Impedance Cardiography for Demonstrating Procedural Efficacy of Percutaneous Mitral Balloon Valvuloplasty

Perkütan Mitral Balon Valvuloplastinin Etkinliğini Değerlendirmede Empedans Kardiyografinin Kullanımı

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ABSTRACT Objective: Impedance Cardiography (ICG) method, facilitates measuring hemodynamic parameters indirectly by recording thoracic impedance variations induced by cyclic changes in blood flow. The aim of this study is to evaluate alterations in hemodynamic parameters obtained by impedance cardiography (ICG) in addition to conventional echocardiographic and catheterization data after percutaneous mitral balloon valvuloplasty (PMBV). **Material and Methods:** 18 patients with severe rheumatic mitral stenosis to whom PMBV had been performed were included in this study. Impedance cardiographic measurements were performed in addition to routine echocardiographic examination and invasive left atrial and pulmonary arterial pressure recordings before and after the procedure. Cardiac output was calculated with direct Fick method before PMBV. Average values of several measurements were used to obtain the most accurate results for atrial fibrillation patients in the study group. **Results:** Following successful PMBV, in impedance cardiographic evaluation an increase in cardiac output (4.69±1.46 and 5.68±1.3 l/min, before and after PMBV, respectively, p<0.001) and cardiac index (2.72±0.81 and 3.29±0.73 l/min/m^2, before and after PMBV, respectively, p<0.001) an evident prolongation in ejection period (246.8±40.3 and 275.2±32.1 msec, before and after PMBV, respectively, p<0.001); and a statistically significant reduction in pre-ejection period (103.7±41.8 and 82.7±16.8 msec, before and after PMBV, respectively, p=0.033), and thoracic fluid content (34.3±11.2 and 27.7±5.31/kΩ, before and after PMBV, respectively, p=0.037) was observed. There was a strong correlation between preprocedural cardiac output calculations of ICG and direct Fick method (r:0.89, p<0.001). **Conclusion:** In addition to the conventional methods, serial recordings of impedance cardiographic outputs may yield beneficial information for the assessment of PMBV efficacy. As a non-invasive and easily applicable method, it might be utilized during in-hospital follow-up.

Key Words: Cardiography, impedance; mitral valve stenosis; mitral valve annuloplasty

ÖZET Amaç: Empedans kardiyografi (EmKG), atımdan atıma değişen kan akımının oluşturduğu göğüs empedans değişikliklerini kaydederek hemodinamik parametrelerin dolaylı olarak ölçülmesine imkân tanıyan bir yöntemdir. Bu çalışmada, perkütan mitral balon valvuloplasti (PMBV) sonrası rutin olarak değerlendirilen ekokardiyografi ve kateterizasyon verilerine ek olarak; EmKG ile elde edilen hemodinamik göstergelerdeki değişimlerin incelenmesi amaçlandı. **Gereç ve Yöntemler:** Çalışmaya PMBV uygulanan 18 ciddi mitral darlığı hastası alındı. İşlem öncesi ve sonrasında, rutin ekokardiyografik inceleme ve invaziv sol atriyum ve pulmoner arter basınç kayıtlarına ek olarak EmKG ölçümleri yapıldı. PMBV öncesi kardiyak debi Fick yöntemiyle hesaplandı. Çalışma grubundaki atriyal fibrilasyon hastalarında ise doğruya en yakın sonucu elde edebilmek için tekrarlayan ölçümlerin ortalaması kullanıldı. **Bulgular:** Başarılı PMBV sonrası, EmKG değerlendirmesinde kardiyak debi (4,69±1,46; 5,68±1,3 l/dk; PBMV öncesi ve sonrası, sırasıyla p<0,001) ve kardiyak indekste (2,72±0,81; 3,29±0,73 l/dk/m^2; öncesi ve sonrası, sırasıyla p<0,001) belirgin artış; ejeksiyon süresinde aşikar bir uzama (246,8±40,3; 275,2±32,1 ms; öncesi ve sonrası, sırasıyla p<0,001); ve preejeksiyon süresi (103,7±41,8; 82,7±16,8 ms; öncesi ve sonrası, sırasıyla p=0,033) ve torasik sıvı içeriğinde (34,3±11,2; 27,7±5,31/kΩ; öncesi ve sonrası, sırasıyla p=0,037) istatiksel olarak anlamlı bir azalma söz konusuydu. İşlem öncesi yapılan EmKG ölçümlerinde elde edilen kardiyak debi değerleri ile Fick yöntemiyle ölçülen değerler arasında güçlü bir korelasyon saptandı (r:0,89; p<0,001). **Sonuç:** EmKG ölçümleriyle elde edilen verilerin takibi, PMBV'nin başarısını değerlendirmede diğer standart yöntemlere ek olarak faydalı bilgiler sunabilir. Non-invaziv ve kolay uygulanabilir olması dolayısıyla hastane içi takipte kullanılabilir.

Anahtar Kelimeler: Kardiyografi, impedans; mitral kapak darlığı; mitral kapak annuloplastisi

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Mitral stenosis was diagnosed in 0.1% of participants at a population-based study (higher in developing countries due to increased prevalence of rheumatic heart disease) and percutaneous mitral balloon valvuloplasty (PMBV), if applicable, is the preferred option of managing severe mitral stenosis.[1,2] Conventional transthoracic and transesophageal echocardiography, invasive left atrial pressure, pulmonary arterial pressure and cardiac output measurements are widely used diagnostic tools to assess the success of PMBV.

In 1870, Fick described a method to estimate cardiac output in humans. Fick postulated that oxygen uptake in the lungs is entirely transferred to the blood. Therefore, cardiac output can be calculated as the ratio between oxygen consumption (VO_2) and arteriovenous difference in oxygen ($AVDO_2$).

Fick equation: $CO = VO_2/AVDO_2$

This estimation is accurate when the hemodynamic status is sufficiently stable to allow constant gas diffusion during the mean transit time of blood through the lungs.[3]

Impedance cardiography (ICG) is designed to measure resistance of tissues to flow and alterations of these during dynamic processes like respiration and cardiac cycle. Thus it is possible to calculate fundamental parameters of hemodynamics by formulas.[4] As mentioned above, ICG is a unique method, fascilitating direct measurement of blood flow instead of utilizing pressure recordings.[5] There are certain investigations readily performed with different concepts, validating ICG in various cardiovascular diseases like acute and chronic heart failure, acute myocardial infarction and valvulopathies.[6-9]

In this study we aimed to determine acute hemodynamic alterations before and after PMBV with ICG in severe mitral stenosis.

MATERIAL AND METHODS

Eighteen consecutive female patients with severe mitral stenosis undergoing PMBV in Kartal Koşuyolu Yuksek Ihtisas Training and Research Hospital were included. The mean age of our study population was 43.7 ± 11.4 years and 5 patients had atrial fibrillation (Table 1). All individuals were evaluated with transthoracic and transesophageal echocardiography for clinical and anatomical eligibility before the procedure. Individuals with characteristics that may cause confusion for impedance measurements like left ventricular systolic dysfunction, severe pulmonary hypertension (mean pulmonary artery pressure >40 mmHg), extremes of body weight and significant aortic valve insufficiency were excluded.

Impedance cardiographic measurements were performed before and 24 hours after the procedure. Planimetric mitral valve area (MVApln) and transvalvular gradients were measured before and 24 hours after the procedure and also, left atrial and pulmonary arterial pressures were recorded just before and immediately after PMBV. Before the procedure cardiac output (CO) was measured invasively and calculated by using the Fick formula. Oral and written informed consents were received from all individuals and the study protocol was approved by our institution's local ethical committee.

BALLOON VALVULOPLASTY AND CARDIAC CATHETERISATION

Right common femoral artery and vein were used for vascular access. 6F pigtail catheters were used for arterial and venous blood sampling before the procedure and CO was calculated. Left atrial and pulmonary arterial pressure tracings were also recorded before and after the procedure using fluid filled 6F pigtail catheters. PMBV was performed by

TABLE 1: Clinical characteristics.

Age (years, mean±SE)	43.7±2.7
BSA (m^2, mean±SE)	1.70±0.35
Rhythm	
SR (%)	13 (72.2%)
AF (%)	5 (27.8%)
NYHA Class	
Class II (%)	14 (77.8%)
Class III (%)	4 (22.2%)

AF: Atrial Fibrillation; BSA: Body Surface Area; F: Female; M: Male; NYHA: New York Heart Association; SD: Standard Deviation; SR: Sinus Rhythm.

the transseptal approach using Inoue balloon (Toray Medical Industries, Houston, TX, USA) technique.

ECHOCARDIOGRAPHIC EXAMINATION

All patients underwent transthoracic echocardiography (TTE) before and 24 hours after the procedure. With TTE (GE, VingMed System Five, Horten, Norway and 3.5 MHz transducer) peak and mean diastolic transmitral gradients were measured by continuous-wave Doppler echocardiography. Estimated valve areas were verified by using the area trace method in all patients. Mitral regurgitation was categorized as absent, mild, moderate, or severe using a combination of qualitative and quantitative parameters. Tricuspid regurgitation (TR) jet flow was assessed from the apical, subcostal, and parasternal views. Systolic pulmonary artery pressure (PAP) was measured with continuous-wave Doppler. The maximum peak TR velocity (V) recorded from any view was used to determine right ventricular systolic pressure with the simplified Bernoulli equation ($PAP = 4V^2 + RAP$). To estimate right atrial pressure, inferior vena cava diameter was measured from the subxiphoid long-axis view. Right atrial pressure was estimated using the caval respiratory index as described by Kircher et al.[10] Pulmonary artery systolic pressure was estimated from the sum of the transtricuspid gradient and right atrial pressure.

IMPEDANCE CARDIOGRAPHIC MEASUREMENTS

The device used at this study (BioZ® CardioDynamics, San Diego, CA), uses electric current stimulations (electrical bioimpedance) for identification of thoracic or body impedance variations induced by cyclic changes in blood flow caused by each heart beat.

Eight ICG electrodes were placed on the carotid arteries and area where midaxillary line intersects with an imaginery line traversing apex at anatomical position. An automatic sphigmomanometry was placed around right arm. Finally all of the cables for data input were attached to the monitor. Measurements were performed before and 24 hours after the procedure. In order to eliminate possible discrepancies caused by beat-to-beat variations in atrial fibrillation patients, five measurements were performed and average values were recorded. The values for CO, cardiac index (CI), ejection period (EP), preejection period (PEP), thoracic fluid content (TFC), left cardiac workload (LCW), systemic vascular resistance (SVR) which had been displayed on the monitor were noted.

ICG utilizes two-dimensional wave forms to estimate hemodynamic status, principally cardiac output. First derivative measures fluid velocity and most of the parameters mentioned in the text are calculated from this data by specific indices. Second derivative measures acceleration and acts as a complementary entity. It also provides accurate coupling with cardiac cycle. Three major waves A, S and O waves correspond to atrial contraction, ventricular systole and mitral valve opening respectively. A wave is absent in atrial fibrillation and may show significant variation during frequent premature contractions. S wave principally, demonstrates cardiac output and larger S waves indicate increased CO. O waves can be barely visible even in healthy young individuals and they are mostly related to diastolic parameters.[4,11]

Extremes of body height and weight, aortic valve insufficency and respiratory artifacts are some other factors that may alter accurate data collection.[4]

STATISTICAL ANALYSIS

Baseline characteristics were expressed as mean ± standard error (SE) for continuous variables, and percentages for categorical ones. Due to the limited sample size (n=18), non-parametric tests were used to compare variables. Pre-test and post-test variables within the study population were compared with the Wilcoxon signed rank test and the results were demonstrated on a table with the corresponding z and p values. The association between measurements of CO by direct Fick and ICG methods was tested by Spearman's correlation analysis. The results of the analysis were shown with a graphic and the corresponding rho and p values. Accuracy of the cardiac output measured by Fick and ICG methods were examined by the Bland and Altman analysis. A 2-tailed p value <0.05 was considered statistically significant. Statistical analysis was performed using MedCalc programme (MedCalc Software, Mariakerke, Belgium).

RESULTS

PMBV was performed by using Inoue balloon with transseptal approach and no complications were observed. Upon echocardiographic and invasive hemodynamic measures; PMBV might be considered as efficacious for all study patients; namely significant decrease in left atrial pressure, invasive pulmonary artery pressure recordings and echocardiographic gradients; and a rise in planimetric valve area were observed (Table 2). Only two patients were found to have moderate mitral regurgitation postprocedurally; others had trivial or mild regurgitation.

In terms of impedance cardiographic measurements before and after the procedure; a significant increase of CO and CI; an evident prolongation in EP; a shortened PEP and a significant decrease in TFC were observed. Reduction of LCW and SVR did not reach statistical significance (Table 3).

According to Spearman's correlation; there was a strong relationship between cardiac output measurements obtained by ICG and direct Fick method (Spearman's rho=0.89, p < 0.001). Correlations between the cardiac output measured by Fick and ICG were also summarized in Figure 1. The Bland-Altman plots revealed a good agreement of CO measured by direct Fick method and ICG (mean difference 0.69±1.09, 95% CI [0.153-1.237]) (Figure 2).

DISCUSSION

Impedance cardiography is a method, which had been used for experimental purposes in early 1960s; and several studies evaluating diagnostic value, validation, variability, cost-effectiveness and contribution to prognosis for diseases including coronary

TABLE 2: Echocardiographic valvular measurements and invasice left atrial and pulmonary artery pressure recordings before and after the procedure.

	Pre-PMBV	Post-PMBV	p value	z score
MVApln (cm^2, mean±SD)	1.14±0.03	1.81±0.04	<0.001 •	-3.75
MEAN GRADIENT, (mmHg, mean±SD)	14.6±1.3	5.2±0.5	<0.001 •	-3.73
LAP, (mmHg, mean±SD)	26.6±1.6	15.9±1.1	<0.001 •	-3.73
PAPsystolic, (mmHg, mean±SD)	57.8±2.9	42±1.7	<0.001 •	-3.63
PAPmean, (mmHg, mean±SD)	38.5±2.2	27.6±1.4	<0.001 •	-3.73
PAPdiastolic, (mmHg, mean±SD)	26±2.2	18.1±1.5	0.001 •	-3.47

LAP: Left atrial pressure; MVApln: Planimetric mitral valve area; PAP: Pulmonary arterial pressure; SD: Standard Deviation.
• Statistical significance.

TABLE 3: Impedance cardiography measurements before and after the procedure.

	Pre-PMBV	Post-PMBV	p value	z score
CO, (l/min, mean±SD)	4.69±0.35	5.68±0.33	<0.001 •	-3.73
CI, (l/min/m^2, mean±SD)	2.72±0,19	3.29±0.17	<0.001 •	-3.73
EP, (msec, mean±SD)	246.8±9.5	275.2±7.6	<0.001 •	-3.53
PEP, (msec, mean±SD)	103.7±9.9	82.7±3.4	0.003 •	-2.98
TFC, (1/kΩ, mean±SD)	34.3±2.6	27.7±1.2	0.022 •	-2.29
LCW, (kg m, mean±SD)	5.8±0.4	5.3±0.4	0.162	-1.4
SVR, (dynes sec/cm^5, mean±SD)	1415.9±157.2	1256.8±88.7	0.396	-0.85

CO: Cardiac output; CI: Cardiac index; EP: Ejection period; PEP: Pre-ejection period; SD: Standard Deviation; TFC: Thoracic fluid content; LCW: Left cardiac workload; SVR: Systemic vascular resistance.
• Statistical significance.

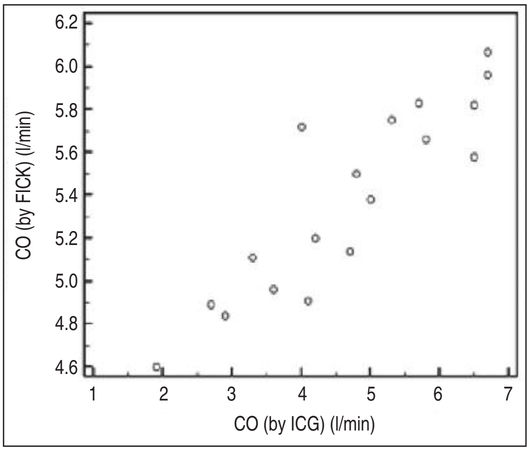

FIGURE 1: Correlation between direct Fick and impedance cardiography measurements of cardiac output.
CO: Cardiac output; ICG: Impedance cardiography; SD: Standard deviation.

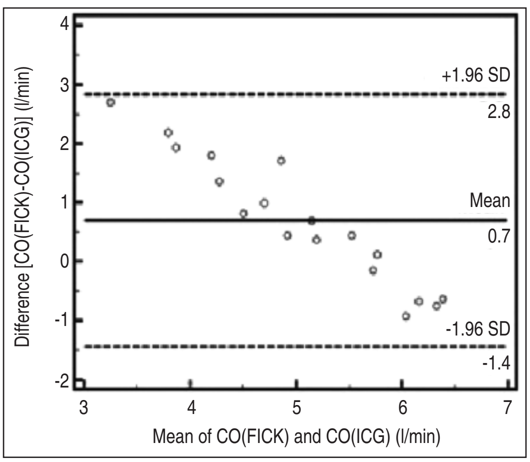

FIGURE 2: Bland-Altman analysis of differences between cardiac output measured by direct Fick and impedance cardiogarphy.
CO: Cardiac output; ICG: Impedance cardiography; SD: Standar deviation.

artery disease, congestive heart failure, systemic hypertension, pulmonary hypertension and various valvular pathologies had been published since then.[6,8,11-14]

In the last decade, ICG had been utilized for monitoring heart failure and tailoring the therapy especially after combination with implantable devices.[15-17]

But the main purpose for utilization of ICG in most of the publications is to estimate cardiac output. At a relatively former article comparing CO measured by ICG with direct Fick method as a part of diagnostic cardiac catheterisation correlation seems tremendous (r:0,93).[18] At publications in early 2000's, it ranges between 0,76 to 0,89.[19-21] Greenberg et al., evaluated the validity of BioZ® CardioDynamics ICG device in heart failure patients and found a close correlation between CO values obtained by ICG and thermodilution method.[22] At the largest randomised trial on heart failure patients -the BIG study as a part of ESCAPE study- only a modest correlation was observed between two techniques.[23] Results of our sample population affirm the strong relationship between invasive and ICG measurements of cardiac output.

There are just a few studies investigating the role of ICG in valvular heart diseases. Aortic valve pathologies, especially significant regurgitation, are known to influence ICG waveforms and decreases the reliability of cardiac output measurements.[24] Thus, patients with aortic insufficiency are invariably excluded in ICG studies. Significant aortic valve disease was also established as a specific contraindication for PMBV and these patients had already been eliminated in the first step of patient selection.

In a study comparing patients who have mitral regurgitation (MR) with healthy individuals, authors concluded that even in MR patients ICG can estimate CO reliably although degree of agreement was decreased.[24]

In comparison with healthy individuals, patients with mitral stenosis are known to have lower stroke volume, consequently cardiac output and cardiac index values measured by ICG.[7]

Same group of authors published another report for mitral valve diseases and defined the restoration of O wave abnormalities after corrective surgery both for stenosis and regurgitation. They also stated that CO values were significantly lower preoperatively in mitral stenosis patients as compared with control group and normalization of these values were observed after surgery.[25]

As expected; in our sample population, an evident increase in CO and related parameters at early stages were observed. And also, due to enhanced flow passing through the expanded valvular orifice, left ventricular filling and ejection periods were altered.

LIMITATIONS

Main limitation of the study is definitely the size of the study population. Despite this disadvantage, statistically significant values were reached. Fick method was used for invasive determination of CO instead of thermodilution for timesaving. Therefore, concerning possible acute procedure-related changes in hemoglobin levels, measurement of CO indirectly by Fick method after the procedure was considered to be unreliable and was not performed.

Another issue is obtaining ICG data in atrial fibrillation patients. A clear signal recording may not be possible in these patients or when frequent premature beats exist. However, in a study comparing ICG with inert gas rebreathing against echocardiographic examination for estimation of CO noninvasively, ICG was found to be superior and acceptable aggreement with echocardiographic measurements was observed.[26] We repeated the examination until we observed at least five clear waveforms for 5 patients with atrial fibrillation in our sample group. We used average values of these serial recordings for statistical evaluation to overcome this predefined adversity.

CONCLUSION

This study defines alterations of the hemodynamic data obtained by ICG before and after PMBV. In addition to the echocardiographic findings and invasive measurements; serial recordings of ICG outputs may yield beneficial and additional information for the assessment of PMBV efficacy.

To the best of our knowledge, hemodynamic changes with ICG after a percutaneous intervention to stenotic valve has not been investigated so far. This is the first study demonstrating the alterations of CO and other parameters calculated by ICG after successful PMBV.

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