New Test Diagnosing Correctly and Guiding Accurately the Management of Acute and Chronic Heart Failure

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Introduction

In the management of patients with acute or chronic heart failure (HF), there are no firm criteria for a definitive diagnosis, for determination of success in the short and long-term management, or prevention of recurrence or re-admission. In this article, the challenges of diagnosing and managing HF are reviewed from a perspective of blood flow and volume, their solutions offered and their therapeutic mechanisms are discussed in details.

Problem 1 Non-specificity of the symptoms and signs of heart failure In the history interview and physical examination of patients with HF, their subjective complaints and objective physical findings are very non-specific. The symptom of shortness of breath (SOB) or the sign of pitting edema in the extremities, the sounds of crackles in the lungs auscultation, the appearance of the jugular venous reflux, etc could be seen in many other medical conditions. They include severe pulmonary embolism, pulmonary hypertension, chronic obstructive pulmonary disease (COPD), etc.

Problem 2 Non-specific strategy in current clinical investigation In the current strategy for investigation of HF, the goal of physical examination is to assess the fluid level in all parts of the body and to detect any fluid overflow at its earliest. The usual areas of examination are listed in table 1.

Table 1 Areas in Focus during the Physical Exam for Heart Failure

1. Lower leg with edema at the ankle or at the shin
2. Abdominal wall with fluid infiltration
3. Dependent areas in the presacral area
4. Liver with hepatomegaly or congestion
5. Extravascular fluid in the lungs with rales on auscultation
6. Jugular vein with distention or induced hepato-jugular reflux

However, the problem is that the current investigation strategy is limited to the assessment of fluid level in the cardiovascular system. Is the search of organs or systems with fluid overload a late reactive tactic or an early pro-active strategy?

Problem 3 Non-specific goals of current management For patients with acute systolic HF, the current management is focused on the removal of fluid from the vital organs such as the lungs, the liver etc. For patients without significant structural heart disease, in the long term management, the goals are to maintain an euvolemic fluid balance and to prevent recurrence of fluid overload. For patients with significant structural heart disease such as moderate aortic stenosis, in the long term medical management, the patient may need to maintain a high preload in order to overcome the decreased opening at the outlet. Beside diuresis, the success of the long term treatment of HF is achieved by betablockade and angiotensin converting enzyme inhibition.

Even so, with the improvement of clinical symptoms and signs, remain many important questions securing persistent clinical success. They are listed in table 2.

TABLE 2. Important Questions in the Management of Heart Failure

1. In the management of acute HF, is the

disappearance of rales in the lungs the hallmark of success?

2. Which are the criteria guaranteeing the long-term success of management for patients with acute systolic HF?

3. Is the disappearance of leg edema the hallmark of success of the long-term management of HF?

4. Can the criteria of fluid removal guarantee the success, without relapse or recurrence, of long term management of HF?

5. What is the mechanism of betablockade and ACEI on fluid dynamic?

6. How much BB and ACEI does a patient need to maintain fluid homeostasis?

SOLUTIONS Discussion of a Comprehensive Strategy: How to Assess the Fluid Volume in the Intravascular Compartment? When is the Venous Compartment Maximally Filled?

In the vascular system, most of the blood is in the veins (70%) while a smaller percentage is in the arteries (21%). (1) The blood volume, which fills up the blood vessels without causing intravascular pressure, is called unstressed volume, while the volume that stretches the blood vessels is called stressed volume. The pressure that exists in the stressed volume compartment is the mean systemic filling pressure (PMSF). The sum of stressed and unstressed volumes is the total blood volume within the venous system. (2)

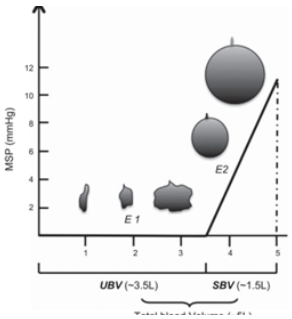


Figure 1 Stressed and unstressed volume

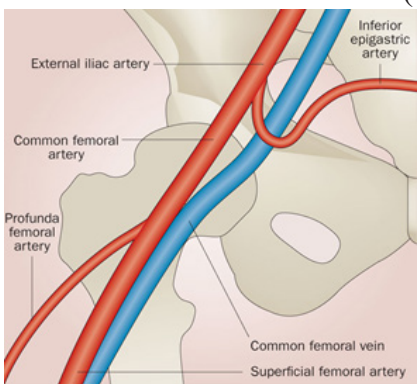
Applying these information to the care of HF patients, if a physician can detect that the veins (stressed volume) are filled at maximal capacity, then the patient needs to be monitored very closely because the patient is in danger of developing fluid overload if the influx of fluid into the venous compartment continues at the current rate. How could a physician assess at the bedside the capacity of the stressed volume?

How to assess the current venous capacity. To supply the blood to the lower extremity, the heart pumps an x amount of blood through the common femoral artery (CFA). This volume of blood arrives to the tissue by the distal arterioles and returns to the right ventricle through the venules, small veins, the common femoral vein (CFV) and the inferior vena cava. This is a harmonious interdependence between the antegrade flow of any artery and the retrograde flow of its corresponding vein. The heart cannot pump more than what it receives. In a patient with normal cardiovascular physiology and in a supine position, the cross section area of the CFA and CFV are measured by ultrasound and found to be of the same size. The similar size implies that the volume flowing across the 2 vessels is the same. This flow depends on the pressure gradient between the proximal and distal arteries or the distal to the proximal veins. Specifically, the flow from the distal vein to the heart depends on the pressure gradient between the mean circulatory filling pressure (MCFP) and the central venous pressure (CVP).

How to assess the current venous capacitance In order to assess the reserve volume (or space) in the venous compartment, we need to measure the capability of the vein to expand when required. For the purpose of estimating the venous capacity and capacitance, the common femoral vein (CFV) offers the best and easiest testing possibility and most accurate results.

The Non-Invasive Measurement of the Size and Expansion of the Common Femoral Vein The measurement of the size and expansion of the common femoral vein (SEFV) is the ultrasound study examining the size of the CFV and its expansion with cough. It is done with an ultrasound equipment (FUJIFILM SonoSite, Inc. Bothell, Washington) or by any echocardiography machine with a vascular probe.

The location of the probe is at the strongest femoral pulsation. The ultrasound plane of the CFA and CFV is the coronal plane immediately proximal to the bifurcation of the superficial and deep femoral artery (CFA). (Figure 2) In patients with normal fluid status, the size of the CFV is similar to the size of the CFA. (Figure 3-4)



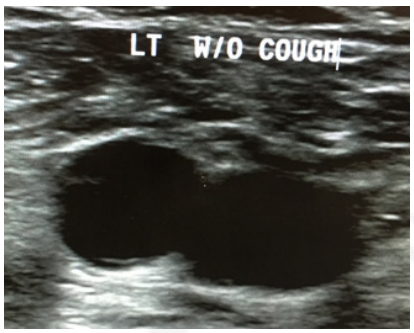


Figure 2. The common femoral vein is measured at the level immediately proximal to the bifurcation of the superficial and deep femoral artery

Figure 3. The common femoral artery is recognized as a round structure in the left and the common femoral in the right.

In a normal person without fluid overload or dehydration, when the person coughs, the femoral vein will expand maximally to twice of the baseline size. (Figure 4)

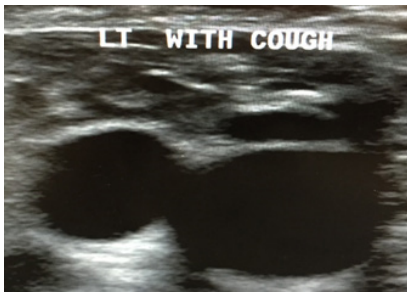
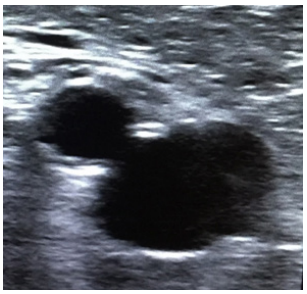


Figure 4. With cough, the size of vein increases to more than twice the size at baseline

If the patient has fluid overload, the size of the CFV is larger than the size of the CFA as seen in Figure 5. When a patient has dehydration, due to bleeding or blood loss, the size of the CFV is smaller than the size of the CFA. (Figure 6) With the SEFV test, this is the first time that assessment the status of the venous and mainly stressed volume could be achieved.



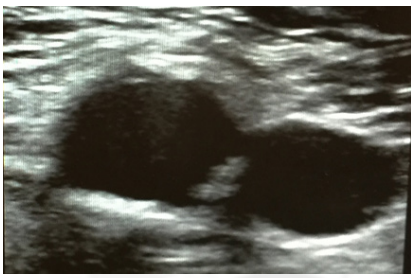


Figure 5. When the patient has fluid overload, the size of the common femoral vein is larger, twice or 3 times larger than the size of the femoral artery

Figure 6. In this picture, the size of the common femoral vein is smaller than the size of the common femoral artery. This patient had bleeding in the stomach due to ulcer.

If the patient coughs and the size of the FV does

not increase, the venous compartment (stressed volume) is full to maximal capacity. This is the most important sign. If the patient coughs and the femoral vein increases its size, the patient is in good condition and can accommodate additional fluctuation of the blood volume during different medical situations or body positions (erect or supine, etc). (Figure 4)

The other veins in the and as a measurement of the venous volume

The inferior vena cava The image of the inferior vena cava (IVC) by ultrasound could be suboptimal or blurred because of large amount of air in the bowel and long interval between the probe and the IVC, especially in very obese patients. Another negative problem is that the size of the studied IVC is compared with an average one while there are a lot of variations in the size of IVC according to body size.

The jugular vein The size of the jugular vein can expand to more than 5 times of its baseline when the patient is talking, especially in patients with pulmonary hypertension. This is why it is difficult to detect subtle changes of intravenous fluid volume by measuring the size of the jugular vein.

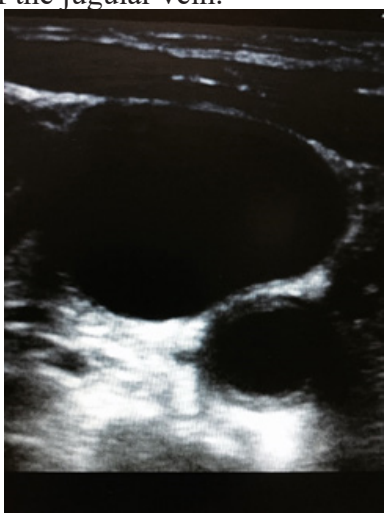


Figure 7. The jugular vein in patient with borderline low blood pressure.

The cubital vein The size of the cubital vein does not change in an ultrasound study of a patient with severe dilated cardiomyopathy and fluid overload. In the case of the CFV, its size is compared with the corresponding CFA so there is no need for a standardized average. (Figure 8-10)

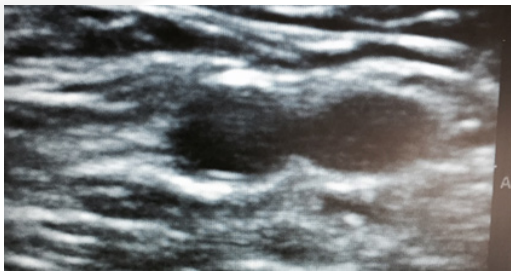


Figure 8. The cubital artery and vein in patient with severe heart failure. The size of the common femoral vein was large. The patient had significant fluid overload, while the size of the cubital vein was normal (as the same size as the cubital artery.

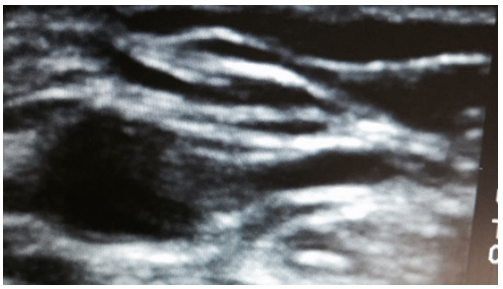


Figure 9. In this picture, the operator pressed the probe in order to depress the vein and by doing so, the operator could identify the cubital vein and artery (not compressed)

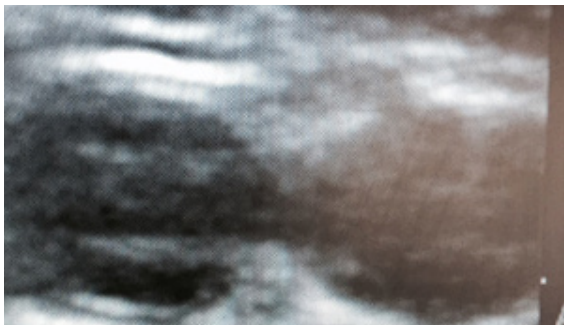


Figure 10. The cubital vein does not expand upon cough.

APPLICATION 1

Accurate Classifications of Patients with Heart Failure

The criteria needed to classify a patient are: (1) ejection fraction (EF), (2) the size of the femoral vein and (3) the expansion of the FV with cough. If the patient has enlarged FV size (fluid overload) and the FV still expands with cough, the fluid overload is mild to moderate. The enlargement of the FV could be reversed and the FV goes back to its normal size (same size as of the femoral artery) when there is sufficient removal of intra- and extravascular fluid. One of the best examples is in the case of patients with HF and preserved EF (HFpEF). These patients do not have permanent HF. Their fluid overload is transient and can be reversed.

If the size of the FV is large and there is no expansion of the FV, the overload is severe, with most likely pulmonary hypertension. The pulmonary artery mean pressure would be above 20mmHg. Even so, the enlargement of the FV could be reversed and the FV goes back to its normal size when there is sufficient removal of intravascular fluid (stressed and unstressed volume).

Some patients with structural heart disease (valvular stenosis or regurgitation, dilated cardiomyopathy, etc.) require high pulmonary artery pressure in order to keep a decent cardiac output. In these patients, the enlarged size of the FV is needed. The above classification of patients with HF is listed in table 3.

Table 3. New Classification of Heart Failure Patients

A. Normal patient Normal EF, size of FV and expansion of FV
B. Early reversible stage of diastolic dysfunction or HFpEF: Normal EF, enlarged size of FV and normal expansion of FV
C. Early reversible stage of systolic dysfunction: Low EF, enlarged size of SFV and normal expansion of FV
D. Advanced reversible stage of diastolic dysfunction: Normal EF, enlarged size of FV and abnormal expansion of FV
E. Advanced reversible stage of systolic dysfunction: Low EF, enlarged size of FV and abnormal expansion of FV
F. Severe advanced stage of diastolic dysfunction: Normal EF, enlarged (not reversible) size of SFV and abnormal (not reversible) expansion of FV
G. Severe advanced reversible stage of systolic dysfunction: Low EF, enlarged (not reversible) size of SFV and abnormal (not reversible) expansion of FV

APPLICATION 2

Fluid status in patients with co-morbidities
There are many patients in whom the physical examination of liver congestion, abdominal wall infiltration, dependent area edema could not be accurately evaluated. These patients could have previous cardiac problems such as coronary bypass graft surgery, or surgical or percutaneous valvular procedure or when the patient is bed-ridden. In these patients, the SEFV test is very sensitive in confirming their volume status (euvolemic or hypervolemic), even when these patients are still asymptomatic. This SEFV test is also very useful in differentiating the causes of shortness of breath (SOB) or fatigue or edema in patients with concomitant chronic obstructive pulmonary disease (COPD), renal failure with or without dialysis, severe obesity etc. In these situations, the SEFV could confirm the presence of absence of fluid overload and by doing so, help the clinical interpretation of SOB from COPD, pulmonary hy-

pertension, HF with or without fluid overload.

APPLICATION 3 Removal of the Extra Fluid With the use of diuretics, fluid is removed from the stressed volume, from the veins where the transmural pressure is higher than zero. The diuretics have no direct effect on unstressed volume where the transmural pressure is less than zero. Mechanism of Fluid Evacuation from the Cutaneous Veins: The Alpha 1- and alpha-2-adrenergic receptors

The splanchnic and cutaneous veins have a high population of alpha 1- and alpha-2-adrenergic receptors and therefore are highly sensitive to adrenergic stimulation, contrary to skeletal muscle veins, which have relatively insignificant sympathetic innervation. So in any patients with or without HF, the alpha agonists act by constricting the cutaneous veins and shunting the blood to the stressed venous compartment in order to increase preload, then indirectly the cardiac output. By constricting the cutaneous veins, the alpha agonists move the blood to the veins and so to the right heart and can aggravate HF if the venous compartment is maximally filled. This observation could explain the negative effect of the alpha blockers (mainly doxazosin) in studies with HF resulting in worsening of HF.

When the patients receive betablockers, the blocking of the beta receptors leave the vasoconstrictive actions of the alpha receptors unopposed so the blood is pushed towards the veins. This is the long term beneficial effect of BB in HF patients. This observation could explain the early worsening of HF when the patients were initiated with BB. With similar mechanisms, the patients on ACEI undergo similar fluid removal by constricting the cutaneous veins

CONCLUSIONS

In the diagnosis and treatment of HF, we need to evaluate accurately the intravascular status (mainly venous) fluid status and start treatment of HF at the early stage even the patient is still asymptomatic. The SEFV test can help us to do that. Once the patient is diagnosed of having imbalance in the fluid status, besides diuretics, evidence based medications such as angiotensin converting enzyme inhibitor or angiotensin receptor blocker, or valsartan and neprilysin inhibitor sacubitril should be used to treat the cause triggering ventricular dysfunction. The mechanism of these drugs is to cause vasoconstriction and shift the fluid to the venous system (stressed volume) so it can be removed. This is why adherence to guideline management would help the patients with HF in the short and long term management.

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