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Correlation between echocardiographic and hemodynamic variables in cardiothoracic intensive care unit

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Highlights:

- Left ventricular systolic dysfunction is frequent in cardiothoracic critically ill patients
- Total isovolumic time and MAPSE correlate with the hemodynamic profile of the patients
- Left ventricular ejection fraction does not correlate with hemodynamics

Title: Correlation between echocardiographic and hemodynamic variables in cardiothoracic intensive care unit

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GT, SP contributed to study design, data collection, data interpretation, and writing the manuscript. VD, CK, FC, BJ, ABP, AV contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

The study was performed at Adult Intensive Care, Royal Brompton Hospital, London UK

All the authors have no conflicts to declare.

Declarations of interest: none

Abstract

Objectives: the echocardiographic indices have not been validated in critically ill population. We investigated the correlation between some echocardiographic and hemodynamics parameters.

Design: Prospective Spontaneous non-interventional observational study.

Setting: Adult cardiothoracic intensive care unit, single center (Royal Brompton Hospital, London UK).

Participants: Consecutive adult patients admitted to cardiothoracic intensive care unit for severe respiratory failure, primary cardio-circulatory failure and post-aortic surgery.

Interventions: Clinical, hemodynamic parameters (stroke volume – SV, cardiac output – CO, mean arterial pressure – MAP, and cardiac power index – CPI) and echocardiographic indices of ventricular function (left ventricular total isovolumic time – t-IVT, mitral annular plane systolic excursion – MAPSE, and left ventricular fraction – LVEF) were evaluated offline.

Measurements and main results: 117 patients were studied (age 57.2 ± 19; 60.6% male). t-IVT showed an inverse correlation with SV, CO, MAP and CPI (respectively r: -67%; -38%; -45%; -51%). MAPSE exhibited a positive correlation with SV, CO, MAP and CPI (respectively r: 43%; 44%; 34%; 31%). LVEF did not show any correlation. In the multivariate analysis the association of t-IVT and hemodynamics was confirmed for SV, CO, MAP and CPI with the highest partial correlation between t-IVT and MAP (R = -58%).

Conclusions MAPSE and t-IVT are two reproducible and reliable echocardiographic indices of systolic function and ventricular efficacy associated with hemodynamic variables in cardiothoracic critically ill patients, while LVEF did not show any correlation.

Key Words: echocardiography – hemodynamics – left ventricular longitudinal function – total isovolumic time

Introduction

Left ventricular (LV) dysfunction and subsequent cardiovascular instability is a significant major cause of morbidity and mortality in intensive care unit (ICU)[1-3]. Echocardiography has widely spread as haemodynamic diagnostic and monitoring tool in critical care settings over the last decades. However, the echocardiographic indices (mainly left ventricular ejection fraction – LVEF) currently used to assess cardiac function and evaluate its response to therapy in ICU, have been adopted from the cardiology outpatient population without being specifically validated in the critically ill population[4, 5]. Stroke volume (SV), cardiac output (CO) and mean arterial pressure (MAP) are some of the indices daily used to evaluate haemodynamic profile at the bedside. Cardiac power index (CPI), which is the product of the flow and the mean arterial pressure, reflects the hydraulic energy of the heart. Both CPI and MAP have been demonstrated to be the strongest indices associate with mortality in patients admitted for cardiogenic shock[6-8].

Mitral annular plane systolic excursion (MAPSE), measured by M-mode echocardiography, is an easy, reliable, and highly reproducible method for the assessment of left ventricular longitudinal function[9-11] even in patients with poor image quality[12]. Furthermore, previous studies have shown that longitudinal function is the earliest and more sensitive indicator of systolic dysfunction[13-15].

Total isovolumic time (t-IVT), the time when the left ventricle (LV) neither ejects nor fills, represents a specific parameter of systo-diastolic interaction and of ventricular efficiency[16].

We sought to determine whether any association exists between echocardiographic parameters (LVEF, MAPSE and t-IVT) and common haemodynamic indices (mean arterial pressure – MAP, stroke volume – SV, cardiac output – CO, and cardiac power index – CPI).

Material and Methods

Subjects

The present study has been approved by the Royal Brompton Hospital NHS foundation Trust ethical committee (IRB approval number 196075). We analysed data from consecutive patients who were admitted to a cardiothoracic adult ICU over a period of 6 months and required a comprehensive echocardiography during the admission.

We divided the enrolled patients in three groups according to the reason for ICU admission: respiratory failure, cardio-circulatory failure and post aortic valve surgery. Patients with acute *cor pulmonale*, congenital heart disease and mitral valve diseases were excluded.

Demographic data, clinical profiles, biochemical data and therapeutic regimens of patients were extracted from the ICU patient data managing system (ICIP® Philips Medical Systems).

Echocardiography

All echocardiographic exams were performed using transthoracic or transoesophageal echocardiography (Philips iE33; Bothell, WA 98041 USA; probe S5-1 Sector Array Transducer or X7-2t Philips, Bothell, WA 98041 USA). Comprehensive echocardiographic studies were performed in accordance with current European Society of Echocardiography guidelines[17, 18] and were reviewed by two independent physicians fully certified in echocardiography blinded to the clinical condition of the patients. All Doppler measurements were recorded at end-expiration and analysed and averaged over 3 cardiac cycles, when in sinus rhythm, and 5-10 cycles, when in atrial fibrillation. All recordings were acquired at a paper speed of 100 mm/s, together with an ECG (lead II). According to the current guidelines, right ventricle (RV) dysfunction was defined as tricuspid annular plane systolic excursion (TAPSE) < 16 mm[19]. TAPSE was measures in deep transgastric view in case TOE was performed[20].

The SV measurement was obtained multiplying the cross sectional area of the left ventricular outflow tract (LVOT) in parasternal long axis view by the LV velocity time integral (VTI) in 4 chambers view[21]. The cardiac output was calculated as the product of heart rate (HR) and SV and it was then indexed by the BSA to obtain the cardiac index (CI)[22].

CPI was calculated as [MAP * (CO/BSA)]/451[6].

LV ejection time (LVET) was measured as the interval between the onset of forward aortic flow and the onset of the aortic valve closure artefact[16]. Pulsed-wave Doppler was used to record mitral inflow at the mitral valve leaflet tips[23]. Left ventricular filling time (LVFT) was measured from the onset of the E wave to the end of the A wave or as the duration of E wave when patients were in atrial fibrillation. Total ejection (t-ET) and filling times (t-FT) were derived as the product of the corresponding time interval and heart rate and were expressed as seconds per minute (i.e. t-ET = [(60,000/RR)*ET]/1,000 and t-FT = [(60,000/RR)*FT]/1,000). t-IVT (also in sec/min) was calculated as 60 – (t-ET + t-FT)[16] (Figure 1). t-IVT normal value is < 12 sec/min (Duncan AM, O'Sullivan CA, Gibson DG, Henein MY. Electromechanical interrelations during dobutamine stress in normal subjects and patients with coronary artery disease: comparison of changes in activation and inotropic state.[24]

Tissue Doppler (TDI) was applied to measure mitral annular early (e’) velocities at the lateral and septal annulus. E/e’ ratios were computed by using the average of the lateral and septal e’.

Mitral annular plane systolic excursion (MAPSE) was determined in two dimensionally guided M-mode on the four portion of the mitral annulus (septal, lateral, inferior and anterior), as described previously[9]. MAPSE was measured as the distance, in millimetres (mm), covered by the atrioventricular plane from the lowest point (corresponding to the onset of contraction) to the peak of the curve (corresponding to the end of contraction and the point closest to the apex)[14]. Left ventricular ejection fraction (LVEF) was obtained using biplane Simpson’s methodology[22].

Transthoracic echocardiography was performed, if the quality of the pictures was insufficient a transoesophageal echocardiography was carried out.

The echocardiography was performed according to the treating physician request

Statistics

Continuous variables are presented as mean ± SD or median and 25^{th}-75^{th} percentiles; categorical variables as counts and percentages. They are compared between reason for admission groups with the one-way analysis of variance (ANOVA) test and the Fisher exact test, respectively.

We assessed the association of MAPSE (the worst one among sites), t-IVT and LVEF with MAP and echocardiographic-derived haemodynamic measurements (SV, CO, and CPI). We used a generalized linear regression model. We computed Huber-White robust standard errors to account for heteroscedasticity. We adjusted for reason for admission. We tested the effect modification by reason for admission by including its interaction with the echo measurement in the model. Also, we carried out a multivariable analysis to adjust the association for the possible confounding of reason for admission, age, left bundle branch block (LBBB) and left ventricle ejection fraction. We computed the (partial) correlation coefficient and its 95% confidence interval (95%CI) from the model. We verified model assumptions with a residual vs. fitted plot. We report the model explained variation to assess model performance.

We analysed data using the statistical package Stata/IC 15.1, StataCorp, College Station,TX, USA). A 2-sided P value less than 0.05 was considered statistically significant. We apply the Bonferroni correction for post-hoc comparison between reason for admission groups ($p < 0.017$ for significance).

We compared hemodynamic and echocardiographic variables according to survival status at 30 days with the Student t test; we computed the mean difference between groups with 95%CI.

Results

Reproducibility

The operator intra-observer variability for MAPSE and t-IVT was respectively 0.996 [(95%CI of 0.998-0.999)] and 0.998 [(95%CI of 0.998-0.999)] and the inter-observer variability was 0.997 [95% CI of 0.97 (0.94-0.99)].

We analysed data from 117 patients (age 57.2 ± 19), of whom 71 (60.6%) were male.

Fifty-seven patients were admitted for respiratory failure (of whom 28 on veno-venous extracorporeal support); 35 patients for cardio-circulatory failure and 25 patients after aortic surgery. Patient features according to reason of admission with group comparison are summarized in Table 1.

The mean LVEF was 43% (± 10.3%) and the mean LV end-diastolic diameter was 4.85 (± 1)cm. 7 patients had atrial fibrillation (5.9%), 15 (12.8%) had left bundle branch block (LBBB) and 6 (5.1%) had right bundle branch block (RBBB). 95 patients (81%) were discharged alive (respiratory: 79%, cardiac failure: 80%, post-surgery: 88%, p = 0.68).

Echocardiography and haemodynamics

Regression models for the association between tested echocardiographic parameters and echocardiographic-derived haemodynamic measures, adjusted for the reason for admission, are shown in Table 2.

t-IVT and MAPSE were inversely correlated (r = - 57% [95%CI -68% to -43%]; $p < 0.001$).

t-IVT demonstrated a significant inverse association with MAP, SV, CO and CPI ($p < 0.001$).

MAPSE showed a significant, though moderate positive association with MAP, SV, CO and CPI ($p < 0.001$).

The LVEF did not correlate with any of the considered haemodynamic parameters (Table 2). We did not find effect modification adjusting by the reason for admission (non-significant p value for interaction, Table 2).

Multivariate analysis

The results of multivariate analysis are shown in Figure 2. t-IVT confirmed the association with all the haemodynamic parameters at the multivariable models for MAP, SV CO and CPI. Whereas MAPSE confirmed a significant weak correlation with SV only. All models were adjusted for the reason for admission, the presence of LBBB, age and LVEF. Based on the explained variation, the model better explaining the data was the model for MAP (explained variation 49%). This model also elicited the strongest partial correlation for t-IVT (R = - 58%).

Outcome

The 30-days mortality was 18,8% (22 patients). T-IVT and MAPSE were both associated with mortality ($p < 0.0001$; respectively [95% CI 10-12.2 and 0.71-0.82]) whereas LVEF was not (p 0.91, [95% CI 41.4 - 45.2]). Additionally, although CO and SV were also associated with mortality (respectively, p 0.0003 [95% CI 49.1 – 56.5] and p 0.003 [95% CI 4.5 -5.2]), MAP and CPI exhibited the strongest correlation ($p < 0.0001$; respectively [95% CI 70.49-75.56 and 0.42-0.53])

Discussion

This is the first study investigating the association between left ventricular echocardiographic parameters and haemodynamic indices in a mixed population composed of critically ill cardio-respiratory patients.

Left ventricular ejection fraction (LVEF) function has been used as marker of systolic function despite it is burdened by a number of potentially biases, including tachycardia, asynchrony and volume conditions, which are frequently seen in ICU patients. Additionally, it is not the earlier index of LV dysfunction. On the contrary longitudinal fibres are the most sensitive to perfusion mismatch[13] as they are mainly found at the level of subendocardium, subepicardium and in the papillary muscles[25, 26] which could represent the strict link between longitudinal function and the MAP, being the coronary perfusion highly dependent by the mean perfusion pressure.

Additionaly, an abnormality of longitudinal systolic function may entail an elongation of systolic contraction and therefore an impairment of diastolic filling time[14, 27]. This mechanism, named post-ejectional shortening[25], may be easily detected by MAPSE and measured by pulse wave Doppler. t-IVT measuring the ejection and filling intervals is the direct expression of such mechanism which turn into an ineffective ventricular efficiency[16, 24]. t-IVT was seen to be related to limitation of cardiac output and oxygen consumption (V'O_2) at peak stress during dobutamine administration in patients with dilated cardiomyopathy (DCM) and coronary artery disease (CAD), resulting the most sensitive indicator of perfusion mismatch[16, 24]. It has also shown to be associated with SV, CO and cardiac index (CI) at different chronotropic status in a small series of patient after cardiac surgery[28].

MAPSE and t-IVT have shown a strong association with 30-days mortality as well as MAP and CPI, although the sample size and the nature of the investigation warrant the cautious interpretation of outcome results.

Recently longitudinal strain echocardiography has gained attention for its reliability and accuracy in detecting early systolic abnormalities[29, 30]. Unfortunately, strain requires high level competency and equipment narrowing its use in ICU settings[29] in contrast to MAPSE that has shown to be feasible, reproducible and able to reflect significantly ventricular function [9] also in the critically ill population[28, 31]

Despite the evidence of t-IVT and MAPSE sensitivity in early detecting ventricular abnormalities, there were no data regarding the integration of these two parameters together and their association to haemodynamic indices, including cardiac power index (CPI), which was proven as one of the most important haemodynamic variables in the assessment of haemodynamic profile and separately associated with 28-day mortality in patients with cardiogenic shock[6, 8, 32]

Echocardiography, is established as the mandatory diagnostic tool for the diagnosis of haemodynamic failure[6, 8, 32-34]. The applicability of early indices of ventricular dysfunction in a mixed population in the acute setting, is promising, although it would need further validation.

Limitations

This study has several limitations: 1) the heterogeneous population with limited sample size; 2) the data recording have been done once during the admission and no repeated measures have been analysed; 3) SV, CO and CI have been measured using echocardiography, although good correlation has been demonstrated[35]; 4)for the purpose of the study, patients with acute *cor pulmonale* have been excluded from the study as they would have represented a confounding factor.

Conclusion

MAPSE and t-IVT are two reproducible and reliable echocardiographic indices of systolic function and ventricular efficacy associated with SV, CO, MAP and CPI in cardio-thoracic critically ill patients, while LVEF did not show any correlation.

Figure legends

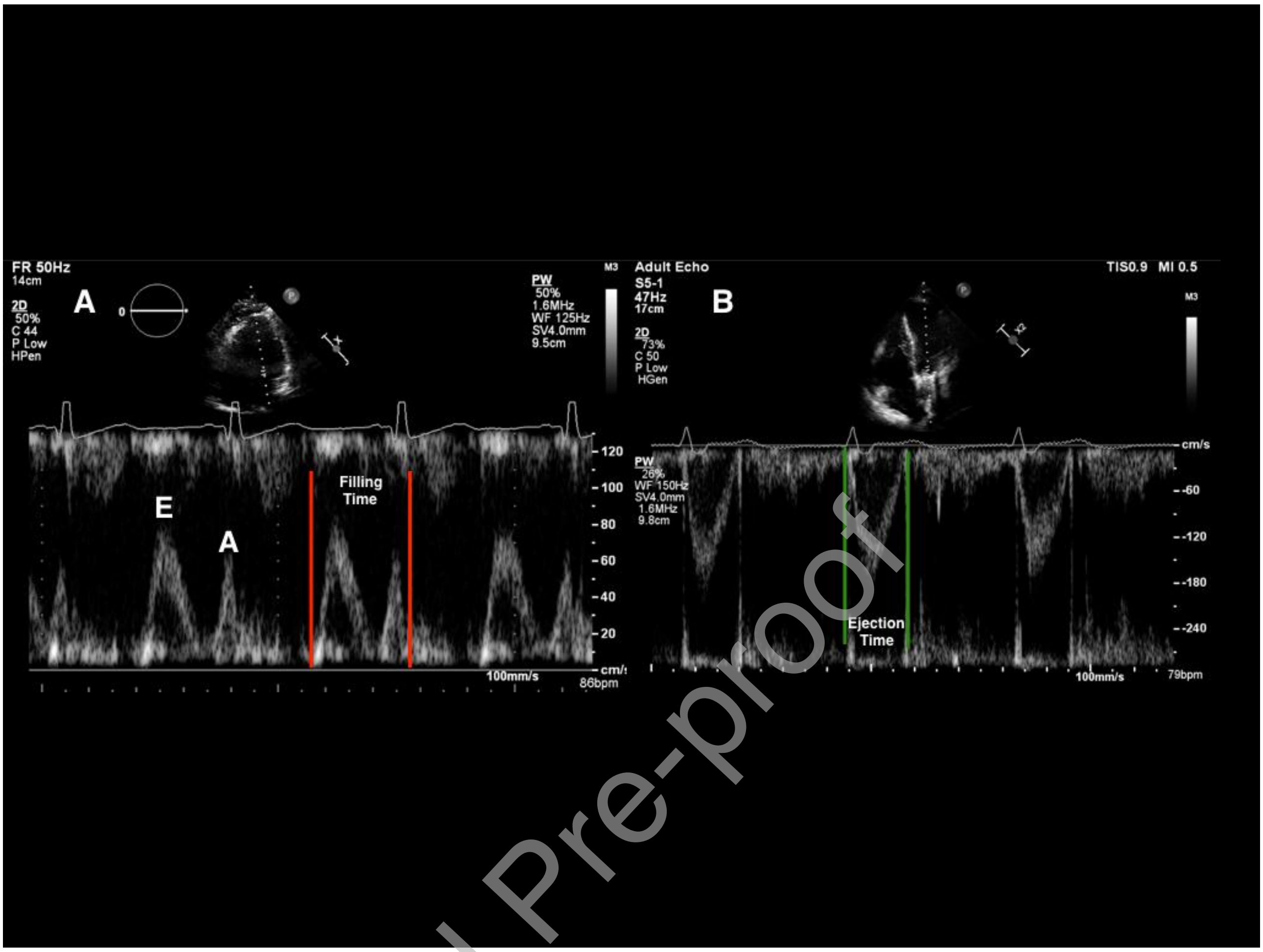

Figure 1. Total isovolumic time measurement. Transthoracic echocardiography.

A) Trans-mitral filling sampled with pulsed-wave Doppler in 4 chambers view. The filling time (red lines) is measured from the onset of the protodiastolic (E wave) to the telediastolic period (A wave) and the total filling time (t-FT) is calculated, measuring the RR interval on the ECG trace, using the following formula: t-FT= [(60000/RR)*FT]/1000.

B) Aortic ejection ejection period sampled with pulsed-wave Doppler. The ejection time (ET) is measured from the onset of the aortic flow to the aortic closure artifact (green line). Total Ejection Time (t-ET) is obtained, measuring the RR interval on the ECG trace, using the following formula: t-ET= [(60000/RR)*ET]/1000. The total isovolumic time is calculated as t-IVT (sec/min) = 60 – (t-FT + t-ET).

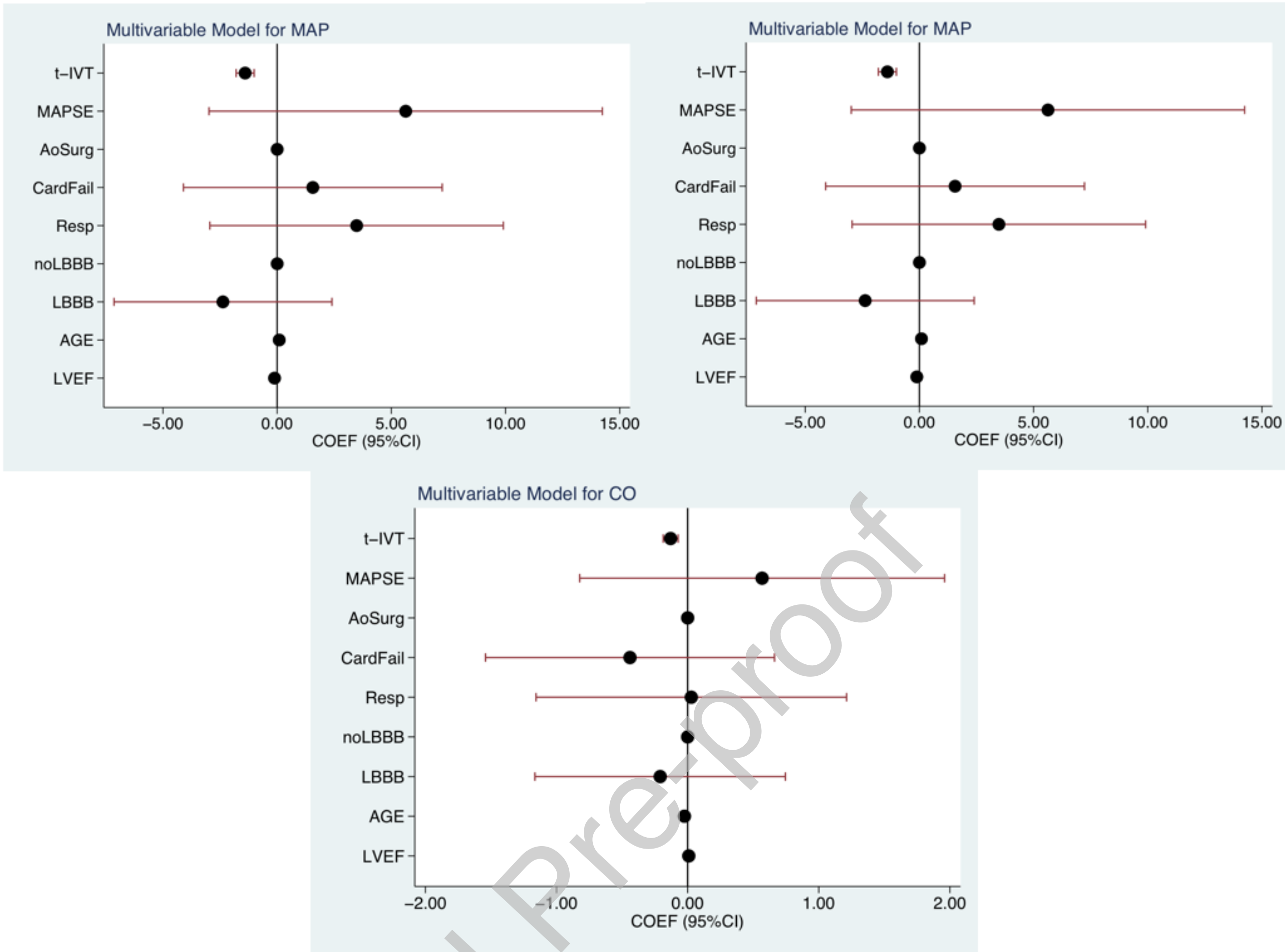

Figure 2. Multivariable models for t-IVT and MAPSE association with MAP, SV and CO. Regression coefficient are shown as dots together with their 95%CI (horizontal red lines). The variable for which the 95%CI line does not cross the null effect line (black vertical line at COEF=0) are significant at the 5% level.

A) Explained variation: 49%, model p < 0.001. Partial correlation with MAP 95%CI) of: t-IVT: -58% (-69% to -44%) p<0.001; MAPSE: 12% (-6% to 30%) p=0.198.

B) Explained variation: 30% , model p < 0.001. Partial correlation with SV (95%CI) of: t-IVT: -19% (-36% to -1%) p=0.027 MAPSE: 27% (10% to 43%) p=0.006

C) Explained variation: 31%, model p < 0.001. Partial correlation with CO (95%CI) of: t-IVT: -35% (-50% to -18%) p<0.001 MAPSE: 7% (-11% to 25%) p=0.420

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Table I - Patients characteristics according to the reason for admission

Characteristics	*Respiratory*	*Cardiac failure*	*Post-surgery*	*p value*
Age	61.5 (±19.2)	63.3 (±17.9)	51.6 (±18.17)	0.006
Male	17 (68%)	23 (66%)	31 (54%)	0.41°
BSA (m^2)	1.73 (± 0.5)	1.81 (± 0.3)	1.71 (±0.3)	0.28
QRS duration (ms)	91.45 (±25.4) *	109 (±37.2)	119.6 (± 36.2)*	0.009
LBBB	5 (20%)	6 (17%)	4 (7%)	0.17
LVEF (%)	46.04 (±10.2)	40.4 (±10.6)	41.28 (± 8.4)	0.019
t-IVT (sec/min)	10.48 (± 6.2)	12.36 (±5.7)	11.14 (± 6.1)	0.36
MAP (mmHg)	74.81 (± 14.7)	70.86 (± 13.1)	72.04 (± 12.5)	0.38
LV EDD (cm)	4.91 (± 0.7)	4.9 (± 1.2)	5.08 (±1)	0.73
MAPSE lateral (cm)	1 (±0.3)	0.81 (± 0.3)	0.9 (±0.2)	0.026
MAPSE septal (cm)	0.9 (±0.2)	0.73 (± 0.3)	0.72 (± 0.3)	0.038
MAPSE inferior (cm)	0.96 (± 0.2)*	0.77 (± 0.2)*	0.88 (± 0.2)	0.011
MAPSE anterior (cm)	1.03 (±0.3)	0.84 (± 0.3)	0.91 (± 0.2)	0.03
Worst MAPSE (cm)	0.83 (± 0.2)	0.67 (±0.2)	0.78 (± 0.2)	0.03
TAPSE	1.87 (±0.67)	1.32 (±0.68)	1.15 (±0.57)	0.001
MV E wave (cm/s)	0.86 (± 0.3)	0.99 (±0.3)	0.99 (± 0.3)	0.07
E/E’	9.68 (± 4.9)	15.59 (± 8.8)	15.81 (± 8.4)	< 0.001
LVOT VTI (cm)	17.96 (±4.3)	15.88 (± 5.5)	15.24 (± 5.9)	0.04
SV (ml)	58.62 (±17.8)*	45.79 (± 19.2) *	49.77 (±23.3)	0.009
CO (L/min)	5.39 (±1.9)	4.23 (± 1.7)	4.8 (±2.5)	0.033
CPI (W/m^2)	0.54 (± 0.28) *	0.39 (± 0.23) *	0.45 (±0.23)	0.008
SAPS II	40.93 (±15.7)	43.83 (± 20.6)	40.16 (±18.5)	0.68
APACHE II	16.2 (± 5.9)	16.1 (± 9.5)	14.2 (±7.1)	0.49

^ Kruskall Wallis test, unless otherwise specified (°Fisher exact test).

P value for the post-hoc comparison between classes of groups: * <0.017 after Bonferroni

BSA: Body Surface Area; LBBB : Left Bundle Branch Block; LVEF: Left Ventricular Ejection Fraction; t-IVT: total isovolumic time (seconds/minute); MAP: Mean Arterial

Pressure; LV EDD: Left Ventricular End-Diastolic Parameter; MAPSE: mitral Annular Pane Systolic Excursion at any site in the group; TAPSE: Tricuspidal Annular Pane Systolic Excursion; MV E wave: mitral valve early ventricular filling velocities; E/E’: ratio between mitral valve early diastolic filling and velocity respectively at transmitral Pulsed wave Doppler and Tissue Doppler imaging; LV VTI: Left Ventricular Velocity Time Intergal; SV: Stroke Volume; CO: Cardiac Output; CPI: cardiac power index; SAPS II: Simplified Acute Physiology Score; APACHE II: Acute Physiology and Chronic Health Disease Classification System

Table 2 - Partial correlation of echo and hemodynamic measurements. The analysis is adjusted for reason for admission

Tested variables	R % (95%CI)	p-value	Interaction with reason for admission p-value
MAP			
MAPSE	43 (27 to 57)	< 0.001	0.8
t-IVT	-67 (-73 to -56)	< 0.001	0.1
LVEF	-04 (-22 to 14)	0.711	0.5
SV			
MAPSE	44 (28 to 58)	<0.001	0.8
t-IVT	-38 (-52 to -21)	<0.001	0.5
LVEF	08 (-10 to 26)	0.421	0.7
CO			
MAPSE	34 (16 to 49)	<0.001	0.7
t-IVT	- 44 (-58 to -28)	<0.001	0.4
LVEF	06 (-12 to 24)	0.520	0.5
CPI			
MAPSE	36 (19 to 51)	<0.001	0.5
t-IVT	-51 (-64 to -37)	<0.001	0.4
LVEF	0.4 (17-18)	0.9	0.7

MAPSE: Mitral annulus Plane Systolic Excursion; t-IVT: total isovolumic time; LVEF: Left Ventricular Ejection Fraction; CPI: Cardiac power index