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Arterial Ventricular Uncoupling with Age and Disease and Recoupling with Exercise

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Abstract

The deterioration in arterial and cardiac function with aging impairs arterial ventricular coupling, an important determinant of cardiovascular performance. However, exercise training improves arterial ventricular coupling especially during exercise during the age and disease process. This review examines the concept of arterial-ventricular coupling, and how age, and disease uncouples but exercise training recouples the heart and arterial system.

Keywords

arterial ventricular coupling; Aging; Cardiovascular Disease; Exercise training

Introduction

By 2050, it is anticipated that approximately 89 million people in the U.S. will be over 65 years of age, more than double the number of older Americans in 2010. This is of particular concern as the process of aging significantly increases cardiovascular (CV) morbidity even in the absence of other risk factors (e.g., hypertension, obesity, diabetes, hypercholesterolemia). As such, the risk of death from heart disease is approximately 60-fold greater in the 8th decade compared to the 4th decade of life. Furthermore, aging is also associated with a drastic increase in subclinical/occult CV diseases (i.e., silent coronary atherosclerosis). Therefore, aging of the U.S. population is one of the major public health challenges that we face.

Compelling evidence has shown that with healthy aging (absence of CV disease), the heart and vasculature undergo considerable remodeling and a deterioration in function, especially in response to stress (such as acute exercise). Although such changes are considered to be representative of ‘normative’ aging, the CV adaptations to aging lower the threshold for the development of CV disease. Indeed, aging in the presence of CV diseases (hypertension,

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diabetes, atherosclerosis) or the clustering of CV risk factors (i.e., metabolic syndrome) accelerates the arterial and cardiac dysfunction. As such, these age and disease interactions impair the coupling between the heart and arterial system, termed arterial-ventricular coupling (E_A/E_{LV}), a key determinant of CV performance and efficiency. The CV system is modulated to provide sufficient pressure and flow to the tissues. Understanding the performance (pressure and flow output) of the heart requires examination of the properties of the left ventricle (LV) itself (power and stroke capacity), and the modulating effects of the arterial system (capacitance and inertial properties of the aorta, and the resistance capacity of the micro-circulation) on LV performance. E_A/E_{LV} allows the examination of the crosstalk between the heart and arterial system.

Importantly, individuals who maintain a physically active lifestyle, or who partake in exercise training later in life, can either ameliorate or delay some, but not all, of the CV alterations that accompany advancing age. This review examines the underlying concept of E_A/E_{LV}, and examines how age and CV disease result in a mismatch in the coupling between the LV and arterial systems, and how exercise training “recouples” the interaction.

What is Arterial-Ventricular Coupling?

LV performance is influenced by the arterial load, and arterial properties are, in turn, influenced by LV performance. Such interactions influence the magnitude and efficiency of transfer of cardiac stroke work to the circulation. By characterizing the arterial system and LV in terms of elastance, we are directly able to examine the crosstalk between the LV and arterial system in the same measurement domain. Typically, arterial load is characterized in the frequency domain as impedance spectra, while LV performance is characterized in the time domain by indexes of pressure and volume. This hinders the ability to directly examine the interaction between the heart and arterial system. Sunagawa and colleagues (51) conceived a measure of arterial load (E_A) that could be directly compared to a measure of LV contraction (E_{LV}; albeit E_{LV} is also influenced by non-contractile aspects; see below for more detail) in the same units (elastance; change in pressure for a given change in volume). Through characterizing the arterial and cardiac systems in terms of pressure and volume, we are able to examine their direct interaction with one another.

Arterial Elastance

Arteries are simply not pipes through which the heart ejects blood to the vital organs and tissues. Rather they act to dampen the pulsatile blood flow from the heart to a steadier flow within the peripheral circulation. The stiffness of the arterial wall affects the blood vessel's ability to ‘store’ stroke volume (SV) from the heart without imposing an excessive afterload, to later recoil during diastole resulting is a progressive reduction in pulsatile blood flow across the arterial tree. As such, the arterial system plays a key role in LV function and determining LV mechanical efficiency (the ratio of energy transferred to the arterial system to the energy consumed for this action). For example, arterial end-systolic pressure (ESP) changes with SV in a roughly linear manner, provided that heart rate (HR) and the diastolic-systolic time intervals remain constant. Thus, the greater the SV ejected into the arterial system, the greater the generated ESP.

In the pressure-volume plane, we can characterize the arterial load on the LV as E_A. Rather than specific arterial properties or location on the arterial tree, E_A simplifies the arterial load into an integrative index that incorporates the principal elements of arterial load (peripheral vascular resistance, total arterial compliance, characteristic impedance, and systolic and diastolic time intervals) (51). As such, E_A can be considered a measure of the net arterial load that is imposed on the LV. Invasively E_A is determined from the pressure-volume loop as the negative slope of the line joining the end-diastolic volume and ESP points (Figure 1). An increase in afterload is depicted by an increase in the slope of the end-systolic pressure to end-diastolic volume relationship to the right, resulting in a higher LV pressure for a given end-diastolic volume. Non-invasively E_A can be calculated from ESP and SV (Equation 1).

$$E_A = ESP/SV \quad \text{Equation 1}$$

ESP can be estimated from the formula [2 × (systolic BP + diastolic BP)]/3, or from ESP = 0.9 × brachial systolic BP. The latter was found to approximate ESP measured invasively (14). However, with recent advances in the imaging field, ESP can also be derived from the arterial waveform, obtained from applanation tonometry, and this method of obtaining ESP was shown to be more reliable than using a calculation (30).

It is important to state that E_A has disadvantages as a measure of arterial load, in that E_A is sensitive to HR, which is a cardiac rather than arterial property. Further, the incorporation of the ‘stiffness’ component of arterial load within E_A has been questioned. Theoretically, an increase in arterial stiffness would lead to an increase in blood pressure pulsatility and a higher ESP. Because E_A is calculated from ESP/SV, a widening of ESP from mean pressure (due to arterial stiffening), would lead to a higher E_A relative to mean resistance load (systemic vascular resistance). Further, it has also been shown that E_A is directly related to arterial resistance, and inversely related to arterial compliance (13). During exercise, the contribution of compliance and resistance to E_A are nearly equal (45). Despite this, evidence collected in human subjects suggested that E_A is mostly dependent on resistance, and is negligibly affect by changes in pulsatile afterload (17). This is important given that the pulsatile component of arterial load is highly relevant with aging and CV disease. As such, it is imperative that E_A not be considered a measure of arterial ‘stiffness’. Although arterial stiffness may not significantly affect E_A, the pulsatile component of arterial load is incorporated in the E_A/E_{LV} paradigm due to the effects of arterial stiffness on LV fibrosis, dysfunction, and failure. Thus, E_A can be considered as a surrogate measure of net arterial load whose advantage is that it can be related to measures of E_{LV}, thus allowing the study of arterial and ventricular interactions.

End-Systolic Elastance

Invasively, the contractile function of the LV is expressed from the slope of the end-systolic pressure-volume relationship (ESPVR; Figure 1), which can be obtained from a series of pressure-volume loops recorded while the preload of the heart is altered. Historically, E_{LV} reflects a relatively (within normal physiological limits) load-independent measure of LV

contraction (chamber stiffness at end systole). An increase in contractility is depicted by an increase in the slope and a shift in the ESPVR to the left, which allows the ventricle to generate more pressure for a given LV volume. In Figure 1, V_0 represents the theoretical volume intercept of the ESPVR. The calculation of E_{LV} assumes that the ESPVR is independent of load, that its slope is linear, and that V_0 is insensitive to inotropic influences. However, ESPVR is generally nonlinear and V_o is not totally independent of the inotropic state. Thus caution is warranted when comparing between groups with different loading conditions. Although E_{LV} reflects the inotropic state of the myocardium, E_{LV} also reflects the geometric (structural remodeling) and biochemical properties (i.e., stiffness or compliance of myocytes, composition of muscle, fibrosis, collagen, etc.) in the LV wall (8). For example, a 'stiffer' LV due to remodeling leads to a higher E_{LV}. E_{LV} should, therefore, be considered an integrated measure of LV chamber performance that can be related to an integrated measure of arterial load (i.e., E_A). Traditionally E_{LV} is assessed from multiple cardiac cycles (acquiring pressure and volume data), however, algorithms have been generated and validated to derive E_{LV} noninvasively from single steady-state data. See Chantler et al. (8) for a more detailed review of the methods to measure E_A and E_{LV}. None-invasively E_{LV} can be calculated from ESP and SV (Equation 2).

$$E_{LV}=ESP/ESV-Vo \quad \text{Equation 2}$$

Arterial-Ventricular Coupling & Clinical Relevance

At rest and in healthy individuals, the properties of the heart and arteries are closely matched so that near maximal cardiac work, power, and chamber efficiency are achieved. Effective coupling between the heart and arteries reflects an optimal transfer of SV without excessive changes in blood pressure, and to provide optimal CV flow reserve without compromising arterial pressures. It is suggested that the mechanical energy (i.e., stroke work) transferred from the ventricular to the arterial system is maximal when the slopes of E_A and E_{LV} are ~equal (52). Further exploration of optimal matching between E_A and E_{LV} revealed, in isolated canine hearts, that stroke work was maximal at E_A/E_{LV} ~ 0.8, while cardiac efficiency was maximal at E_A/E_{LV} ~ 0.7 (20). In healthy humans the optimal range of E_A/E_{LV} to cardiac efficiency and stroke work range from 0.7 to 1.0. None-invasively the coupling ratio can be calculated from E_A and E_{LV} (Equation 3).

$$E_A/E_{LV} \quad \text{Equation 3}$$

How E_A and E_{LV} interact with each other has significant implications on the transfer of blood from the LV through the circulatory system and the preservation of CV reserve. For example, at rest, a stiffer LV (increased E_{LV}), or an increase in arterial load (increased E_A) means that systolic blood pressures are much more sensitive to changes in cardiac volumes (32). Thus, situations that alter cardiac volumes acutely, such as a change in posture, overeating, or use of medications would result in an exaggerated change in pressures and

increase the amount of myocardial oxygen consumption required to deliver a given SV. In turn, such a response can negatively impact systolic and diastolic LV function and worsen regional coronary ischemia (32). The clinical importance of E_A/E_{LV} was reflected by its ability to predict outcome (all-cause mortality, stroke, and myocardial infarction) in patients with heart failure (33), acute coronary syndrome (38), and myocardial infarction (1). E_A/E_{LV} was also shown to correlate with B-type natriuretic peptide levels, which is released from the myocardium in response to myocyte stretch and transmural pressure load in patients with a history of myocardial infarction (1). Finally, recent data suggests the application of E_A/E_{LV} for risk stratification of patients undergoing stress echocardiography, whereby an small E_A/E_{LV} reserve capacity was associated with a higher prevalence of adverse outcomes (5).

Aging and Arterial-Ventricular Coupling

At Rest

Age is the dominant risk factor for CV disease, and is linked to the age-associated changes to the structure and function of the heart and arteries. The CV changes with age occur in everyone but not necessarily at the same rate or to the same extent, and this may account for the difference noted in the development of CV disease between individuals of the same chronological age. In the resting state, invasive assessments of E_A have reported an increase in E_A of 44%-73% between 20 to 79 years of age (15, 19), indicating a deterioration in arterial health. However, these data provided limited insight into the influence of healthy aging on E_A, as patients with coronary artery disease, and on chronic CV medications were included. Non-invasive cross-sectional studies in healthy individuals have reported an increase in E_A with age (45-95 years) between 7-12%, and that inclusion of individuals with existing CV disease further increased the age-associated change in E_A by 17-20% (47). The increase in E_A with age reflects the age-associated alterations in conduit and microvascular structure and function, including an increase in conduit arterial lumen diameter, wall remodeling and stiffness (increases in collagen deposition and decreases in elastin), and endothelial dysfunction (in both conduits and microvessel) via reduced bioavailability of nitric oxide, which likely reflect the age-associated accumulation of oxidative stress and inflammation (34, 35). However, the gradual increase in E_A with healthy aging was not confirmed in a longitudinal study over 4 years, and in individuals with CV disease, E_A decreased slightly (2%) (7), highlighting the importance of performing longitudinal studies.

In healthy individuals, cross-sectional studies have shown that resting E_{LV} increased between 10-28% with age (20-79 years) (15, 19, 47). Further, unlike E_A, longitudinal examination of the change in E_{LV} with healthy aging confirmed the cross-sectional reports of a gradual increase in E_{LV} (11%) and that inclusion of people with CV disease did not alter the age-associated increase in E_{LV} (8% increase) (7). It is important to note that the increase in E_{LV} with age is unlikely to be a reflection of an increase in LV contractility, but rather reflects passive stiffening and LV remodeling, reflective of a reduction in the number of cardiac myocytes, an increase LV wall thickness and collagen deposition, with non-enzymatic cross-linking within the heart (34, 35). An important implication of this finding is that a significant component of LV stiffening seems to be mediated by processes that are independent of elevations in arterial load.

A consequence of the age-associated increase in E_{LV}, with a minimal change in E_A, ensured that the E_A/E_{LV} ratio gradually decreased with increasing age. However, E_A/E_{LV} values remained in a narrow range, allowing for optimal energetic efficiency at the expense of mechanical efficacy (7, 15, 19, 47). Although, having a lower resting E_A/E_{LV} would mean that older individuals would have less reserve capacity to call upon during times of stress.

With certain disease states, the resting E_A/E_{LV} ratio remained stable in people with hypertension, obesity and metabolic syndrome (MetS). We have previously shown that in patients with the MetS who have a clustering of metabolic risk factors (mild hypertension, obesity, elevated glucose and hyperlipidemia) that at rest E_A, E_{LV}, and therefore E_A/E_{LV}, were similar to healthy controls. However, other groups have shown that with hypertension and obesity, E_A and E_{LV} were increased between 15-60% and 16-95% respectively, compared to controls (9, 16, 18, 36, 49). Such elevations in E_A and E_{LV} at rest reflect further increases in wall stiffness, wall thickness, with increased reflected pressure waves, (augmenting central systolic pressure).

Although the age-associated increase in E_A and E_{LV} maintains E_A/E_{LV} within a normal range, the absolute magnitude of both the numerator (E_A) and denominator (E_{LV}) is equally important, and has detrimental effects on hemodynamic stability and CV reserve. In young healthy individuals, the low resting E_A and E_{LV}, with optimal coupling, maintains an optimal transfer of blood from the LV to periphery without excessive changes in blood pressure, and provides optimal CV flow reserve without compromising arterial pressures (31). However, with increasing age or the presence of CV diseases, the increased resting E_A and E_{LV} results in a large change in LV pressures for a given change in LV volume (15, 32). Consequently, the stroke work (myocardial demand) required to perform this task is increased and can potentially have negative consequences on systolic and diastolic function, including coronary flow (i.e., greater dependence upon systolic pressure for coronary flow) (32). Thus, older individuals are working at a higher set point regarding changes in pressure for a given change in loading conditions and this disadvantage is further exaggerated in CV disease. Because the absolute level of any given hemodynamic variable during exercise is determined in part by the resting value for that variable, any elevation in resting E_A and E_{LV} (despite matched coupling) would likely reduce the coupling reserve capacity, i.e., rest minus peak values (see next section for more detail).

During Exercise

Exercise provides a powerful tool to examine the response of the CV system to stress, to assess its functional reserve capacity, and to reveal pathophysiological changes that are often hidden from sight at rest. The CV system meets the demands of the exercising tissues by modifying a complex combination of alterations in HR, LV contractility, preload, and afterload. During exercise, the goal of the CV system is to prioritize cardiac efficacy over energetic efficiency, and this is manifested by a decrease in the coupling ratio (i.e., a greater relative increase in E_{LV} than E_A). In other words, during exercise the reduction in the coupling ratio reflects a suboptimal set point from the standpoint of LV performance and metabolic efficiency, however, it does reflect an optimization of LV stroke work. The decrease in E_A/E_{LV} during exercise is supported from data collected in both animal and

human models. In adult dogs, Little and Cheng (43) reported a 25% decrease in E_A/E_{LV} from rest to submaximal exercise. In healthy human subjects undergoing supine cycle ergometry, Asanoi et al. (3) observed that E_A/E_{LV} decreased by 35% and 54% at workloads corresponding to 30% below and 30% above the anaerobic threshold, respectively; and Chantler et al. (15) found that E_A/E_{LV} decreased by approximately 65% (from an average of 0.58 to 0.34, and 0.52 to 0.27 in men and women, respectively) from rest to peak exercise. In these scenarios, the reduction in E_A/E_{LV} with exercise is due to an acute increase in E_{LV} which reflects an increase in LV contractility. The response of E_A during exercise is dependent on the changes in its components. E_A is linearly related to HR and peripheral resistance, and inversely related to compliance (10, 13, 44). Both resistance and compliance usually decrease during exercise (reflecting less resistance to blood flow in the microcirculation, but increased stiffness of the conduit arteries) and the relative contribution of the pulsatile component (compliance) to E_A increases, so that by 80% of peak exercise the resistive and the pulsatile components provide nearly equal contributions to E_A (44).

With aging, the ability to increase HR, and lower resistance, during exercise is blunted (34, 35), however, the change in E_A during exercise was not affected by age (40). Perhaps the blunted changes in resistance, compliance, and HR with age are compensated for by the greater increase in blood pressure during exercise in older vs. younger healthy individuals (43). We have shown that some of the components of the changes in E_A seem to be related to each other (11). That is, greater preservation of compliance during exercise is associated with a greater reduction in systemic vascular resistance. This suggests that the tandem changes in vascular resistance and compliance appear to be linked. Further, the change in E_A during exercise is also linked to a specific pattern of change in ventricular volumes and function, whereby the change in E_A is inversely related to the recruitment of end-diastolic volume, and the enhancement of SV and cardiac output with exercise. Indeed individuals who expressed a large increase in E_A during exercise demonstrate a reduced ability to augment SV via the Frank-Starling mechanism (11).

In contrast to E_A, there is a clear limitation in the increase in E_{LV} during exercise with age, with noticeable deficits at submaximal workloads, and an approximately 40-55% smaller maximal E_{LV} in individuals 60 vs. 40 years of age (40). This would suggest a decrease in LV contraction during exercise with increasing age are evident at lower exercise workloads, which is clinically significant given that most individuals spend more time during low levels of physical activity. As such, older individuals are working harder at the same submaximal workload than younger individuals. It is known that with aging that LV emptying is substantially impaired during maximal exercise, likely reflecting a stiffer heart, impaired intrinsic myocardial contraction, and reduced cardiac response to β-adrenergic receptor stimulation (26). As a consequence of the impaired E_{LV} response during exercise there is a corresponding blunted reduction in E_A/E_{LV} with increasing age (40). Importantly, we have shown that acute pharmacologic reduction in both cardiac and vascular components of LV afterload by sodium nitroprusside (nitric oxide donor) in older, healthy individuals lowered maximal E_A/E_{LV}, and therefore represents an enhanced peak exercise CV response similar to levels noted in younger individuals (12, 42). The improved CV response was due to an increase in maximal E_{LV} as the effects of sodium nitroprusside on E_A waned at higher levels of exercise, such that peak E_A was similar during both sodium nitroprusside and placebo

infusions. Further examination of the components of E_A reveal that sodium nitroprusside did not alter arterial resistance or compliance at peak exercise. However, as discussed above, E_A is less sensitive to changes in compliance, and given the known effects of sodium nitroprusside on reducing arterial wave reflection (and thus pulsatile afterload), the increased peak exercise E_{LV} (and decreased E_A/E_{LV}) may have been also due to a reduction in peak exercise arterial wave reflection, especially given the reduction in systolic blood pressure at rest that persisted throughout exercise. Thus, at peak exercise in the old heart, sodium nitroprusside was able to augment the CV performance predominately through increasing LV contractility directly and via a reduction in LV wall stress, and possibly via a reduction in pulsatile component of arterial load.

To what extent the age-associated deterioration in peak exercise E_A/E_{LV} is further blunted in the presence of CV disease is limited to a handful of studies, and those studies suggest that the alteration in peak E_A/E_{LV} is dependent on the type of disease state. Borlaug et al. (6) showed that hypertensive individuals expressed a similar increase in E_A, and E_{LV}, and a decrease in E_A/E_{LV} at submaximal and maximal exercise compared to normotensive individuals matched by age and sex. Although a closer look at these data would suggest that the decrease in E_A/E_{LV} at peak exercise had started to become blunted with hypertension, and significant differences may have been obtained if the hypertensive response was compared to a healthy control group without obesity or elevated cholesterol. In contrast, we have previously shown that in individuals with systolic hypertensive, but otherwise healthy people, that E_A/E_{LV} at 50% of peak exercise, and at peak exercise did not differ compared to healthy age-and sex matched controls, i.e., both groups had a similar decrease in E_A/E_{LV} (9). This would suggest that E_A/E_{LV} performance at peak exercise is not affected by the presence of hypertension in persons without overt cardiac disease. However, due to the lower resting E_A/E_{LV} (i.e., less optimal coupling) in systolic hypertensive women, the E_A/E_{LV} reserve (peak-rest E_A/E_{LV}) was reduced, which was not evident in men (9). Further, we found that the E_A reserve was also reduced in systolic hypertensive men and women, which may a reflect a compensatory response to prevent an excessive increase in arterial load, and therefore permit an adequate E_{LV} increase during exercise. However, what is clear is that more research is needed to tease out how the various forms of hypertension affect the sex-specific coupling response during exercise.

Another modern CV risk factor is obesity, which is at epidemic levels. Similar to hypertension, peak E_A/E_{LV} values (and E_A/E_{LV} reserve) were similar between obese and none-obese individuals (22). However, this was despite a smaller increase in peak exercise E_A (by 27%) and E_{LV} (by 39%) in obese compared to none-obese individuals. Recently, we have shown that when multiple CV/metabolic risk factors cluster together in a given individual, namely MetS, that the reduction in E_A/E_{LV} during exercise is blunted compared to healthy age- and sex-matched controls. This limited E_A/E_{LV} response was due to a smaller increase in E_{LV} (but not E_A) from rest to peak exercise in MetS (28), suggesting that peak exercise LV contractility is reduced in MetS. The discrepancy between the impaired peak coupling response with obesity vs. MetS (for which obesity is a key determinant) suggests that the added CV risk factors that determine MetS (elevated blood pressure and glucose, hyperlipidemia) have a critical role in uncoupling peak arterial and LV interactions. Further, our data in MetS demonstrate that pathophysiological CV alterations occur in the

earliest stages of MetS development, prior to any evidence of chronic disease such as diabetes and/or overt CV disease, and that impaired LV systolic function during exercise occurs prior to evidence of LV systolic dysfunction at rest.

So what is the clinical significance of a reduced ability to lower E_A/E_{LV} during exercise with age or with certain CV disease states? The reduced E_A/E_{LV} reserve with age that is further exacerbated in MetS suggests an inability to attain maximal efficacy, manifested by a limited increase in LV contractility during exercise. Given that E_A/E_{LV} is a determinant of CV performance, it is not surprising that the E_A/E_{LV} reserve is inversely correlated with peak aerobic capacity in various populations (6, 25, 27). A reduction in peak aerobic capacity represents one of the most important age-and disease-associated physiological changes with regard to quality of life and functional independence. Indeed, peak aerobic capacity is a predictor of all-cause and CV-specific mortality (39). The alterations in resting and exercise E_A and E_{LV} likely contribute to this reduced peak aerobic capacity. Whereby, an increased E_{LV} at rest would translate into a less effective increase in E_{LV} during exercise thereby limiting CV performance (6). For example, individuals who start at a higher E_{LV} at rest likely have a limited capacity to further increase SV, and the limited SV response is further exacerbated when a stiff heart is connected to a stiff artery (15, 32). Further, acute infusion of verapamil improved E_A/E_{LV} and corresponded with an improved exercise capacity (11). These data suggest a direct link between E_A/E_{LV} and aerobic capacity, in that a blunted coupling likely results in a reduced effective transfer of blood from the heart to periphery, thereby reducing functional reserve capacity.

Can Exercise Re-Couple the Heart and Vasculature?

People are living longer, and with an increase prevalence of CV diseases, it is therefore imperative to identify and implement strategies/interventions that will reverse or at the very least delay the development of CV disease. Habitual exercise has been shown to be an effective intervention to improve various aspects of arterial and cardiac systems that impact E_A and E_{LV}, although the effects of exercise training on CV performance are in certain circumstances dependent on sex and exercise activity/intensity (aerobic, resistance, aquatics etc.). In general, moderate aerobic exercise interventions reduce blood pressure and aortic arterial stiffness in healthy middle/older men/women (46) and in patients with MetS (23), but do not improve arterail stiffness in the more muscular femoral arteries (41). We have also shown that exercise training can improve central blood pressure, augmentation pressure, and arterial wave reflection in MetS (23). Similarly, brachial artery endothelial function has also been shown to be affected by habitual exercise training. In older men, brisk walking restored brachial artery endothelial function to levels noted in young healthy individuals (21). The improved endothelial function was likely due to an increase in nitric oxide bioavailability and an upregulation in endothelial nitric oxide synthase protein expression and phosphorylation (21). In contrast, the influence of regular aerobic exercise on macrovascular endothelial function with aging in women is far less clear with either no improvements (46) or an increase in endothelial function was noted (53).

Important exercise-induced adaptations also occur to the aged heart including physiological eccentric LV remodeling (3), lower resting HR, improved peak exercise cardiac function

(increased SV and reduced end-systolic volume) and aerobic capacity (29, 50). However, in terms of resting LV function (SV, end-diastolic volume, ejection fraction, or LV contractility), moderate/high intensity exercise training for 8-48 weeks in previously healthy sedentary older persons had limited effects (4, 24, 50). Thus, regular exercise training seems to be an effective strategy, for the most part, for combating several adverse cardiac and arterial changes associated with aging. We have previously shown that E_A/E_{LV} is moderately correlated with peak aerobic capacity again suggesting a relationship between E_A/E_{LV} and fitness (27). However only a handful of studies have examined how exercise training affects E_A/E_{LV} at rest and during exercise. We hypothesize that exercise training is an effective therapeutic intervention to “recouple” the interactions between the LV and vasculature.

In young healthy men and women, 8 weeks of aerobic exercise training increased E_{LV} and lowered E_A/E_{LV} at rest, but only in women (37). This increase in E_{LV} likely reflected an increase in LV contractility rather than an increase in passive LV stiffness (as evidence with aging or the presence of CV disease), or an attempt to offset an increase in E_A, which was not evident in this study. Indeed, irrespective of sex, aerobic exercise did not alter resting E_A. This was despite both groups showing lower central pulse wave velocities (a measure of arterial stiffness) (37). Further, the increase in E_{LV} was accompanied by a reduction in ESP which likely allowed for a more efficient CV system, i.e., improved transfer of SV without an excessive increase in pressure. To what extent exercise training in young healthy individuals only showed beneficial effects on resting E_A/E_{LV} in women is unknown and highlights the importance of examining the sex-specific changes in CV function after exercise training.

In an older population free of CV disease, Schulman et al. (50) explored the role of exercise training and detraining on CV performance. Although the focus of the study was not on E_A/E_{LV}, one can obtain a rough idea as to how E_A/E_{LV} was impacted in this study by calculating E_A/E_{LV} and its components from reported average data. In healthy older men, 6 months of aerobic exercise training (3-4 times/week) slightly lowered resting E_A and E_{LV}. As such, no change in E_A/E_{LV} was noted (Figure 2). This is important given that E_A and E_{LV} are elevated at rest with age and have important consequences on resting CV efficiency. Thus a decrease in E_A and E_{LV} likely improve mechanical efficiency at rest. Whereas at peak exercise, exercise training lowered E_A (~8%) and increased E_{LV} (~46%), resulting in a lower E_A/E_{LV} (~37%) (Figure 2). The greater reduction in E_A/E_{LV} during exercise would have allowed for a greater stroke work and an improved peak aerobic capacity. In this case, the improved E_A/E_{LV} was due to a combined effect of E_A and E_{LV}. Whereby, the reduction in peak exercise E_A after exercise training likely, in part, contributed to the improved E_{LV} (i.e., the LV has less arterial load to contract against). In the same study, 8 master athletes stopped their endurance training for 12 weeks. Exercise detraining had minimal effects on E_A and E_{LV} with a slight increase in E_A/E_{LV} at rest. However, significant deficits were noted at peak exercise with a decreased E_{LV} (~12%) and a blunted reduction in E_A/E_{LV} (~32%). This would suggest that highly trained individuals, who have undergone decades of training, are to some extent protected from brief periods of physical inactivity, at least at rest. In contrast, the coupling response to acute exercise is most impacted by deconditioning in highly trained master athletes, and the most significant deconditioning response is a reduced LV contractility.

Exercise training also has beneficial effects on arterial-ventricular coupling in diseased states. We have previously shown that in patients with MetS, who are associated with a three-fold increase risk of CV morbidity and mortality, that aerobic exercise training did not alter resting E_A/E_{LV}, E_A, and E_{LV} but resulted in a significant increase in peak exercise E_{LV} and consequently a decrease in peak exercise E_A/E_{LV} which also corresponded with an improved aerobic capacity in patients with the MetS (Figure 3) (27). Of note, exercise training in these patients also improved lifetime risk score (a predictor for future CV mortality), which was also correlated with E_A/E_{LV} ($r = 0.50$, $p<0.05$) and E_{LV} ($r = - 0.50$, $p<0.05$) reserve, suggesting that the higher the CV risk, the smaller the reduction in E_A/E_{LV} and increase in E_{LV} during exercise. We also have unpublished data in older women with MetS (n=9, mean age = 58 years) that 8 weeks of deep water aerobic exercise training did not alter resting E_A, E_{LV}, or $E_A/E_{LV,}$ however at peak exercise, a 19% increase and a 22% decrease in E_{LV} and E_A/E_{LV} was noted respectively (Chantler, PD, unpublished manuscript/ observations, October 2016). These data suggest that aquatic-based exercise training can improve LV contractility at peak exercise, resulting in a larger E_A/E_{LV} reserve and a greater optimization of CV performance. Such data highlight that various forms of aerobic exercise training are beneficial in improving E_A/E_{LV}, in particular exercising in an aquatic environment could benefit obese people who find exercising on a treadmill difficult, or for people with arthritis, etc. These findings have clinical importance as they provide insight that some of the pathophysiological changes associated with MetS can be improved and lower the risk of CV disease.

Improvements in arterial-ventricular coupling have also been noted in other disease populations. In patients with coronary artery disease, 12 months of aerobic exercise training did not alter resting E_A/E_{LV}, or E_{LV} (albeit a slight reduction in E_A was evident) (48). However, the major effects of exercise training in this population was noted during hand grip exercise performed at 30% of maximal voluntary contraction, whereby after exercise training a 37% increase in E_{LV} and a 23% reduction in E_A/E_{LV} was evident. Similarly, 20 sessions of exercise-based cardiac rehabilitation in heart failure with reduced ejection fraction increased resting E_A/E_{LV} from 0.56+0.18 to 0.67+0.21 via a slight (9%) reduction in E_A. As such, resting cardiac energetic efficiency was improved, i.e., the ratio of energy transferred to the arterial system (external work) to the energy consumed for this action (2). Collectively, exercise training induces significant CV adaptations during exercise in various populations with different severities of CV disease. Figure 4 summarizes the change in E_A/E_{LV} with age and CV disease.

Conclusion

Analyses of the LV and arterial system in the pressure-volume plane, and characterizing these data in a simplified, intuitive and useful approach (E_A/E_{LV}), permits the global evaluation of the specific contributions of the arterial system and LV in determining SV and mechanical energetics (external mechanical energy, potential energy, and energetic efficiency). Importantly, to gain further insights into the role of the vasculature and heart on determining CV performance, E_A/E_{LV} should be complemented by more specific parameters of arterial (pule wave velocity, pulse wave analysis, characteristic impedance, conduit remodeling, etc.) and cardiac (myocardial contractility, wall stress, chamber size, and

thickness) load that provide additional physiological insights into the role of aging and disease.

With advancing age, silent changes occur within the CV systems that uncouple the crosstalk between the heart and arteries, affecting CV efficiency that is further exacerbated in the presence of CV disease (Figure 5). Such age-disease changes limit the CV response to exercise, decreasing E_{LV} and E_A/E_{LV} reserve capacity. Importantly, aerobic exercise training has the capacity, at least in part, to “recouple” the interaction between the heart and arterial systems irrespective of disease state (Figure 4).

Important future contributions to this topic should include the following. The type, frequency, intensity, and duration of exercise training required to preserve/improve E_A/E_{LV} with advancing age is incompletely understood. It remains unknown how other exercise modalities, such as resistance training or high intensity interval training affects E_A/E_{LV}. Given the reported sex differences in CV function with exercise training, future studies should ensure sufficiently numbers of males and females to adequately compare sex-specific E_A/E_{LV} responses.

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References

1. Antonini-Canterin F, Enache R, Popescu BA, et al. Prognostic value of ventricular-arterial coupling and B-type natriuretic peptide in patients after myocardial infarction: a five-year follow-up study. J Am Soc Echocardiogr. 2009; 22(11):1239–45. [PubMed: 19783121]
2. Aslanger E, Assous B, Bihry N, Beauvais F, Logeart D, Cohen-Solal A. Effects of Cardiopulmonary Exercise Rehabilitation on Left Ventricular Mechanical Efficiency and Ventricular-Arterial Coupling in Patients With Systolic Heart Failure. J Am Heart Assoc. 2015; 4(10):e002084. [PubMed: 26464425]
3. Baggish AL, Wang F, Weiner RB, et al. Training-specific changes in cardiac structure and function: a prospective and longitudinal assessment of competitive athletes. Journal of Applied Physiology. 2008; 104(4):1121–8. [PubMed: 18096751]
4. Beere PA, Russell SD, Morey MC, Kitzman DW, Higginbotham MB. Aerobic Exercise Training Can Reverse Age-Related Peripheral Circulatory Changes in Healthy Older Men. Circulation. 1999; 100(10):1085–94. [PubMed: 10477534]
5. Bombardini T, Costantino MF, Sicari R, Ciampi Q, Pratali L, Picano E. End-systolic elastance and ventricular-arterial coupling reserve predict cardiac events in patients with negative stress echocardiography. Biomed Res Int. 2013; 2013:235194. [PubMed: 24024185]
6. Borlaug BA, Olson TP, Lam CSP, et al. Global Cardiovascular Reserve Dysfunction in Heart Failure With Preserved Ejection Fraction. Journal of the American College of Cardiology. 2010; 56(11): 845–54. [PubMed: 20813282]
7. Borlaug BA, Redfield MM, Melenovsky V, et al. Longitudinal changes in left ventricular stiffness: a community-based study. Circ Heart Fail. 2013; 6(5):944–52. [PubMed: 23811963]

8. Chantler PD, Lakatta EG, Najjar SS. Arterial-ventricular coupling: mechanistic insights into cardiovascular performance at rest and during exercise. Journal of Applied Physiology. 2008; 105(4):1342–51. [PubMed: 18617626]

9. Chantler PD, Melenovsky V, Schulman SP, et al. The sex-specific impact of systolic hypertension and systolic blood pressure on arterial-ventricular coupling at rest and during exercise. American Journal of Physiology-Heart and Circulatory Physiology. 2008; 295(1):H145–H53. [PubMed: 18456731]

10. Chantler PD, Melenovsky V, Schulman SP, et al. Use of the Frank-Starling Mechanism during Exercise is Linked to Exercise-Induced Changes in Arterial Load. Am J Physiol Heart Circ Physiol. 2011

11. Chantler PD, Melenovsky V, Schulman SP, et al. Use of the Frank-Starling mechanism during exercise is linked to exercise-induced changes in arterial load. American Journal of Physiology - Heart and Circulatory Physiology. 2012; 302(1):H349–H58. [PubMed: 22003052]

12. Chantler PD, Nussbacher A, Gerstenblith G, et al. Abnormalities in arterial-ventricular coupling in older healthy persons are attenuated by sodium nitroprusside. American Journal of Physiology - Heart and Circulatory Physiology. 2011; 300(5):H1914–H22. [PubMed: 21378146]

13. Chemla D, Antony I, Lecarpentier Y, Nitenberg A. Contribution of systemic vascular resistance and total arterial compliance to effective arterial elastance in humans. Am J Physiol Heart Circ Physiol. 2003; 285(2):H614–20. [PubMed: 12689857]

14. Chen CH, Fetics B, Nevo E, et al. Noninvasive single-beat determination of left ventricular end-systolic elastance in humans. J Am Coll Cardiol. 2001; 38(7):2028–34. [PubMed: 11738311]

15. Chen CH, Nakayama M, Nevo E, Fetics BJ, Maughan WL, Kass DA. Coupled systolic-ventricular and vascular stiffening with age: implications for pressure regulation and cardiac reserve in the elderly. J Am Coll Cardiol. 1998; 32(5):1221–7. [PubMed: 9809929]

16. Chirinos JA, Rietzschel ER, De Buyzere ML, et al. Arterial load and ventricular-arterial coupling: physiologic relations with body size and effect of obesity. Hypertension. 2009; 54(3):558–66. [PubMed: 19581507]

17. Chirinos JA, Rietzschel ER, Shiva-Kumar P, et al. Effective arterial elastance is insensitive to pulsatile arterial load. Hypertension. 2014; 64(5):1022–31. [PubMed: 25069668]

18. Cohen-Solal A, Caviezel B, Himbert D, Gourgon R. Left ventricular-arterial coupling in systemic hypertension: analysis by means of arterial effective and left ventricular elastances. J Hypertens. 1994; 12(5):591–600. [PubMed: 7930560]

19. Cohen-Solal A, Caviezel B, Laperche T, Gourgon R. Effects of aging on left ventricular-arterial coupling in man: assessment by means of arterial effective and left ventricular elastances. J Hum Hypertens. 1996; 10(2):111–6. [PubMed: 8867565]

20. De Tombe PP, Jones S, Burkhoff D, Hunter WC, Kass DA. Ventricular stroke work and efficiency both remain nearly optimal despite altered vascular loading. Am J Physiol. 1993; 264(6 Pt 2):H1817–24. [PubMed: 8322910]

21. DeSouza CA, Shapiro LF, Clevenger CM, et al. Regular Aerobic Exercise Prevents and Restores Age-Related Declines in Endothelium-Dependent Vasodilation in Healthy Men. Circulation. 2000; 102(12):1351–7. [PubMed: 10993851]

22. DeVallance E, Fournier SB, Donley DA, et al. Is obesity predictive of cardiovascular dysfunction independent of cardiovascular risk factors? Int J Obes (Lond). 2014

23. Donley DA, Fournier SB, Reger BL, et al. Aerobic exercise training reduces arterial stiffness in metabolic syndrome. J Appl Physiol (1985). 2014; 116(11):1396–404. [PubMed: 24744384]

24. Ehsani A, Ogawa T, Miller T, Spina R, Jilka S. Exercise training improves left ventricular systolic function in older men. Circulation. 1991; 83(1):96–103. [PubMed: 1984902]

25. Fahs CA, Rossow LM, Yan H, et al. Resting and post exercise arterial-ventricular coupling in endurance-trained men and women. J Hum Hypertens. 2013; 27(9):552–6. [PubMed: 23426069]

26. Fleg JL, Tzankoff SP, Lakatta EG. Age-related augmentation of plasma catecholamines during dynamic exercise in healthy males. J Appl Physiol. 1985; 59(4):1033–9. [PubMed: 4055584]

27. Fournier SB, Donley DA, Bonner DE, Devallance E, Olfert IM, Chantler PD. Improved arterial-ventricular coupling in metabolic syndrome after exercise training: a pilot study. Med Sci Sports Exerc. 2015; 47(1):2–11. [PubMed: 24870568]

28. Fournier SB, Reger BL, Donley DA, et al. Exercise reveals impairments in left ventricular systolic function in patients with metabolic syndrome. Exp Physiol. 2014; 99(1):149–63. [PubMed: 24036595]
29. Fujimoto N, Hastings JL, Carrick-Ranson G, et al. Cardiovascular Effects of One year of Alagebrium and Endurance Exercise Training in Healthy Older Individuals. Circulation: Heart Failure. 2013
30. Kappus RM, Ranadive SM, Yan H, et al. Validity of predicting left ventricular end systolic pressure changes following an acute bout of exercise. J Sci Med Sport. 2013; 16(1):71–5. [PubMed: 22721862]
31. Kass DA. Ventricular Arterial Stiffening: Integrating the Pathophysiology. Hypertension. 2005; 46(1):185–93. [PubMed: 15911741]
32. Kawaguchi M, Hay I, Fetics B, Kass DA. Combined ventricular systolic and arterial stiffening in patients with heart failure and preserved ejection fraction: implications for systolic and diastolic reserve limitations. Circulation. 2003; 107(5):714–20. [PubMed: 12578874]
33. Ky B, French B, May Khan A, et al. Ventricular-arterial coupling, remodeling, and prognosis in chronic heart failure. J Am Coll Cardiol. 2013; 62(13):1165–72. [PubMed: 23770174]
34. Lakatta EG. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part III: cellular and molecular clues to heart and arterial aging. Circulation. 2003; 107(3):490–7. [PubMed: 12551876]
35. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part II: the aging heart in health: links to heart disease. Circulation. 2003; 107(2):346–54. [PubMed: 12538439]
36. Lam CS, Roger VL, Rodeheffer RJ, et al. Cardiac structure and ventricular-vascular function in persons with heart failure and preserved ejection fraction from Olmsted County, Minnesota. Circulation. 2007; 115(15):1982–90. [PubMed: 17404159]
37. Lane AD, Yan H, Ranadive SM, et al. Sex differences in ventricular-vascular coupling following endurance training. Eur J Appl Physiol. 2014; 114(12):2597–606. [PubMed: 25142819]
38. Milewska A, Minczykowski A, Krauze T, et al. Prognosis after acute coronary syndrome in relation with ventricular-arterial coupling and left ventricular strain. Int J Cardiol. 2016; 220:343–8. [PubMed: 27390953]
39. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise Capacity and Mortality among Men Referred for Exercise Testing. New England Journal of Medicine. 2002; 346(11):793–801. [PubMed: 11893790]
40. Najjar SS, Schulman SP, Gerstenblith G, et al. Age and gender affect ventricular-vascular coupling during aerobic exercise. J Am Coll Cardiol. 2004; 44(3):611–7. [PubMed: 15358029]
41. Nualnim N, Barnes JN, Tarumi T, Renzi CP, Tanaka H. Comparison of central artery elasticity in swimmers, runners, and the sedentary. Am J Cardiol. 2011; 107(5):783–7. [PubMed: 21247521]
42. Nussbacher A, Gerstenblith G, O'Connor FC, et al. Hemodynamic effects of unloading the old heart. Am J Physiol. 1999; 277(5 Pt 2):H1863–71. [PubMed: 10564141]
43. Ogawa T, Spina RJ, Martin WH 3rd, et al. Effects of aging, sex, and physical training on cardiovascular responses to exercise. Circulation. 1992; 86(2):494–503. [PubMed: 1638717]
44. Otsuki T, Maeda S, Iemitsu M, et al. Contribution of systemic arterial compliance and systemic vascular resistance to effective arterial elastance changes during exercise in humans. Acta Physiol. 2006; 188(1):15–20.
45. Otsuki T, Maeda S, Iemitsu M, et al. Systemic arterial compliance, systemic vascular resistance, and effective arterial elastance during exercise in endurance-trained men. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology. 2008; 295(1):R228–R35.
46. Pierce GL, Eskurza I, Walker AE, Fay TN, Seals DR. Sex-specific effects of habitual aerobic exercise on brachial artery flow-mediated dilation in middle-aged and older adults. Clin Sci (Lond). 2010; 120(1):13–23.
47. Redfield MM, Jacobsen SJ, Borlaug BA, Rodeheffer RJ, Kass DA. Age- and Gender-Related Ventricular-Vascular Stiffening: A Community-Based Study. Circulation. 2005; 112(15):2254–62. [PubMed: 16203909]

48. Rinder MR, Miller TR, Ehsani AA. Effects of endurance exercise training on left ventricular systolic performance and ventriculoarterial coupling in patients with coronary artery disease. American Heart Journal. 1999; 138(1):169–74. [PubMed: 10385782]

49. Saba PS, Ganau A, Devereux RB, Pini R, Pickering TG, Roman MJ. Impact of arterial elastance as a measure of vascular load on left ventricular geometry in hypertension. J Hypertens. 1999; 17(7): 1007–15. [PubMed: 10419075]

50. Schulman SP, Fleg JL, Goldberg AP, et al. Continuum of Cardiovascular Performance Across a Broad Range of Fitness Levels in Healthy Older Men. Circulation. 1996; 94(3):359–67. [PubMed: 8759077]

51. Sunagawa K, Maughan WL, Burkhoff D, Sagawa K. Left ventricular interaction with arterial load studied in isolated canine ventricle. Am J Physiol. 1983; 245(5 Pt 1):H773–80. [PubMed: 6638199]

52. Sunagawa K, Maughan WL, Sagawa K. Optimal arterial resistance for the maximal stroke work studied in isolated canine left ventricle. Circ Res. 1985; 56(4):586–95. [PubMed: 3978773]

53. Yoshizawa M, Maeda S, Miyaki A, et al. Additive beneficial effects of lactotripeptides intake with regular exercise on endothelium-dependent dilatation in postmenopausal women. Am J Hypertens. 2010; 23(4):368–72. [PubMed: 20075849]

Key Points

- It is known that healthy aging impairs the coupling between the heart and arterial system.
- The age-associated impairment in arterial-ventricular coupling is further increased, especially during exercise, in the presence of cardiovascular diseases.
- Exercise training is known to have beneficial effects on the heart and blood vessels.
- It is relatively unknown to what extent exercise training can improve the coupling between the heart and blood vessels at rest and during peak performance.
- This review article examines how aging and cardiovascular disease alters resting and peak arterial-ventricular coupling and provides evidence indicating that exercise training can recouple this interaction.

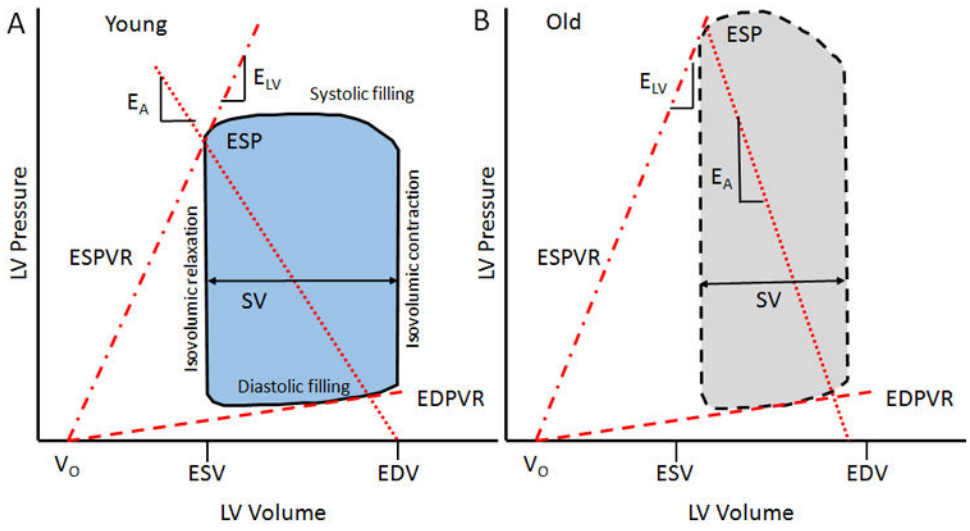

Figure 1.

Pressure volume loop. A representative depiction of the pressure-volume relationship comparing the slope of the end-systolic pressure-volume relationship (ESPVR) and the slope of the line joining the ESP and EDV points (E_A) from a healthy young control (A) and an older individual with hypertension (B). End-systolic elastance (E_{LV}) reflects a load-independent measure of left ventricular (LV) contraction, and is steeper in an older hypertensive individual. Effective arterial elastance (E_A), a measure of net arterial load on the LV, is increased (thereby reducing SV and increasing ESP) in an older individual compared to a young healthy individual. Vo represents the theoretical volume intercept of the ESPVR; ESP, end systolic pressure; SV, stroke volume; ESV, end systolic volume; EDV, end diastolic volume; and EDPVR, end diastolic pressure volume relationship.

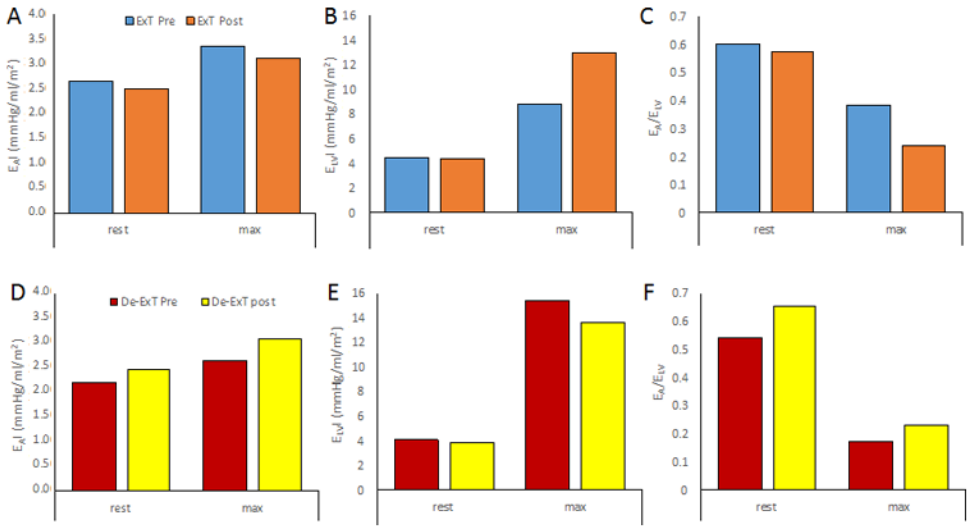

Figure 2.

The change in arterial ventricular coupling after aerobic exercise training or detraining. Aerobic exercise training in healthy older individuals had minimal effects on (A) resting arterial elastance indexed to body surface area (E_AI) and (B) end-systolic elastance indexed to body surface area ($E_{LV}I$), but a slight increase in E_A/E_{LV} (C) at rest. However, at peak exercise aerobic exercise improved $E_{LV}I$ and lowered E_A/E_{LV} in previously sedentary older individuals. In contrast, in master athletes who stopped their endurance training, resting E_AI (D), $E_{LV}I$ (E), and E_A/E_{LV} (F) was minimally affected by this detraining, whereas exercise detraining decreased E_{LV} (~12%) and blunted E_A/E_{LV} (~32%) at peak exercise. Created from previously published data Schulman et al. (50).

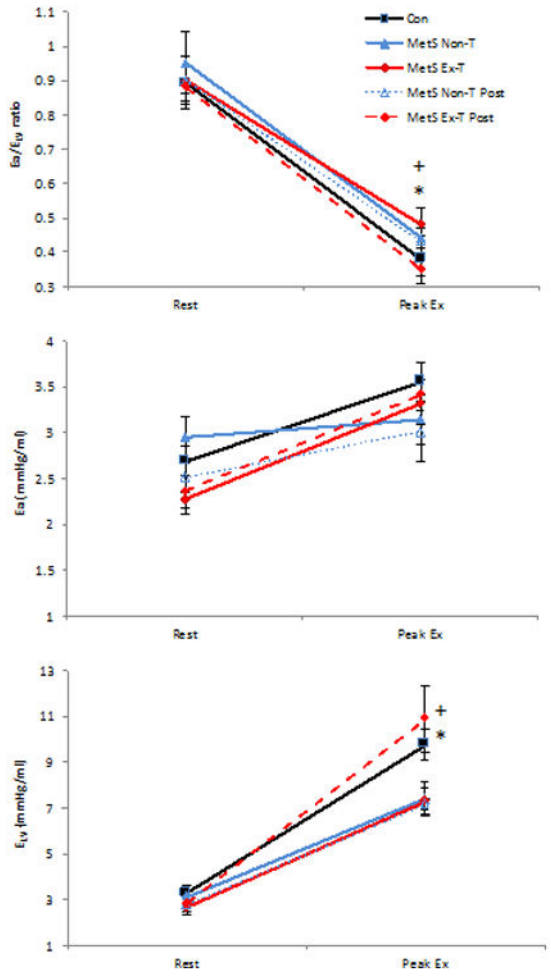

Figure 3.

The effects of exercise training on resting and peak exercise arterial-ventricular coupling in patients with the metabolic syndrome (MetS). Change in arterial-ventricular coupling (Ea/E_{LV}), LV end-systolic elastance (E_{LV}), and arterial elastance (Ea) from rest to peak exercise in Mets patients who underwent exercise training (MetS-ExT, diamond) and in MetS who remained inactive (MetS-NonT, triangles). Healthy age- and sex-matched controls are depicted by the solid black line and closed squares. Post intervention for both MetS groups are depicted by a dashed line. Control healthy age-matched individuals are depicted by black squares with a solid line. Exercise training significantly reduced peak Ea/E_{LV}, and increased peak E_{LV} in MetS, and there was a significant time (pre- and post-intervention) by group (MetS-ExT vs. MetS-NonT) for Ea/E_{LV} and E_{LV}. *P<0.05 illustrates significant differences pre and post intervention in MetS Ex-T; +P<0.05 time by group interaction. Data presented as means ± SEM. Created from previously published data, Fournier et al. (27).

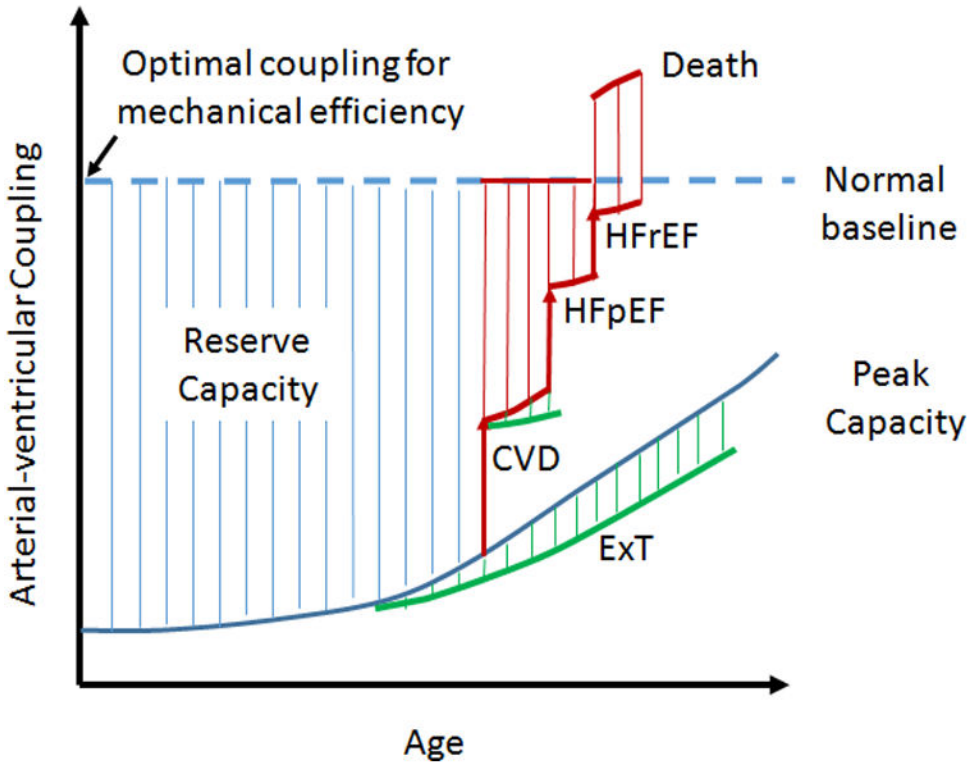

Figure 4.

Schematic representation of the changes in Arterial-ventricular coupling as a consequent of age, and cardiovascular disease (CVD: hypertension, obesity, metabolic syndrome). The dashed blue line represents resting E_A/E_{LV} and the solid blue line maximal E_A/E_{LV}. The hatched area between represents the reserve capacity of E_A/E_{LV}. This can be affected by age or cardiovascular disease, and is further acerbated in the presence of heart failure either with preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF). However, we hypothesize that exercise training (ExT) improves the E_A/E_{LV} reserve capacity with age, and the presence of CVD.

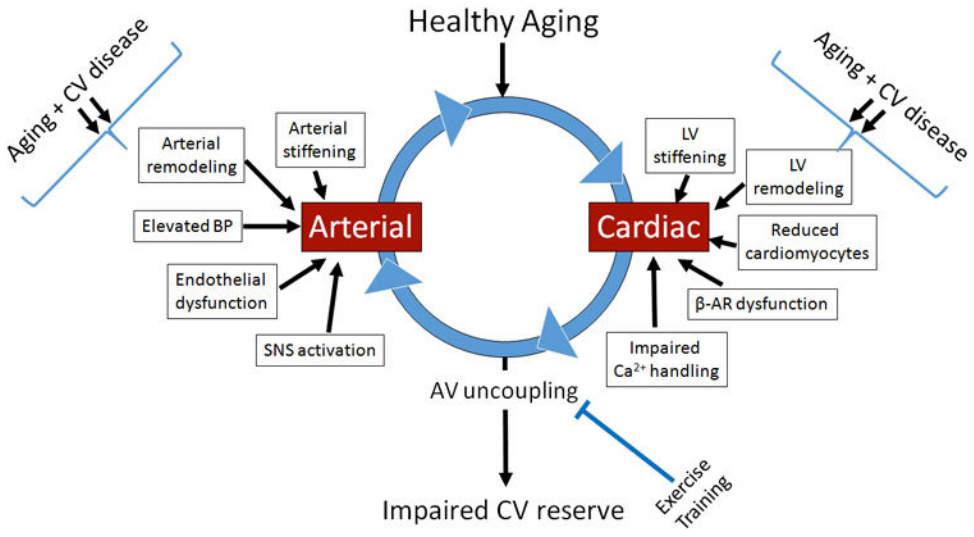

Figure 5.

Arterial and cardiac adaptations with healthy aging and the relationship with arterial-ventricular coupling. With healthy aging the arterial and cardiac systems undergo considerable remodeling (change in collagen, reduced elastin, accumulation of advanced glycation end products, loss in cardiomyocytes, and altered autonomic tone), which uncouple the heart and arterial system at rest and during exercise. This uncoupled arterial and cardiac interaction (AV uncoupling) is further exacerbated (double arrows) in the presence of cardiovascular (CV) diseases (such as hypertension and metabolic syndrome) especially during exercise. However, evidence suggests that exercise training can re-couple the interaction between the heart and arterial systems. SNS, sympathetic nervous system; BP, blood pressure; Ca^{+}, calcium; LV, left ventricle; Beta-adrenergic receptors.