The Safety and Hemodynamic Effects of Pneumatic Sleeves in Patients with Severe Left Ventricular Dysfunction

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ABSTRACT: **Background:** Pneumatic sleeves (PS) are often used during laparoscopic surgery and for prevention of deep vein thrombosis in patients who cannot receive anticoagulation treatment. There is very little information on the hemodynamic changes induced by PS and their effect on brain natriuretic peptide (BNP) in patients with severely reduced left ventricular ejection function (LVEF).

Objectives: To determine the safety and hemodynamic changes induced by PS and their effects on BNP.

Methods: This study comprised 14 patients classified as New York Heart Association (NYHA) II–III with severely reduced LVEF (‹ 40%). We activated the PS using two inflation pressures (50 or 80 mmHg, 7 patients in each group) at two cycles per minute for one hour. We measured echocardiography, hemodynamic parameters, and BNP levels in each patient prior to, during, and after the PS operation.

Results: The baseline LVEF did not change throughout the activation of PS (31 ± 10% vs. 33 ± 9%, $P = 0.673$). Following PS activation there was no significant difference in systolic or diastolic blood pressure, the pulse measurements, or central venous pressure. BNP levels did not change after PS activation ($P = 0.074$).

Conclusions: The use of PS, with either low or high inflation pressures, is safe and has no detrimental effects on hemodynamic parameters or BNP levels in patients with severely reduced LVEF following clinical stabilization and optimal medical therapy.

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KEY WORDS: brain natriuretic peptide (BNP), heart failure, hemodynamics, laparoscopic surgery, pneumatic sleeves (PS)

Pneumatic sleeves (PS) are widely used following prolonged surgeries to prevent venous stasis and improvement of venous circulation. PS were originally designed to treat severe limb edema (elephantiasis) and were recently shown to improve cardiovascular hemodynamics during positive pressure pneumoperitoneum (PP), which is essential in abdominal laparoscopic operations [1]. Hemodynamic derangements, such as reduced venous return, stroke volume and cardiac output, and increased systemic vascular resistance (SVR) may follow PP and prohibit its use in patients with significant cardiovascular diseases [2-11]. Activation of PS to create pressure equilibration is effective in eliminating undesired systemic and visceral hemodynamic changes associated with PP [1,12-14]. Decreased sympathetic autonomic activity during laparoscopic operations may be an additional mechanism explaining the reduced SVR caused by the PS [15].

We previously conducted a study measuring echocardiographic indices during PS application in healthy subjects [16] and found an improvement in cardiac activity as expressed by increased cardiac output and decreased SVR, without an accompanying increase in heart rate. However, the increased venous return and a possible increase in pulmonary blood flow might be deleterious in patients with congestive heart failure (CHF). In another study, we showed that the use of PS in patients with chronic CHF does not exacerbate symptoms and transiently improves cardiac output through an increase in stroke volume and a reduction in SVR [17].

In the current study, we evaluated the effects of prolonged use of PS in patients with chronic CHF, using low or higher inflation pressures (50 or 80 mmHg), and studied the hemodynamic changes, as well as the changes in brain natriuretic peptide (BNP) – a marker of heart failure severity – throughout the activation of the PS.

PATIENTS AND METHODS

The institutional ethics committee approved the study. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave their informed consent prior to their inclusion in the study. The study is an extension and modification of a previously reported study [17].

We connected each patient to the PS device (Lympha-press, Mego-Afek AC Ltd, Afek, Israel) soon after arrival to the procedure room. We wrapped each leg in a PS from the tip of the toes to the proximal thigh below the inguinal region. Each sleeve

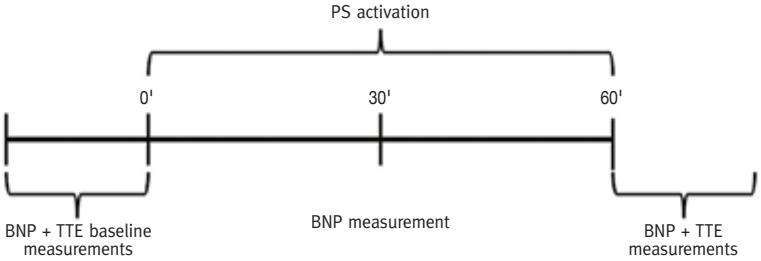
is composed of 10 air cells separately connected by an inflation tube to a computerized compressor. The sleeves inflate sequentially to a maximal pressure of 50 or 80 mmHg, at a rate of 2 cycles per minute (separated by a short interval), to enable maximal venous refilling before any successive pneumatic squeeze. The Lympha-press device produces pressures in the range of 20–80 mmHg. In our previous studies, we applied 50 mmHg as this pressure is commonly used in laparoscopic surgery. We decided to also use the maximal pressure produced by the device to emphasize the safety of using such a high pressure in patients with severe left ventricular dysfunction. We randomly assigned patients to 50 or 80 mmHg in a sequential order. The total activation of PS lasted 60 minutes [Figure 1]. Transthoracic echocardiography (TTE) and brain natriuretic peptide (BNP) levels were measured prior to PS activation. We performed cardiac assessments, which lasted 10 minutes, 30 minutes after PS activation, and measured BNP levels. After completion of 60 minutes of continuous PS activation, we performed our second TTE assessment and measured BNP levels for the third time. Each participant served as his own control.

An experienced echocardiography specialist conducted the echocardiographic measurements. During assessments, the patients were in the left lateral decubitus position. SVR was calculated according to the relationship between mean arterial pressure (MAP), cardiac output, and central venous pressure (CVP) (directly reflected by measuring cubital vein pressure through a 17 Gauge intravenous cannula). This method has been previously validated in surgical patients [18].

STATISTICAL ANALYSIS

IBM SPSS software version 19 (SPSS, Inc, Chicago, IL) was used to perform statistical analysis. Quantitative data is expressed by means, medians, and standard deviations. Qualitative data is presented as frequencies and percentages. Paired sample *t*-test or Wilcoxon signed-rank test were used to compare measures between time points when appropriate (evaluating the significance of the mean change in echocardiographic parameters before and following activation of the PS device). We assumed that the differences, calculated for each pair, had an approximately normal distribution. We used repeated measures model to evaluate changes over time, which was appropriate for mean arterial pressure and CVP. Multiple comparisons were performed (Bonferroni test) for measures performed over time presented for the CVP measure. A P value < 0.05 was considered statistically significant.

Figure 1. Timeline of the pneumatic sleeve activation study



BNP = brain natriuretic peptide, PS = pneumatic sleeve, TTE = transthoracic echocardiography

RESULTS

We activated the PS only after treatment with intravenous diuretics and symptomatic improvement. Therefore, none of the patients had clinical signs of severe pulmonary congestion (i.e. pulmonary rales or crackles) at the time of the study. However, an increased jugular venous pressure and lower extremities pitting edema were noted in 21% of the patients. None of the patients had a cardiac resynchronization therapy device [Table 1].

There was no significant difference in any hemodynamic parameter before and after PS activation in either the 50 or 80 mmHg

Table 1. Patient characteristics at baseline (n=14)

	n (%)
Patient characteristics	
Average age (years)	65 ± 8
Gender, male	11 (78)
Previous myocardial infarction	11 (78)
Dilated cardiomyopathy	4 (28)
Paroxysmal atrial fibrillation	4 (28)
Previous coronary artery bypass graft	4 (28)
NYHA II	9 (64)
NYHA III	5 (36)
Right heart failure	5 (36)
Peripheral arterial disease	5 (36)
Arterial hypertension	13 (92)
Diabetes mellitus	12 (86)
Chronic renal failure	4 (21)
Chronic lung disease	3 (22)
Anemia	4 (28)
Medications	
ACEI / ARB	8 (57)
Beta blockers	13 (92)
Spironolactone	9 (64)
Two of the three medications	11 (78)
Echocardiographic findings	
Mean ejection fraction	31 ± 10.1%
Restrictive pattern of diastolic dysfunction	7 (50)
Severe mitral regurgitation	3 (22)
Moderate to severe pulmonary hypertension	6 (43)

ACEI = angiotensin-converting-enzyme inhibitor, ARB = angiotensin II receptor blockers, NYHA = New York Heart Association

groups [Table 2]. We found the same results for the mid-term measurement, post 30 minutes of PS activation (data not presented). There was also no effect on diastolic function parameters.

The changes in BNP levels for each patient are presented in Figure 2. The baseline BNP level varies between the patients reflecting their clinical stability. In the patients with higher LVEF (mean 36%) and lower baseline BNP levels, we applied a higher inflation pressure (80 mmHg) and yet noted no significant difference in the hemodynamic or clinical outcomes.

DISCUSSION

We previously reported the safety of a short application of PS, at low inflation pressure (50 mmHg), in patients with severe cardiac dysfunction [17]. In this study, we have demonstrated the safety of prolonged activation of PS in patients with severely reduced left ventricular cardiac function who were admitted for acute decompensated heart failure and were studied after clinical stabilization. We also demonstrated the safety of PS in using either low or high inflation pressure (50 mmHg or 80 mmHg, respectively). There was no increase in BNP levels from baseline in both groups. In addition, adverse pulmonary effects (clinical, auscultative, or oxidative worsening) did not accompany the expected increase in venous return. Our previous study [17] included 19 patients. An interim analysis after studying 14 patients showed similar results. Therefore, we did not expand the study sample size.

The mechanism of action of PS may aggravate or even induce signs and symptoms of CHF. The increase in venous return may elevate pulmonary pressure, increase left ventricular preload and afterload, and thereby increase left ventricular myocardial strain and stress, leading to myocardial ischemia. The expected increase in venous return due to PS activation did not result in any adverse cardiac or pulmonary effects (clinical, auscultative or oxidative worsening).

In our previous study [17], we found an early improvement in cardiac function, with immediate return to baseline towards the end of the PS activation, which lasted 40 minutes in total. In this current study, we did not find such an increase in cardiac output throughout the PS activation. We attribute this to the stable condition of the patients and to the improved medical treatment they received.

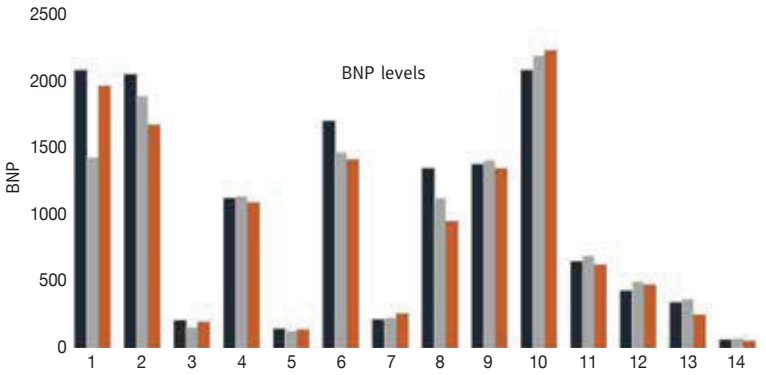
Our study is somewhat limited by the small number of patients. Our patients did not undergo the anesthetic and physiological insult associated with a surgical procedure, so our data may not be extrapolated to real surgical patients. As stated, we did not study postoperative patients due to possible inconvenience during mobilization for examinations, yet we do believe that our study population is representative of these patients as well. In addition, the optimal pneumatic pressure to be used in PS is as of yet undetermined and remains arbitrary, and our results might not be applicable to other types of PS.

Table 2. Hemodynamic parameters pre- and post-pneumatic sleeve activation

	Pre-PS mean	Post-PS mean	*P* value	Pre-PS mean	Post-PS mean	*P* value
Inflation pressure	50 mmHg (n=7)			80 mmHg (n=7)		
SBP (mmHg)	121 ± 19	114 ± 19	0.13	122 ± 23	122 ± 23	0.61
DBP (mmHg)	65 ± 11	64 ± 10	0.15	62 ± 8	64 ± 8	0.59
HR (beats/min)	79 ± 15	78 ± 15	0.23	76 ± 7	76 ± 10	0.86
CVP (cmH_2O)	10 ± 4	9 ± 4	0.91	8 ± 3	7 ± 3	0.23
SVR ($dyn{\cdot}s{\cdot}cm^{-5}$)	1519 ± 487	1364 ± 487	0.13	1036 ± 367	1106 ± 337	0.23
LVEF (%)	30 ± 5	30 ± 6	0.91	36 ± 13	36 ± 13	0.86
CO (l/m)	4.3 ± 1.4	4.6 ± 1.3	0.27	6.3 ± 2.2	5.8 ± 1.7	0.17
SV (ml)	56 ± 19	59 ± 19	0.39	74 ± 29	75 ± 18	0.86
O_2 saturation (%)	93.9 ± 7.2	93.7 ± 7	0.68	94.1 ± 6.9	93.8 ± 7.1	0.62

CO = cardiac output, CVP = central venous pressure, DBP = diastolic blood pressure, HR = heart rate, LVEF = left ventricular ejection function, PS = pneumatic sleeves, SBP = systolic blood pressure, SV = stroke volume, SVR = systemic vascular resistance

Figure 2. The changes in brain natriuretic peptide levels before, during, and after pneumatic sleeve activation



	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Baseline	2073	2045	211	1120	148	1696	218	1343.3	1374	2074	649.2	431.3	343.7	67.7
During PS	1425	1885	163	1138	135	1465	234	1124.8	1405	2184	694.9	501.9	373.9	78.8
Post PS	1959	1668	201	1087	142	1410	261	951.3	1345	2221	627.1	476.3	253.2	60

BNP = brain natriuretic peptide, PS = pneumatic sleeve

The use of PS during laparoscopic surgery should probably be used with caution in patients with high right atrial pressures, severe tricuspid regurgitation, or severe right ventricular systolic dysfunction as abruptly increasing venous return will not translate to improvement in left ventricular stroke volume and cardiac output, despite the decrease in systemic vascular resistance. It must be emphasized that our study included only optimized CHF patients after diuresis in stable condition. Extrapolation to those undergoing laparoscopic surgery should be done with extreme caution.

CONCLUSIONS

The extensive use of PS in laparoscopic procedures, together with the increasing number of elderly patients, as well as

patients with severe CHF who undergo surgery, makes the selection of the PS highly important for improved clinical outcome. We have demonstrated that a prolonged use of PS, even in high inflation pressure, may be safely used in patients with severe LV dysfunction after clinical stabilization and on optimal medical therapy.

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Capsule

A haven for T cells in the bone marrow

Memory T cells (MTCs) help the host respond quickly and effectively to subsequent challenges by the same pathogen. During times of nutritional stress, the host may have to balance productive immune responses with competing claims on limited resources. In mice subjected to dietary restriction, **Collins** et al. found that MTCs translocate to the bone marrow where they enter a quiescent, energy-conserving state accompanied by reduced mechanistic target of rapamycin signaling. Glucocorticoid hormones mediated accumulation of several cell types, not only other immune cells, but also adipocytes in bone marrow. Adipocytes were important for recruitment and survival of MTCs in this niche. This adaptive response ensures that immune responses can persist during periods of caloric restriction.

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Capsule

Priming responses to checkpoint blockade

Activation of intracellular DNA sensing has been proposed as a means to promote antitumor immunity, but molecules that regulate sensing of intracellular RNAs have received less attention. **Heidegger** and colleagues found that expression of the RNA sensor RIG-I in tumor cells plays a vital role in promoting responsiveness to an immune checkpoint therapy in mouse models of cancer. The authors used engineered melanoma cell lines to map the relative importance of various pathways in regulating antitumor immunity and responsiveness to checkpoint blockade. Activation of RNA sensing may be used to increase the immunogenicity of poorly immunogenic tumors.

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