Influence of pneumoperitoneum on left ventricular filling pressures and NT-proBNP levels

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Abstract. – BACKGROUND: We recently demonstrated that pneumoperitoneum affects diastolic echocardiographic findings in healthy women scheduled for gynaecologic laparoscopy. No reports have been conducted in order to assess the echocardiographic consequences in hypertensive subjects during laparoscopic procedures.

AIM: The aim of this study was to evaluate Left Ventricular filling pressures in hypertensive women with and without diastolic dysfunction, combining the tissue Doppler imaging technique and the plasmatic levels of amino terminal proBNP.

MATERIALS AND METHODS: Doppler recordings of mitral inflow, tissue Doppler imaging of mitral annulus and N-terminal-proBNP plasmatic levels were obtained in 40 hypertensive women with or without diastolic dysfunction. Measurements were executed in awake patients (T0), after the induction of anesthesia (T1), 10 and 20 minutes after the creation of the pneumoperitoneum (T2 and T3, respectively) and at the end of the surgery (T4). Furthermore, we collected the last blood sample after 12 hours (T5).

RESULTS: The E/Ea ratio for the evaluation of left ventricular filling pressures were higher in the diastolic dysfunction group than in the non diastolic dysfunction and significantly increased after pneumoperitoneum. Pneumoperitoneum increased the plasmatic levels of natriuretic peptide in both groups. At the end of the procedure we did not observe any further significant alteration.

CONCLUSIONS: Pneumoperitoneum produces a consistent increase of ventricular filling pressures in a population of hypertensive patients with and without diastolic dysfunction. Moreover, there is a significant but transient rise in NT-proBNP after gas insufflation in both groups, most accentuated in the diastolic dysfunction group.

Key Words:
- Laparoscopy, Pneumoperitoneum, Echocardiography, Natriuretic peptides.

Introduction

Diastolic dysfunction (DD) is the sum total of a complex sequence of multiple interrelated events, including prolonged ventricular relaxation, loss of ventricular suction, increased myocardial fibrosis, and increased chamber stiffness, that result in symptoms of angina and dyspnea. Hypertension now day is a common causes of DD and it is responsible for a large amount of heart failure cases in a population-based sample. Doppler echocardiography is widely used for the non-invasive assessment of diastolic filling of the left ventricle. In the past, cardiac catheterization was required to determine the extent of diastolic dysfunction by direct measurement of left ventricular (LV) filling pressures.

Thanks to the improvements of non-invasive Doppler indices (such as tissue Doppler imaging (TDI) and transmirtal flow velocities) it has become practicable the non-invasive estimation of filling pressures in subsets of patients. TDI of the heart is a Doppler technique that measures the frequency of ultrasound returning from moving myocardium to estimate the velocity of the myocardial wall. TDI allows the determination of velocity and extent of mitral annular displacement in systole and diastole. The indices of relaxation are suitably related with the early diastolic velocity at the annulus (E’), and it is not influenced significantly by preload. Since mitral velocity E is preload dependent and E’ is related to LV relaxation, the ratio E/E’ can be used to estimate LV filling pressures. An E/E’ ratio =15 is highly specific for elevated left ventricular end diastolic pressure, whereas E/E’ = 10 is very specific for normal to low filling pressures. The combination of mitral annulus and mitral inflow velocities has been shown to provide better esti-
mates of LV filling pressures than other methods. Brain-natriuretic peptide (BNP) is a cardiac neurohormone secreted from the ventricles in response to ventricular volume expansion and pressure overload.\(^6\)\(^7\)

BNP levels may also reflect diastolic dysfunction.\(^8\)\(^9\)\(^10\) This hormone has become firmly established as a biomarker for heart failure diagnosis and prognosis across the spectrum of cardiovascular disease.\(^11\)\(^12\) The relationship between the B-type peptides and echocardiographic measures of cardiac structure and function has been explored. The strongest correlations have been reported for BNP with LV diastolic wall stress consistent with stretch-mediated BNP secretion.\(^13\) In a small substudy to the LIFE study, high amino terminal pro-brain natriuretic peptide levels predicted cardiovascular events in patients with hypertension, without LV systolic dysfunction.\(^14\) Recently, Dokainish published a review in which was demonstrated the utility of combined tissue Doppler imaging and B-type natriuretic peptide in estimation LV filling pressures in patients presenting with dyspnea. Laparoscopic surgery involves less trauma than open operation. However, there is concern about the cardiovascular changes that may be induced by the carbon dioxide pneumoperitoneum (Pnp) needed to create workspace. These are characterized by an increase in arterial pressure and systemic and pulmonary vascular resistances early after the beginning of intraabdominal insufflation, with no significant changes in heart rate (HR). We recently demonstrated abnormalities in diastolic filling times after Pnp in healthy women during gynaecological laparoscopy.\(^16\) Intraperitoneal insufflation of carbon dioxide significantly affect the cardiac afterload.\(^15\) In the light of this, it is understandable that consistent changes may occur in cardiac function in hypertensive patients.

Unfortunately, no study has considered the potential clinical applications of echocardiography integrated with the amino-terminal pro-BNP testing in the setting of operating room during a laparoscopic surgery.

Therefore, the aim and major outcome of this work was to estimate left ventricular filling pressures by TDI intraoperatively in conditions of elevated intraabdominal pressure in hypertensive patients with and without diastolic dysfunction. We also combined the use of a blood sample measuring the concentrations of a natriuretic peptide.

### Materials and Methods

After obtaining approval from the institutional Ethics Committee of the Catholic University of the Sacred Heart of Rome, and written informed consent, 40 American Society of Anesthesiologists (ASA) standard 1 or 2 patients undergoing laparoscopic hysterectomy (LH) were studied. Exclusion criteria were renal and metabolic diseases and recent use of any cardiological drugs. We divided the patients into two groups: in the first we allocated those patients (n=20) with echocardiographic diagnosis of diastolic dysfunction (group DD); in the second group patients (n=20) without diastolic dysfunction (group nDD). Oral midazolam, 3 mg, was given as a premedication 1 hour prior to anesthesia. A Ringer’s solution was infused intravenously at 10 ml per kg per hour. Anesthesia was induced with a bolus of propofol (1.5-2 mg/kg). Patients received fentanyl (5 µg/kg). Muscle paralysis to facilitate tracheal intubation and to maintain muscle relaxation were obtained with vecuronium (0.1 mg/kg). General anesthesia was maintained with sevoflurane (2%-2.5%, end-Tidal concentration. Patients were mechanically ventilated with 40% oxygen in air and Tidal volume was set at 8 ml/kg initially and then adjusted to achieve an end-Tidal (ETCO\(_2\)) concentration of 30 ± 3 mm Hg at a respiratory rate (RR) of 12 breaths per minute. Further parameters monitored were continuous electrocardiography, non-invasive blood pressure and pulse oximetry.

Pneumoperitoneum was established by introduction of a Veress needle into the navel, insufflating carbon dioxide using an Olympus CO\(_2\) insufflator. All patients underwent transthoracic echocardiography (TTE) and fasting blood sample before surgery in a preoperating room (T0), after induction of anesthesia (T1), 10 and 20 min after the creation of pneumoperitoneum (T2 and T3), and at the end of the operation (T4). A single experienced investigator performed all Doppler recordings with a multifrequency Doppler transducer.

Parasternal and apical projections were obtained according to the recommendations of the American Society of Echocardiography (ASE). Global diastolic function measurements, including peak velocities of E and A waves and the ratio E/A, deceleration time of E wave (DT) were determined. Abnormal left ventricular relaxation and filling were classified according to the European Study Group on Diastolic Heart Failure.
The diagnosis of diastolic dysfunction was based on: E/A < 50 y < 1.0 and DT < 50 y > 220 ms, E/A > 50 y < 0.5 and DT > 50 y > 280 ms. Patients with a Doppler pattern of pseudonormalization were excluded and we enrolled those hypertensive patients at first grade of diastolic dysfunction. Pulsed wave tissue Doppler recordings from the septal and lateral sites were also recorded from the apical four chamber view. A pulsed sample volume of 5 mm was placed over the mitral annulus and the average peak diastolic velocities (Ea) during early filling over three consecutive cardiac cycles were measured. Mean Ea were estimated by averaging the septal and lateral values. Left ventricular filling pressures were estimated by calculating the E/Ea mean ratio.

Statistical Analysis

Statistical analysis was performed by Statistical Package for Social Science (SPSS), release 15.0 (SPSS Inc., Chicago, IL, USA). All data were expressed as mean±SD. All data were first analyzed for normality of distribution using the Kolmogorov-Smirnov test of normality. When comparing differences in the groups, the Kruskal-Wallis non parametric test was used for non-normally distributed continuous variables and analysis of variance was used for normally distributed variables. A p < 0.05 was considered statistically significant.

Results

Comparison of demographic, clinical and echocardiographic data between DD and nDD group is shown in Table I. The two groups were comparable with respect to age, ASA physical status and body mass index (BMI) and for operation times. The day before surgery all recruited subjects underwent an ambulatory blood pressure monitoring and were classified as first hypertensive stage (OMESH). We excluded three patients for the presence of valvular abnormalities and pulmonary hypertension. The systolic function, as expressed by the ejection fraction, was preserved for all patients. No significant (p > 0.05) differences were observed for heart rate during surgery. We observed a consistent (p < 0.001) increase in mean arterial pressure (MAP) at T2 in both groups. We analysed the E/A ratio and deceleration time (DT) to divide the patients into the two groups. We measured left atrial volume index (LAVi) as a surrogate in estimation of the atrial filling pressures and we found significant difference between DD and nDD group (p < 0.001). In Table I we show that patients with diastolic dysfunction had impaired relaxation while those without diastolic dysfunction had normal echocardiographic findings. As shown in Figure 1 nDD patients had a normal myocardial relaxation. In this group capnoperitoneum caused a significant decrease of Ea velocity (T2 and T3). The DD group had an impaired myocardial relaxation and the creation of Pnp led to a significant drop of Ea (Figure 1, T2 and T3). For nDD group baseline values demonstrated a normal myocardial relaxation which is altered after the gas insufflation (T2 and T3) (Figure 1). At all times the values of Ea for both groups remain above the lower limits. The gas insufflation also affected the Left Ventricular Filling pressures as for both groups we observed a consistent rise of E/Ea ratio (Figure 2, T2 and T3). As shown in
both figures, at the end of surgery (T4) all parameters were normalized. Furthermore, as expected, patients in group DD presented higher values of NT-proBNP than patients in group nDD ($p < 0.05$) (Figure 3). Thus we found that the augmented intraabdominal pressure (T2 and T3) led to a significant increase of the cardiac hormone in both groups ($p < 0.001$). Its plasmatic levels approximated baseline values only 12 hours after the end of surgery (T5).

**Discussion**

In our study we describe the combined use of Tissue Doppler imaging and NT-proBNP test to assess the cardiac consequences which occurred during laparoscopic surgery. We enrolled hypertensive patients with and without diastolic dysfunction. The systolic function, as expressed by the ejection fraction, was preserved for all patients studied. Furthermore, we focused on the possibility to evaluate LV filling pressures and correlate these to the plasmatic levels of B-type natriuretic peptide. Mak et al.\(^1\) demonstrated the correlation of BNP levels with E/E’ ratio as a surrogate in estimation of LV filling pressures. Ea distinguishes a normal transmitial filling pattern (normal relaxation with normal left ventricular filling pressures) from a pseudonormal pattern (impaired relaxation with elevated left ventricular filling pressures), because both of these are seen as transmitial early diastolic velocity > late diastolic velocity (E > A). Dividing E by Ea results in a ratio (E/Ea) that reflects left ventricular filling pressure. An E/Ea = 10 indicates normal left ven-
Tricuspid filling pressures, while an E/Ea = 15 indicates elevated left ventricular filling pressures. An E/Ea from 11 to 14 is a gray zone, in which case other variables are needed to determine whether left ventricular filling pressures are elevated: left atrial volume indexed to body surface area (normal volume, < 32 mL/m²), rules out significant left atrial pressure elevation. BNP was used only as a surrogate in estimation of LV filling pressures. It is widely accepted the relationship between the concentration of this hormone and structural and functional cardiac diseases.

Several Authors described the hemodynamic effects of the Pnp created for laparoscopic surgery. Increases in heart rate, mean arterial blood pressure (MAP) and systemic vascular pressure are the main haemodynamic changes associated with carbon dioxide Pnp22-23. Our group7 demonstrated that the gas insufflation affects the diastolic filling times in healthy women but systolic function remained unchanged. In the same population study we recently found that Pnp led to augmented left ventricular wall stress and stroke work, but no influence on NT-proBNP levels and on LV filling pressures. We extended our investigation performing the TDI technique in order to evaluate the consequences of capnoperitoneum in those hypertensive patients with preoperative diastolic dysfunction comparing to those without diastolic dysfunction. Furthermore, we investigated the plasmatic levels of BNP since its relationship with vascular volume expansion and cardiac pressure overload has been well demonstrated. We examined the E/Ea ratio as an estimation of the LV filling pressures and our data showed that the increased intraabdominal pressure (T2) produced a significant increase of LV filling pressures, higher in those with established diastolic dysfunction.

Furthermore, we found that at the same time (T2) NT-proBNP levels significantly increased in both groups, but approximating the baseline values after 12 hours (T5). These changes are more evident in those patients with diastolic dysfunction. According to our findings an augmented intraabdominal pressure significantly affects the filling pressures of the left ventricle in hypertensive women. Moreover, the augmented afterload during capnoperitoneum led to an increase in LV filling pressures greater extent for patients with cardiac impaired relaxation (Figure 2), such hypertensives with diastolic dysfunction. Our study doesn’t offer any relevance to short or longer term clinical morbidity and mortality but reiterates the importance of a preliminary and accurate evaluation of those patients with increased cardiovascular risk, such hypertensives. Furthermore, our results suggest the possibility of an acute secretion of the ventricular B-type natriuretic peptide. In conclusion, pneumoperitoneum negatively affects cardiac diastolic function in both DD and nDD hypertensive patients as assessed by E/Ea and NT-proBNP concentration.

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