Update

Determination of Hemodynamic Parameters Using Doppler Two-dimensional Echocardiography: A Searching Tool for Therapeutic Optimization in Patients with Congestive Heart Failure on an Outpatient Care Follow-up

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One of the major problems in the management of patients with severe heart failure is frequent hospital readmissions due to lack of compensation, which, in addition to causing a great burden to the public health system, is one of the major causes of loss in quality of life of those patients. On average, 30 to 50% of the patients are readmitted 3 to 6 months after hospital discharge [1]. A recent meta-analysis indicated that the frequency of hospital readmissions may be reduced through a constant follow-up by a multidisciplinary team of physicians and nurses in a specialized heart failure clinic[2,3]. Therefore, a careful follow-up with individualized treatment directed to the specific and current situation of each patient can have medium- and long-term benefits in the outpatient care of chronic patients with moderate to severe congestive heart failure. In this article, we report the potential applications of methods, such as echocardiography, for the optimized management of patients with congestive heart failure and present the initial results of the use of such an instrument for guiding the therapy.

Peculiarities of the development and manifestations of congestion and low cardiac output in congestive heart failure - In patients with congestive heart failure, an important cause of re-hospitalization or visits to the emergency unit, or both, is related to congestive states [4,5]. On the other hand, the clinical diagnosis of congestive states may be particularly difficult in chronic patients, due to several pathophysiological adaptations that make the clinical manifestations of congestion subtle in those patients, frequently leading to underuse of diuretics and vasodilating agents [6], which, in turn, contributes to increase the risk of decompensation.

The identification of elevated ventricular filling pressures in congestive heart failure does not follow the same pattern of the semiotic clinical findings in the acute settings considered in therapeutic decision making processes. One of the major signs and symptoms of congestion is an elevation in jugular venous pressure

and orthopnea. The clinical assessment of jugular venous pressure requires a careful technique, because it seems to be the most important clinical sign for assessing the real congestive status of patients with congestive heart failure [7].

In congestive heart failure, the concordance between the estimates of right- and left-sided pressures is known to be 80%, because Drazner et al [8] have shown that, through a right atrial pressure (RAP) > or < 10 mmHg, the left atrial pressure (LAP) may be estimated as > or < 22 mmHg, respectively [8,9]. Other factors, such as abdominal compression with positive hepatojugular reflux, a "square root"-type pressure response to the Valsalva maneuver, and increased intensity of the second cardiac sound may also indicate an elevation in the right-sided chamber cavities, which, in turn, may estimate high left-sided pressures [9,10].

Due to the compensatory lymphatic drainage chronically present in patients with congestive heart failure, pulmonary rales are lacking in more than 80% of cases, even in the presence of elevated filling pressures. The symptoms of dyspnea and fatigue are due to the fact that although the residual interstitial fluid does not hinder oxygenation it may restrict inspiration and reduce pulmonary compliance [6].

Lower limb edema occurs in only 25% of patients with congestive heart failure below the age of 70 years, while in older patients it may rather be caused by local factors than by an elevation in the central venous pressure itself. These data allow us to suggest that peripheral edema and elevated jugular venous pressure are more specific than sensitive for detecting elevated left-sided filling pressures.

The third cardiac sound is present in most patients with congestive heart failure, although in some patients it may never be identified. It is worth emphasizing that the degree of concordance about the presence of the third cardiac sound, even within experienced physicians, is moderate or low. This fact may be related to the loss of auscultatory acuity in a time of more sophisticated and accessible diagnostic methods [11-13]. Some authors have suggested that the third cardiac sound is not a reliable parameter for assessing the congestive status of patients with congestive heart failure [6]. Nevertheless, the presence of the third cardiac sound and the elevation in jugular venous pressure in congestive heart

failure are independently associated with a higher incidence of hospitalization due to heart failure (RR=1.32, P<0.01), death, or hospitalizations due to heart failure (RR=1.30, P<0.005) death due to heart failure (RR=1.37, P<0.05) [4].

The reason why the elevation in jugular venous pressure or the presence of the third cardiac sound is associated with an elevated risk in congestive heart failure progression is not clear. The elevated jugular venous pressure reflects an increase in right atrial pressure, which, by itself, correlates with elevated left pressures in patients with congestive heart failure. The elevated left pressures, in turn, are associated with a poor prognosis perhaps because of the apoptosis triggered by the myocardial parietal tension and by the activation of the sympathetic nervous system [14,15]. The third cardiac sound, which relates more to low left ventricular compliance and the elevated filling pressures and velocities, has also been associated with a poor prognosis due to a disorder in diastole in patients with systolic dysfunction [4].

One of the few useful clinical bedside instruments for patients with congestive heart failure is pulse pressure (systolic pressure - diastolic pressure/systolic pressure), which, when < 25%, estimates a cardiac index of 2.2 $L/min/m^2$ [2-6]. The ratio between the pulse pressure obtained with normal breathing and the pulse pressure during the Valsalva maneuver may also be used to estimate left atrial pressure with a 93% accuracy [16].

In addition to those characteristics, in patients with congestive heart failure and enlarged ventricular diameters, the degree of mitral regurgitation is usually significant, significantly contributing to the appearance of signs and symptoms of congestion and low cardiac output. The mechanism responsible for mitral regurgitation in congestive heart failure is the lack of appropriate coaptation of the mitral leaflets due to dilation of the mitral valve annulus and impairment of the geometry of the subvalvular apparatus [17]. With compensation of the congestive setting and the reduction in left ventricular and atrial volumes, mitral regurgitation and the effective regurgitant orifice decline significantly. Thus, the systolic volume "steal" greater than 50%, which occurs in symptomatic patients at rest, is redistributed and the effective left ventricular systolic volume increases [18]. Because the dominant symptoms are secondary to congestion, the consequent relief in symptoms at rest is mainly due to the reduction in the elevated filling pressures. Other factors positively affected by the reduction in filling pressures are as follows: the improvement in coronary percussion; the reduction in neurohormonal activation with a reduction in norepinephrine release and parietal stress [14,19,20]; the improvement in functional capacity [21]; a reduction in the circulating cytokines, in the natriuretic peptides, in liver congestion, and, later, in the progressive malnutrition of chronic patients [22].

Contrary to that which occurs in patients after acute myocardial infarction, whose stiff myocardium, not yet dilated, benefits from high filling pressures, patients with chronically dilated ventricles have maximally elongated sarcomeres, in which a greater pressure or volume overload will not elongate them any more, but increase the wall tension and valvular incompetence. Therefore, the decrease in the filling pressures to normal or low levels with diuretics and vasodilators reflects in systolic volume increase. This increase is due not to an improvement in the ejection fraction, which elevates just a little, but to a great reduction in the systolic volume lost during mitral regurgitation [23].

Hemodynamic optimization in heart failure - The basic objectives of the clinical therapy of heart failure guided by hemodynamic optimization are those defined by Stevenson et al [24], which are as follows: left atrial pressure of 15 mmHg or lower; right atrial pressure ≤8 mmHg; systemic vascular resistance around 1200 $dynes/sec/cm^5$; and systolic blood pressure ≥ 80 mmHg. Classically this strategy requires an intensive care environment with the use of a catheter in the pulmonary artery. By redesigning therapy for 24 to 72 hours according to hemodynamics, essentially using a vasodilator (sodium nitroprusside) and intravenous loop diuretic (furosemide), the hemodynamic profile may be optimized and the patient may be maintained clinically stable for the following months, with a reasonable improvement in symptoms, which allows the patient's withdrawal, although temporarily, from the heart transplantation list [25-28]. Although the strategy of hemodynamic optimization using a catheter in the pulmonary artery has repeatedly resulted in an improvement in functional and clinical outcomes, these are observational data, which have not been tested in a clinical trial. Therefore, the multicentric randomized study called ESCAPE is being carried out, comparing the invasive strategy and clinical management in congestive heart failure [29]. Such studies should clarify whether that strategy in fact alters the outcomes, creating survivors, or whether it simply identifies those with greater chances to survive, regardless of the therapeutic strategy used.

In addition to providing an adequate hemodynamic profile with that approach, a recent study [30] has shown that in patients with severe hemodynamic impairment, interventions with diuretics and vasodilators, with no inotropic agents, directed to normalize the conditions of overload and systemic resistance reduce the markers of neurohumoral activation, such as atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and the vasoconstrictors endothelin and norepinephrine. Thus, intensification of the congestive heart failure therapy with diuretics and angiotensin-converting enzyme inhibitors (ACEI) has been shown to reduce BNP serum levels, and, in addition, patients treated with a therapy guided by BNP values had a 35% reduction in cardiovascular events (P=0.02) as compared with those undergoing clinical follow-up only [31]. On the other hand, recent data indicate that 54% of patients with baseline BNP levels of 480 pg/mL or greater will have a new congestive episode within 6 months [32]. These data indicate that the guidance of the treatment of decompensated congestive heart failure, aiming at reducing the filling pressures, either through numeric hemodynamic data, or through a reduction in BNP levels (a marker whose increase indicates distension of the sarcomeres), has clinical benefits to the patients.

Alternative tools for characterizing the hemodynamic parameters - Most data recommending the search for hemodynamic optimization result from studies using a pulmonary artery catheter for invasive assessment of the hemodynamic parameters. It is evident that that strategy is necessarily restricted to the intensive care therapy and applies to those patients with decompensated congestive heart failure who seek hospital care. Considering the importance of maintaining the patients with congestive heart failure euvolemic to avoid or protect them from decompensation due to congestion, tools to be used in the outpatient care environment are required. Therefore, other noninvasive methods for assessing cardiac output and filling pressures, such as Doppler echocardio-

graphy with a bioimpedance device, may be useful for the follow-up and individualization of the congestive heart failure therapy[33,9].

A recent study [34] was carried out using a hemodynamic monitor of right ventricular pressure (Medtronic Incorporation) implanted as a pacemaker to guide daily clinical management of 32 patients with congestive heart failure, which resulted in a 57% reduction in hospitalizations (P<0.01).

Echocardiographic hemodynamic assessment - Echocardiography may be an attractive alternative as a tool of hemodynamic assessment, because, in most patients with heart failure, it may provide hemodynamic data with an excellent correlation with those concomitantly collected by using right catheterization [35,36]. Right-sided pressures, for example, may be obtained 97% of the time when assessing the diastolic (89%) and systolic (73.5%) pressures in the pulmonary artery [37].

In congestive heart failure, right-filling pressures may be estimated by using echocardiographic parameters, such as the inferior vena cava diameter associated with its collapse index during inspiration. The tendency of the inferior vena cava towards total or partial collapse occurs because, during inspiration, the negative intrathoracic pressure increases, and, as long as the inferior vena cava and the right cavities are not overloaded, blood flow should increase towards the right atrium, causing a partial or total collapse of that vessel. When, due to technical reasons, the assessment of the inferior vena cava is not possible and no evidence of elevation in the pressures of the right cavities exists, the simple use of an arbitrary mean value of 10 mmHg is the general consensus [38].

Pulmonary artery pressure may be obtained by measuring the velocities of regurgitation between the right cavities, basically tricuspid and pulmonary regurgitation. With the complete assessment of all echocardiographic "windows", the tricuspid transvalvular gradient and pulmonary regurgitation may be recorded in 86 and 89% of the tests, respectively. It has been shown that, by adding the 2 possibilities, a pressure value was detected in the pulmonary artery in 97% of a series of 200 patients [37,39]. In patients who do not have a sufficient degree of pulmonary regurgitation to estimate the gradient, tricuspid regurgitation is used at the moment of pulmonary valve opening to estimate the diastolic pressure in the pulmonary artery. This simple technique showed a correlation with cardiac catheterization (r=0.92), except for the patients with severe tricuspid regurgitation and those undergoing mechanical ventilation [40,41].

Another important hemodynamic parameter, cardiac output, can also be calculated by use of echocardiographic data and shows a correlation coefficient of r=0.97 with the data obtained through right catheterization [35]. For such, one should multiply heart rate by the time of the velocity integral (TVI) and the area of left ventricular outflow tract, corrected to body surface, for obtaining the cardiac index values.

Pulmonary capillary pressure is a well-established parameter for assessing heart function and left ventricular filling. In patients with congestive heart failure, an elevated pulmonary capillary pressure is associated with a poor prognosis, frequent decompensations of symptoms and low exercise tolerance [42-45]. The reduction in those values after adequate treatment improves the patients' quality of life [46]. The use of data referring to those values may help in the routine therapeutic management of patients with congestive heart failure.

Pulmonary capillary or left atrial pressure may be estimated by assessing blood flow velocity in the pulmonary artery, if the patient has no pulmonary disease, or by assessing the transmitral and pulmonary venous flow in the left side. Transmitral flow analysis also provides information on left atrial pressure and heart failure prognosis. However, it depends on multiple conditions, such as heart rate, ventricular relaxation and suction, left atrial and ventricular compliance, and mitral valve conditions. To avoid the interference of these factors, other parameters, such as pulmonary venous flow, the response of transmitral flow to different volume loads, color M mode, and Doppler tissue imaging of the mitral ring, may be used. Left atrial pressure cannot be estimated by using isolated rules, but after assessing several parameters and respecting the limitations of each one. For practical purposes, pulmonary capillary pressure and left atrial pressure are considered equivalent, because the pulmonary capillaries, the pulmonary veins, and the left atrium communicate freely, forming a large chamber. Simultaneous measurements of right catheterization and left atrium through transeptal catheterization have already confirmed the similarity of those pressures [47-49]. The several calculations used to obtain hemodynamic data through echocardiography are shown in table I.

Other methods - Doppler tissue imaging is a relatively new technique that records the systolic and diastolic myocardial velocities at the level of the mitral valve annulus, preferentially medial or lateral. Filters should be used to eliminate the high frequencies, and the Nyquist limit should be maintained between –15 and 20 cm/s. Contrary to the transmitral flow (E wave), the velocity recorded at the mitral valve annulus by using Doppler tissue imaging (E_a) does not undergo the influence of left atrial pressure and reflects isolated left ventricular relaxation. Thus, it is an excellent

Table I - Echocardiographic formulas used for obtaining hemodynamic data	
CO, L/min	SV x HR
SV, mL	tVI x ALVOT
ALVOT, cm^2	0.785 D^2
CI, L/min/m^2	CO/BS
BS, m^2	[height (cm) + weight (kg)] - 60/100
ISVR, dynes.cm $^{-5}$	MBP – RAP/CI $\times$ 80
LAP, mmHg (Henry)	65 – (0.5 TPA)
LAP, mmHg (Dabestani)	57 – (0.39 TPA)
LAP, mmHg (TIVR and Vp)	4.5 (10^3/ [2 TIVR] + Vp) - 9
LAP, mmHg (Vp and E')	5.27 [E/Vp]+ 4.6
LAP, mmHg (Doppler tissue imaging)	1.24 (E/E') + 1.9
SPPA, mmHg	Δ RA/RV + RAP
DPPA, mmHg	Δ EDP PR + RAP
MPPA, mmHg	90 – (0.6 TPA)
RAP, mmHg	Ø IVC + % inspiratory collapse

CO - cardiac output; SV - systolic volume; tVI - flow velocity integral; ALVOT - area of the left ventricular (LV) outflow tract; D - diameter in the LV outflow tract; CI - cardiac index; BS - body surface; ISVR - index of systemic vascular resistance; MBP - mean blood pressure; RAP - estimated right atrial pressure; LAP - estimated left atrial pressure; TPA - time of flow acceleration in the pulmonary artery; TIVR - time of isovolumetric relaxation; Vp - velocity of propagation of the transmitral flow according to the color M mode; E - maximum velocity of the transmitral valve flow; E' - maximum velocity of the tissue E wave; SPPA- systolic pressure in the pulmonary artery; Δ RA/RV - pressure gradient in tricuspid regurgitation; DPPA - diastolic pressure in the pulmonary artery; MPPA - mean pressure in the pulmonary artery; Δ EDP PR - end-diastolic pressure gradient in pulmonary regurgitation; Ø IVC - inferior vena cava diameter.

index for assessing the relaxation deficit, even in pseudo-normal cases, and, when coupled to nontissue transmitral valve flow, it may estimate left atrial pressure. An E/E_a ratio > 10 may foretell a LAP > 12 mmHg with 91% sensitivity and 81% specificity, or an E/E_a ratio > 10 may foretell a LAP > 15 mmHg with 97% sensitivity and 78% specificity. Ommen et al [50] have shown a correlation level between the $E/E_{a\ medial}$ ratio and the mean left ventricular diastolic pressure of r=0.64, greater in patients with ejection fraction lower than 50%, as compared with those without ventricular dysfunction. These authors have also shown a positive predictive value of 64% for a left ventricular end-diastolic pressure > 12 mmHg, if E/E_a is > 15 mmHg, and a negative predictive value of 97% for low left atrial pressures, if the E/E_a ratio is < 8. In the presence of infarction in the laterobasal wall, atrial fibrillation, and severe mitral regurgitation, significant technical limitations exist and may render those measurements unfeasible [51,52].

In addition to the already cited methods, several other formulas may be used to estimate left atrial pressure, using the following echocardiographic parameters: time of isovolumetric relaxation; velocity of propagation of the transmitral valve flow obtained by using color M mode (TMVF) [53-57]; velocity of deceleration of the early transmitral valve flow [58-60]; systolic fraction of the pulmonary venous flow; time of deceleration of the diastolic pulmonary flow[61]; systolic fraction of the integral of velocity of the anterograde pulmonary venous flow [62]; and ratio between the time of atrial contraction of the retrograde pulmonary venous flow and the anterograde transmitral valve flow [63]. The choice of the most appropriate technique may vary according to the individual characteristics of the patients.

Therefore, the noninvasive hemodynamic assessment with information provided by echocardiography may be obtained with a good accuracy by using more than one parameter and knowing the advantages and limitations of each method. Technically, it requires time and training of the echocardiographer, and its performance depends on the need of the clinical cardiologist in patients' management.

Clinical application of echocardiography in the search for optimum hemodynamic parameters - Our group is carrying out a randomized clinical trial comparing the echocardiography-guided outpatient care, which aims at tailoring the hemodynamic profile (a reduction in the filling pressures and peripheral resistance), with the conventional clinical management, which aims at improvement of symptoms. Our study comprised 99 patients diagnosed with congestive heart failure of any etiology, in functional class II-IV, with an ejection fraction ≤40%, who were hospitalized or visited the emergency unit due to decompensated heart failure in the prior 3 months. Our preliminary study comprised 70 patients, 31% of whom had congestive heart failure of ischemic etiology, a mean age of 60±15 years, an ejection fraction of 27±7%, and 60% were males. The preliminary data have shown that, in the group with the echocardiography-guided treatment, a reduction occurred in the right atrial pressure from 10.1±5 to 7.8±4 mmHg (P=0.004), in the maximum systolic pressure of the pulmonary artery from 47±12 to 39±12 mmHg (P=0.003), and in the systemic vascular resistance index from 3821±1265 to 3390±1142 dynes/sec/cm^5 (P=0.048). No significant difference was observed in those parameters in the conventional clinical management group. These data and the conduction of this study so far have

indicated that the use of echocardiography-guided treatment based on hemodynamic data is feasible and more effective than the treatment based on traditional clinical management for obtaining a favorable profile of reduction in the filling pressures and peripheral resistance in patients with heart failure being followed up on an outpatient care basis.

Role of the hemodynamic profile for prognosis of chronic heart failure and predictive factors - The importance of the volemic status in the prognosis of patients with congestive heart failure may also be observed in data indicating that survival may range from 80% in 2 years in patients without congestion to less than 50% in 6 months in patients with refractory symptoms at rest [64]. The maintenance of a clinical status free from congestion, aiming at low or normal filling pressure levels within 4 to 6 weeks after hospital discharge in patients with functional class IV was associated with survival improvement in the following 2 years [65].

Hemodynamic monitoring may also be useful to stratify risk, because patients with normal initial filling pressures had a one-year survival of 95%, while in those with elevated initial pressures, a better prognosis was attributed to the therapy for reducing the pressures rather than to the level of initial congestion [66].

In addition to the congestive status of patients with congestive heart failure, the following important prognostic data may be obtained by use of echocardiography: degree of preservation of right ventricular function[67,68]; left ventricular end-diastolic diameter[69]; left atrial pressure; restrictive pattern in transmitral diastolic flow[70-72]; and degrees of mitral and tricuspid regurgitation[73,74]. The BNP levels, which are elevated in congestive heart failure perhaps indicating the degree of congestion, also correlate with sudden death[75], NYHA functional class[76], and future events[77].

Filling pressures, therefore, are useful in the management of patients with congestive heart failure, because they may foretell outcomes even after adjustments in therapy [66] and may be inferred not only through BNP levels, but also through echocardiographic parameters, such as those already cited.

Final considerations - The treatment of systolic heart dysfunction has advanced considerably in the past 20 years, mainly in the pathophysiological field due to the discoveries of the role of the neurohormonal factors[78], which led to the use of drugs that proved to reduce mortality, such as ACEI[79-81], beta-blockers[82,83], and spironolactone[84]. The participation of multidisciplinary teams has been important for specifically reducing hospital readmissions[85,86].

Despite these advances, mortality and hospital readmission due to symptoms of decompensation are still high [87,88], and this is partially due to the limitation in the clinical setting to indicate adequacy of the treatment before hospital discharge, especially in defining the congestive/volemic status of those patients. Conventional tests, such as echocardiography, have not been routinely used in their plain potential to provide additional information to clinical examination in regard to the real hemodynamic conditions of the patient. On the other hand, the frequent use of right cardiac catheterization in managing patients with decompensated heart failure is not feasible, not only due to the risks and high costs of the procedure, but also because it requires the use of intensive care unit beds [89-92]. Therefore, alternative methods should be sought to provide information about the volemic status of patients with congestive heart failure. The measurement of the BNP neurohormone has shown positive initial results for monitoring the

long-term outpatient care treatment of those patients. The current ample availability of echocardiography in cardiology practice may allow better control of patients with congestive heart failure on an outpatient care basis, if the potential of that method for deter-

mining the hemodynamic profile is mastered in a more comprehensive form by cardiologists/echocardiographers, providing precious information to the clinician and allowing a pattern of differentiated management for that difficult group of patients.

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