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Integrative Approach for the Management of Diabetes Mellitus and Cardiovascular Disease

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Abstract: ***Diabetes Mellitus and Cardiovascular disease are one of important non-communicable, lifestyle-related endocrine disorders. According to the International Diabetes Federation (IDF), the number of people with diabetes is expected to increase from 366 million in 2011 to 552 million in 2030. The use of an integrative approach to medicine Traditional and modern medicine needs to be considered to address the multiple challenges posed by diabetes. Integrated strategy involves self-management and lifestyle changes and is a new term emphasizing the combination of conventional and alternative approaches to address biological, psychological, society and the spirit of health and disease. When considered an alternative, integrated treatments to diabetes, all patients must realize the importance of careful monitoring of blood sugar levels. blood and potential side effects, as well as regular contact with the medical care team. In the present study, the integrative approach for the management of Diabetes Mellitus and Cardiovascular disease.***
Keywords: Diabetes , Ayurveda , Medicine , Integrative therapy, HFpEF

I. INTRODUCTION

Diabetes mellitus is one of the oldest and common disease conditions . Ayurvedic studies describe about the etiology, etiology, prognosis, complications, their management, and the causal relationship between diet, lifestyle, environment, and genetic factors. Despite recent advances or advances in medicine, the management of diabetes still presents some challenges that require special attention to develop unexplored areas of medical knowledge. Ayurveda provides a comprehensive, safe and effective approach to the treatment of such diabetes. The development of relevant research models is an important challenge in studying the safety and effectiveness of Ayurvedic interventions that are consistent with their basic principles and system approach.[1]. Integrative medicine is a new term that emphasizes a combination of traditional and alternative approaches to addressing the biological, psychological, social and psychological aspects of health and illness. It emphasizes respect for human ability for healing, the importance of physician-patient relationships, a collaborative approach to patient care between practitioners, and the practice of "evidence-based" traditional complementary and alternative medicine. Diabetes is a chronic disease in which the body does not properly produce or use insulin and affects the way the body uses glucose as energy.

The burden of diabetes lies not only in the management of hyperglycemia, but also in the associated microvascular and macrovascular complications that can lead to visual impairment, amputation, and renal failure. Globally, the number of diabetics is projected to increase from 153 million in 1980 to 347 million in 2008 and to 552 million by 2030. Insulin must be present in order for cells to use glucose for energy.

In people with diabetes, the pancreas produces little or no insulin (type 1) or cells do not respond appropriately to the insulin produced (type 2 and gestational diabetes). Regarding the pandemic state of diabetes mellitus and the recent number of afflicted people in the world, i.e., 422 million and 1.5 million deaths per year, attributed directly to diabetes, an integrative approach was used to treat patients suffering from the condition. [2] The three main types of diabetes are: (a) Type 1, also known as juvenile diabetes (b) Type 2 diabetes (c) Gestational diabetes (occurs in pregnant women during the pregnancy, but resolves after delivery) The high sugar level leads to complications such as blindness, kidney failure, circulatory problems, coronary heart disease, neuropathy etc. Diabetes is treated with insulin (always in type 1 and sometimes in type 2) by monitoring blood sugar levels and oral medication (type 2).

Lifestyle changes are critical in diabetes management, and they are an expected part of a conventional medical care plan. It includes: (a) Healthy, lowfat, highfiber, nutritious diet, minimizing simple and processed sugars (b) Exercise (c) Weight loss (if appropriate) or maintenance of a healthy weight Patients with type2 diabetes mellitus are increasingly interested in integrative medical strategies, most of which involve selfmanagement and lifestyle changes. [3]

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II. INTEGRATIVE THERAPIES FOR DIABETES MELLITUS

These therapies are considering an alternative that integrates treatments for diabetes, all patients should recognize the importance of careful monitoring of their glucose levels. blood pressure and potential side effects, as well as regular communication with the medical care team. The following therapies and therapies can be used to manage type 1 diabetes and manage or eliminate type 2 diabetes (T2DM), optimizing function and minimizing complications.

A. Nutrition and Weight Loss

Type 2 diabetics are advised not to take trans fat supplements and limit saturated fat to less than 7% of total calories to reduce heart disease risk factors circuit. Moderate weight loss (5% of body weight) improves insulin action, lowers fasting blood sugar, and reduces the need for diabetes medications. [6] It was found that almost 10% of the weight loss was associated with a decrease in glycosylated hemoglobin (HbA1c) [7] and weight maintenance is also an important part of diabetes weight management.

The American Diabetes Association (ADA) [8] has recommended three types of diets for patients with type 2 diabetes, such as the low glycemic index (GI) diet. Mediterranean and vegetarian diets and have emphasized that the best diet for a particular patient is the one that best matches their dietary and lifestyle goals. The low glycemic index emphasizes carbohydrates and other low glycemic index foods, leading to a gradual increase in sugar levels. It also showed a significant increase in high-density lipoprotein (HDL) cholesterol on the low-glycemic diet. The Mediterranean diet is high in fruits, vegetables and unsaturated fats, and low in glycemic index fish and whole grains. It is higher in carbohydrates and fats than a portion-controlled diet. The vegetarian weight loss program makes a speciality of culmination and veggies and ingredients low in saturated fats and it has a tendency to be better in fiber and decrease in energy than different diets. [9] and improvement of T2DM because of the maintenance of beta cells and vegan diets enhance glycemic manipulate. Cinnamon changed into determined to assist lessen blood sugar, LDL cholesterol and overall LDL cholesterol in human beings with kind 2 diabetes. Omega-three fatty acids, a kind of ―good fats determined in fish oil and flaxseed-oil dietary supplements, may also assist lessen infection and insulin resistance in human beings with diabetes. [10].

B. Exercise

Regular exercising allows each weight loss or weight reduction and glucose uptake and it's miles crucial in dealing with diabetes. Higher depth hobby did now no longer enhance glycemic manipulate any extra than mild depth exercising. [11]

C. Vitamins And Mineral Dietary Supplements

The diabetic sufferers have been at improved chance for deficiencies following very-low-calorie diets, the aged and strict vegetarians may also gain from multi-diet and mineral dietary supplements. Individuals with maximum diet D ranges have decrease chance of growing diabetes. [12] A fats-soluble antioxidant determined in vegetable oil, nuts, and inexperienced leafy veggies, diet E`s best-studied aspect is alphatocopherol. Chromium is a hint mineral and concept to be a vital cofactor for insulin law and glucose metabolism and aids glucose with delivery into the cell. Chromium reduces HbA1c and fasting blood sugar ranges and its deficiency induces hyperglycemia and impaired glucose tolerance. This detail is found in many ingredients, mainly brewer`s yeast, liver, carrots, potatoes, broccoli and spinach. It additionally reduced glycosylated hemoglobin (HbA1c). [13] Magnesium is concerned in insulin secretion, binding and hobby and a deficiency of magnesium is related to reduced absorption in sufferers with diets excessive in processed meals or improved removal in folks who ingest huge portions of alcohol or caffeine or take diuretics or beginning manipulate pills. Magnesium is concerned with extra than three hundred enzymatic reactions and is essential to glucose metabolism and insulin homeostasis. Low serum and plasma ranges of magnesium are related to changes in nerve, muscle, and cardiac conduction. This contributes to nephropathy and quit degree renal disease. Increased nutritional consumption of magnesium advanced metabolic manipulate and decreased the chance of T2DM and dyslipidemia. [5] Dietary reasserts of magnesium encompass complete grains, leafy inexperienced veggies, legumes and nuts. Magnesium dietary supplements cause an development in fasting blood glucose, however did now no longer substantially decrease HbA1c in sufferers with kind 2 diabetes.

[14] Alpha lipoic acid (ALA) is a robust antioxidant determined in very small quantities in ingredients, has proven promise withinside the remedy of diabetic neuropathy. It improves glucose uptake and stops glycosylation, a method withinside the frame in which sugars are inappropriately hooked onto proteins and fats. The crucial fatty acids found in ALA can defend towards the nerve and blood vessel harm from diabetes via way of means of growing insulin secretion and decreasing ldl cholesterol ranges. The research have determined that ALA may also lessen oxidative strain and enhance insulin sensitivity in sufferers with diabetes. There changed into a sizeable lower in fasting blood glucose.

D. Plant Medicine

There are herbs that have been recommended for the treatment of diabetes in Ayurvedic and traditional Chinese medicine and its anti-diabetic effects have been reported by many researchers. These reports are confirmed by in vitro studies and in vivo models. Herbal remedies, especially Gymnemasylvestre, Momordicacharantia, and Trigonellafoenumgraecum, have clinical evidence of antidiabetic effects. Therefore, it seems likely that physicians could rely on these herbs, at least as an adjunct, as well as current hypoglycemic drugs to improve the management of patients with diabetes mellitus. [16] Vitamin C acts as a potent antioxidant that improves insulin resistance and reduces tissue damage caused by free radicals. It is important for healthy immunity and wound healing. Ginkgo biloba also contains antioxidant compounds that stabilize pancreatic beta cell membranes and aid in peripheral circulation. A variety of plant secondary metabolites such as alkaloids, terpenoids, phenols, flavonoids and many others show promising antidiabetic potential. Herbal and natural products are the most commonly used forms of complementary and alternative medicine. Current findings suggest that CAM can help advance a participatory and integrated model of diabetes care, based on provider knowledge of evidence-based therapies and disclosures of patients about CAM use. Emerging evidence for positive outcomes with certain natural products has been reported in glycemic parameters, cardiovascular risk markers, and quality of life in individuals with type 2 diabetes.[18-21]

E. General Medicine

There is evidence of the use of therapeutic modalities such as acupuncture, massage/energy therapy, acupressure and chiropractic and others, as an approach An integrative approach to the treatment of diabetes and its complications. These treatment modalities are collectively known as manual drugs. Although acupuncture has long been reported to improve glycemic control in patients with diabetes and prediabetes, the evidence is limited and of poor quality.

F. Chelation Therapy

The Chelation Therapy Evaluation Trial (TACT) is one of the most promising advances in the treatment of Coronary Artery Disease (CAD). TACT was designed to determine if future cardiac events could be reduced for patients at least 50 years of age who had already suffered at least one heart attack and it reduced future cardiac events by lowering the death rate of diabetic patients who had a previous myocardial infarction. It was a randomized, doubleblind, clinical trial of 1708 patients, who were given more than 55,000 intravenous treatments and half of the patients were given high dose vitamins. Stress management helps individuals more effectively regulate their diet and physical activity, both of which are important in managing diabetes.

III. CLINICAL RESEARCH PROSPECT

RCTs is beyond the scope of the present work and can be found elsewhere.[22],[23] Interestingly, lifestyle changes such as exercise and calorie restriction suggest most promising results in short-term trials, [24-25] likelihood The lack of progress in pharmacological management of patients not only justifies better-designed trials with recruitment and selection criteria clearly defined criteria, but also a clearer understanding of the pathophysiology.Yo date, translation and After a long period of omission, in the last few years there have been many trials of heart failure with preserved ejection fraction (HFpEF).

Epidemiological trends suggest that with increasing life expectancy and increasing disease burden, the prevalence of HFpEF may reach epidemic proportions. Mortality rates vary from 30 to 60% at 5 years, hospitalization is high, and quality of life (QOL) is severely impaired. Several randomized clinical trials (RCTs) have attempted to halt disease progression and improve morbidity and mortality by targeting different underlying pathophysiological mechanisms, all of which have inconclusive or neutral results. A detailed overview of these basic science have not been able to support the development of therapy.

Indeed, while a wealth of data from experimental models have been collected ranging from visceral baths to intracellular mechanisms involved in cardiac relaxation and compliance, vascular function and inflammation , mechanistic knowledge, biochemistry, and detailed molecular data from basic science have yet to be linked. mostly complex preclinical models and patient phenotypes. This positional article focuses on current knowledge of the pathophysiology of HFpEF, available animal models, and experimental methods. From these data, we suggest directions for future research in the field of translation.

A. Diagnosis Of Heart Failure With Maintained Ejection Fraction

Diastolic function is determined by the relaxation and compliance of the left ventricle (LV), which together enable low pressure swelling [26].

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Confusion in any of these areas causes diastolic heart failure (DD). Asymptomatic DD [sometimes called preclinical heart failure (HF) is common in society. When evaluated carefully, patients often show a decrease in quality of life and an increased cardiovascular risk. Importantly, follow-up studies have shown general progression to HFpEF11. Simply put, the diagnosis of HFpEF depends on the signs and symptoms of pulmonary congestion, not on other causes, or markers of normal ejection fraction and diastolic dysfunction.[27]. The gold standard for diagnosing HFpEF clearly documents the development of heart failure during exercise (due to the inability to increase filling pressure and cardiac output), so invasive hemodynamics from exercise tests Evaluation is [28-29] but invasive testing is risky and not feasible in all patients, clearly guaranteeing a non-invasive surrogate. The diagnosis of HFpEF remains controversial. At a minimum, the 2016 ESC guidelines require symptoms, objective evidence of heart failure, and some structural or functional deficiencies. The latter is usually measured by echocardiography and can include left ventricular hypertrophy (LVH), increased left ventricular volume, and various abnormalities associated with DD.

DD has always been considered an important factor, but only two-thirds of patients present with DD at rest and in some patients RCTs.[30]. To simple observation emphasizes the lack of a firm consensus on the diagnosis of HFpEF. In fact, DD is a major function of HFpEF, but most experts today say that DD is a complex syndrome in which multiple cardiac, vascular, and non-cardiac determinants act to impair cardiovascular reserves. [31-32]. HF with reduced ejection fraction (HFrEF), sudden attacks cause muscle cell loss, dysfunction, and a self-enhancing neurohumoral cascade, whereas HFpEF is a slow-growing process without index events. Aging and comorbidity cause increasingly dysfunction through changes in stress conditions, inflammation, and complex systemic changes. The direct effects of aging explain the superiority of HFpEF in the elderly with long-term comorbidity and decreased cardiovascular reserve. For practical reasons, a single organ, single stressor approach is usually preferred in basic research.

Indeed, it is difficult to mimic aging and multiple comorbidities in the laboratory. It should be emphasized that ejection fraction (EF) is load dependent and is overestimated in cases of myocardial hypertrophy. based on their diagnostic criteria on EF. Follow-up showed that patients who were later classified into HFpEF or HFrEF fell into the opposite category, [33] echocardiograms poorly monitored individual progress, [34]and were dependent on resting parameters is not sufficient because HFpEF begins with exercise intolerance. Guidelines do not incorporate this concept well, relying mainly on data obtained from hospitalized patients with decompensated HF and abnormally elevated levels of diuretic sodium peptides. Unsurprisingly, sensitivity is low when applied to RCTs recruiting stable patients or outpatients with dyspnea.exerxise testing can improve the sensitivity of ESC HFpEF diagnostic guidelines current at the expense of reduced specificity.

B. Mechanism And Phenotype Of Heart Failure With Preserved Ejection Fraction (Heref)

1) Cell Mechanism

Endocardial biopsy revealed cardiomyocyte hypertrophy and greater myofibril density in HFpEF than in HFrEF, but no difference in collagen volume fraction. cardiomyocyte stiffness, both by N2B-favorable isoform displacement (stiff) and by hypophosphorylation, although hypophosphorylation appears to predominate. Other post-translational edits may also contribute. In addition, the titin-actin interaction accounts for 40% of LV viscosity and thus plays an important role in the slow relaxation process. Transient Ca2+ decay, which may contribute to decreased relaxation. Similarly, the ratio between the endoplasmic reticulum Ca2 + ATPase content and the phospholamban content in HFpEF was reduced compared with the myocardium of HFrEF patients.

2) Aging

Aging prolongs relaxation and increases LV stiffness through collagen accumulation and crosslinking, myocardial cell loss, and reactive hypertrophy. [35] Neuroendocrine disorders, mitochondrial dysfunction body, increased oxidative stress and fibroblast activation are well-established pathways associated with aging. Repetitive heartbeats rupture the elastin layer of the central vessels, causing dilation and stiffening, loss of the Windkessel effect and distant propagation of oscillation pressure.[36] Increased wave speed causes earlier wave reflections. Although initial studies in hypertensive patients have shown that wall stress does indeed decrease towards the end of systole, at the time of wave reflection,[37-38] population-based studies have shown wave reflexes and increased Late systolic wall tension contributes to decreased relaxation capacity. [39] In addition, in patients referred for coronary angiography, wave reflection was less predictive of cardiovascular outcomes, particularly when systolic function was preserved. In turn, increased wall stress increases endosystolic elasticity and volume sensitivity while fluctuating pressure transmission leads to endothelial dysfunction (ED). An increase in arterial stiffness with exercise has been shown in HFpEF.[40].

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Measurements of LVH, left atrial size, DD, and age-dependent diuretic sodium peptides, suggest that senile age expressed to some extent physiological HFpEF. Clearly, aging is a progressive process in itself, so the line between aging and HFpEF remains unclear. Therefore, one of the main challenges will be to provide a more uniform description of the aging cardiac phenotype, to distinguish it from HFpEF.

3) Gender

Although it is now recognized that not only older women but also younger men with obesity and diabetes (DM) are also at risk for HFpEF, [38]omen tend to predominate in the HFpEF groups. This result may be explained by the fact that women often reach an older age, but also by pathophysiological mechanisms. Sex differences in vascular biology and sex hormones may account for postmmenopausal aortic stiffness and elasticity maintenance in perimenopause. Aortic elasticity is lost after menopause, constituting a potential explanation for hypertrophic remodeling and HFpEF.[41]. Loss of ovarian function also leads to erectile dysfunction and inflammation

4) Comorbidities

It has also been found that a higher burden of comorbidities exists in HFpEF. The most important of these comorbidities are systemic hypertension, obesity, and diabetes, but a long list of other comorbidities such as chronic obstructive pulmonary disease, renal dysfunction, arrhythmias Sleep apnea, hypothyroidism, and anemia have also been reported. Adverse events, other than the typical HF endpoint, such as pump failure and sudden death, were common,[43].

Conversely, comorbidities themselves are an integral part of the HFpEF syndrome, and actively contribute to dysfunction and remodelling in HFpEF Obesity and metabolic syndrome associate with DD well before DM, while DM may ultimately lead to cardiomyopathy.[44].

HFpEF is not just the outcome of comorbidities. Abnormalities in cardiovascular structure and function go beyond those explainable by comorbidities alone. Comorbidities, however, do influence phenotype and outcome should be managed.

5) Microvascular And Epicardial Coronary Artery Disease

Recent progress in HFpEF research has suggested that HFpEF may in fact be a disease of the microvasculature. Studying the role of comorbidities and inflammation created a new hypothesis based on coronary microvascular ED, [45], which was supported by findings at autopsy. HFpEF patients show systemic microvascular dysfunction as well as coronary microvascular ED and rarefaction.[46]. CAD is documented in many of HFpEF patients, pooled analysis of prospective HFpEF studies suggests that it is present in approximately 50% of patients and contributes to a worse prognosis. In a HFpEF cohort that underwent coronary angiography, patients with CAD showed increased mortality and EF deterioration that was mitigated by revascularization.[47].

6) Pulmonary Hypertension And Right Ventricular Dysfunction

Large community mostly studies demonstrate that pulmonary hypertension is prevalent and often severe and independently predicts mortality in HFpEF.[48]. It may discriminate between HFpEF and hypertension suggesting a role in symptom development.

7) Peripheral factors

Effort intolerance, which is the core HF sign and symptom in HFpEF, is not solely due to low cardiovascular reserve but also to poor peripheral oxygen extraction by the skeletal muscle.[49].Indeed, chronotropic incompetence and low systolic reserve lead to further reliance on peripheral oxygen extraction to meet demands in HFpEF but peripheral extraction also fails due to abnormalities of both skeletal muscle and the microvasculature [50]improvements in exercise capacity due to exercise training appear to derive primarily from improved peripheral (arterial and/or skeletal muscle) function, highlighting the important contribution and plasticity of peripheral factors.[51]

8) Experimental models

Given its complex ,tough pathophysiology, none of the current models is fully emulates the HFpEF and probably none ever will. The Preclinical tests should build upon the robust features of each model .[52]. A detailed overview of available animal models is provided in the supplementary material.

9) Small Animals

Only saltsensitive rats and obese hypertensive and diabetic ZSF1 rats have a clear demonstration of increased lung weight, which could relate to HF. [Saltsensitive rats however have been criticized because they develop / show LV dilatation and there is decreased EF.[53-55]. As for ZSF1 obese rats, they have low peak maximum oxygen consumption and effort intolerance, which puts the model one step ahead towards clinical translation.[56]. Additionally, microvascular injury, ischaemia, inflammation and titin hypophosphorylation have been demonstrated. ZSF1 obese rats have a convenient hypertensive lean control and mimic many features of HFpEF. Valuable insights into alternatives to effort testing have been proposed.[57]. Nevertheless, we must highlight several drawbacks. They are young adults with untreated metabolic syndrome and do not recapitulate the scenario of an elderly patient, they progress to renal failure at an older age, the fullblown phenotype is very hard to recapitulate in mostly in reproductive age females, and they mostly show mild extracellular matrix changes. An animal model of pulmonary hypertension associated with HFpEF is also needed, and a two-hit model has recently been proposed. [58]. In mice, few models can mimic HFpEF. Myosin binding protein C phosphorylation-deficient mice develop LVH and rigidity, delayed relaxation, pulmonary congestion, and decreased spontaneous activity, but unfortunately EF [59] is also slightly reduced, obese and diabetic Leprdb / db mice.

10) Big animals

Large animal models are highly desirable as they better mimic human physiology. HFpEF has been modeled in older hypertensive dogs by renal encapsulation.[58] they present with hypertrophy, fibrosis, and impaired relaxation. Recently, a new model has been developed on young female Landrace pigs. Pigs with deoxycorticosterone have increased blood pressure associated with a high-salt diet while hyperlipidemia due to a high-cholesterol diet. They did not show increased fibrosis, but showed remodeling and hardening of concentric hypertrophy. Although the animals were asymptomatic, the disturbances were aggravated at high excitation frequencies. The authors attribute their findings to attenuation of PKG signaling, titin isoform displacement, and reduced phosphorylation. This model has disadvantages such as marked hypercholesterolemia, young age, and mild hypertension. HFpEF has also been mimicked in dogs by repeated coronary microvascularization, the only model that partially addresses the association with coronary artery disease. Finally, large animal models are very needed for device development and interventional therapies, such as recently reported with the proof of concept percutaneous pericardectomy in pigs.

11) Skinned Cardiac Cells

Some of the most influential pathophysiological findings from HFpEF patients have been obtained in dermal cardiomyocyte preparations. These studies indicate that LV stiffness is mainly due to passive stiffness. of the cardiac muscle cells themselves. Mechanistically, titin isoform change and hypophosphorylation are directly associated with higher passivation intensity. Results are reproduced in animal models of HFpEF. Access to biopsies from HFpEF patients is rare because there is no formal indication for endocardial biopsy beyond clinical suspicion of cardiomyopathy. restriction, infiltration or inflammation. This leads to selection bias, as biopsies are often obtained from younger patients without coronary artery disease. Another concern is that the source of HFpEF cardiomyocytes is usually from the endocardium, and their controls are often obtained from the right ventricle of transplant patients or donor hearts. Finally, studies were performed with the lattice gap widened at low temperature. Studies on intact cardiomyocytes at physiological temperature have shown that dermal cardiomyocyte preparations lack the contribution of actomyosin. Advantages and disadvantages of different experimental settings, from Cell function to cardiovascular function in vivo.

12) Cardiac Muscle Cells Are Intact

An important aspect of diastolic function is that the intracellular handling of Ca2+ and Na+ is disturbed. While in HFrEF, a decrease in the amplitude of intracellular Ca2+ transition plays a dominant role in contractile dysfunction, it remains unclear what changes in Ca2+ in cells actually contributes to DD in HFpEF. Cellular ion manipulation is commonly analyzed in intact and isolated cardiac cells stimulated by electric field stimulation, especially from animal models. The advantage of these studies on dermal cardiomyocyte preparations is that with cell shortening, cellular ion manipulation and its changes can be analyzed with a fluorescence probe, while the Percutaneous myocytosis only analyzes sarcomere function. It remains unclear to what extent mitochondrial dysfunction and/or oxidative stress contribute to diastolic (and/or mild systolic) dysfunction also in HFpEF. Studies of isolated cardiomyocytes allow to investigate the redox state of pyridine nucleotides, membrane potentials, and reactive oxygen species in mitochondria embedded in their physiological cellular context by using fluorescence imaging combined with excitation.

One drawback of both techniques is that the muscle cells sit on a sheet of paper without any physical workload. This underestimates the physiological workload and may have important implications for mitochondrial energy and excitatory-contractile coherence. A major recent advance has been the development of techniques allows to stretch and impose varying degrees of preload and load on isolated cardiomyocytes when fixed to thin glass.

C. Evaluation Of Heart Failure With Preserved Ejection Fraction In Experimental Models

1) Hemodynamic Assessment

This approach is invasive, requires deeper anesthesia, and is usually limited to end-stage evaluation. However, serial evaluation and telemetry are possible. Traditional approaches are based on separate assessment of active relaxation and passive stiffness at end-diastolic but newer methods, based on global optimization, can provide added value. is derived from the end-diastolic pressure-volume relationship. In closed thoracic preload mode, the first beats after preload reduction are often influenced by right ventricular loading, which accounts for approximately 30-40% of resting end-diastolic pressure,and this must be is taken into account. The LV stiffness constant has units of vol. and therefore depends on the shape and size of the LV. Their was several approaches have been tried to solve this problem. One approach is to take stress analog values, including estimation of LV mass or wall thickness, other is volume indexing. Assess a single pressure point and end-diastolic volume highly dependent and imprecise. Although useful in large community studies, the single span method raises concerns in experimental scenarios. Even after pressure correction for the relaxant's active component, they are subject to error in individual estimates, especially in incubation preparations. Methods based on normalized data Volumes obtained in different species are also better when applied to groups than low pressure. range and limitations in HFpEF. Finally, inotropic reserve is impaired in HFpEF and should also be evaluated in experimental models, abrupt loading indicates low inotropic.

2) Image method

Non-invasive imaging methods are favored both in clinical practice and experimental research. Echocardiography is the first choice.Most standard clinical approaches can be converted to animal studies using high-frequency linear transducers, even with ultrasonographic devices. normal heart sounds. has conflicting results. It should be emphasized that relying on a single parameter is often less informative than integrated analysis. Tension analysis is primarily a research tool, but it has potential far beyond tissue Doppler imaging. It can evaluate all segments of the myocardium and takes into account the geometry of the chambers. It remains to be determined whether stress-derived echocardiographic parameters can add value to the diagnosis of HFpEF. Spot tracking has an advantage over tissue Doppler, which is not affected by alignment angle but is also limited by its lower temporal resolution. In rodents, the resolution must be high enough for tracking points and requires high frequency probes and specialized machinery.

3) Exercise testing (diastolic stress tests) and other alternative methods

Several limitations to cardiovascular reserve have been shown in HFpEF during dynamic exercise but their relative role is disputed. It must be emphasized that most HFpEF patients are elderly and have various comorbidities that may preclude dynamic exercise or confound interpretation. Still, a cardiopulmonary exercise test is an invaluable diagnostic tool, measures of submaximal and peak effort were shown to be reliable in HFpEF patients and have been used as strong endpoints in RCTs. Stress and effort testing is increasingly advocated also in echocardiography, but it remains unclear which variables should be sought and under which protocol. A reasonable alternative when dynamic exercise is not feasible might be load or pharmacological manipulation. Although it may be technically challenging to have joint hemodynamic evaluation and effort testing with maximum oxygen consumption, such an integrated evaluation of all determinants of effort intolerance could be an important contribution from experimental models of HFpEF. Joint afterload and preload elevation with selective vasopressors is potentially helpful as appraised experimentally. Pacinginduced tachycardia is another alternative, whereas the role of dobutamine is debated, as some studies suggest it may impair E` response in HFpEF, while others show smaller increases in systolic wall tension than dynamic exercise, even decreasing enddiastolic volume and myocardial oxygen consumption in the hypertrophic heart, without worsening [60-62].

IV. CONCLUSION

Diabetes care requires a multidisciplinary approach through a concerted effort to deliver different support services in a timely and effective manner.

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The principles of Ayurveda have been developed over time using clinical evidence, observations, and philosophical assumptions. Translational Ayurveda implements ideas of translation medicine, taking into account Ayurveda's unique principles of health care and their application in patient care. Thus it is a need of integrated interdisciplinary studies to validate and translate that knowledge into dynamic science. Diagnosis and treatment must correlate with systems biological concepts. Final goal of drugs convert is to help patients with grow faster than out of new diagnoses, drugs, and ant treatments medical formula diseases, enabling everyone to access care at a reasonable cost. An integrative medicine approach that combines conventional and alternative therapies with a focus on natural, minimally invasive and evidence-based selection is well suited for the management of diabetes.

As the mechanisms and characteristics of HFpEF are gradually elucidated in clinical and epidemiological studies, basic researchers and epidemiologists should be aware of its complexity and possibly benefit from it. Advice both on experimental model and choice of experimental set-up as well as on the most relevant topics of investigation. Additional access to myocardial samples from representative cohorts of HFpEF patients allows for guaranteed functional and molecular phenotypes. Animal models should be selected based on their specific characteristics, favoring those that are intolerant of exercise or with impaired cardiovascular reserve as clinical subjects, at least for pre-therapeutic testing. Clinical. The roles of aging, sex, and specific comorbidities in the progression of HFpEF are largely underexplored and need to be addressed in these experimental models. To gain a systemic biology view of HFpEF, the systemic effects and higher-order crosstalk with other organs need to be further investigated, as well as the disrupted intercellular communication mechanisms in the heart.

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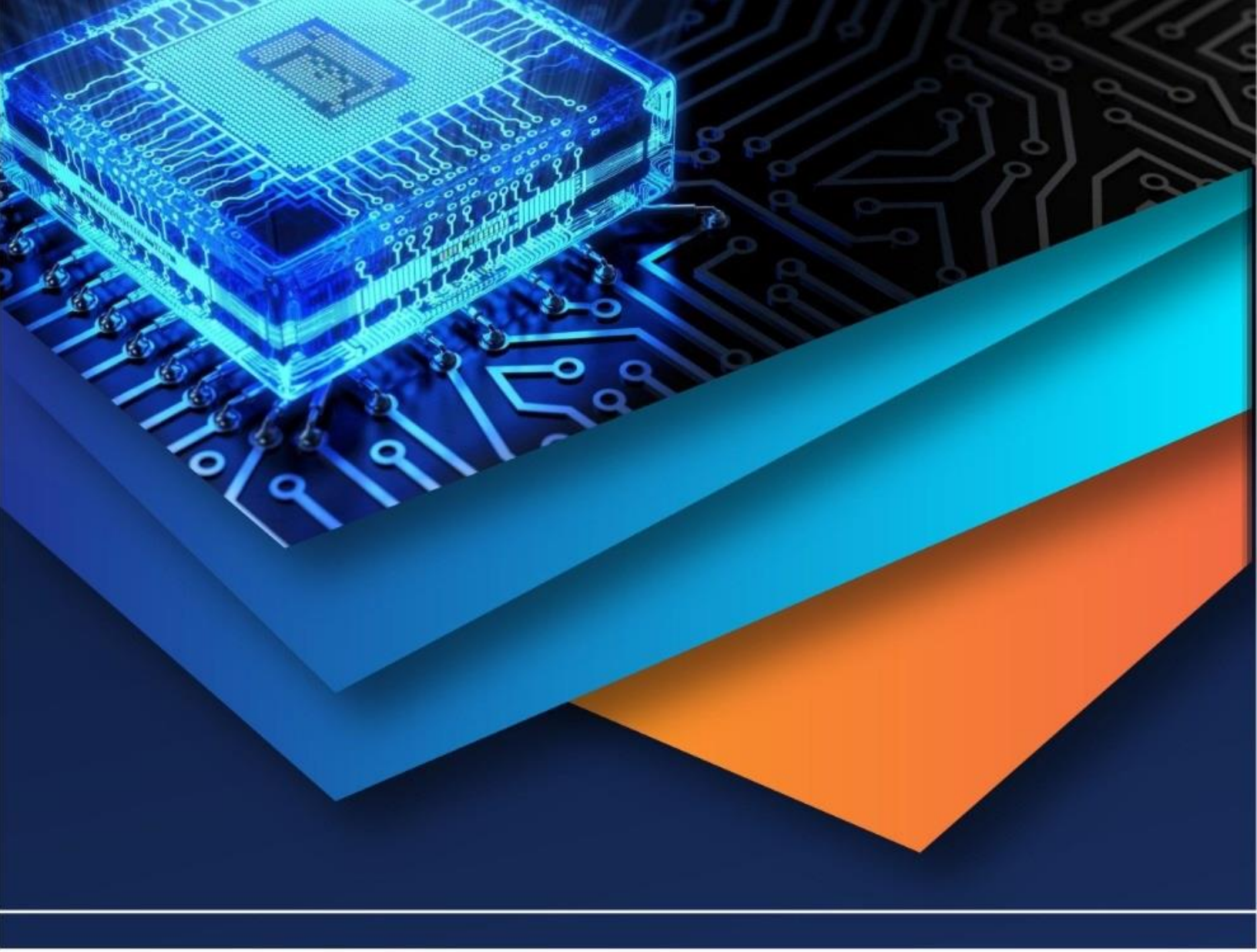
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