Review paper

A reappraisal of concepts in heart failure: Central role of cardiac power reserve

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Abstract

Of all cardiological conditions, heart failure (HF) is by far conceptually the most difficult to grasp. For over a century, it has been beset with a number of misconceptions, which require reappraisal. Central to these misleading concepts is the absence of a reliable means of evaluating what constitutes heart failure and how to assess and ameliorate its severity. To attain this necessitates our moving away from the easier assessments at rest to measurements at peak exercise. Taking the key function of the cardiac pump as the delivery of adequate hydraulic energy to maintain the requisite circulation, it becomes apparent that the parameter we require is cardiac power output reserve, which incorporates both the flow- and pressure-generating capacity of the heart. Evidence available so far has shown that this variable is a major determinant of exercise incapacity and prognosis in patients with heart failure.

Key words: cardiac power output, cardiac functional assessment, peak oxygen consumption, chronic heart failure.

Introduction

Despite major advances in heart failure (HF) therapy in recent decades [1-3], confusion about the condition still abounds, as indicted by the conclusion drawn from a survey by the journal Cardiovascular Research which stated "heart failure is the label for a cardiovascular syndrome that is lacking uniform criteria for definition" [4]. Fundamental to this debate is that the experts who were surveyed patently had very different concepts about heart failure arising mainly because physicians have so far been unclear about what method(s) should be employed to measure the condition. The objective of this short review is to reappraise the prevailing concepts and ascertain which ones might be conceptually misleading, and explore an avenue whereby our conceptual framework about heart failure may be put on the right track.

Some misleading concepts of heart failure

There are some conceptual cul-de-sacs that have been rather influential in the field of heart failure. The first one is the reliance by clinicians on

measurements made with the patients comfortably resting using sophisticated imaging techniques. A fundamental flaw in this approach is the confusion between structure and function, as exemplified by the widespread use of left ventricular ejection fraction (LVEF) in clinical practice as an indicator of cardiac "function". The second pertains to the fundamental misconception that heart failure is a problem of myocardial contractility, which needs to be "extracted" and be independent of the loading conditions affecting the myocardial contraction. The third is the belief that heart failure is exemplified by its inability to meet "the needs of the body" [5] or "to pump blood at a rate commensurate with the requirements of the metabolizing tissues" [6]. The fourth is the belief that measurements made at rest are sufficient to define the overall state of heart failure.

Imaging and LVEF

Echocardiographic representation of LVEF is perhaps the most widely used indicator of cardiac function. Although entrenched in cardiological practice and widely employed as an inclusion requirement into clinical trials, it is not a panacea. It is usually measured at rest. It has previously been shown to correlate well with mortality [7-9], but does not correlate with functional capacity as measured by exercise duration, METS achieved or peak VO2 [10-14]. When the heart begins to fail, a key manifestation is exercise intolerance. For a measurement purported to represent cardiac function to show very poor correlation with exercise capacity, questions should be asked whether such a measure is truly a reliable representation of HF.

LVEF is equal to stroke volume (SV) divided by the LV end-diastolic volume (LVEDV), LVEF=SV/LVEDV. End-diastolic dimensions or volume are essentially an indication of the structure of the LV, just as a necessary part of the description of the structure of a container is given by describing its dimensions. Therefore, in this equation, only the numerator is possibly an indication of cardiac function. However, it is also known that compensatory mechanisms are triggered following an insult to the heart in an attempt to maintain the SV as constant as possible. In other words, the decrease in LVEF following cardiac impairment is largely a relative constant divided by the enlarging LVEDV. Thus, LVEF can be viewed as the reciprocal of LVEDV, and therefore an indicator of structure. This is probably why LVEF correlates poorly with exercise capacity or cardiac function [15].

The operative concept in HF is impairment of function, of instead structure which may or may not have contributed to the dysfunction. It is therefore vitally important, when viewing images of the heart, to distinguish information pertaining to function versus to structure, and the relation between the two. A commonly used term in modern HF literature is 'remodelling', which is often assumed to connote adverse remodelling (meaning ventricular chamber dilatation), although the dilatation itself may actually be physiological and compensatory [16]. To assume that all remodelling (dilatation) is adverse and should be prevented or reversed is rather simplistic. A deeper understanding of the mechanistic processes involved is necessary to avoid confusion [1].

Contractility

In the 1960s, a notion emerged that became a prevailing concept that the crucial difference between a failing and a normal heart is that the former has compromised myocardial contractility [17-19]. This led to the hunt for an "index of contractility" that was totally independent of ventricular loading conditions, especially preload and afterload [18-20]. A major objective of therapy thus became primarily to increase myocardial contractility to reverse HF. This led to a systematic development of positive inotropic agents and the emergence and testing of milrinone, enoximone, xamoterol, flosequinan, vesnarinone, and more recently levosimendan [21, 22]. However, meta-analyses of data from clinical trials of inotropic agents point to worryingly high mortality rates [23-25]. Paradoxically, powerful negative inotropic agents such as β-adrenoceptor blockers have been shown in clinical trials to produce the opposite effect of lower mortality rates [26, 27], and not all of these were due to reduction in sudden cardiac deaths [28].

With hindsight, it has become evident that the concept of increasing myocardial "indices of contractility" is flawed. After a major injury to the left ventricle, such as after a sizeable myocardial infarction or acute myocarditis, the remaining viable myocardium becomes vital in maintaining the cardiac function and provides an adequate circulation. Stimulating these remaining viable myocardium to enhance cardiac pumping by neurohormonal, pharmacological or other means would improve the indices of "contractility" (e.g. LV dp/dt_{max}, V_{max}, E_{max}), but also hasten the demise of these vital cardiomyocytes, leading to vicious downward spiral of progressive LV dysfunction [1]. Rather than stressing the cardiomyocytes, the objective should be to improve impaired ventricular mechanics, such as in the presence of dyssynchrous contraction that can be corrected by cardiac resynchronisation therapy, thereby possibly sparing the need for the viable myocytes to hypercontract leading to prolonged survival [3].

Failure to meet the needs of body tissues

The concept that heart failure is exemplified by its inability to meet "the needs of the body" [5] or "the requirements of the metabolizing tissues" [6] has been so deep-seated as to be sanctioned in many

formulations of definitions of heart failure [4]. Of all the nutrient needs of the body, because of the lack of any storage capacity in the tissues, the one that is most dependent on the continuous delivery via the blood propelled by the pumping action of the heart is oxygen, not glucose, free fatty acids or other ingredients of biochemical fuel. This is so crucial that apart from the heart, the only other organ in the body that receives the entire cardiac output is the lungs, in order to acquire oxygen. However, such a concept of not meeting tissue needs was debunked over two decades ago by Harris [29] who pointed out that "neither the consumption of oxygen by the body is reduced in cardiac failure" nor is there any tissue sensor that detects tissue hypo-oxygenation or hypo-metabolism and thereby triggers compensatory mechanisms [30]. Instead, he expounded that the body naturally detects the insufficiency in cardiac pumping output via the arterial baroreceptors that secondarily trigger a whole series of compensatory mechanisms in an attempt to prop up the arterial pressure. At length, he explained that nature does not cater for the heart failure condition, and in effect, these detection and compensatory systems triggered by heart failure are erroneous because they were designed not to cope with heart failure but for other purposes such as haemorrhagic shock or exercise. Subsequent clinical counteraction of these effects through pharmacotherapy (using diuretics, ACE inhibitors, β-adrenergic, angiotensin and aldosterone receptor blockers, etc) has proven to be beneficial to the patients [1, 2, 26-28, 31]. These therapies are nevertheless dealing with the secondary effects of heart failure. Dealing with the primary defect of cardiac pump dysfunction is even more fundamental, but the present clinical predicament is whether there is a reliable way of measuring the primary functional inadequacy of cardiac pumping, that also takes into account the natural detection system already in place through evolution [29].

Measurements made at rest are unrepresentative of cardiac reserve

It is axiomatic that patients with HF are more troubled by symptoms during exertion than at rest, mainly because the reserve function of the heart becomes exposed as being limited during exertion [32]. More than a century ago, Sir William Osler [33] wrote "that in these hearts, the reserve force is lost, and with it the power of meeting the demands in maintaining the circulation during severe exertion" [34]. This was probably one of the earliest recognitions by a physician (without the benefit of measuring cardiac function *in vivo*) that the prime cause of heart failure is the loss of cardiac reserve, and implied that its evaluation should include means of revealing such limitations through some form of maximal stress, such as severe exertion or maximal exercise testing. Conceptually, HF is primarily the failure of the cardiac pump to function adequately to support the more dynamic circulation required during exercise [15]. Conversely, the extent of impairment in pump function is indirectly represented by the diminution in exercise capacity, best measured by peak exercise oxygen consumption (VO_2), but approximated by exercise duration [15]. However, in the event that the exercise diminution is likely to be caused by non-cardiac factors as well, direct evaluation of how much cardiac function is impaired will be required. In this case, the choice of variable to represent cardiac function requires careful consideration, as such a variable will need to be reliably indicative of cardiac impairment.

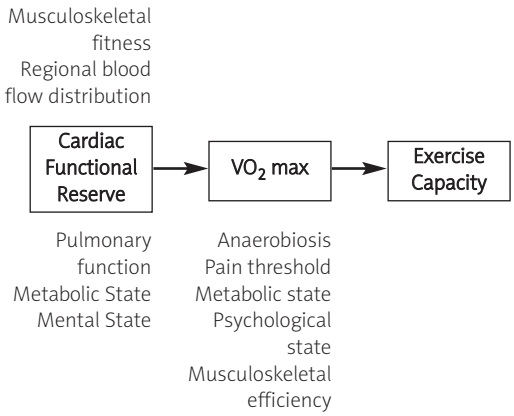

Figure 1. Factors influencing exercise capacity
How much exercise a person can perform depends on physical and psychological factors, although the bulk of it is determined by aerobic capacity (peak oxygen consumption, VO_2 max). In a patient with heart failure, and assuming the absence of other organ impairment, then the functional reserve of the heart is the major determinant of VO_2 max and exercise capacity. As a corollary, both VO_2 max and exercise capacity can be viewed as indirect indicators of cardiac functional reserve

Cardiac functional reserve

What is clear from the above is that when measured at rest, unless the heart is in extremis and the patient is symptomatic with minimal or no exertion, it will not be able to predict how much reserve function the failing heart still possesses. The most reliable estimate of the reserve is necessarily measured at peak stimulation of the heart, during "severe exertion", as stipulated by Osler in 1895 [33].

Peak oxygen consumption

HF is a disease of exercise; exercise limitation is its principal symptom and the degree of exercise limitation is its principal prognostic indicator [32]. The addition of respiratory gas analysis to standard exercise testing has become increasingly important

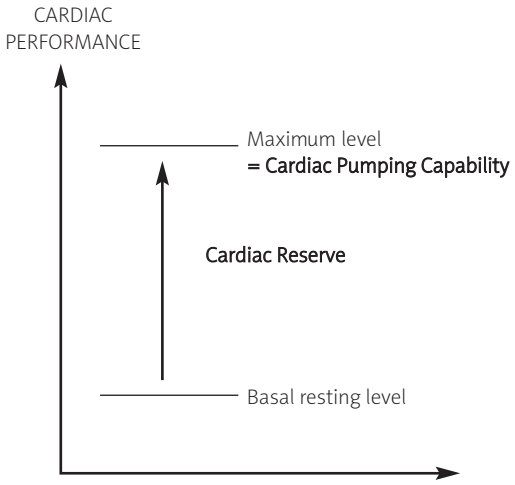

Figure 2. Cardiac pumping reserve
The performance of the heart varies from basal (unstimulated, non-zero) levels at rest, necessary for maintaining baseline metabolism, to a peak ceiling level that cannot be superseded for a given set of mechanical properties of an individual heart. The span between these two levels represents the reserve functional capacity of the heart. Measurements at basal resting state do not provide any information about the amount of reserve function available, except when the reserve is exhaustively used in order to maintain life (e.g. in cardiogenic shock, see Figure 3)

over the years, especially in the assessment of HF. There is a steady growth in recent years of patients awaiting transplantation relative to the availability of donor hearts. The use of peak oxygen consumption (VO_2) in prognostic assessment and monitoring of this condition has become, and continues to be, standard practice [35, 36].

Exercise capacity (Figure 1), expressed as exercise duration or workload achieved has been recognised for several decades as an important prognostic marker in cardiac disease [37]. Myers and colleagues [38] showed peak exercise capacity to be the strongest predictor of all cause mortality amongst both normal subjects and those with cardiovascular disease. Exercise capacity outperformed other traditional markers of cardiovascular risk, including smoking, hypertension, diabetes, previous history of myocardial infarction or HF and hyperlipidaemia. This study concluded that, in terms of reducing mortality from any cause, improving exercise tolerance warranted at least as much attention from physicians as other major risk factors. Exercise capacity itself is a key item of the quality of life of patients with HF, which can be perceived by the patients and verified through formal exercise testing. Improving it is a major objective of therapeutic trials.

Peak VO_2 (Figure 1) is a more reliable index of exercise capacity than exercise duration or workload as it represents a more precise, reproducible and physiological measure of cardiopulmonary function [32, 35]. Numerous studies published in the last decade demonstrate peak VO_2 to be an independent predictor of mortality. Several small studies were published in the mid 1980's showing peak VO_2, along with other factors, to be important in risk stratification in patients with HF [39-41]. Studies followed in the 1990's all indicating peak VO_2 to be an independent predictor of mortality using a multivariate analysis [13, 42-48].

Some of these studies highlighted that a single cut off point for peak VO_2 provided a clinically meaningful separation between patients with a high or low likelihood of survival. The study by Szlachcic and colleagues [39] was the first to suggest that a cut-off point of peak VO_2 (in this case, 10 mls/kg/min) played an important role in risk stratification. More recently, a peak VO_2 of 14 mls/kg/min has been used and is commonly applied in the context of selecting patients for transplantation [49]; it appears that for patients who achieve values greater than 14 mls/kg/min, the 1-year survival is similar to those who receive a transplant. This value is currently recommended as a relative indication for accepting patients for transplantation in the American Heart Association Scientific Statement on Transplantation [50]. Peak VO_2 also correlates well with quality of life and symptoms [51, 52] and hospitalisation rates [53].

Limitations of peak oxygen consumption

However, peak VO_2 has several key limitations in the assessment of cardiac disease. It is influenced by non-cardiac factors (Figure 1) such as muscle deconditioning, motivation for performing exercise and obesity [52, 54]. The expected peak VO_2 varies according to the age and sex of the subject [55, 56] and evaluation using a percentage of the predicted peak VO_2 has been suggested to be more predictive of mortality than peak VO_2 alone [57]. Also, no statistical difference in survival between patients with peak VO_2 levels of 10-14 mls/min/kg and those with levels of 14-18 mls/min/kg has previously been shown in some studies [39,43,49]. A large study consisting of 664 patients during a 10 year period of follow-up was carried out by Myers and colleagues [58]. A multivariate analysis revealed peak VO_2 to be an independent predictor of mortality above and below a range of 10-17 mls/min/kg, rather than at a cut-off point of 14 mls/kg/ml. The non-predictive value of peak VO_2 may be linked to the fact that it is only an indirect indicator of peak exercise cardiac output [39, 59, 60] and cardiac functional reserve [15]. This has led investigators to look beyond peak VO_2 at other cardiopulmonary exercise derived data in the assessment of cardiac function.

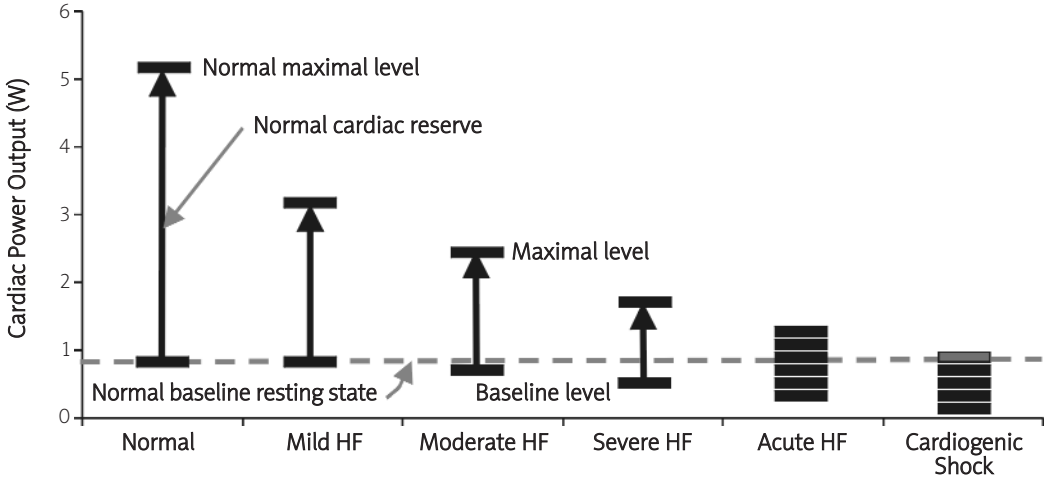

Figure 3. Schematic diagram depicting cardiac functional reserve of individual hearts in a normal functional state, in various degrees of heart failure (HF) and in cardiogenic shock.
In acute heart failure and cardiogenic shock, due to activation of compensatory mechanisms, the baseline levels span from markedly depressed performance to augmented states approaching the individual hearts' maximal pumping capability

Haemodynamic assessment of cardiac function

Parameters such as the blood pressure response to exercise [61-65], the ratio of minute ventilation to carbon dioxide production (VE/VCO_2) [66-69] and oxygen recovery post exercise [70] have emerged in recent years as independent predictors of outcome. However, these variables are only indirectly related to cardiac function, and therefore can only be considered as markers of severity of organ failure, with direct means to improve these values not necessarily indicating an improvement in cardiac function. More direct measurements of cardiac work, represented by peak stroke work index [71, 72], cardiac output (CO) response to exercise [73] or cardiac power output, CPO [74, 75], have emerged as powerful independent predictors of prognosis over peak VO_2.

Cardiac pumping capacity and cardiac reserve

The heart is a mechanical pump; its performance ranges from zero to a finite maximum. Two important terms can be applied to cardiac performance: (a) **cardiac pumping capability** – the maximum performance that can be achieved during stimulation, and (b) **cardiac pumping reserve** – the difference in performance between resting and maximally stimulated states. This concept was initially proposed by Barringer [76] in 1917 and has since been re-evaluated and modified by subsequent investigators [77-80].

Each heart has its own ceiling peak pumping performance, above which it is physically impossible to exceed (Figure 2). This value would alter only if the intrinsic condition of the heart is altered, e.g. after an acute myocardial infarction or after successful relevant cardiac surgery. When compared, these maxima of individual cardiac function are direct and objective indicators of how relatively good or impaired the hearts are as fluid pumps. They provide a means of grading the degree of functional impairment in heart failure along the scales below the norm (Figure 3), and conversely, the degree of superiority in the function of athletic hearts [79, 80].

The performance of the cardiac pump, if considered in the context of its function, can be defined by paraphrasing William Harvey's original concept as "the maintenance of the circulation to transport nutrients to meet the metabolic demands of body tissues" [81]. The delivery of oxygen to an organ depends on the rate of blood flow into the vascular bed of that organ. Thus, the first determinant of the demand imposed on the heart is the production of an adequate cardiac output (CO). One way of increasing blood flow to any tissue is by reducing its vascular resistance. Once maximum vasodilatation is achieved, the only way to increase blood flow into the tissue is by increasing arterial perfusion pressure. This increase in pressure assumes an even greater importance in the perfusion of exercising skeletal muscle because of the higher tissue pressure developed during muscle contraction, in particular during isometric exercise. Hence, the second demand imposed on the heart is the maintenance of an adequate arterial pressure. The product of cardiac output and arterial pressure is defined as **cardiac power output (CPO)**. This term represents the overall function, equivalent to the rate of hydraulic energy imparted by the cardiac pump into the circulation to facilitate the perfusion of various metabolising tissues. By virtue of containing the arterial pressure term, CPO

measurement, especially at maximal exercise, may well represent the best way of detecting and monitoring primary cardiac pump inadequacy in heart failure patients, complementing the natural detection of inadequate BP levels already afforded through evolution [29].

Cardiac pumping capability can thus be defined as the power output achieved by the heart during maximal stimulation, and cardiac pumping reserve as the increase in power output as the heart's performance is increased from resting to the maximally stimulated state. Figure 3 illustrates cardiac functional reserve of individual hearts in a normal functional state, in various degrees of HF and in cardiogenic shock.

Clinical application of cardiac work and cardiac power output

CPO has been used by several investigators in the evaluation of cardiac disease. It is calculated as the product of the mean arterial pressure (MAP) and the cardiac output multiplied by a correction factor (2.22 X 10^{-3}) and is expressed in watts. Maximal CPO was shown by Tan [78] in 1986 to be an accurate predictor of prognosis in a group of ambulatory patients with New York Heart Association (NYHA) functional class III-IV of heart failure. Sixty three patients with a mean LVEF of 24.2% were studied. Several invasive haemodynamic measurements were recorded at rest: Cardiac index (CI) = CO/body surface area in l/min/m^2, pulmonary artery wedge pressure (PAWP), left ventricular stroke work index (LVSWI) = MAP x PAWP/HR x 0.133 J.m^{-2}). Dobutamine was then infused as a stress agent increasing in increments of 5mcg/kg/min to a maximum of 40 mcg/kg/min.

The hypothesis tested was that a maximal CPO of <1 watt via pharmacological stimulation (assumed to be normal resting value for an average sized man) could discriminate between survivors and non-survivors at one year follow up. Of the 23 patients with a maximal CPO <1 watt, 19 died of progressive heart failure. Four patients died in the group of 40 with a maximal CPO of >1 watt. No pattern was seen with any resting parameter. Conclusions were drawn therefore that a maximal CPO of <1 watt was indicative of a poor 1-year survival, although no statistical comparison was made with the other haemodynamic parameters in order to assess which provided the most accurate prognostic information. We can conclude from this study, however, that haemodynamic parameters under stress are more predictive of mortality than resting values.

In a similar study, Tan and Littler [82] studied the application of CPO in patients with acute cardiogenic shock. Twenty eight consecutive patients admitted to the coronary care unit (CCU) with the condition were studied (24 of these patients had sustained a myocardial infarction, MI). Invasive measurements of the haemodynamic parameters were taken, at rest and after dobutamine stress (until no further rise in CPO occurred or a maximum dose of 40 mcg/kg/min was reached). The study showed differences between survivors and non-survivors in resting and maximal LVSWI, maximal CI and maximum CPO. All the patients with a resting CPO <0.35 watts died, as did all the patients with a maximum CPO of <1 watt or a LVSWI <0.25 J/m^2.

Over two decades later, the SHOCK trial registry [83] confirmed the prognostic value of resting. In a multivariate analysis, CPO and CPI (cardiac power index) were found to be the only haemodynamic predictors independently associated with in-hospital mortality after adjusting for age and a history of hypertension.

Stress represented by exercise (a more natural physiological index of stress) has also been found to correlate with dobutamine stimulation for maximal CPO [84]. In this study, LVSWI also showed no significant difference between the two modes of stress, but maximal CO values were higher in the dobutamine group. This may have been due to the fact that dobutamine caused more vasodilatation than exercise and the heart converted more of its pressure generating capacity into a flow generating capacity.

Roul and colleagues [74] were the first group to evaluate the prognostic value of peak CPO during maximal exercise testing of patients with CHF. This group assessed 50 patients with NYHA class II-III CHF using invasive measurements of the haemodynamic parameters during maximal supine exercise on a flywheel. The mean follow-up was 21.2±1.17 months. The multivariate analysis revealed the peak CPO to be an independent predictor of death or a major cardiac event and a peak CPO <2 watts was found to accurately identify patients with a poor short term prognosis.

Non-invasive estimation of cardiac power output

One of the drawbacks of using peak CPO and other haemodynamic parameters as indicators of cardiac function, is that invasive measures use a right heart catheter, which is not without risk to the patient and also impractical for everyday clinical use. Investigators have therefore looked at non-invasive ways of measuring haemodynamic parameters using either echocardiography [85,86] or carbon dioxide (CO_2) re-breathing techniques [87]. The non-invasive assessment has the advantage that it does not have the complications associated with Swan-Ganz catherisation, e.g. pneumothorax. From the patients' point of view, it obviates the discomfort associated with in-situ intravenous (± intra-arterial) catheters which can result in indeterminate extents of vaso-vagal reaction. With less constraints, patients are more likely to attain their true maximum exercise

capability. Non-invasive measurements are therefore more likely to provide a true reflection of peak exercise haemodynamic data.

Further statistical evidence in favour of using maximal CPO and cardiac reserve (assessed non-invasively by echocardiography) as prognostic indicators was reported by Marmor and Schneeweiss [88]. Forty two patients with CHF (NYHA functional class I-IV) and 10 healthy volunteers were followed-up for 3 years after haemodynamic assessment at rest and after incremental dobutamine stimulation. CPO was estimated non-invasively as the maximal product of systolic pressure and aortic flow. Aortic flow was determined using Doppler ultrasonography to calculate the velocity time integral and aortic cross sectional area. Central aortic pressure was calculated by a computer controlled device producing a non-invasive waveform previously validated against invasive measurements [89]. By aligning the beginning of the flow with the simultaneously recorded central aortic pressure, instant power measurements were obtained. This study showed that those subjects with a cardiac reserve >1.5 watts (i.e. ability to increase cardiac power output on stress) survived and 8 out of the 9 patients with a cardiac reserve <1.5 watts died. Cardiac reserve was found to be the only significant predictor of survival in a multivariate analysis.

That a cut-off point exists for the prognostic power of peak exercise CPO (assessed non-invasively using CO_2 re-breathing methods) in a group of patients with stable CHF was confirmed by Williams and colleagues [75]. A cohort of 219 unselected consecutive patients underwent cardiopulmonary exercise testing with non-invasive measurements of haemodynamic parameters over a mean follow up period of 4.64 years. Peak and resting CPO, peak MAP peak and resting CO, and peak VO_2 were all predictive of outcome in univariate analyses. Peak CPO, either entered continuously or categorically with a cut-off value of 2.0 watts, was the only independent predictor of mortality using a multivariate model - outperforming peak VO_2. The mortality rate of those patients with a peak CPO <2.0 watts was considerably higher than those with a peak CPO >2.0 watts in Kaplan-Meier survival analysis, a result in close agreement with previous published work using invasive measurements of CPO [74].

"Surrogate" markers of cardiac power output

Methods of measuring cardiac output and mean systemic arterial pressures, especially at peak exercise, are not as straightforward as measuring of O_2 consumption with available non-invasive equipments nowadays. For practical purposes, approximations to CPO are being sought. After all, VO_2 contains CO, multiplied by a factor, the systemic arteriovenous difference in O_2 content. At peak exercise, if we can assume that systemic oxygen extraction to be maximal, then the difference in O_2 content can be assumed to be relatively constant.

Taking the above into account, Cohen-Solal et al. [90] assessed the prognostic value of a new "surrogate" variable of CPO, "circulatory power" (CircP, the product of peak VO_2 and peak systolic blood pressure). Although easier to measure, systolic blood pressures are generally exaggerated in stiffened arterial systems, such as those found in the elderly. Despite these confounders, circulatory power was found to be the only cardiopulmonary variable predictive of prognosis in a population of 175 patients with CHF. Scharf et al. [91] also confirmed the prognostic significance of the circulatory power, which also outperformed peak VO2 in a multivariate analysis, in 154 patients with CHF.

Williams et al. [92] evaluated the relationship between the more direct CPO and the indirect index of cardiac pumping capacity, circulatory power in 219 ambulatory patients with CHF. CircP was found to have a direct and consistent relationship with CPO, both overall and at peak exercise. The results suggest CircP to be an adequate measure of cardiac pumping capacity when the more directly measured CPO is not available. This finding was not unexpected as VO_2 contains the term CO, multiplied by a factor, the systemic arteriovenous difference in O_2 content ($[O_2]_{a-v}$). For the approximation of CO from VO_2 to hold, it requires that we assume at peak exercise the $[O_2]_{a-v}$ is invariable, which implies that systemic oxygen extraction is maximal in each patient. If this assumption holds, then peak VO_2 and hence peak CircP would provide similar information about cardiac function as peak CO and CPO, respectively.

However, this raises the question whether in clinical practice we can rely on such approximations and assumptions when making important decisions on individual patients, such as whether to undergo cardiac transplantation or not. The answer depends on each clinician's decision about how much trade-off between accuracy and ease of measurement is clinically acceptable. As technology for measuring CO and MAP continuously and non-invasively, especially at peak exercise, is not as well developed as that for measuring VO_2, it would therefore seem reasonable to use CircP as a valid and practical surrogate. However, when more critical decision making is required, then the clinician can fall back and rely on the more direct indicator of cardiac function, CPO [15,93].

Cardiac power output and relationship to exercise capacity

The studies outlined above have highlighted the prognostic importance of CPO, cardiac reserve and the "surrogate" circulatory power, in the assessment of various cardiac disorders. Assessment of exercise

capacity and quality of life is as important as mortality in the evaluation of cardiac disease. CPO and cardiac reserve, like peak VO_2, have previously been shown to correlate with exercise capacity and quality of life. Bain and colleagues [94] studied 41 CHF patients with NYHA functional class II-IV, using invasive haemodynamic measurements at rest and maximal exercise. Peak exercise CPO was shown to correlate with exercise duration to a greater extent than either maximal cardiac index or left ventricular stroke work index. Cardiac reserve correlated with exercise duration, to a similar extent as peak exercise CPO. A later study by Cooke et al. [87], using non-invasive haemodynamic assessments, was performed to test the hypothesis that CPO and cardiac reserve correlated with peak VO_2. Seventy subjects with a wide range of cardiac function, from trained athletes to transplant candidates performed treadmill cardiopulmonary exercise tests with estimation of haemodynamic parameters. CPO at peak exercise was found to correlate significantly with peak VO_2. Non-invasive measurements of data were reproducible with coefficients of variation of 4.7% for peak VO_2, 7.08% for maximal CO and 9.08% for CPO. Marmor et al. [85] showed NYHA functional class, the classical tool used for symptom assessment of cardiac disorders to significantly correlate with peak CPO, suggesting that NYHA is an easily obtainable clinical surrogate of cardiac function.

Conclusions

Compared to other aspects of cardiology (e.g. coronary artery or valvular diseases, hypertension or arrhythmia), heart failure is conceptually more challenging, and historically, it has also been beleaguered by misleading concepts. At the crux of these difficulties lies the question, what is the most representative measure of cardiac pump dysfunction. To find the answer, we need to acknowledge that heart failure is indeed a disease of exercise intolerance, and that no amount of measurements at basal resting states can accurately depict or predict the true extents of loss of functional reserve. Similarly, any selection of parameter to represent cardiac dysfunction must be cognizant of the fact that the prime role of the mechanical pump is to impart hydraulic energy to maintain an adequate circulation, and that the cardiovascular control system operative in compensating for the failing heart works by detecting the inadequacy of pressure and flow generating capacity of the heart. Evidence available so far supports the concept that there is a central role for measuring cardiac power reserve in understanding how best to evaluate and treat patients with heart failure.

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