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Article

Effect on The Physiological Changes in Terms of Force, Contraction and Relaxation of Failing Left Ventricle

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Abstract: This study investigates the physiological changes in force contraction and relaxation of the failing left ventricle, addressing the gap in understanding myocardial dysfunction in heart failure. Using a prospective design, 65 cardiac tissue samples were analyzed from June 2022 to April 2023, categorized into non-failing, failing ischemic, and failing non-ischemic groups. The methodology involved preparing cardiac trabeculae and assessing contractile properties at a baseline frequency of 1 Hz. Findings indicate that failing myocardium exhibits lower active developed force, prolonged time to peak tension, and slower relaxation dynamics compared to non-failing myocardium, with statistically significant differences noted primarily in the failing non-ischemic group. These results suggest impaired contractile function and altered myocardial kinetics in failing hearts, providing critical insights for developing targeted therapeutic interventions to enhance cardiac performance in heart failure patients.

Keywords: Ischemic, failing heart, myocardium, infarction, ischemia, heart failure.

1. Introduction

The heart is composed of the endocardium, myocardium, and pericardium. Pathology within these sections can result in heart failure. Left ventricle failure occurs when the left ventricle becomes dysfunctional resulting in insufficient blood delivery to crucial body organs. Left ventricle failure can be further subdivided as heart failure with preserved ejection fraction reduced ejection fraction or mid-range ejection fraction. Etiologies of left heart failure are hypertension and coronary artery disease. Hypertension can lead to heart failure through left ventricular hypertrophy and serves to be a risk factor associated with coronary artery disease. A sedentary lifestyle, diabetes, male gender, smoking, and obesity are risk factors associated with heart failure. These causes can be prevented and control of these risk factors remains crucial for preventing heart failure [1]. Heart failure is much more prevalent in elderly populations. Nearly 5.7 million populations in the U.S. have been diagnosed with heart failure. Nearly 50% of the patients suffering from heart failure have been considered to suffer from HFrEF and the diagnosis is becoming much more prevalent with the passage of time. HFpEF in comparison to HFrEF is much more prevalent in women and affects elderly populations.

Left heart failure occurs due to several mechanisms. Chronic controlled hypertension leads to increased afterload and enhanced cardiac workload that lead to hypertrophy of the left ventricle. The hypertrophy serves to be a compensatory mechanism and plays a crucial role in maintaining cardiac output. However, long-term hypertrophy inhibits myocardium relaxation resulting in impaired cardiac filling and diminished left ventricular failure. Coronary arterial disease leads to myocardial damage directly resulting in scar formation and remodeling that diminish cardiac output and contractility [4]. Arrhythmias result in remodeling and reduce cardiac output by impairing ventricular filling and reducing ventricular relaxation. Cardiomyopathies include a diverse

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pathologic spectrum and several mechanisms that lead to cardiac dysfunction. Figure 1 shows that Coronary artery disease and is shown below:

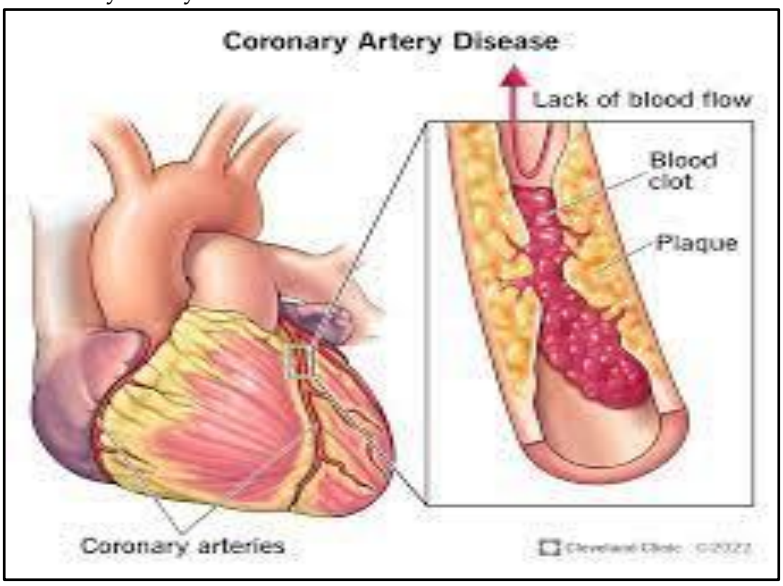

Figure 1: Coronary artery disease

Patients suffering from left heart failure go through shortness of breath, weight gain, and increase in abdominal girth, orthopnea, and pain in the upper quadrant due to congestion in the liver. However, some patients suffering from the advanced disease often experience cardiac cachexia or weight loss. Heart failure diagnosis is clinical. However, numerous examinations are available for evaluation. Brain Natriuretic Peptide (BNP) tests are much more helpful as it is helpful in differentiating acute heart failure from causes that lead to shortness of breath. Laboratory tests further include complete blood count, liver function examination, and troponin T for detecting myocardial infarction. Electrocardiography showcases hypertrophy of the left ventricle. Echocardiography serves to be helpful in distinguishing HFrEF from HFpEF by determining ejection fraction [2]. Coronary angiography is indicated among individuals with angina symptoms and is indicated among patients suffering from symptoms of heart failure. Left heart failure can be often complicated with volume overload resulting in respiratory distress and arrhythmias, cardiogenic shock, and death. It has been further reported that acute coronary syndrome, cerebrovascular accidents, and pulmonary embolism are prevalent causes of mortality rate among patients suffering from heart failure. Figure 2 shows the Brain Natriuretic Peptide test process as shown below:

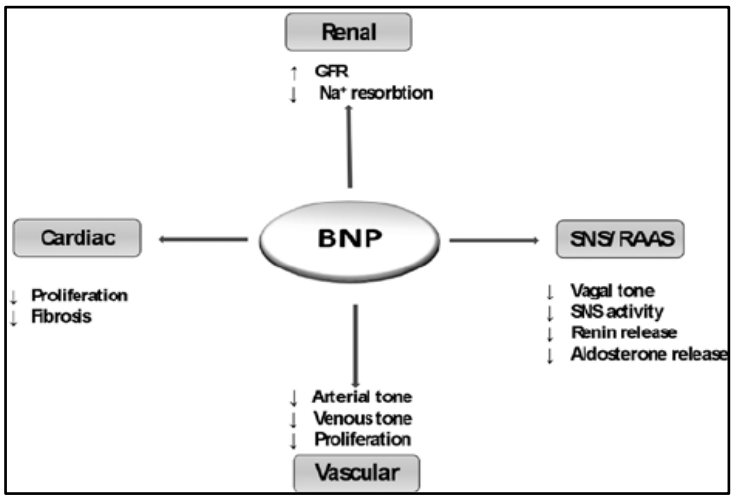

Figure 2: Brain Natriuretic Peptide

The heart is involved with supplying oxygen as well as metabolite substrate to peripheral tissues. Heart failure is a pathological state as the organ is unable to pump blood

at the required amount. Heart failure occurs due to left heart abnormalities. Mechanical events occurring during the cardiac cycle highlight the occurrence of systole and diastole [3]. The heart is unable to pump sufficient amounts of blood due to the inability of LV to eject or fill. Diastolic and systolic heart failure are quite similar in LV functional and structural characteristics involving enhanced LV mass and diastolic pressure. LV is a crucial part associated with the cardiovascular system. Contraction of LV forces oxygenated blood through the aortic valve and is distributed to the whole body. Heart failure occurs due to poor functioning of the left ventricle. Diminished diastolic filling as well as ejection fraction leads to limited blood leaving the heart in case of systemic circulation. HF is correlated with structural changes in the ventricle and mural thinning. Myocardium alterations occur before ventricular changes like fibrotic replacement and focal loss of myocytes. Myocardial changes result in a decrease in the potentiality of contraction of individual myocytes with enough force and speed for maintaining cardiac output required to maintain bodily requirements. The primary function of LV is to provide a sufficient amount of cardiac output for maintaining blood flow [6]. Systolic contraction of LV leads to cardiac output that can be easily influenced by contractility, preload, and afterload. Cardiac output is the amount of blood pumped out of the heart at a specific time.

Preload is referred to as load on ventricle muscle in the case of diastole. Load occurs when blood volume fills the ventricle during rest position between times of contractions. Increased preload volumes enhance contractility through the Frank-Starling mechanism. The occurrence of the mechanism is recorded when preload volume increases sarcomere length much more closely to the overlapping of myosin and actin. Afterload is the pressure that LV pushes against during contractions. Conditions like aortic stenosis, hypertension, and atherosclerosis require LV to work harder for overcoming increased afterload pressure. Contractility is considered an inotropic condition of the heart muscle. Intracellular calcium concentration affects heart contractility with increased levels inducing high contraction. Several medications, for instance digoxin are administered for increasing heart contractility via the contractile performance of myocytes. Medications are considered to be therapeutic for individuals who suffer from chronic left ventricular dysfunction. Therapy normalizes action potential features and leads to enhanced functioning of LV pumps [5]. LV pumps blood with high pressure in comparison to other heart chambers as it faces a high workload as well as mechanical afterload. Electrophysiology associated with LV initiates at a SA node that initiates an action potential. The action potential goes through the atria, leading to the contraction of the AV node. Electrical current in AV nodes is delayed by about 100ms prior to transmission of an impulse to the atrioventricular bundle. The electrical impulse is then recorded to travel to the left and right bundle of Purkinje fibers. Action potential upon reaching ventricular contractile fibers and excitation-contraction coupling induces calcium influx resulting in synchronized contraction initiating at the apex of the heart and progressing in an upward direction.

2. Materials and Methods

This prospective study was conducted from June 2022 to April 2023, analyzing 65 samples of cardiac tissue taken from patients in different pathophysiological states, divided into three groups: control non-failing (NF), end-stage failing ischemic (FI), and failing but non-ischemic (FNI) hearts. Non-failing human hearts were obtained from donors without a history of heart failure, while failing hearts were collected from patients with end-stage heart failure after informed consent was obtained. Immediately after removal, the hearts were flushed with an ice-cold cardioplegic solution and transported to the lab. Cardiac trabeculae from the left ventricle were carefully dissected and stored in a modified Krebs-Henseleit buffer. The trabeculae were then electronically stimulated at a frequency of 0.5 Hz and allowed to stabilize. Contractile properties were assessed by raising the stimulus frequency to a baseline of 1 Hz, corresponding to the average resting human heartbeat. Measurements included active developed force, diastolic force, time to peak tension, time to 50% and 90% relaxation, and total twitch duration. Statistical

analysis was performed using ANOVA, with significant data defined as a p-value of 0.05. The study included samples from patients aged 20-70, excluding those with cardiac or pulmonary abnormalities and damaged samples. Ethical approval was obtained from the hospital's review board, and patient consent was secured. Data were analyzed to compare contractile and relaxation dynamics across the three groups, aiming to elucidate the physiological alterations in failing hearts and provide a foundation for developing targeted therapies to improve cardiac performance in heart failure patients.

3. Results

Table 1 presents the baseline force and contraction/relaxation dynamics of isolated left ventricular (LV) trabeculae from human hearts with different conditions: non-failing (NF), failing ischemic (FI), and failing non-ischemic (FNI). Table 1 also provides various parameters measured in each group, including Fdev (force development), TTP (time to peak tension), Fdia (diastolic force), TT90 (total twitch duration), RT50 (time from peak tension to 50% relaxation), RT90 (time from peak tension to 90% relaxation), -dF/dt (the highest rate at which force is generated during relaxation), dF/dt (the highest rate at which force is generated during contraction), -dF/dt/Fdev (maximal rate of kinetic relaxation), and dF/dt/Fdev (maximal rate of kinetic contraction).

The results show that compared to NF trabeculae, failing trabeculae (both FI and FNI) generally has lower values for most parameters, indicating impaired contractile function. Specifically, failing trabeculae have lower Fdev, -dF/dt, dF/dt/Fdev, and higher Fdia, TT90, RT50, and RT90 values compared to NF trabeculae, suggesting decreased contractile strength and prolonged relaxation times. However, some of these differences are statistically significant only in certain groups (e.g., FI or FNI) compared to NF trabeculae, as indicated by asterisks (*) in the table.

These findings suggest that both ischemic and non-ischemic failing hearts exhibit impaired contractile and relaxation dynamics compared to non-failing hearts. The parameters measured in this study provide insights into the functional differences between these heart conditions, which may help in understanding the underlying mechanisms and potential therapeutic interventions.

Table 1 shows the baseline force of relaxation and contraction of isolated trabeculae. The hearts collected from patients were divided into two groups control NF and test group failing (n=35) and further two groups FI (n=10) and FNI (n=25). When compared to failed trabeculae, NF trabeculae showed a much greater Active Developed Force , while failing trabeculae displayed a significantly longer Time taken from peak tension to 90% relaxation and Total Twitch Duration as well as a significantly slower dF/dt, -dF/dt, and -dF/dt/Active Developed Force . In etiology-based stratification, FNI trabeculae showed considerably longer Time taken from peak tension to 90% relaxation and significantly slower dF/dt, -dF/dt, and -dF/dt/Active Developed Force compared to NF trabeculae, but no significant changes in Active Developed Force, Diastolic Force, Time to Peak Tension, Time taken from peak tension to 50% relaxation, Total Twitch Duration, or dF/dt/Active Developed Force. It was determined that there were no significant variations between HF groups in the baseline force and kinetic parameters.

Table 1: Baseline force and contraction/relaxation dynamics of isolated LV trabeculae from human hearts with NF, FI, and FNI.

Parameter	NF (n=30)	Failing (n=35)	FI (n=10/35)	FNI (n=25/35)
Active Developed Force, mN/mm2	17.1 ± 1.9	12.9 ± 1.6*	13.2 ± 2.9	12.4 ± 1.7
Time to Peak Tension, ms	205 ± 7	202 ± 6	204 ± 11	202 ± 6
Diastolic Force , mN/mm2	7.5 ± 0.5	7.6 ± 0.6	6.5 ± 0.9	8.2 ± 0.9
Total Twitch Duration, ms	475 ± 13	508 ±12*	489 ± 19	516 ± 16
Time taken from peak tension to 50% relaxation, ms	139 ± 5	149 ± 5	141 ± 7	156 ± 6
Time taken from peak tension to 90% relaxation, ms	271 ± 11	306 ± 9*	289 ± 16	315 ± 11*
-dF/dt, mN/mm2/s	-94.9 ± 10.1	-60.9 ± 7.1 *	-73.1 ± 17.2	-55.3 ± 5.6*
dF/dt, mN/mm2/s	125.2 ± 11/5	91.5 ± 7.9*	93.1 ± 16.5	90.4 ± 8.9*
-dF/dt/Active Developed Force , s-1	-5.9 ± 0.5	-5.4 ± 0.6*	-5.7 ± 0.6	-4.6 ± 0.6*
dF/dt/Active Developed Force, s-1	8.3 ± 0.6	8.2 ± 0.6	8.0 ± 0.7	8.2 ± 0.6

dF/dt/Active Developed Force, maximal rate of kinetic contraction; −dF/dt/Active Developed Force , maximal rate of kinetic relaxation; Time taken from peak tension to 90% relaxation, time from peak tension to 90% relaxation; Total Twitch Duration, total twitch duration; Diastolic Force , diastolic force; FNI, failing non-ischemic; FI, failing ischemic; LV, left ventricular; Time taken from peak tension to 50% relaxation, time from peak tension to 50% relaxation; NF, non-failing; Time to Peak Tension, time to peak tension; dF/dt, the highest rate at which force is generated during contraction; − dF/dt, the highest rate at which force is generated during relaxation;

Figure 3 shows the Gender distribution of 3 groups in this study; the Failing group (n=35) consists of FI (n=10) and FNI (n=25).

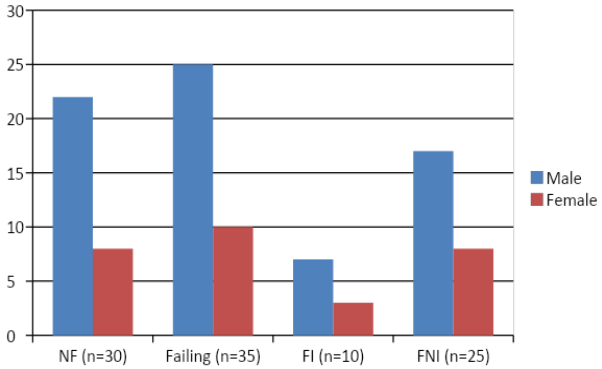

Figure 3: Gender distribution of 3 groups in this study; Failing group (n=35) consists of FI (n=10) and FNI (n=25).

Figure 4 presents data on active developed force and diastolic force in three different types of myocardium: normal functioning (NF), failing ischemic (FI), and failing non-ischemic (FNI) myocardium, at various time intervals ranging from 100 ms to 1100 ms.

Active Developed Force:

Active developed force refers to the force generated by the myocardium during contraction, and is an indicator of its contractile strength. Figure 4 also shows the values of active developed force in NF, FI, and FNI myocardium at different time intervals. In general, as the time from stimulation increases (from 100 ms to 1100 ms), the values of active developed force also tends to increase in all three types of myocardium. However, the rate and magnitude of force development vary among the three types of myocardium. At each time interval, it is observed that NF myocardium generates the highest active developed force, followed by FI myocardium, and then FNI myocardium. This suggests that normal functioning myocardium has the highest contractile strength, while failing ischemic and failing non-ischemic myocardium exhibit reduced force generation capabilities.

Diastolic Force:

Diastolic force refers to the force present in the myocardium during its relaxation phase, and is an indicator of its ability to relax and return to its baseline tension. Figure 4 also shows the values of diastolic force in NF, FI, and FNI myocardium at different time intervals. At each time interval, it is observed that NF myocardium has the highest diastolic force, followed by FNI myocardium, and then FI myocardium. This suggests that normal functioning myocardium has the highest ability to relax and return to baseline tension during diastole, while failing ischemic and failing non-ischemic myocardium exhibit impaired relaxation capabilities.

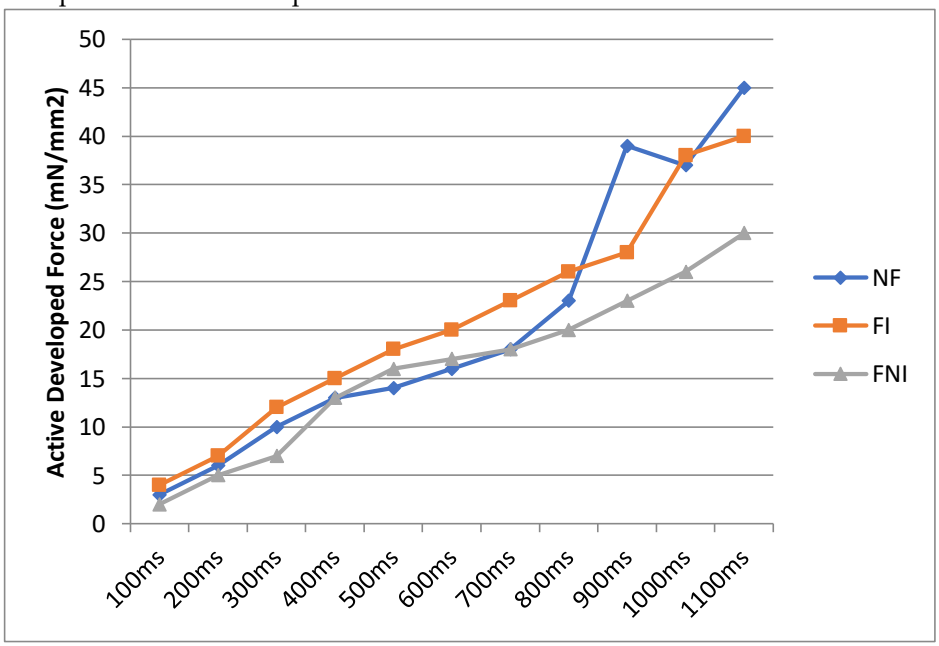

Figure 4: (a) Active Developed Force

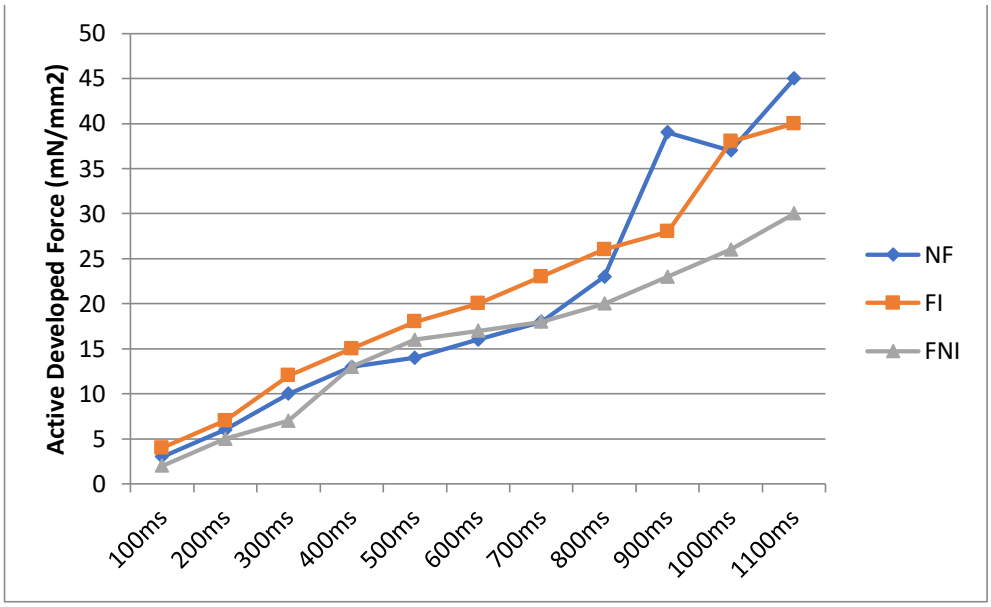

Figure 4: (b) Diastolic Force between the groups

Overall, Figure 4 suggests that there are differences in the contractile strength and relaxation dynamics among normal functioning, failing ischemic, and failing non-ischemic myocardium, with normal functioning myocardium generally exhibiting higher active developed force and diastolic force compared to failing myocardium. These findings may indicate alterations in myocardial function and contractility associated with myocardial dysfunction, such as ischemia or heart failure.

Figure 5 describes and interprets the kinetics of myocardium, specifically the time to peak tension; time is taken from peak tension to 50% relaxation, and total twitch duration, in non-failing (NF) and failing hearts.

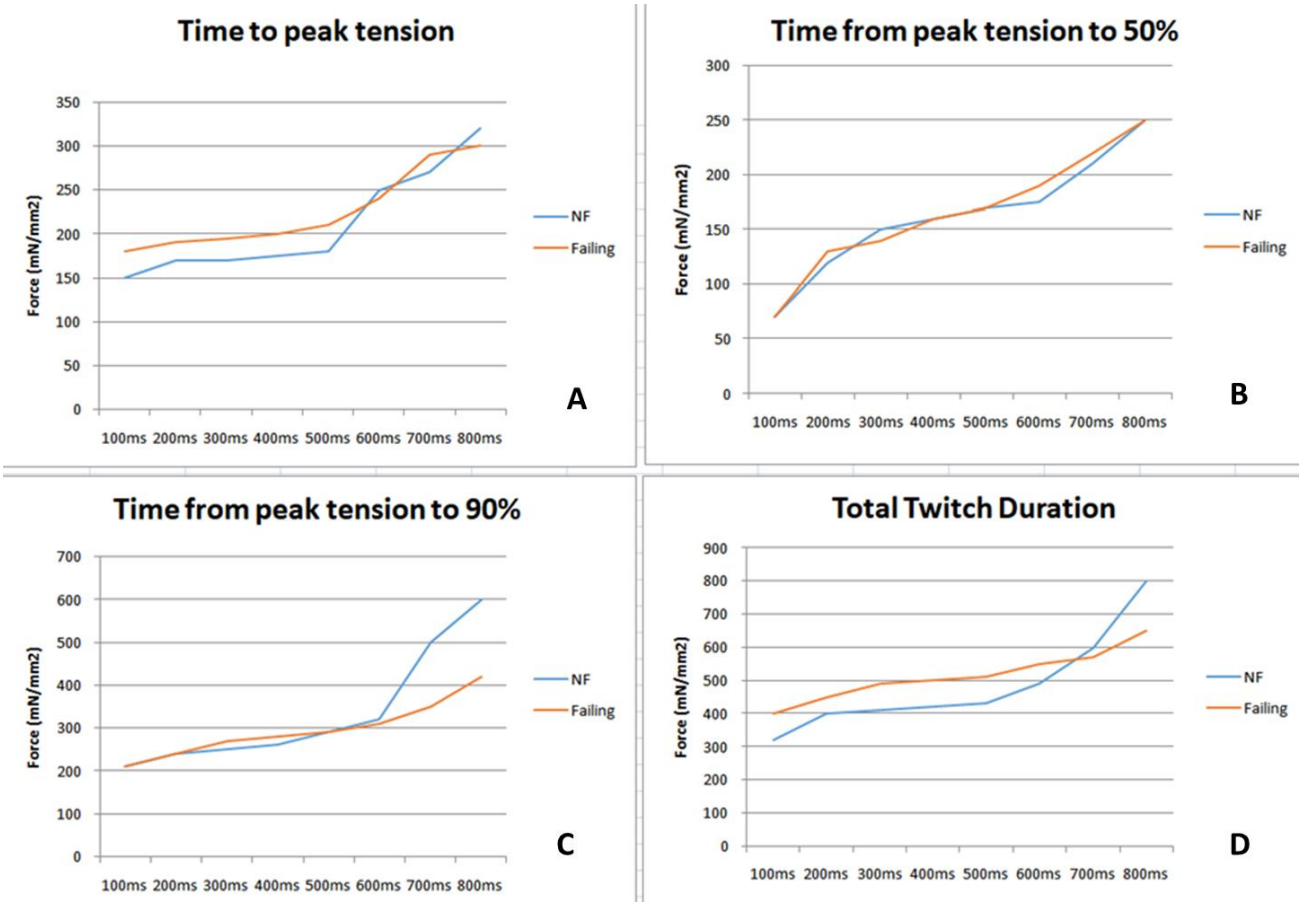

Figure 5: Kinetic characteristics of failing and non-failing myocardium

Time to Peak Tension:

Figure 5 also shows the time taken in milliseconds for myocardium to reach peak tension in non-failing (NF) and failing hearts. In general, as the time from stimulation to peak tension increases (from 100 ms to 800 ms), the values for NF and failing hearts also increase. However, it is observed that failing hearts take longer to reach peak tension compared to NF hearts at each time interval. For example, at 100 ms, NF hearts take 150 ms to reach peak tension while failing hearts take 180 ms. This trend continues throughout the time intervals, with failing hearts consistently taking longer to reach peak tension compared to NF hearts.

Time taken from peak tension to 50% relaxation:

Figure 5 also presents the time taken in milliseconds for myocardium to relax to 50% of its peak tension after reaching peak tension. Similar to time to peak tension, failing hearts generally take longer to relax to 50% of peak tension compared to NF hearts. However, the difference in relaxation time between NF and failing hearts is less pronounced compared to time to peak tension.

Total Twitch Duration:

The total twitch duration refers to the time taken for myocardium to contract and relax completely, from the time of stimulation to the return to baseline tension. Figure 5 also shows that the total twitch duration generally increases with longer time intervals from stimulation (from 100ms to 800ms) in both NF and failing hearts. However, it is notable that failing hearts exhibit longer total twitch duration compared to NF hearts at each time interval, indicating slower contraction and relaxation dynamics in failing hearts.

Overall, the figure below suggests that failing hearts exhibit slower kinetics of myocardium compared to non-failing hearts, as evidenced by longer time to peak tension, longer time taken from peak tension to 50% relaxation, and longer total twitch duration. These findings may indicate impaired contractile function in failing hearts, which could be associated with underlying cardiac dysfunction or disease conditions.

Discussion

4. Heart failure is one of the major causes of mortality rate among the majority of individuals in the UK. Pharmacotherapies associated with heart failure with reduced ejection fraction phenotype include beta-blockers, Na-glucose cotransporter inhibitors, and neprilysin inhibitors. Irrespective of significant advancement in therapies and prevention, HF remains involved with poor clinical outcomes. It is highly crucial to obtain detailed insight into contractile forces and kinetic changes that occur in cardiac muscles during end-stage HF. It serves to be beneficial in developing therapies that lead to improved cardiac performance. Besides contractile force, the speed of relaxation and contraction is crucial for determining cardiac performance. It is crucial to obtain detailed insight into kinetic changes and forces at the cardiac muscle level during end-stage HF while taking into consideration primary etiology which can lead to the development of effective targeted therapies that can improve cardiac performance. One of the significant causes of HF is reduced LV myocardial function; LV tissues are used for investigating myocardial dysfunction and are considered to be clinically significant. The assessment was conducted under baseline conditions while considering three physiological modifiers that lead to the alteration of myocardial contractions: length-dependent activation, frequency-dependent stimulation and response to ß-adrenergic stimulation by isoproterenol. Study results highlighted NF trabeculae showcased high Active Developed Force in comparison to failing trabeculae. Failing trabeculae showcased prolonged Total Twitch Duration as well as Time taken from peak tension to 90% relaxation and reduced -dF/dt/Active Developed Force , dF/dt, and -dF/dt in comparison to NF trabeculae without any significant difference in dF/dt/Active Developed Force, Diastolic Force, Total Twitch Duration, and Time taken from peak tension to 50% relaxation [8].
5. Results further highlighted frequency-relied activation shown in the case of NF trabeculae where enhancement in frequency of stimulation at Lopt resulted in enhancement in Active Developed Force. However, on the other hand, the Bowditch effect was impaired in the case of FI. FNI myocardium showcased a decrease in Active

Developed Force. Production of Active Developed Force by NF trabeculae was higher at every frequency than at the 0.5Hz baseline. FI trabeculae on the other hand showed a reduction in Active Developed Force values at every frequency in comparison to the preceding reduced frequency. In the FNI group, Active Developed Force values remained almost unchanged between 05Hz to 1.5Hz. Significant differences were not observed in Diastolic Force within or between each group at varied frequencies except at 3Hz where Diastolic Force values were higher in comparison to FNI and NF groups. Furthermore, NF trabeculae have been recorded to have short Time taken from peak tension to 50% relaxation in comparison to Time taken from peak tension to 50% relaxation of FNI trabeculae at 0.5Hz to 2Hz.

6. Length-dependent activation was observed in trabeculae that were isolated from failing heart and NF where an increase in muscle length led to enhancement of Active Developed Force generation. Stretching of cardiac muscles resulted in enhancement in Active Developed Force in comparison to L95, L85, and L90 among all groups. In the case of all groups, Diastolic Force increased following enhancement in the length of muscles. An increase in muscle length Time taken from peak tension to 50% relaxation, and Time to Peak Tension slowed down and thus resulted in the observation of Total Twitch Duration [7]. FNI trabeculae along with NF showed longer Total Twitch Duration, Time to Peak Tension, and Time taken from peak tension to 50% relaxation at L100 in comparison to the preceded length of muscle except for Time taken from peak tension to 50% relaxation. No significant differences were observed. FI trabeculae showcased rapid dF/dt, and dF/dt at muscle length in comparison to FNI trabeculae. However, differences failed to reach statistical significance at L100.
7. Studies have observed that "Active Developed Force (ADF) increases in all groups after enhancing isoproterenol. When normalizing ADF values to the baseline of muscles, NF trabeculae demonstrated higher ADF compared to HF trabeculae at concentrations of 30nM to 1 μM of isoproterenol. Previous studies have utilized isolated myocardium in both exvivo and in vitro settings to investigate kinetic reserve and its regulations. The studies have further revealed a high degree of variation, whereas several other studies have reported statistically high development of force in NF in comparison to failing myocardium. The finding was consistent with the idea regarding failing myocardium that has been reported to be weak in case of contractile strength. Studies on the other hand indicate significant enhancement of tension development in failing myocardium.
8. The development of baseline contractile force in human myocardium has been studied to determine the impact of heart failure (HF) on the ability to generate force, and these studies have revealed a high degree of variation. Some studies have reported statistically significant differences in force development between normal and failing myocardium, with NF myocardium showing higher ADF compared to failing myocardium, consistent with the concept that failing myocardium is weaker in terms of contractile strength. However, other studies have reported significant enhancement of tension development in failing myocardium [9] [10]."

In one study, NF myocardium showed higher ADF compared to failing myocardium, but significant differences among groups were absent when stratified by etiology. Since cardiac output at rest is nearly identical in patients with end-stage heart failure and healthy subjects, and the amount of myocardium may vary slightly, it is expected that normalized forces are similar. However, there are several factors that can lead to high variation in contractile outcomes for failing myocardium, depending on the underlying etiology, which may reveal varied responses. Failing trabeculae upon stratification by etiology resulted in the development of force that is higher in the case of NF trabeculae into being significantly different between FI trabeculae, NF and FNI.[11] Previous studies were carried out on limited human muscles due to the irregular availability and scarceness of human tissues. Past studies mainly focused on using 2-to5 NF controls. Small sample sizes often lead to type I errors or identification of an effect as significant while no differences exist. Studies using large sample sizes further lead to much more

reliable quantitative outcomes [5]. Studies further highlighted the fact that the human heart has specific metabolic, functional, electrophysiological, and embryological origins and mechanisms associated with ventricular failure, which varies among two ventricles. However, it is not clear whether both ventricles showcase similar mechanical properties in the case of healthy hearts as well as in end-stage HF. Experimental conditions for instance mechanical loading conditions, temperature, and pacing plays significant role in discrepancies. It has been further highlighted that myocardial contractility largely relies upon temperature where developed force enhances temperature reduction in NF as well as in failing myocardium. A large number of past studies were performed by utilizing physiological temperature (37 degree Celsius), and several other studies were conducted at 30-degree temperatures. Different temperatures often affect contractile outcomes. Temperature-dependent changes in contractile performance often differ in diseased and healthy myocardium. Experimental conditions like baseline stimulation frequencies have been utilized in several past studies where myocardium was placed at different frequencies ranging from 0.25 Hz to 1 Hz. Sub-physiological pacing rate affected force development in NF myocardium.

Conclusion

The study has concluded that kinetics of relaxation and contraction of myocardium were found to be impaired in end stage failing samples under the baseline conditions. Failing myocardium also showed slower kinetic parameters than others under the increasing condition of stimulation frequency, stretching muscle length. All these changes show that the myocardium kinetics pattern is affected in failing heart or myocardial tissue in progression of failure. This study has contributed in understanding the physiological changes of myocardium in failing heart. Diagnosis of heart failure is clinical, but several examinations are available for evaluation. Timely management of heart failure is important to prevent complications such as volume overload and mortality caused by acute coronary syndrome, cerebrovascular accidents, and pulmonary embolism. Obtaining detailed insight into contractile forces, kinetic changes, and primary aetiology at the cardiac muscle level during end-stage HF can aid in developing targeted therapies that improve cardiac performance.

REFERENCES

Alhakak, A.S., Teerlink, J.R., Lindenfeld, J., Böhm, M., Rosano, G.M. and Biering-Sørensen, T., 2021. The significance of left ventricular ejection time in heart failure with reduced ejection fraction. European Journal of Heart Failure, 23(4), pp. 541-551.

Awinda, P.O., Bishaw, Y., Watanabe, M., Guglin, M.A., Campbell, K.S. and Tanner, B.C., 2020. Effects of mavacamten on Ca2+ sensitivity of contraction as sarcomere length varied in human myocardium. British Journal of Pharmacology, 177(24), pp. 5609-5621.

Chen, Y.J., Chien, C.S., Chiang, C.E., Chen, C.H. and Cheng, H.M., 2021. From genetic mutations to molecular basis of heart failure treatment: an overview of the mechanism and implication of the novel modulators for cardiac myosin. International Journal of Molecular Sciences, 22(12), p. 6617.

Dashwood, A., Cheesman, E., Wong, Y.W., Haqqani, H., Beard, N., Hay, K., Spratt, M., Chan, W. and Molenaar, P., 2021. Effects of omecamtiv mecarbil on failing human ventricular trabeculae and interaction with (−)-noradrenaline. Pharmacology research & perspectives, 9(3), p. e00760.

Heinzel, F.R., Hegemann, N., Hohendanner, F., Primessnig, U., Grune, J., Blaschke, F., de Boer, R.A., Pieske, B., Schiattarella, G.G. and Kuebler, W.M., 2020. Left ventricular dysfunction in heart failure with preserved ejection fraction—molecular mechanisms and impact on right ventricular function. Cardiovascular diagnosis and therapy, 10(5), p. 1541.

Longobardi, S., Sher, A. and Niederer, S.A., 2022. Quantitative mapping of force–pCa curves to whole-heart contraction and relaxation. The Journal of Physiology, 600(15), pp. 3497-3516.

Mashali, M.A., Saad, N.S., Canan, B.D., Elnakish, M.T., Milani-Nejad, N., Chung, J.H., Schultz, E.J., Kiduko, S.A., Huang, A.W., Hare, A.N. and Peczkowski, K.K., 2021. Impact of etiology on force and kinetics

of left ventricular end-stage failing human myocardium. Journal of molecular and cellular cardiology, 156, pp.7-19.

Naqvi, T.Z. and Chao, C.J., 2021. Adverse effects of right ventricular pacing on cardiac function: prevalence, prevention and treatment with physiologic pacing. Trends in cardiovascular medicine.

Saad, N.S., Mashali, M.A., Elnakish, M.T., Hare, A., Campbell, C.M., Kiduko, S.A., Peczkowski, K.K., Huang, A.W., Fazlollahi, F., Torres Matias, G.S. and Ahmed, A.A., 2022. Effect of hypothyroidism on contractile performance of isolated end-stage failing human myocardium. Plos one, 17(4), p.e0265731.

Saleh, S. K., Mohammed, S. L., & Al-Askery, A. (2022). A Review of Techniques Used to Suppress Tremor. Journal of Techniques, 4(4), 61-70.

Hameed, B. H., Al-Rayahi, I. A., & Muhsin, S. S. (2022). Evaluation of Preoperative CA15-3 Level and its Relationship with Clinico-Pathological Characteristics in Primary Breast Cancer Patients. Journal of Techniques, 4(2), 21-26.