The mystery of diastolic heart failure (DHF), described by authorities as a “puzzle” and a “clinical paradox,” stems from the following misperception: (1) that the normal ejection fraction implies normal cardiac output (CO), (2) that therefore low CO is not operative (it is rarely mentioned in relation to the pathophysiology of DHF), and (3) the congestive phenomena are due to the stiff left ventricle. In fact, a normal ejection fraction is not a reliable indicator of normal CO; low CO is the fundamental pathophysiologic abnormality of all heart failure (HF), whether systolic and/or diastolic (or, indeed, “high output”); and increased ventricular stiffness is not the principal cause of congestion in DHF. Pathophysiologic explorations supporting these understandings further reveal the following: (1) the premise that a clinical event as dramatic as acute pulmonary edema (systolic and/or diastolic) would be contingent on similarly dramatic acute hypertensive or ischemic ventricular dysfunction, while intuitive, is unsubstantiated, and there is an alternate explanation satisfying both theoretical and clinical observations; (2) contrary to general perception, DHF is no more vulnerable to diuretic-induced hypotension than systolic HF; (3) heart rate reduction should not yet be considered an established therapeutic goal in DHF; (4) since HF is HF whether systolic and/or diastolic, studies are likely to show that therapeutic similarities outweigh differences except as the various agents might modify the underlying structural and/or functional pathology; (5) although long evident that HF occurs by only two mechanisms (systolic dysfunction and/or diastolic dysfunction), it has only recently been acknowledged that the mere exclusion of one is diagnostic of the other; and (6) the definition of HF currently in widespread use is unnecessarily confounded by neglect of the fundamental distinction between ventricular dysfunction and failure.

**Key words:** cardiac output; diastole; diastolic function/dysfunction; diuretics/therapeutic use; ejection fraction; end-diastolic volume; end-systolic volume; heart failure; pulmonary edema

**Abbreviations:** ACE = angiotensin-converting enzyme; CO = cardiac output; DDf = diastolic dysfunction; DHF = diastolic heart failure; EDP = end-diastolic pressure; EDV = end-diastolic volume; HF = heart failure; HR = heart rate; LV = left ventricle, left ventricular; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; PED = pulmonary edema; RAAS = renin-angiotensin-aldosterone system; RAASAT = renin-angiotensin-aldosterone system activation threshold; RV = right ventricle, right ventricular; RVEDP = right ventricular end-diastolic pressure; SDf = systolic dysfunction; SHF = systolic heart failure

But I think the most likely reason of all
May have been that his heart was two sizes too small.

*How the Grinch Stole Christmas,* by Dr. Seuss

### The Mystery

**How Can the Heart Fail if the Ejection Fraction Is Normal?**

It is well understood and accepted that the mechanism of systolic heart failure (SHF) is impaired ventricular contractility, that is, systolic dysfunction (SDf) defined as a left ventricular ejection fraction (LVEF) <50%.1 Diastolic dysfunction (DDf) is defined as impaired ventricular filling and is the mechanism of diastolic heart failure (DHF), heart failure (HF) with an LVEF ≥ 50%.1 But even experts have found DHF difficult to (a) understand: (“...we do not really understand what is wrong with patients who seem to have heart failure and apparently preserved systolic function,”2 “...we do not understand it or know how to treat it,”3 and “...the precise mechanisms...are incompletely understood...”) or to (b) accept: (“it’s uncertain...if an LVEF value of 45% is depressed enough to initiate...congestive HF,”4 and “many suspected of having this syndrome...may not have heart failure at all”5). Indeed, Gandhi et al1 characterized a normal

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LVEF within 72 h of hospitalization for congestive HF as a “clinical paradox” and hypothesized that “many ... with acute [hypertensive] pulmonary edema ... have transient left ventricular systolic dysfunction, which is no longer present ... after treatment.” They compared the LVEF during the initial treatment of 38 patients presenting within 6 h of the onset of acute hypertensive pulmonary edema (PED) to a second LVEF 2 to 3 days later after hypertension and congestion had resolved (Table 1). Unexpectedly, the “during” LVEF was essentially identical to the “after” LVEF not only in the 18-patient DHF group but also in the remaining SHF group (Table 1). The hypothesis was refuted, the enigma of HF in the context of a normal LVEF preserved; however, close inspection of the important work of Gandhi et al along with a focused review of circulatory physiology reveals the true mechanism of DHF and why it is not a mystery.

**The Neglected Role of Low Output and the Ejection Fraction Illusion**

As suggested, “our tools [have] constrained our thinking” and in this case the tool is the echocardiograph. Its ready ability to supply an LVEF soon preoccupied clinicians and researchers alike and was largely responsible for the emergence of the “ventricular function model” of HF. Unfortunately, this, along with other popular models of HF, including the neurohormonal, cellular, molecular, genetic, and inflammatory models, has obscured the essential reality of HF (whether systolic and/or diastolic) and the key to its understanding—that HF, as its proper definition states, is inability of the heart “... to pump blood at a rate commensurate with the requirements of the metabolizing tissues. ...” Simply stated, low cardiac output (CO) is not merely a feature of HF, but is its primary pathophysiologic abnormality. Thus, parameters of myocardial function (including the LVEF) relate to HF only insofar as they accurately reflect CO. The LVEF does not accurately reflect CO.

To illustrate, Table 2 is derived from standard left ventricular (LV) volume data. Compared to the SHF example, the LVEF in the DHF-1 example (DHF due to mild- to-moderate DDf) is 30 percentage points higher but CO is identical, 30% below normal. Remarkably, the LVEF in the DHF-2 example (DHF due to severe DDf) is another 10 percentage points higher yet provides the same low CO. A normal LVEF can thus be very effective camouflage for low CO.

Gandhi et al (Table 1) showed a mean LVEF 20% higher (proportionally approximately 45% higher) in the patients with DHF than in the patients with SHF. Nevertheless, stroke volumes differed by at most only 4 mL (7%). CO was actually lower in the higher LVEF (DHF) patients, more a result of lower heart rate (HR) than lower stroke volume. The point remains that unless LV volumes, particularly LV end-diastolic volume (LVEDV), are considered along with the LVEF, and they rarely are, the LVEF does not and cannot accurately predict stroke volume, hence CO. It therefore cannot predict HF.

Thus, the mystery of DHF stems from the misperception that the LVEF is a valid surrogate for CO. The normal LVEF of DHF is then taken to imply that low CO is not pathophysiologically operative, and the congestive phenomena are attributed to the stiff LV.

**HF (Systolic and/or Diastolic)**

**The Obligatory Role of Low CO**

Low CO is the pathophysiologic basis not only of advanced HF (systolic and/or diastolic) but also of the earliest stages of the underlying SDf and/or DDf, long before HF is symptomatic or detectable at the bedside.

<table>
<thead>
<tr>
<th>Variables</th>
<th>SHF (n = 20)</th>
<th>DHF (n = 18)</th>
<th>DHF Compared to SHF (n = 18), %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>During</td>
<td>After</td>
<td>During</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>131</td>
<td>138</td>
<td>85</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>78</td>
<td>83</td>
<td>36</td>
</tr>
<tr>
<td>LSV, mL</td>
<td>53</td>
<td>55</td>
<td>49</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>87</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>40</td>
<td>40</td>
<td>58</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>4.6</td>
<td>4.3</td>
<td>3.9</td>
</tr>
</tbody>
</table>

*Derived from Gandhi et al. Since their article included no HR or volume data for the SHF group, these data were computed via spreadsheet from the published DHF and combined DHF-SHF values. To achieve the best approximation of the original observations (available from the author), LVEF values were then calculated from the computed volumes, minor deviations anticipated due to precision/rounding error. LVEDV = LV end-diastolic volume; LVESV = LV stroke volume; LVEDV = left ventricular end-diastolic volume.
Table 2—LVEF: Meaningless in Terms of Cardiac Output Without the Coexisting LVEDV*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal</th>
<th>SHF</th>
<th>DHF-1</th>
<th>DHF-2</th>
<th>SDf</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV, mL</td>
<td>120</td>
<td>250</td>
<td>100</td>
<td>85</td>
<td>200</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>50</td>
<td>200</td>
<td>50</td>
<td>35</td>
<td>130</td>
</tr>
<tr>
<td>LSV, mL</td>
<td>70</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60</td>
<td>20</td>
<td>60</td>
<td>60</td>
<td>35</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>4.2</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>4.2</td>
</tr>
<tr>
<td>ΔCO, from normal, %</td>
<td>0</td>
<td>-30</td>
<td>-30</td>
<td>-30</td>
<td>0</td>
</tr>
</tbody>
</table>

*Derived from Braunwald et al.9 whose angiographic volume indexes are converted here to absolute volumes using nominal body surface area (1.73 m²) and liberal rounding to facilitate interpretation (but in all cases < 2%). DHF-1 = DHF due to mild-to-moderate DDF; DHF-2 = DHF due to severe DDF; SDf = systolic dysfunction without HF; see Table 1 for expansion of abbreviations.

Hemodynamic and Autonomic Responses to Low CO: It is axiomatic that, except for transient imbalances, right ventricular (RV) and LV output must be equal. Since SDf and/or DDF rarely, if ever, impair the ventricles symmetrically, their earliest effect is to unbalance the circulation, that is, to lower the output of one ventricle more than the other.10,11 An example is shown in Figure 1, where SDf and/or DDF transforms a normal LV output curve (Starling curve), curve I, into curve II. With no immediate change in LV end-diastolic pressure (LVEDP), LV output drops11 from 5 to 2 L/min, point x. Meanwhile the RV continues pumping 5 L/min (right-heart curves are omitted from Fig 1 for clarity). The LV is thus unable to empty the pulmonary circuit as fast as the RV fills it, and pulmonary blood volume expands. This shifts the normal pulmonary venous return12/vascular function13 (Guyton) curve, A, upward to B, re-setting the Starling-Guyton intersection to a higher LVEDP and a partially compensating LV output, 4.5 L/min (intersection II-B).10 Since total blood volume is fixed, the volume expanding the pulmonary circuit is equally and simultaneously removed from the systemic circuit. This shifts the systemic Guyton curve and RV end-diastolic pressure (RVEDP) downward. Thus, by Starling’s law of the heart and within a few heartbeats, the altered Guyton curves simultaneously raise the lowered LV output while lowering the normal RV output until biventricular output re-equilibrates at an intermediate CO (intersection II-B).10,11 Low CO also evokes a reflex sympathetic response proportional to its hypotensive effect, the cardiostimulatory component tending to shift the Starling curve back toward normal.

The Neurohormonal Response to Low CO: The renin-angiotensin-aldosterone system (RAAS) is so exquisitely sensitive to low CO/reduced renal perfusion that it is activated physiologically by mere postural changes.14 Thus, to the degree that CO after ventricular re-equilibration and autonomic adjustments (Fig 1, intersection II-B) remains below the RAAS activation threshold (RAASAT), the RAAS is activated, stimulating renal fluid retention. This in turn shifts the Guyton curves upward (pulmonary, B to C; systemic, not shown) increasing biventricular end-diastolic pressure (EDP), thence CO, until CO reaches the RAASAT (intersection II-C). CO thus compensated is maintained by persistent RAAS activation at the new higher set point. With further ventricular dysfunction (Fig 1, Starling curve III), the greater CO shortfall after hemodynamic and autonomic stabilization (intersection III-D) requires additional RAAS activation to compensate (intersection III-D to III-E).

For every Starling curve, there is a point of optimum EDP, roughly coinciding with the onset of the Starling “plateau,” above which ventricular output no longer significantly increases irrespective of further increases in EDP. Note that the Figures reverse the conventional axes of the Starling curve to show the “height” of the EDP column more intuitively on the vertical axis (as did Starling himself15). Thus, the Starling “plateau” is represented not horizontally as a plateau but vertically, as a “wall,” an appropriate descriptor in the current vernacular as it defines the maximum achievable output if the ventricle is “pushed to the wall” by EDP exceeding optimum EDP. In the case of (normal) Starling curve I, optimum EDP is 11 mm Hg (intersection I-G). Compared to SDf, the Starling slope in DDF is steeper, ensuring a higher optimum EDP and a higher LVEDP at any given output.

With marked systolic dysfunction and/or DDF, the Starling curve is confined to a position to the left of the RAASAT (Starling curve IV). The RAAS is thus persistently activated in an attempt to raise the intractably low CO to the RAASAT.16 Since the RAAS control loop is now endless, it will continue raising EDP at a rate proportional to the RAASAT-CO shortfall ad infinitum above optimum EDP (intersection IV-F) until therapy, reduced circulatory demand, improved ventricular function, or death in PED intervenes. This process is not only congestive, excessive, futile, and cardiovasculopathic,14 but also at least partly accounts for failure of effective (HF) therapy to reverse the renal sodium retention that requires continued diuretic therapy17 and the transience of aldosterone suppression during angiotensin-converted enzyme (ACE)-inhibitor therapy17,18 (the ACE-inhibitor escape phenomenon), observations authorities have found difficult to explain.
Perspective: It should be noted that the determinants of LV output and EDP (the Starling and Guyton curves and the RAASAT) are in a constant state of flux. Thus, the static intersections in Figure 1 actually represent the aggregate of many intersections over time. In other words, low CO could be compensated/normal at rest while uncompensated with activity and other circulatory stresses, the aggregate yielding a substantial CO RAASAT deficit.

It is advantageous that resting CO remains compensated (not absolutely/measurably low) until LV dysfunction is advanced; however, it comes at the cost of persistent RAAS activation with its cardiovascular sequelae. This could account for the long-term benefit of ACE-inhibitor therapy in ventricular dysfunction even before overt HF develops.

Compensation also helps to conceal the pivotal role of low CO. Indeed, some authors go as far as to dismiss low CO altogether as the stimulus to sustained RAAS activation in HF, attributing it to hypovolemia. The misperception is compounded when, having to concede that HF is a hypervolemic state, RAAS activation is then mischaracterized as “inappropriate,” inviting the distorted view that HF is primarily a disorder of neurohormonal control (the “neurohormonal model”) rather than of fully or partially compensated low output.

Acute Hypertensive PED (Systolic or Diastolic)

The foregoing explains the chronic indolent course of (systolic or diastolic) HF with its congestive and hypoperfusive features but not its presentation as acute hypertensive PED. The work of Gandhi et al provides further insight.

Evidently based on the unchanged normal LVEF during and after acute hypertensive PED in their DHF group, they considered it a “high probability that the pulmonary congestion was due to isolated transient DDF.” While admirably obtaining data at the earliest feasible opportunity after acute PED onset, technically their study did not include events leading up to or initiating acute PED, as they acknowledge. Thus, although it seems intuitive that a clinical event as dramatic as acute hypertensive PED would be predicated on a similarly acute change in LV function, the data of Gandhi et al do not establish this.

Even if their data did include events up to and initiating acute PED, Gandhi et al did not specify how they identified transient DDF, although lacking evidence of transient SDF it is possible they simply (and properly) accepted DDF as the only possible alternative (see section on “Diagnosis”). It is intriguing that transient DDF remained attractive as the...
likely precipitator of diastolic acute hypertensive PED even though evidence that transient SDf precipitated systolic acute hypertensive PED (intuitively even more likely) was notably absent. Also, they were unable to identify a triggering mechanism for acute transient DDf (or SDf). They considered acute ischemia, but neither they nor their colleagues in an earlier study could confirm it, a finding supported by the ordinary clinical observation that even the most overt expressions of myocardial ischemia (angina pectoris and acute myocardial infarction) are infrequently complicated by acute PED. They considered acute hypertension but did not interpret their data as corroborative. Moreover, by ordinary clinical observation, acute hypertension is also a clinical event only occasionally associated with acute PED even in the context of LV dysfunction.

These considerations thus cast reasonable doubt on the premise that acutely impaired cardiac performance is the usual mechanism of acute hypertensive PED. Could there be another explanation? Could most acute hypertensive PED simply be an extension of the chronic process of systolic and/or diastolic HF?

The effect of chronic RAAS activation is cumulative, inexorably raising extracellular volume and biventricular EDP until CO reaches the RAASAT. If this is not achieved at an LVEDP at or below optimum EDP, LVEDP will operate on the near-vertical Starling wall, maximizing the effect of additional volume retention on LVEDP. This could set the stage for acute volume loads to sharply elevate LVEDP beyond the pulmonary capillary transudation point and precipitate acute PED (see section on “Diuretics”). Since many acute myocardial infarctions are first cardiac events, venous pressure before the event is likely to be normal, possibly accounting for the infrequency of complicating acute PED, its occurrence essentially confined to those with the greatest acute ischemic insult and/or preexisting ventricular dysfunction/low output.

However, disorders known to raise intravascular and interstitial volume predispose to acute PED despite normal or only minimally impaired ventricular function. Such is the case with bilateral renal artery stenosis where acute PED is effectively prevented by successful renal revascularization alone.

Thus, an “over-stuffed” circulation seems to be a key predisposing substrate to acute PED, which might then be precipitated by a relatively modest additional volume load without necessarily involving acute ventricular dysfunction. Such loads can result from dietary indiscretion, lapse in HF therapy, or postural change as occurs to lesser consequence in orthopnea and paroxysmal nocturnal dyspnea. Further loss of renal perfusion has a similar effect as when acute bradyarrhythmia/tachyarrhythmia lowers CO. Increased physical activity or inflammatory illness also lower renal perfusion. Here, the hypermetabolic/inflamed (vasodilated) tissues create an AV fistula effect. When CO is low and fixed, blood flow thus diverted is at the expense of the kidneys. The net effect is to shift the RAASAT to the right, which, parenthetically, is also the basis of high-output failure—low output (relative to the “...the requirements of the metabolizing tissues...” as represented by the RAASAT) is the unifying mechanism of all HF.

Once LVEDP exceeds the pulmonary capillary transudation point, free fluid rapidly passes into the pulmonary interstitial and alveolar spaces. The resulting acute respiratory and emotional distress then triggers an acute adrenergic response. Its vasocostrictive component would explain the associated acute hypertension. The chronotropic component would tend to elevate HR and, as Gandhi et al noted, the inotropic component could mask acute hypertension-induced systolic dysfunction. In any case, CO during acute hypertensive PED was in fact higher than the chronic/“after” value. Thus, whatever the mechanisms operative during the acute event, the net effect seems to be more compensatory than contributory.

Accordingly, the evidence that acute ventricular dysfunction precipitates acute hypertensive PED is weak at best, and there is good theoretical evidence to the contrary. Thus it seems plausible, if not likely, that it results from the combination of chronic low CO with its attendant cumulative fluid retention and a superimposed acute, often relatively modest, volume challenge (see section on “Diuretics”). The associated acute hypertension is most likely an adrenergic sequela. Ambulatory hemodynamic monitoring holds the promise of clearer insight.

**DHF**

**Mechanism**

**Low CO:** Because CO is perceived as normal in DHF, it is rarely considered, descriptions such as: “... inability to ... expel sufficient blood,” and “the major ... manifestations relate to inadequate CO” conspicuously applied to SHF but not to DHF. Meanwhile in DHF, the focus is on the DDf “stiffness”/“backward failure” component: “... a primary impairment of diastolic function that results in the need for elevated atrial pressure to maintain/ensure adequate filling” and “the major ... manifestations relate principally to the elevation of filling pressures.”

Of course the ventricle is always adequately filled; indeed, it is reasonably viewed as overfilled not only in DHF but also in SHF. The point is that in DHF,
as in any restrictive cardiomyopathy, the end-diastolic capacity (EDV) to which it can be filled is low, "two sizes too small." Low stroke volume/CO further requires an end-systolic volume "two sizes too big" to match the low EDV, presumably the result of (1) the inherent mechanical limit to cardiomyocyte shortening, and/or (2) Frank-Starling forces constrained by the constrained EDV.

**Ventricular Stiffness:** While DD/ventricular "stiffness" has captured the spotlight as the presumed cause of pulmonary congestion in DHF, Figure 1 shows that it cannot be the dominant factor. Indeed, without the ability of the normal pulmonary Guyton curve (Fig 1, curve A) to shift upward, LVEDP could never exceed its y-intercept (11 mm Hg) regardless of LV stiffness. The Guyton y-intercept (hence the vertical position of the entire Guyton curve on the pressure axis) varies inversely with the capacity and directly with the volume contained by the vascular circuit it represents, the slope varying with vascular resistance. Guyton curves are unaffected by DD or any other characteristic of their downstream ventricle. They shift upward purely because of the increased vascular volume and tone resulting from the hemodynamic, autonomic, and neurohormonal responses to low output. This occurs most dramatically with type IV left ventricle Starling curves—the associated pulmonary Guyton y-intercept, hence LVEDP will rise ad infinitum above optimum EDP (intersection IV-F) with no additional ventricular dysfunction.

Starling curves of type IV, representing advanced ventricular dysfunction, cannot by definition be compensated at a LVEDP below the pulmonary capillary transudation point. Moreover, they have a near-vertical Starling wall that predisposes to abrupt increases in LVEDP. Thus, they are a likely substrate for acute PED. Accordingly, the "after" stroke volume observed by Gandhi et al1 could represent the uncompensated/intractably low CO state characteristic of these curves, and it was essentially identical in the SHF and DHF groups (55 mL and 57 mL, respectively). Alternatively, the "after" stroke volumes could be normal/compensated. If so, the occurrence of acute PED 2 to 3 days earlier could only be explained, in either group, by an antecedent aggregate RAASAT-CO deficit. Thus, whether the "after" stroke volumes were low or compensated, they were essentially equal in both groups—if there is no mystery/paradox in SHF, there should likewise be no mystery/paradox in DHF.

**Therapy**

**Diuretics:** The notion that DHF is more vulnerable than SHF to the hypotensive effect of diuretics and other preload-reducing agents is widely echoed. The premise seems to be that since a stiffer LV requires a higher EDP to maintain a given EDV/stroke volume, stroke volume will fall faster as EDP falls.

This premise, like all partial truths, is misleading. Figure 2 shows normal RV and LV Starling curves as examples of greater and lesser ventricular compliance, respectively. As EDP falls from point a to b, LV stroke volume falls < 9 mL (point c to d), but RV stroke volume falls > 12 mL (point e to f). Thus,
when EDP varies, stroke volume, CO, and BP vary less, not more, in DHF than in SHF.

The "stiff LV" premise is not only flawed, it is unrelated to the effect of diuretics on stroke volume/CO/BP. While it is true that the LV Starling curve determines LVEDP and the output at which both ventricles equilibrate when the LV is the weaker/"rate-limiting" ventricle, once the circulation equilibrates to this output it is actually the RV that determines any diuretic-induced change in CO.31 This is simply because the initial effect of diuretics is to lower central venous pressure/RVEDP. This lowers RV output. To comply with the imperative of circulatory balance, the then relatively higher LV output will progressively deplete pulmonary blood volume, thus lowering LV output until it re-equilibrates with the diuretic-induced lower RV output. Thus, it is the RV, not the LV, that is the principal determinant of CO when central venous pressure is the primary hemodynamic disturbance,10 its effect directly proportional to RV compliance.

While the RV determines LV output in this context, the LV Starling curve determines the LVEDP at which this occurs (Fig 2, acute PED).31 After venesection, RVEDP fell 5 mm Hg (point g to b), lowering stroke volume 1 mL (point h to i). This required LVEDP to fall 13 mm Hg (point j to k) for ventricular output to re-equilibrate. Thus, the Starling slope disparity magnified the change in RVEDP by a factor of 13/5.31 These observations explain how a modest diuresis (and/or systemic veno-}

cartely avoided in either only if a “cushion” of jugular venous pressure (2 to 3 mm Hg above top normal) is preserved.

LV Volume: It was recently recommended that the “initial step in treating DHF is to reduce pulmonary congestion by decreasing LV volume . . .”3; but since inadequate LV EDV is the very basis of DHF, its additional primary lowering, without a concomitant greater lowering of LV end-systolic volume, could only further limit stroke volume/CO. This would increase, not decrease, LVEDP/pulmonary congestion.

Heart Rate: Finally, recommendations to reduce HR in DHF, “The initial step in treating . . . DHF [includes] . . . reducing heart rate”29 and by how much, “Although the optimal heart rate must be individualized, an initial goal might be a resting heart rate of 60 to 70 bpm [beats/min] with a blunted exercise-induced increase in heart rate”29 merit careful scrutiny. Gandhi et al1 showed that EDV and stroke volume were indeed lower during (but not necessarily a direct result of) the higher HR of acute PED (Table 1). Nevertheless, CO was in fact slightly higher suggesting a net benefit (or at least no detriment) to the higher HR, a benefit that might be even greater at higher HRs. In any case, the premise that prolonging the diastolic filling interval will increase EDV/stroke volume enough to overcome the lower HR is tenuous since resistance to further filling is fundamental to DHF. The resting HR goal of “60 to 70 bpm” attributed by this author29 to Levine35 was based on the presumption that DDF is hydraulically analogous to mitral stenosis (H. J. Levine, MD; personal communication; May 2002). It is evident that ventricular filling past an obstruction will be time dependent, but in DDF filling is restricted, not obstructed; therefore, the applicability
of primarily lowering a normal HR in patients with DHF is dubious.

Controlling supraventricular (including sinus) tachycardia might well be another matter, particularly if it is perceived as having a causal or aggravating role in an acute decompensation. However, tachycardia occurred in only a small minority of the patients of Gandhi et al1 (only 17% had a HR > 97 beats/min assuming a normal HR distribution).

Moreover, by ordinary clinical observation, treating the congestive phenomena to prompt and substantial effect alone commonly controls, if not spontaneously converts, nonchronic supraventricular tachycardias. Therefore, it is reasonable to infer that they, too, are frequently secondary phenomena in acute HF. Also, in the context of acute HF and its associated hyperadrennergic state, supraventricular tachycardia is relatively resistant to control/conversion. This often necessitates an aggressive pharmacologic regimen, itself inviting an unfavorable risk/benefit ratio. Indeed, with a 95% short-term survival using only standard treatment excluding antiarrhythmics except digitalis,30 the adage “the enemy of good is better” might apply to more aggressive antiarrhythmic therapy, at least in terms of mortality. In any case, an imperative to apply specific antichronotropic or antiarrhythmic measures is exceptional unless there is associated acute ischemia, hypotension, or lack of a prompt response to anticongestive therapy, in which case rate control and/or direct current cardioversion is appropriate, as long established.

Overview: Other presumed therapeutic distinctions are the subject of ongoing trials; but, as we have seen, whereas the structural or functional pathology underlying systolic dysfunction and DDF might vary, its pathophysiological sequelae (low CO) does not: HF is HF whatever its cause, and it is truly the final common pathway of cardiac disease. Thus, except where the underlying pathology might be affected, therapeutic similarities are likely to outweigh differences. This is supported by ordinary clinical observation and the limited data presently available.37–41

Diagnosis

The diagnosis of DHF has for some time been encumbered by the perceived need to specifically document DDF. Assuming an adequate HR, whatever the primary pathology—myocardial, valvular, pericardial, etc.—there are two, and only two mechanisms by which any pump (including the heart) can fail to deliver an adequate output: inadequate ventricular discharge (SDf) and/or insufficient ventricular charge (DDf). Thus, not surprisingly, Zile et al42 confirmed that a normal LVEF has in fact always accurately identified DHF, obviating the vexatious43 task of specifically documenting the subtle, multiple, indirect, technically challenging, variable, and unreliable echocardiographic and Doppler signs of DDF.

DEFINING HF (SYSTOLIC AND/OR DIASTOLIC)

The foregoing groundwork provides an opportunity to address the equally vexatious issue of defining HF. As has long been evident and as Table 2 attests, “not all patients with congestive HF have systolic dysfunction,” and “not all those with systolic dysfunction have symptoms of congestive HF.”44 These observations prompted the suggestion that “the term congestive HF used in the traditional way is no longer useful,”44 implying that the “traditional” definition equates or at least correlates HF with LVEF. In fact, just as “coronary artery disease” and “coronary heart disease” are associated but not synonymous, LVEF and HF are associated but not synonymous. The disturbing reality is that despite the manifest nonequivalence of LVEF and HF, many clinicians and researchers and at least one prominent clinician and influential classification of heart disease45 continue to accept a low LVEF as an independent diagnostic criterion of HF. Conceptual clarity, not to mention rational therapy and research, would be served if the diagnosis of ventricular dysfunction were strictly distinguished from the diagnosis of HF.

Setting what exactly is the optimum definition of HF is arguably a lot less problematic than might be presumed. Thus, while low CO is the pathophysiological essence of HF, its disadvantage as a diagnostic test is that its measurement requires an imaging or invasive procedure; it is compensated at rest in all but marked ventricular dysfunction, thus requiring an exercise procedure in this large subset; and its “normal” range is always relative to the individual’s contemporaneous (and labile) RAASAT over time, thus limiting the utility of a “snapshot” value.

Fortunately, as allowed by the full proper definition of HF: “...[inability of the heart]...to pump blood at a rate commensurate with the requirements of the metabolizing tissues or...can do so only from an elevated filling pressure,”78 the constant feature in untreated HF is high ventricular EDP with or without congestive sequelae (see Fig 1 legend for diagnostic criteria). Thus, until other markers such as plasma natriuretic peptides are better established, high EDP remains (1) the most clinically accessible (as jugular venous pressure), (2) timely (radiographic and renal function markers typically lag 24 to 72 h), and (3) useful criterion of HF despite its limitations—jugular hypertension has been shown 81% sensitive46 (the undetected 19% presumably due to...
Starling height disparity), and 80% specific-46 (the false-positive 20% presumably due to a rate-limiting right ventricle) for an LVEDP \(\geq 18\text{ mm Hg}\). It is certainly the most economical. It is also the most diagnostically rational and clearly preferable to the certain the most economical. It is also the most diagnostically rational and clearly preferable to the present state of confusion—diagnostic limitation is one thing, diagnostic misdirection another.

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