a wide range of CO values.

According to the protocol, hemodynamic measurements were performed twice: at the initiation of hemodynamic monitoring within the first 6 hours after admission (first measurement) and after 24 hours (second measurement which is usually associated with improvement or stabilization of clinical status, despite temporary or permanent they were).

A Swan-Ganz flow-directed triple-lumen catheter was inserted through either subclavian or internal jugular vein, with continuous pressure and electrocardiographic monitoring. Selected measurements of right atrial, pulmonary artery, and pulmonary capillary wedge pressures and cardiac output were carried out. ITD measurements were performed by standard procedure flushing 10 mL of sodium saline injectate via the proximal lumen of pulmonary artery catheter.

ICG signal was recorded using the standard technique of eight electrodes (7, 8). Stroke volume and CO was calculated using a modified equation suggested by Kubicek *et al.*, which was modified by D. P. Bernstein (7) and B. B. Sramek (8):

$$SV = \frac{(0.17H)^3}{4.2} \times \frac{(dZ/dt)_{max} \times T_{Lve}}{Z_0}$$

$$CO = SV \times HR$$

Where: SV – stroke volume; CO – cardiac output;

HR – heart rate; Z_0 – baseline impedance between recording electrodes; H – patient's height; dZ/dt_{max} – the maximum of the first derivative of impedance; T_{Lve} – left ventricle ejection time.

ITD and ICG measurements were made simultaneously in all the patients.

Statistical analysis. SPSS software was used for data analysis. Correlation between the ITD and ICG techniques was determined using linear regression. A plot of the differences between techniques was done according to method described by J. M. Bland and D. G. Altman (1). Values are presented as means and standard deviations (SD).

The study was approved by the Ethics Committee of Kaunas Regional Biomedical Research (protocol No. 169/2004).

Results

A total of 64 paired measurements were carried out in 34 patients: first measurement (34 paired measurements) upon initiation of hemodynamic monitoring within 6 hours after admission to Cardiac Intensive Care Unit and second measurement after 24 hours (30 paired measurements as 2 patients died within 24 hours due to refractory cardiogenic shock).

CO values obtained by two different methods of hemodynamic monitoring are presented in Table.

Higher CO values, as it was expected, were obtained during the second measurement after improvement or stabilization of patient's status.

Regression analysis plots of the first (initial measurement at the beginning of hemodynamic monitoring; status of patients compromised by cardiogenic shock, pulmonary edema) and the second (carried out after 24 hours, usually associated with stabilization of the patient's status) measurements are presented in Fig. 1

and 2.

A very strong positive correlation was observed for the second measurement (r=0.98, P<0.0001), while for the first measurement, a weak positive linear correlation was found (r=0.373, P=0.03).

Fig. 3 and 4 show Bland–Altman plots of the first measurement carried out at the beginning of hemodynamic monitoring and the second measurement carried out after stabilization of patients' status.

Discussion

Application of Bland–Altman analysis for the comparison of two methods of measurement still remains insufficient. K. Dewitte *et al.* screened articles starting from 1995 to 2001. It was observed increasing use of the Bland–Altman plots over the years, from 8% in 1995 to 14% in 1996 and 31–36% in 2000–2001. In addition to the Bland–Altman method, method comparisons were performed using correlation and regression analysis and the concordance plot. Most authors also used correlation and regression analysis, suggesting that difference plots are viewed as complementary to, rather than substitutes for, regression analysis (9). According to our observation and experience, mainly linear regression is used for the evaluation of two methods in the studies of Lithuanian researchers.

Application of correlation and regression analysis as the only approach for the comparison of two methods is misleading. This was observed in our study by application of ITD and ICG techniques and further comparison of their data.

On the other hand, application of Bland–Altman analysis allows the validation of the application of newly introduced method in certain conditions. As it was observed in our study, patients with severe

Table. **Values of cardiac output according to method of monitoring**

| Variable	First measurement		Second measurement	
	ITD	ICG	ITD	ICG
CO, L/min	3.85	5.88	4.71	4.88
SD, L/min	1.79	2.19	1.93	2.35
Maximum value, L/min	7.8	8.8	8.9	9.4
Minimal value, L/min	0.36	2.1	1.95	1.8
Correlation coefficient*	0.373		0.98	

* Estimated comparing the values of cardiac output obtained by impedance cardiography and intermittent thermodilution.

CO – cardiac output; ITD – intermittent thermodilution; ICG – impedance cardiography;
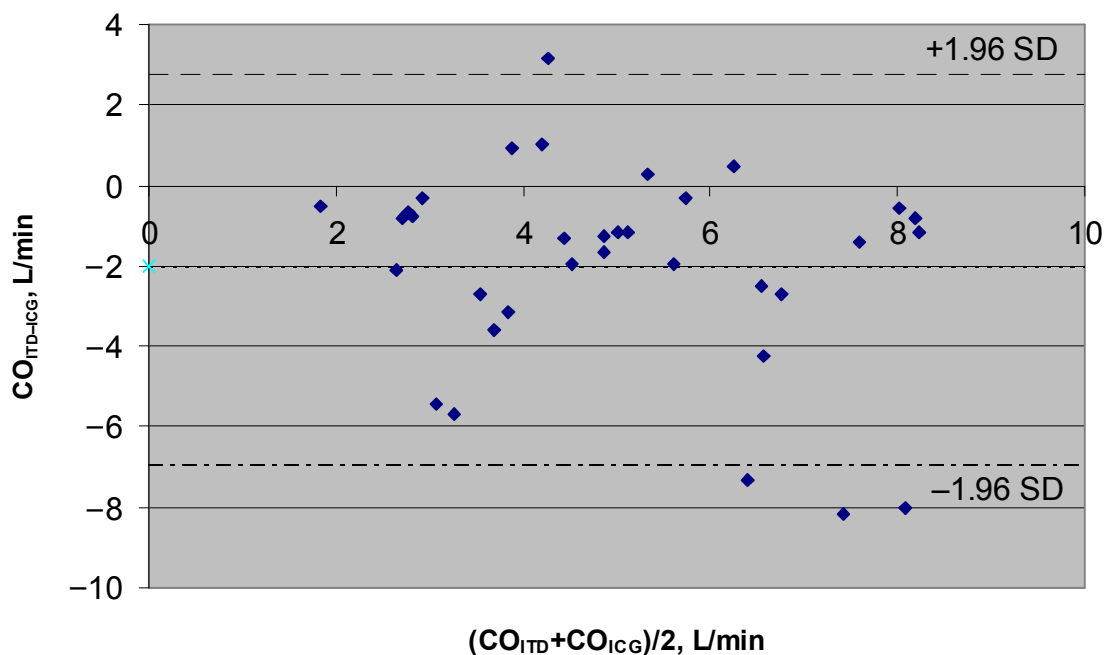SD – standard deviation.

r=0.373, P=0.03
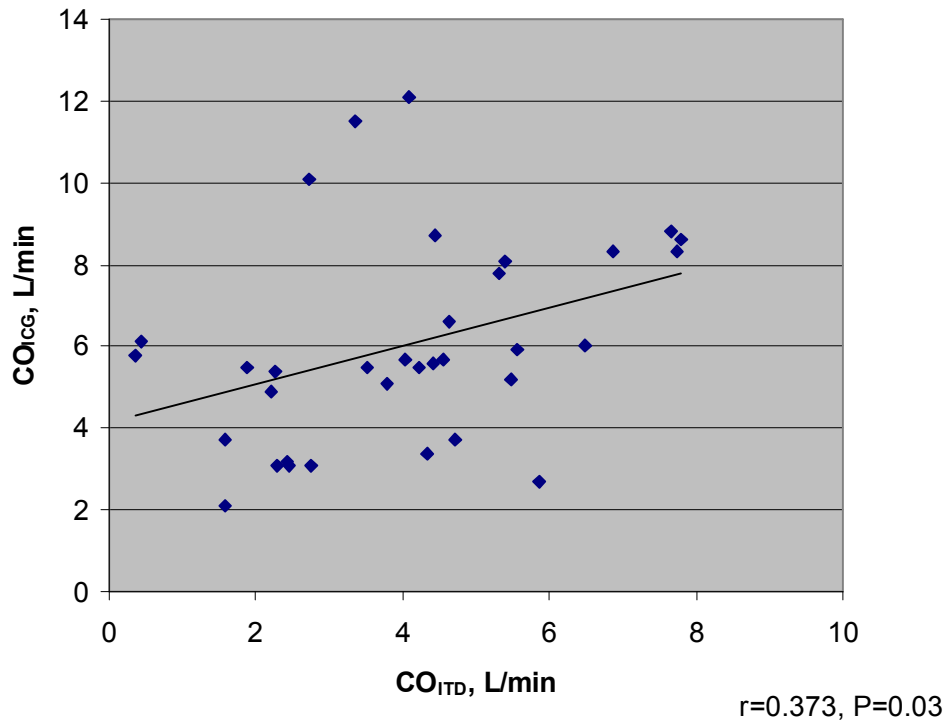
Fig. 1. Regression analysis: correlation of CO$_{ITD}$ and CO$_{ICG}$ (first measurement)
CO$_{ITD}$ – cardiac output measured by intermittent thermodilution.
CO$_{ICG}$ – cardiac output measured by impedance cardiography.

r=0.98, P<0.0001
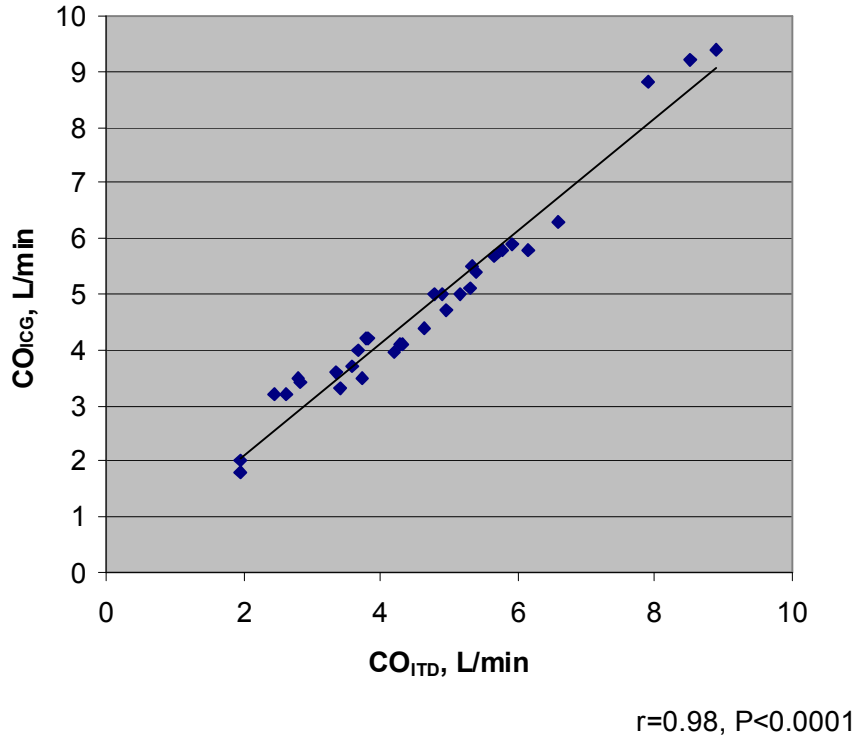
Fig. 2. Regression analysis: correlation of CO$_{ITD}$ and CO$_{ICG}$ (second measurement)
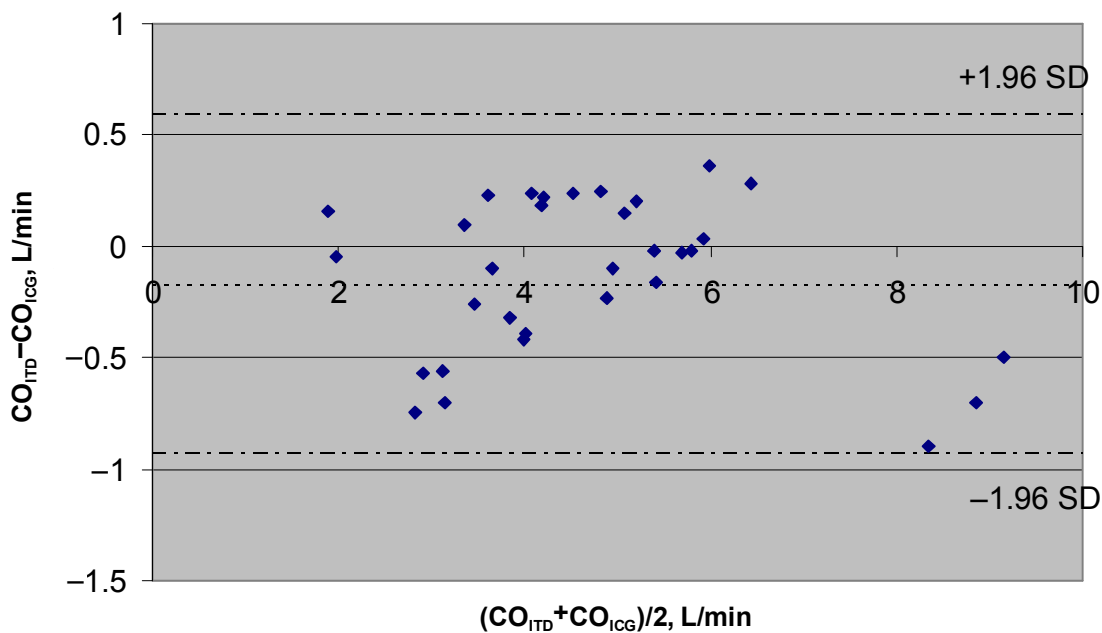CO$_{ITD}$ – cardiac output measured by intermittent thermodilution.
CO$_{ICG}$ – cardiac output measured by impedance cardiography.

Fig. 3. Bland–Altman analysis: correlation of CO_{ITD} and CO_{ICG} (first measurement)
CO_{ITD} – cardiac output measured by intermittent thermodilution.
CO_{ICG} – cardiac output measured by impedance cardiography.

Fig. 4. Bland–Altman analysis: correlation of CO_{ITD} and CO_{ICG} (second measurement)
CO_{ITD} – cardiac output measured by intermittent thermodilution.
CO_{ICG} – cardiac output measured by impedance cardiography.

cardiogenic shock seemed to be ineligible candidates for the application of ICG technique for the assessment of hemodynamics.

Comparing a new method of measurement with a standard method, one of the things we want to know is whether the difference between the measurements by two methods is related to the magnitude of the measurement. A plot of the difference against the standard measurement is sometimes suggested, but this will always appear to show a relation between

difference and magnitude when there is none. A plot of the difference against the average of the standard and new measurements is unlikely to mislead in this way (10). We show this theoretically and by a practical example.

J. M. Bland and D. G. Altman noted that in the analysis of measurement method comparison data, neither the correlation coefficient nor techniques such as regression analysis are appropriate (11). It was suggested to replace these misleading analyses by a method that is simple both to do and to interpret (1).

Previously, in our articles, we also exceptionally used regression analysis for the comparison of two measurement methods (5, 6). So there is a question, given by J. M. Bland and D. G. Altman, "Why has a totally inappropriate method, the correlation coefficient, become almost universally used for this purpose?" (1). Medical statisticians who ask, "Why did you use this statistical method?" will often be told, "Because this published paper used it" (1).

On the other hand, in our study, we observed hemodynamic improvement after 24 hours among survivors, and this was accompanied by improvement in the correlation between invasive and noninvasive methods for hemodynamic measurement either in linear regression analysis or in Bland–Altman analysis. This supports the idea that impedance cardiography as noninvasive method for hemodynamic assessment should be used in noncomplicated cases rather than in complicated ones.

Conclusions

Bland–Altman analysis is an alternative method for assessing the agreement between two methods of clinical measurement.

According to regression and Bland–Altman analysis, impedance cardiography as a noninvasive technique for hemodynamic monitoring have limitations for its application in cases of acute myocardial infarction complicated by cardiogenic shock. In patients with improved left ventricular function or in cases of noncomplicated acute myocardial infarction, impedance cardiography seems to be a reliable method for its application in clinical practice.

Bland–Altman analizė – alternatyvus būdas statistiniam hemodinamikos tyrimo metodų naudojimui įvertinant ūminį miokardo infarktą

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Raktažodžiai: ūminis miokardo infarktas, impedanso kardiografija, plaučių arterijos kateteris, Bland–Altman analizė, linijinė regresija.

Santrauka. Hemodinamikos rodiklių įvertinimas ligoniams, susirgusiems ūminiu miokardo infarktu, yra svarbus norint užtikrinti adekvatų ištyrimą ir gydymą. Klinikinėje praktikoje vertinant naujo diagnostikos metodo įdiegimo galimybes, paprastai jis lyginamas su jau naudojamu metodu. Palyginimui dažniausiai naudojamas plačiausiai paplitęs regresinės analizės metodas. Dabar tyrimo duomenims palyginti D. G. Altman ir J. M. Bland pasiūlyta Bland–Altman statistinė analizė.

Tiriamųjų kontingentas ir metodai. Į tyrimą įtraukti 34 ligoniai, iš jų 20 (58,8 proc.) vyrų ir 14 (41,2 proc.) moterų. Prospektyvioji studija atlikta siekiant palyginti du klinikinėje praktikoje naudojamus hemodinamikos tyrimo metodus – tai intermituojančiąją termodiliuciją ir impedanso kardiografiją. Širdies minutinis tūris ligoniams, susirgusiems ūminiu miokardo infarktu, dviem hemodinamikos tyrimo metodais vertintas sinchroniškai. Straipsnyje pateikiamas statistinis duomenų vertinimas atliktas taikant regresinę analizę ir jau statistiniams tyrimams pradėtu naudoti alternatyviu Bland–Altman analizės būdu.

Rezultatai. Tyrimo metu atlikti poriniai hemodinamikos rodiklių matavimai pradėjus hemodinamikos stebėseną ir 30 – pagerėjus ar stabilizavusis ligonių būklei. Koreliacijos koeficientas tarp hemodinamikos tyrimo metodų svyravo nuo 0,37 iki 0,98. Hemodinamikos rodikliai lyginti taikant Bland–Altman grafinę analizę.

Išvados. Bland–Altman analizė yra tinkamas būdas dviejų skirtingų tyrimo metodų, naudojamų klinikinėje praktikoje, palyginimui. Mūsų tyrimo duomenimis, impedanso kardiografija gali būti sėkmingai taikoma nekomplikuotos eigos ūminiu miokardo infarktu sergančių ligonių hemodinamikos rodiklių stebėsenai.

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