Gerontology & Geriatric Medicine
Volume 7: 1–8

DOI: 10.1177/23337214211018933
journals.sagepub.com/home/ggm
SAGE

# Cardiovascular Health in Individuals with Exceptional Longevity Residing in Arkansas

**Brandi M. Mize[1], Brandon Duke[1], Amanda K. Pangle[1], Jeanne Y. Wei[1], and Gohar Azhar[1]**

**Abstract**

Cardiovascular disease is a common comorbidity associated with an aging population. However, there is a unique group of individuals whose age-defying qualities are still being investigated.

This retrospective chart review analyzed various cardiac and metabolic health parameters to characterize the prevalence of heart failure and metabolic derangements in individuals aged 90 years old or older in central Arkansas. Only 236 of the 291 patients in our study cohort had blood pressures recorded. Of these, 50% had systolic blood pressures ≥140 mmHg. Additionally, 77% had pulse pressures ≥50 mmHg. Of the 96 patients with BNP data, 44% had values ≥300 pg/mL. There was a slight positive correlation between aging and HDL cholesterol, while there was a negative correlation between aging and both total cholesterol and LDL cholesterol. A majority of our patients had both elevated systolic blood pressures and elevated pulse pressures. A majority also had high BNP values, indicative of some degree of heart failure. Additionally, atrial fibrillation was a common arrhythmia identified on EKG. However, these oldest of the old patients had fewer documented metabolic derangements. These findings lay important groundwork for further investigation into lifestyle and genetic components that allow them to live exceptionally long with such comorbidities.

**Keywords**

heart failure, oldest old, cardiovascular disease, heart disease risk factors, longevity

**Manuscript received:** January 22, 2021; **final revision received:** April 22, 2021; **accepted:** April 28, 2021.

## Introduction

A notable outcome of improved healthcare systems includes a significant impact on population longevity. The most robust generation in the United States, termed the Baby Boomers, is expected to have all members aged 65 years or older by 2030 (America Counts Staff, 2019). As the number of individuals 65 years old or older has rapidly grown over the decades—12.4% in 2000 to 16.0% in 2018, the comorbidities have trended similarly with nearly 75% of older adults being burdened with multiple medical comorbid conditions (America Counts Staff, 2019; U.S. Department of Health and Human Services, 2016).

Heart failure (HF) remains ubiquitous in the aging population and continues to be a significant cause of hospital admission and healthcare dollar spending with the total cost predicted to increase to $70 billion in 2030 up from $31 billion in 2012 (Ambrosy et al., 2014; Benjamin et al., 2019; Heidenreich et al., 2013; Jackson et al., 2018). There are two major clinical subtypes of HF: heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). HFpEF occurs with greater frequency at an older age due to a higher burden of cardiovascular risk factors such as hypertension, arrhythmias, atherosclerosis, and dyslipidemias in addition to decreased automaticity of intrinsic pacemakers with age (Dharmarajan & Rich, 2017; Samuel et al., 1999; Wei, 1992).

HF is the number one cause of death in both men and women in the United States (Heron, 2019), hence it is relevant to investigate its prevalence in nonagenarians and centenarians. Previous work from our group has explored associations among common comorbid conditions, cardio metabolic characteristics, and hematological profiles in the geriatric population in the southern

[1]UAMS, Little Rock, AR, USA

**Corresponding Author:**
Gohar Azhar, Reynolds Institute on Aging, University of Arkansas for Medical Sciences, 4301 West Markham, Little Rock, AR 72205, USA.
Email: azhargohar@uams.edu

United States (Azhar et al., 2015, 2017; Joshi et al., 2017). However, there has been little exploration into prevalence of heart failure associated with exceptional longevity in Arkansas. Assessment of the clinical cardiovascular profile is of particular interest in Arkansas, the state that ranked third in the nation in 2017 for heart disease related deaths (CDC Stats of States, 2018). We performed a retrospective study of the oldest of the old residing in central Arkansas to explore the spectrum of heart failure with common associated co-morbidities of hypertension, arrhythmias, and hyperlipidemia in those with exceptional aging.

## Methods

### *Study Population*

This was a retrospective, descriptive study based on data requisition from electronic medical records (EMR) of nonagenarians and centenarians using the Data warehouse. The inclusion criteria included age >90 years, both genders and all ethnicities seen at the University of Arkansas for Medical Sciences (UAMS). Exclusion criteria included age <90 years and charts that had key missing data such as vital signs. These included patients who had been seen by the optometrist and had no other physical exam or medical history. All duplicate records were removed, and a total of 291 unique patient records were identified who had received care between 2011 and 2016. The EMR for each patient was queried from their most recent visit for data that consisted of demographic, physiologic, metabolic, biochemical, and medication information. This study proposal was approved by the UAMS Institutional Review Board (Protocol #201959).

Anthropometric measurements and hemodynamic values were obtained from the last documented visit of the patient. Body mass index (BMI) was subdivided into the following groups: ≤25 (underweight), 25 to 29.9 (normal weight), 30 to 34.9 (overweight), and ≥35 (obese). Systolic blood pressures were divided into the following categories based on the current American Heart Association guidelines: <120 (normal), 120 to 129 (pre-hypertension/elevated), 130 to 139 (Stage I hypertension), and ≥140 (Stage II hypertension). Pulse pressure was calculated by finding the difference between systolic blood pressure and diastolic blood pressure measurements. Other cardiometabolic measurements of lipids and brain naturetic peptide (BNP) were obtained from the EMR. Data from EKG was available in $n = 108$ subjects and was queried for any dysrhythmias including, atrial fibrillation, premature atrial complexes, premature ventricular complexes, atrioventricular and sinonodal blocks, and bundle branch block. Presence of a pacemaker and any arrhythmias associated with pacing was recorded. Echocardiograms were only available in $n = 25$ and we focused on ejection fraction. The record of out-patient medication history was reviewed and medications noted. The data gathered were either associated with the last clinic visit or closest available to the last clinic visit.

**Table 1.** Study Population Demographics. The Majority of Patients were White/Caucasian Female Nonagenarians, and More Than Half of the Patients were Classified as Underweight. Systolic Blood Pressure was Categorized in Accordance with the American Heart Association Blood Pressure Guidelines. The Majority of the Study Population had Systolic Blood Pressures Consistent with Stage II Hypertension.

| Age (years) | *N* (%) |
|---|---|
| 90–99 | 214 (73.5) |
| 100–109 | 73 (25.1) |
| 110–119 | 4 (1.4) |
| Race | |
| White/Caucasian | 216 (74.2) |
| Black/African American | 67 (23.0) |
| Hispanic/Latino | 1 (0.3) |
| Unknown | 7 (2.4) |
| Gender | |
| Male | 49 (16.8) |
| Female | 242 (83.2) |
| BMI | |
| <25 | 75 (56.8) |
| 25–29.9 | 46 (34.8) |
| 30–34.9 | 9 (6.8) |
| >35 | 2 (1.5) |
| Cardiovascular profile | |
| Hypertension status | |
| Normal | 48 (20.3) |
| Pre-HTN | 34 (14.4) |
| Stage 1 HTN | 35 (14.8) |
| Stage 2 HTN | 119 (50.4) |
| Pulse pressure ranges | |
| <50 mmHg | 54 (22.8) |
| 50–70 mmHg | 84 (35.4) |
| >70 mmHg | 99 (41.8) |

Statistical tests: Categorical variables were presented as counts and percentages and data were reported as mean ±SD. The standard *t*-test was employed and scatterplots and Pearson's correlation coefficients were calculated using Graphpad Prism 9.1 to examine associations between different variables of interest. An alpha cut-off of 0.05 was used for significance.

## Results

For this study, the average age of the sample was 98 ± 3.0 years, with 83.2% females. Approximately 74.2% of the population was White/Caucasian and 23.0% of the population was Black/African American. Of the 291 patients, 132 patients had BMI data available. The average BMI for this study population was 24 ± 5.1 kg/m$^2$, with 56.8% underweight, and only 8.3% overweight or obese (Table 1).

Hypertension was categorized based on the latest American Heart Association guidelines. Of the 291 patients, 236 patients had systolic blood pressure data

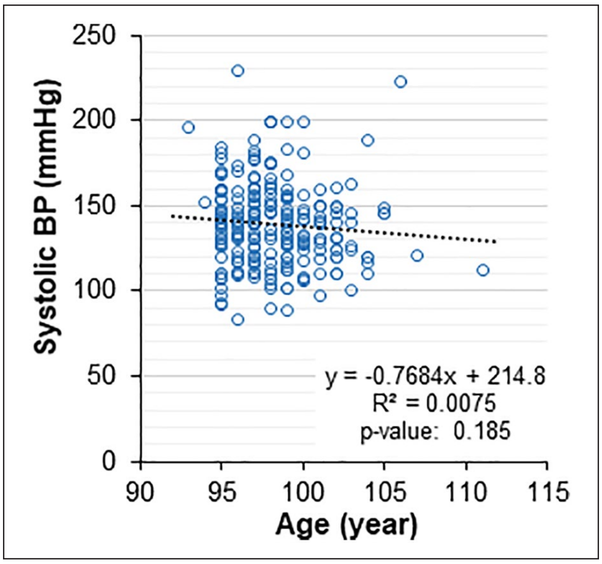


**Figure 1.** Scatterplot of systolic blood pressures (SBP) versus age; $N = 236$. SBP values ranged from 83 to 229 mmHg. Pearson's correlation showed no significant association between SBP and age.

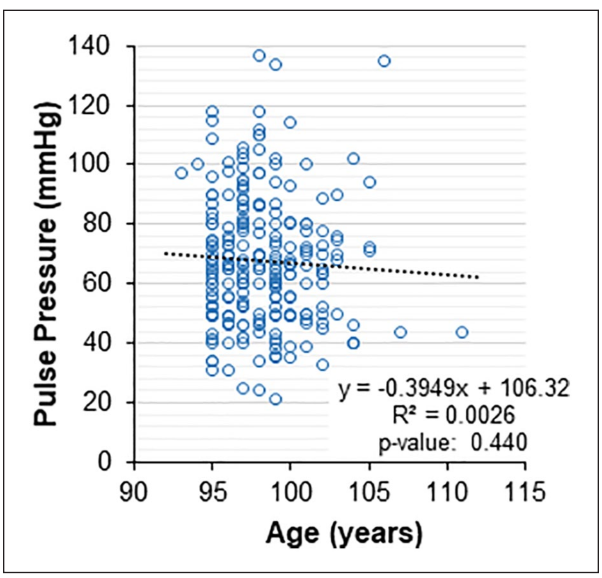


**Figure 2.** Scatterplot of pulse pressures (PP) versus age; $N = 237$. PP values ranged from 21 to 180. The majority of patients in the study had elevated pulse pressures with values greater than or equal to 50, signifying less arterial compliance. Pearson's correlation showed no significant association between PP and age.

available. Approximately 50.4% of patients had systolic blood pressures categorized as Stage II HTN, while 20.3% of patients had systolic blood pressures that were considered normal (Figure 1). 77.2% of patients had pulse pressures that were ≥50 mmHg with a mean of 68 ± 23.2 (Figure 2).

When evaluating cardiac function in this sample, we assessed ejection fractions, BNP levels, and ECG abnormalities. Only 25 patients had echocardiograms, out of which 16.0% had ejection fractions between 25% and 45%, which qualifies as heart failure with reduced ejection fraction (HFrEF), while 84.0% had ejection fractions greater than 50% which is categorized as heart failure with preserved ejection fraction (HFpEF) (Figure 3). BNP values were available in 96 patients (Figure 4). The average BNP level in this study

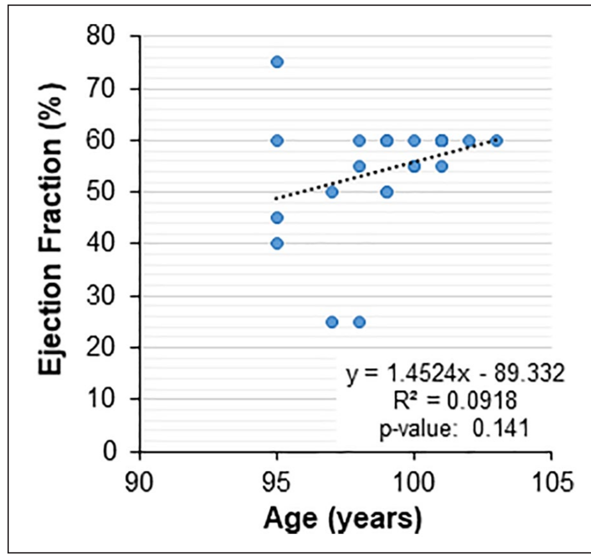


**Figure 3.** Scatterplot of ejection fraction versus age. Ejection fraction was available in only 25 patient charts for this study population. The majority of patients with this assessment in their chart had ejection fractions in the normal range between 50% and 60%. Pearson's correlation showed no significant association between ejection fraction and age.

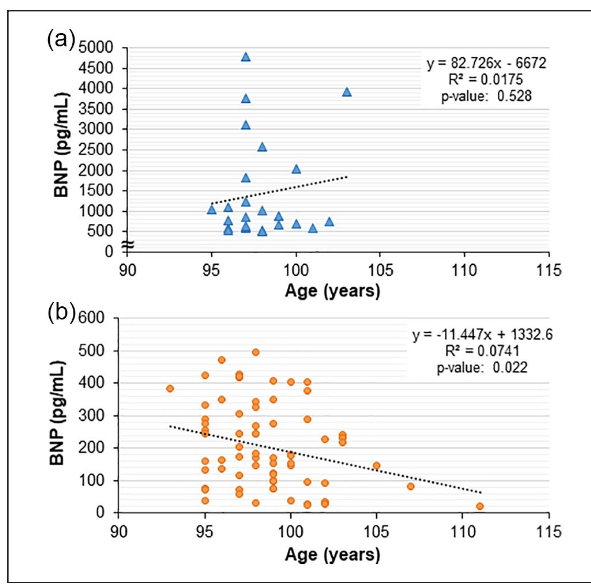


**Figure 4.** B-type natriuretic peptide values vs. age. BNP values ranged from 21 to 4800 pg/mL: (a) scatterplot of BNP values 500 pg/mL and above (moderate to severe HF) versus age; $N = 25$ and (b) scatterplot of BNP values below 500 pg/mL (normal to mild HF) versus age; $N = 71$. Pearson's correlation showed a significant negative association between BNP values under 500 pg/mL and aging, however, there was no association seen for BNP values 500 pg/mL and above.

**Table 2.** Common ECG Abnormalities ($N = 108$) Found in this Study Population, with the Majority of Abnormalities Being Arrhythmias, Especially Atrial Fibrillation.

| Cardiac pacing | *N* (%) |
|---|---|
| Atrial pacing | 2 (1.8) |
| Ventricular pacing | 5 (4.6) |
| AV pacemaker | 1 (0.9) |
| Nodal abnormalities | |
| AV blocks | 13 (12.0) |
| LBBB | 3 (2.8) |
| RBBB | 3 (2.8) |
| SA nodal dysfunction | 1 (0.9) |
| Arrhythmias | |
| Atrial fibrillation | 54 (50.0) |
| Sinus arrhythmias | 4 (3.7) |
| Sinus bradycardias | 7 (6.5) |
| Dysrhythmias | 1 (0.9) |

*Note.* PAC = premature atrial complexes; PVC = premature ventricular complexes; AV = Atrioventricular; LBBB = left bundle branch block; RBBB = right bundle branch block; SA = sinoatrial node.

**Table 3.** Common Diuretic Medication Regimens ($N = 291$) Used in the Oldest of the Old with Single Therapy with Loop Diuretics Being the Predominant Drug of Choice Despite Nearly 62% of Patients Not Being on a Diuretic Medication.

| Diuretic regimens | *N* (%) |
|---|---|
| Loop | 81 (27.8) |
| Loop; *K*-sparing | 1 (0.3) |
| Loop; thiazide | 2 (0.7) |
| *K*-sparing | 1 (0.3) |
| Thiazide | 26 (8.9) |
| None | 180 (61.9) |

*Note. K*-sparing = potassium sparing diuretics (i.e., spironolactone).

**Table 4.** Common CV Medicine Regimens ($N = 291$), with Single Therapy-BB Being the Predominant Drug of Choice. However, Nearly 47% of Patients in Our Population Were Not on Any CV Medication.

| CV medicine regimens | *N* (%) |
|---|---|
| ACEi | 27 (9.3) |
| ARB | 3 (1.0) |
| BB | 35 (12.0) |
| BB; Amiodarone | 1 (0.3) |
| BB; ACEi | 14 (4.8) |
| BB; ARB | 8 (2.7) |
| BB; dCCB | 6 (2.1) |
| BB; dCCB; ACEi | 7 (2.4) |
| BB; dCCB; ARB | 2 (0.7) |
| BB; dCCB; NG; ACEi | 1 (0.3) |
| BB; ndCCB | 3 (1.0) |
| BB; ndCCB; ARB | 1 (0.3) |
| BB; NG | 1 (0.3) |
| BB; NG; ACEi | 1 (0.3) |
| dCCB | 24 (8.2) |
| dCCB; ACEi | 4 (1.4) |
| dCCB; ARB | 2 (0.7) |
| Digoxin; ARB | 1 (0.3) |
| ndCCB | 9 (3.1) |
| ndCCB; ACEi | 2 (0.7) |
| ndCCB; ARB | 2 (0.7) |
| NG | 1 (0.3) |
| None | 136 (46.7) |

*Note.* ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BB = beta-blockers; CV = cardiovascular; dCCB = dihydropyridine calcium channel blocker; NG = nitroglycerin; ndCCB = non-dihydropyridine calcium channel blocker.

population was 523 ± 830.6 pg/mL. A BNP level ≥300 was found in 43.8% of this group of patients. For BNP levels under 500 pg/mL, there was a significant negative correlation between BNP level and age ($R^2 = 0.074$, $p < 0.022$), while BNP levels 500 pg/mL and higher did not show any correlation ($R^2 = 0.018$, $p > 0.528$). Over half of these patients were not on a diuretic medication, including one patient with a BNP of 4,800 pg/mL and an ejection fraction less than 45%. There were 108 patients that had ECG results available. Arrhythmias constituted 61.1% of ECG abnormalities with 50.0% of the arrhythmias being atrial fibrillation, 18.5% nodal and conduction abnormalities, while pacemakers were present in 7.5% (Table 2). 24% of the patients with EKG on file had normal sinus rhythm.

When considering common medication regimens for heart failure we found that diuretics and anti-hypertensives were the predominant medication categories. Amongst diuretics, 27.8% of patients were managed with a single loop diuretic, followed by 8.9% that were managed solely with thiazide diuretics. While there was a small percentage of our study sample on combination diuretic therapy, 61.8% of patients were not on any diuretic medications (Table 3). Amongst cardiac medications, 12.0% of patients were treated with only a beta-blocker (BB) while 9.3% were treated with only an angiotensin-converting enzyme inhibitor (ACEi) and 8.3% were treated with only a dihydropyridine calcium channel blocker (dCCB). Combination therapy with a BB and ACEi was used in 4.8% of patients. While various other medication combinations were also documented, 46.7% of patients in our sample were not on any cardiovascular medications (Table 4).

Review of lipid data revealed that total cholesterol and low-density lipoprotein (LDL) were negatively correlated with age, respectively ($R^2 = 0.040$, $p < 0.056$; $R^2 = 0.057$, $p < 0.023$). Conversely, high-density lipoprotein (HDL) showed a trend toward positive correlation with age ($R^2 = 0.035$, $p < 0.077$). Total triglycerides (TG) did not have any correlation with age ($R^2 = 0.0057$, $p > 0.48$; Figure 5).

## Discussion

This retrospective study is unique in providing data on cardiovascular parameters specifically in the nonagenarian

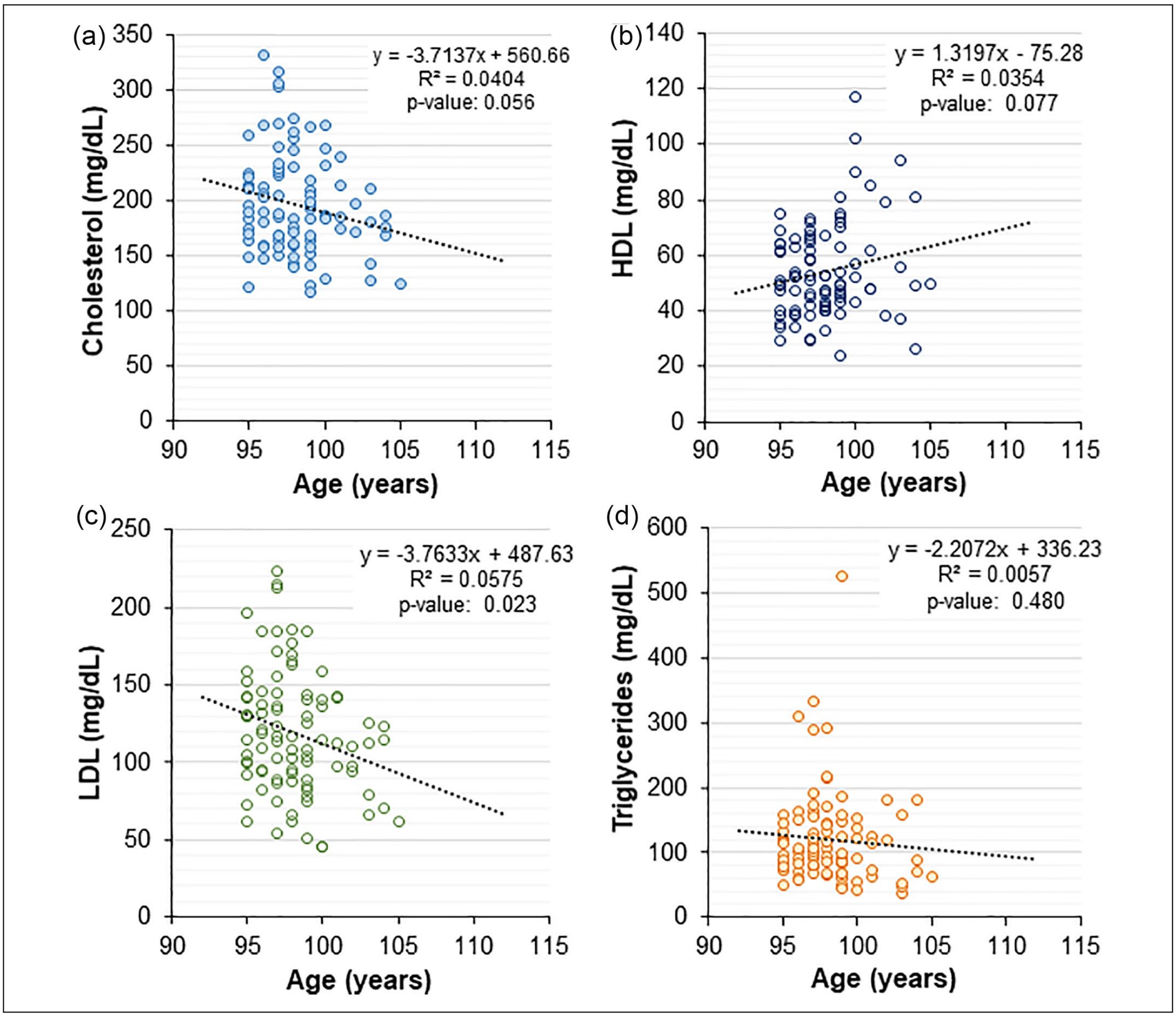


**Figure 5.** (a) Scatterplot of cholesterol levels versus. age; $N = 91$. Cholesterol levels ranged from 117 to 332 mg/dL. Pearson's correlation showed a slight negative association between cholesterol and age, (b) scatterplot of high-density lipoprotein (HDL) versus age; N = 89. HDL levels ranged from 24 to 117 mg/dL and showed a slight positive correlation with age, (c) scatterplot of low-density lipoprotein (LDL) versus age; $N = 90$. LDL levels ranged from 45 to 215 mg/dL. This plot demonstrates a significant negative correlation between LDL and age, and (d) Scatterplot of total triglyceride versus age; $N = 90$. Triglyceride levels ranged from 36 to 526 mg/dL. There appeared to be no correlation between total triglyceride and age.

and centenarian population from a south-central rural state. A number of notable findings in our study included documentation of: (1) elevated BNP values indicative of some degree of heart failure in the majority of patients; (2) a majority of patients were not on any diuretic medications; (3) presence of high systolic blood pressure and pulse pressure in a large percentage of patients; (4) high frequency of ECG abnormalities, with atrial fibrillation being the predominant arrhythmia.

## *Hemodynamic Profiles*

Our data demonstrates the well-known association between hypertension and aging, with approximately 65% of our study population having systolic blood pressures consistent with Stage I or II hypertension (HTN) (Figure 1). Pulse pressure can be considered a surrogate measure of aortic stiffness given that vasculature tends to lose compliance with age, resulting in an increase in systolic blood pressure and thereby increased pulse pressure with age (Buford, 2016; Sun, 2015). It is no surprise that elevated pulse pressure has also been associated with an increased risk of all cause morbidity (i.e., heart failure, acute myocardial infarction) and mortality (Kostis et al., 2001). Similar to previous findings, our sample population also had 77.2% of patients that had pulse pressures greater than or equal to 50, which is typically considered the lower threshold for cardiac event risk (Figure 2). Our data with high systolic blood pressures in nonagenarians and centenarians is at odds with the results of the highly cited Systolic Blood Pressure Intervention Trial (SPRINT) that showed that intensive control of systolic BP goal of less than 120 mm Hg versus less than 140 mm Hg reduced cardiovascular events and all-cause mortality among nondiabetic older adults with high cardiovascular risk (Supiano & Williamson, 2017). However, a more recent analysis of the SPRINT trial showed that older patients without cardiovascular or chronic kidney disease did not significantly benefit from intensive BP therapy. Hence, the risk of intensive BP therapy, including hypotension, dizziness, syncope, and falls outweighs the benefits of tight BP control (Rostomian et al., 2020). In heart failure patients there is a J shaped-curve for all-cause mortality, with both upper and lower ends of the blood pressure resulting in higher mortality (Schmid et al., 2017). In our study, more than 70% of the patients fell between normal to Stage II hypertension, which probably contributed to their reduced morbidity.

While cognitive function was not included in the database, it would have been of interest to know. This is because our group recently found that those who have elevated blood pressure in middle age tended to show a decrease in blood pressure in later years that preceded their cognitive decline (Wilson et al., 2020). Our data are supported by follow-up study of SPRINT-MIND, which associated a statistically significant greater decrease in hippocampal volume with intensive blood pressure control compared with standard treatment (Nasrallah et al., 2021).

## Cardiac Function

Cardiovascular disease, most notably heart failure, is commonly associated with aging and is a significant source of morbidity and mortality (Heron, 2019). B-type natriuretic peptide (BNP) has been used as a surrogate marker for heart failure severity and to aid in diagnosis of acute heart failure exacerbations. The Rugao Longevity and Aging Study from China and another study from Kyoto University Graduate School of Medicine in Japan has recently examined associations between frailty and BNP levels, finding that elevated BNP levels are associated with increased frailty measures including decreased gait speed (Nishiguchi et al., 2016; Yao et al., 2019). Frailty indices, which typically increase with age, have been shown to help predict mortality in elderly patients as well (Kojima et al., 2018). The patient population in our study consisted of nonagenarians and centenarians with an average age of 98 ± 3.0 years (Table 1). Our sample also had average BNP levels of 523 ± 830.6 pg/mL with 43.8% of patients in this study having BNP levels greater than or equal to 300 pg/mL, which is the lower threshold for clinical diagnosis of heart failure (Figure 4). Based upon both age and BNP, this shows that our sample consisted of individuals with increasing clinical concern for heart failure and frailty. Koca et al. (2020) found that severity of atrial fibrillation, based on symptoms, is associated with both frailty and elevated BNP in older adults. This is consistent with the findings in our study, with half of our patients having a diagnosis of atrial fibrillation (Table 2). However, despite having nearly half of our sample having elevated BNP levels and diagnoses of atrial fibrillation, approximately 61.8% and 46.7% of patients were not being prescribed diuretic or cardiovascular medications (Tables 3 and 4). Elevated BNP levels have been associated with non-cardiac conditions such as renal failure or cancer (Di Marca et al., 2018). Di Marca et al. have also shown that BNP has prognostic implication in non-heart failure conditions with values of >600 pg/ml predicting re-hospitalization (OR = 12.28) within 3 months and worse 30 day mortality (OR 2.7). For the purpose of this study, we did not evaluate all non-cardiac conditions but it is possible that they could have contributed to the high BNP values in some of the subjects.

## Lipid Profiles

Lipid metabolism and its effects on aging has been investigated for many years to evaluate trends in lipid profiles and genes that may be upregulated or downregulated to provide advantages for exceptional longevity. Much of this data has come from yeast, nematodes, fruit flies and mouse models, which have found varying associations between longevity and different lipid metabolic profiles (Johnson & Stolzing, 2019). Current research on lipid metabolism, biomarkers, and associations with aging in humans have produced differing results, especially with regards to sex. Some studies have showed a positive correlation with triglyceride levels increasing as people age, in addition to acting as a predictor of coronary artery disease in females and the elderly (Xia et al., 2017; LaRosa, 1997). Our descriptive data shows no substantial correlation between triglycerides and age in the oldest of the old (Figure 5d), which contradicts this general theme that triglycerides increase with aging. This may be attributed to the unique genetic composition of our sample, considering that this trend was not specifically noted in this cohort containing only nonagenarians and centenarians.

The Framingham study also provided insight into lipid metabolism, showing trends and effects of cholesterol during normal aging. They found that HDL cholesterol, which typically decreases with age, tends to be cardio-protective while LDL cholesterol, which usually increases with age, is detrimental (Abbott et al., 1983; Morgan et al., 2016). The data regarding lipids in the oldest old remains controversial. Some studies report that HDL cholesterol in adults decreases with age in both men and women (Wilson et al., 1994). Baggio et al. (1998) reported that the mean HDL levels of (both female and male) centenarians are 20% lower than those of 65-year-old subjects. On the other hand, some investigators have shown that HDL cholesterol actually increases with exceptional longevity (Barzilai et al., 2001; Rader et al., 1993). In addition, a few observational studies have shown that centenarians tend to have a predominance of the larger, more lipid–rich HDL2 subclass (Arai & Hirose, 2004). Although in our retrospective study, we could not define the HDL subtype, we showed a favorable lipid profile in our subjects with a tendency towards higher HDL and lower total cholesterol and LDL levels, similar to Barzilai et al. There is also a paradox with TG levels in the oldest old. A large prospective study of elderly individuals with a mean age of 94 showed that a higher concentration of TGs were associated with a lower risk of cognitive decline and function, less frailty and reduced mortality (Lv et al., 2019). TG are used as alternative sources of energy and it is possible that the lower level of TG in our study population is reflective of that, especially since a significant number of elderly were underweight. Lower LDL and total cholesterol in our data might also be indicative of poorer nutritional intake of patients with heart failure.

However, there needs to be more investigation into how genetics factor into lipid metabolism differences with aging, alongside factors like nutritional intake and other co-morbid conditions.

### *Study Limitations and Strengths*

Among the several limitations of this study, the prevailing limitation is the retrospective and descriptive nature of this study. As with retrospective studies, our data was limited by the incomplete or irregular recording of data points of interest in this study, resulting in varying sample sizes for each calculation performed. Additionally, the descriptive nature of the study simply provides information on the trend of health parameters in nonagenarians and centenarians in a rural state, both of which may limit the generalizability of the findings in the study. However, a strength of our study is that our data was pulled from patients in our geriatric clinic, which is one of the largest outpatient clinics in the country. Additionally, given that there is currently limited information regarding nonagenarians and centenarians, this study contributes to the continued study of those with exceptional longevity and further aids in discovering common trends that occur in this unique population.

## Conclusion

Amongst diseases associated with aging, HF continues to be costly in regard to healthcare spending and in overall patient morbidity and mortality. However, nonagenarians and centenarians are a unique population to study given their exceptional longevity and ability to withstand typically detrimental health comorbidities as they age, including HF. Here we investigated the profile of HF and associated co-morbidities seen amongst the oldest of the old in rural Arkansas, a state that commonly ranks towards the top in the nation for heart disease related deaths. In future studies we hope to identify factors that contribute to the exceptional longevity in rural elderly residing in the south-central part of the United States.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

### ORCID iDs

Amanda K. Pangle https://orcid.org/0000-0001-5974-618X
Gohar Azhar https://orcid.org/0000-0002-6810-5189

### References

Abbott, R. D., Garrison, R. J., Wilson, P. W., Epstein, F. H., Castelli, W. P., Feinleib, M., & LaRue, C. (1983). Joint distribution of lipoprotein cholesterol classes. The Framingham study. *Arteriosclerosis*, *3*(3), 260–272. https://doi.org/10.1161/01.atv.3.3.260

Ambrosy, A. P., Fonarow, G. C., Butler, J., Chioncel, O., Greene, S. J., Vaduganathan, M., Nodari, S., Lam, C. S. P., Sato, N., Shah, A. N., & Gheorghiade, M. (2014). The global health and economic burden of hospitalizations for heart failure: Lessons learned from hospitalized heart failure registries. *Journal of the American College of Cardiology*, *63*(12), 1123–1133.

America Counts Staff. (2019). By 2030, all baby boomers will be age 65 or older. Retrieved April 11, 2020, from https://www.census.gov/library/stories/2019/12/by-2030-all-baby-boomers-will-be-age-65-or-older.html

Arai, Y., & Hirose, N. (2004). Aging and HDL metabolism in elderly people more than 100 years old. *Journal of Atherosclerosis and Thrombosis*, *11*(5), 246–252.

Azhar, G., Abraham, R. R., Girotra, M., Wei, J. Y., & Foster, S. R. (2015). A study of metabolic health in very old individuals residing in Central Arkansas. *Journal of Aging Science*, *3*(136), 2.

Azhar, G., Pangle, A. K., & Wei, J. Y. (2017). Heart failure, metabolic risk factor and dementia in South-Central United States. *of*, *6*(1), 29–34.

Baggio, G., Donazzan, S., Monti, D., Mari, D., Martini, S., Gabelli, C., Dalla Vestra, M., Previato, L., Guido, M., Pigozzo, S., & Cortella, I. (1998). Lipoprotein (a) and lipoprotein profile in healthy centenarians: A reappraisal of vascular risk factors. *The FASEB Journal*, *12*(6), 433–437.

Barzilai, N., Gabriely, I., Gabriely, M., Iankowitz, N., & Sorkin, J. D. (2001). Offspring of centenarians have a favorable lipid profile. *Journal of the American Geriatrics Society*, *49*(1), 76–79.

Benjamin, E. J., Muntner, P., Alonso, A., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Chang, A. R., Cheng, S., Das, S. R., Delling, F. N., Djousse, L., Elkind, M. S. V., Ferguson, J. F., Fornage, M., Jordan, L. C., Khan, S. S., Kissela, B. M., Knutson, K. L., & Virani, S. S. (2019). Heart disease and stroke statistics-2019 update: A report from the American Heart Association. *Circulation*, *139*(10), e56–e528.

Buford, T. W. (2016) Hypertension and aging. *Ageing Research Reviews*, *26*, 96–111.

CDC Stats of States. (2018). Stats of the state of Arkansas. Retrieved April 17, 2020, from https://www.cdc.gov/nchs/pressroom/states/arkansas/arkansas.htm

Dharmarajan, K., & Rich, M. W. (2017). Epidemiology, pathophysiology, and prognosis of heart failure in older adults. *Heart Failure Clinics*, *13*(3), 417–426.

Di Marca, S., Rando, A., Cataudella, E., Pulvirenti, A., Alaimo, S., Terranova, V., Corriere, T., Pisano, M., Di Quattro, R., Ronsisvalle, M. L., & Giraffa, C. M. (2018). B-type natriuretic peptide may predict prognosis in older adults admitted with a diagnosis other than heart failure. *Nutrition, Metabolism and Cardiovascular Diseases*, *28*(6), 636–642.

Heidenreich, P. A., Albert, N. M., Allen, L. A., Bluemke, D. A., Butler, J., Fonarow, G. C., Ikonomidis, J. S., Khavjou, O., Konstam, M. A., Maddox, T. M., Nichol, G., Pham, M., Piña, I. L., & Trogdon, J. G. (2013). Forecasting the impact of heart failure in the United States a policy statement from the American Heart Association. *Circulation: Heart Failure*, *6*(3), 606–619.

Heron, M. (2019). Deaths: Leading causes for 2017. *National Vital Statistics Reports*, *68*(6), 1–77.

Jackson, S. L., Tong, X., King, R. J., Loustalot, F., Hong, Y., & Ritchey, M. D. (2018). National Burden of Heart Failure Events in the United States, 2006 to 2014. *Circulation Heart Failure*, *11*(12), e004873.

Johnson, A. A., & Stolzing, A. (2019). The role of lipid metabolism in aging, lifespan regulation, and age-related disease. *Aging Cell*, *18*(6), 1–26.

Joshi, K. P., Priyambada, P., Pangle, A., Wei, J. Y., & Azhar, G. (2017) Favorable hematological profile of the oldest old residents from South Central United States. *International Journal of Gerontology & Geriatric Research*, *1*(1), 1–6.

Koca, M., Yavuz, B. B., Tuna Doğrul, R., Çalışkan, H., Şengül Ayçiçek, G., Özsürekçi, C., Balcı, C., Eşme, M., Ünsal, P., Halil, M., & Cankurtaran, M. (2020) Impact of atrial fibrillation on frailty and functionality in older adults. *Irish Journal of Medical Science*, *189*(3), 917–924.

Kojima, G., Iliffe, S., & Walters, K. (2018). Frailty index as a predictor of mortality: A systematic review and meta-analysis. *Age and Ageing*, *47*(2), 193–200.

Kostis, J. B., Lawrence-Nelson, J., Ranjan, R., Wilson, A. C., Kostis, W. J., & Lacy, C. R. (2001). Association of increased pulse pressure with the development of heart failure in SHEP. *American Journal of Hypertension*, *14*(8), 798–803.

LaRosa, J. C. (1997). Triglycerides and coronary risk in women and the elderly. *Archives of Internal Medicine*, *157*(9), 961–968.

Lv, Y. B., Mao, C., Gao, X., Yin, Z. X., Kraus, V. B., Yuan, J. Q., Zhang, J., Luo, J. S., Zeng, Y., & Shi, X. M. (2019). Triglycerides paradox among the oldest old: “The lower the better?” *Journal of the American Geriatrics Society*, *67*(4), 741–748.

Morgan, A. E., Mooney, K. M., Wilkinson, S. J., Pickles, N. A., & Mc Auley, M. T. (2016). Cholesterol metabolism: A review of how ageing disrupts the biological mechanisms responsible for its regulation. *Ageing Research Reviews*, *27*, 108–124.

Nasrallah, I. M., Gaussoin, S. A., Pomponio, R., Dolui, S., Erus, G., Wright, C. B., Launer, L. J., Detre, J. A., Wolk, D. A., Davatzikos, C., & Williamson, J. D. (2021). Association of intensive vs standard blood pressure control with magnetic resonance imaging biomarkers of Alzheimer disease: Secondary analysis of the SPRINT MIND randomized trial. *JAMA Neurology*. Advance online publication. https://doi.org/10.1001/jamaneurol.2021.0178

Nishiguchi, S., Nozaki, Y., Yamaji, M., Oya, K., Hikita, Y., Aoyama, T., & Mabuchi, H. (2016) Plasma brain natriuretic peptide level in older outpatients with heart failure is associated with physical frailty, especially with the slowness domain. *Journal of Geriatric Cardiology*, *13*(7), 608–614.

Rader, D. J., Schaefer, J. R., Lohse, P., Ikewaki, K., Thomas, F., Harris, W. A., Zech, L. A., Dujovne, C. A., & Brewer, H. B., Jr. (1993). Increased production of apolipoprotein A-I associated with elevated plasma levels of high-density lipoproteins, apolipoprotein A-I, and lipoprotein A-I in a patient with familial hyperalphalipoproteinemia. *Metabolism - Clinical and Experimental*, *42*(11), 1429–1434.

Rostomian, A. H., Tang, M. C., Soverow, J., & Sanchez, D. R. (2020). Heterogeneity of treatment effect in SPRINT by age and baseline comorbidities: The greatest impact of intensive blood pressure treatment is observed among younger patients without CKD or CVD and in older patients with CKD or CVD. *The Journal of Clinical Hypertension*, *22*(9), 1723–1726.

Samuel, R. S., Hausdorff, J., & Wei, J. Y. (1999) Congestive heart failure with preserved systolic function: Is it a woman’s disease? *Women’s Health Issues*, *9*(4), 219–222.

Schmid, F. A., Schlager, O., Keller, P., Seifert, B., Huang, R., Fröhlich, G. M., Lüscher, T. F., Ruschitzka, F., & Enseleit, F. (2017). Prognostic value of long-term blood pressure changes in patients with chronic heart failure. *European Journal of Heart Failure*, *19*(7), 837–842.

Sun, Z. (2015). Aging, arterial stiffness, and hypertension. *Hypertension*, *65*(2), 252–256.

Supiano, M. A., & Williamson, J. D. (2017). Applying the systolic blood pressure intervention trial results to older adults. *Journal of the American Geriatrics Society*, *65*(1), 16–21.

U.S. Department of Health and Human Services. (2016). About the multiple chronic conditions initiative. Retrieved April 11, 2020, from https://www.hhs.gov/ash/about-ash/multiple-chronic-conditions/about-mcc/index.html

Wei, J. Y. (1992). Age and the cardiovascular system. *New England Journal of Medicine*, *327*(24), 1735–1739.

Wilson, C., Pangle, A., Wei, J. Y., & Azhar, G. (2020). A study of heart failure patients and their blood pressure trends preceding the dementia diagnosis. *Journal of Gerontology and Geriatric Research*, *9*, 183–189.

Wilson, P. W. F., Anderson, K.M., Harris, T., Kannel, W. B., & Castelli, W. P. (1994) Determinants of change in total cholesterol and HDLC with age: The Framingham study. *Journal of Gerontology*, *49*(6), M252–M257.

Xia, X., Chen, W., McDermott, J., & Han, J. D. J. (2017). Molecular and phenotypic biomarkers of aging. *F1000Research*, *6*, 860.

Yao, S., Guo, J., Shi, G., Zhu, Y., Wang, Y., Chu, X., Jiang, X., Jin, L., Wang, Z., & Wang, X. (2019). Association of BNP with frailty in elderly population: Rugao Longevity and Ageing Study. *The Journal of Nutrition, Health & Aging*, *23*(1), 73–78.