

# Characteristics of Associated Diseases in Older Patients with Cardiovascular Disease

Shrooq S. Alyami<sup>1</sup>, Abrar Algharbi<sup>1</sup>, Salem Alsuwaidan<sup>2\*</sup>

<sup>1</sup>Family Medicine Academy, Riyadh, Kingdom of Saudi Arabia

<sup>2</sup>Research and Innovation Center, Riyadh, Kingdom of Saudi Arabia

Email: \*sa.alsuwaidan@ksmc.med.sa

**How to cite this paper:** Alyami, S.S., Algharbi, A. and Alsuwaidan, S. (2022) Characteristics of Associated Diseases in Older Patients with Cardiovascular Disease. *Advances in Aging Research*, 11, 151-161. <https://doi.org/10.4236/aar.2022.116011>

**Received:** October 9, 2022

**Accepted:** November 21, 2022

**Published:** November 24, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## Abstract

**Background:** Cardiovascular disease (CVD) affects the heart and blood vessels. Older people are considerably more likely to suffer from a heart attack or stroke or to develop coronary heart disease (commonly called heart disease) and heart failure than younger people. Caring for older patients with cardiac conditions is markedly different from caring for younger patients with the same diagnosis. **Objective:** This study aimed to explore the characteristics and prevalence of CVD and its associated comorbidities in older patients. **Methods:** This study reviewed the medical files of all patients aged 65 years and older with CVD. Data such as sociodemographic characteristics and CVD findings were collected from 1614 patients with CVD. **Design and Setting:** Single-center retrospective cross-sectional study. **Subjects:** Almost two-thirds (1044, 64.7%) of the patients were male, and one-third (570, 35.3%) were female; all had various comorbidities. **Results:** Two main comorbidities associated with CVD were hypertension (HTN) (1092, 67.7%) and diabetes mellitus (DM) (927, 57.4%). The mean number of comorbidities associated with CVD was 2.61 ( $\pm 1.1$  SD), with a higher average in males than in females (2.74 [ $\pm 1.07$ ] vs. 2.54 [ $\pm 1.06$ ]). **Conclusion:** Up to six associated comorbidities were found in older patients with CVD, mostly with three comorbidities per patient. Males accounted for two-thirds of the overall study population. HTN and diabetes mellitus were the main CVD-associated comorbidities. Furthermore, almost 95.2 patients were reduced every 5 years of age progression.

## Keywords

Cardiovascular Disease, Elderly, Comorbidities, Associated Disease

## 1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality globally, and it

increases with age, with the annual mortality expected to reach 23.6 million by 2030 [1] [2]. CVD affects the heart and blood vessels. It includes coronary artery diseases, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, abnormal heart rhythms, congenital heart disease, valvular heart disease, carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, and venous thrombosis. CVD is also associated with arterial damage in organs such as the brain, heart, kidneys, and eyes [3]. CVD is mostly caused by atherosclerosis, and its most common risk factors include hypertension (HTN), unhealthy blood cholesterol levels, diabetes mellitus (DM), and obesity [4]. In people older than 75 years, the most common heart condition is HTN [5].

Three-quarters of CVD mortality worldwide occur in low- and middle-income countries. Compared with high-income countries, these countries often do not have integrated primary healthcare programs for the early detection and treatment of people with risk factors [6].

In this study, older people were defined as males or females aged 65 years or higher [7]. Changes in the cardiovascular system associated with aging include the elasticity reduction and stiffness increase of the arterial system. These changes result in increased afterload on the left ventricle, systolic blood pressure increase, and left ventricular hypertrophy, as well as other changes in the left ventricular wall that prolong relaxation of the left ventricle during diastole [8]. By 2030, 20% of the population is expected to be at 65 years or older; in this age group, CVD will account for 40% of all deaths and rank as the leading cause [9].

Older people aged 65 years and older are considerably more likely to suffer from a heart attack or stroke or to develop coronary heart disease (commonly called heart disease) and heart failure than younger people. Heart disease is also a major cause of disability, which limits activity and declines the quality of life of millions of older people [10]. Common concerns of older people are independence and the psychosocial and financial burdens of disease on themselves and their families [11].

In Australia, 26% of people aged 75 years and over have heart disease, stroke, and vascular disease [12]. In the Netherlands, atrial fibrillation mostly occurs in people at  $62 \pm 9$  years of age and males (70%). Of the 265 participants with incident atrial fibrillation, 60 (23%) received the diagnosis at a PREVENT visit, and the other 205 (77%) received the diagnosis during a hospital visit or admission [13]. The prevalence of heart failure in Italy rises with age (from 2% - 3% to 10% - 20% at 70 - 80 years of age) [14], similar to that in South Korea (40 - 59 years, 1.0%; 60 - 79 years, 5.5%;  $\geq 80$  years, 12.6%) [15]. In India, more than 50% of people over 70 years of age suffer from one or more chronic conditions. Chronic illnesses usually include HTN, coronary heart disease, and cancer. According to the Government of India statistics, CVD accounts for one-third of mortality in older people [16].

Caring for older patients with CVD is considerably different from caring for younger patients with the same diagnosis. The primary outcome is mortality

prevention. Other goals important to these older patients include the ability to ambulate, decreased hospitalizations, and decreased symptoms, implying prolongation of a symptom-free life.

Although this study is not the first to investigate older patients with CVD and its associated diseases, it focused more on how far the associated diseases are considered CVD risk factors or whether CVD can induce other comorbidities. This study also aimed to explore age progression as a risk factor together with the associated diseases. Considering the progression of age-related mortality, this study focused on the associated diseases.

## **2. Aim and Objectives**

This study mainly aimed to identify the CVD and comorbidities of older patients and to explore the association between age and the CVD to determine the prevalence of CVD in this age group.

## **3. Patients and Methods**

This retrospective cross-sectional study examined the records of older patients with CVD presenting with comorbidities admitted to King Saud Medical City in Riyadh between January 2017 and December 2019. From the institution's database, the data of all patients aged 65 years and older with CVD that may or may not be associated with other diseases were included. However, those who were below 65 years old or had any effect of COVID-19 were excluded.

In this study, older patients were defined as patients aged 65 years and higher. The data of older patients were reviewed to determine the prevalence of CVD.

A total of 1614 older patients had cardiovascular issues. The main measurable variable was the number and category of diseases associated with CVD in these patients. Other variables such as age and sex were also recorded. Only qualified and professional candidates were chosen for data entry and data verification to present quality and accurate data. The main comorbidities were HTN, DM, asthma, dyslipidemia, cardiac diseases, lung diseases, renal diseases, rheumatic diseases, cancer, neurological diseases, psychiatric (mental) diseases, and others (including gastric diseases).

### **3.1. Ethical Statement**

This study was approved by the KSMC-Institutional Review Board, IRB Registration Number with KACST, KSA: H-01-R-053 under a reference number: H1RI-02-Jul20-02.

### **3.2. Statistical Considerations**

The main variables, such as age, sex, and the associated diseases, were collected and saved in a Microsoft Excel sheet. The most important variable is the total number of associated diseases for every older patient with CVD. Descriptive statistics, frequency, and percentage of such diseases were determined.

## 4. Results

A total of 1614 patients with CVD and comorbidities were included, with an average age of 74.5 years (+7.7 SD). Almost two-thirds of the patients (1044, 64.7%) were male, and one-third were female (570, 35.3%) (**Table 1**). However, the percentage of associated diseases was higher in males than in females, except for mental diseases. The average number of comorbidities associated with CVD in all patients was 2.61 ( $\pm 1.1$ ), with a higher average in males than in females (2.74 [ $\pm 1.07$ ] vs. 2.54 [ $\pm 1.06$ ]).

The two main comorbidities associated with CVD were HTN (1092, 67.7%) and DM (927, 57.4%). Up to six comorbidities were found, but most of them were only found in these patients by approximately 10% or less. For instance, only 8 (0.5%) of the patients with CVD had rheumatic disease, as well as psychiatric problems. Other CVD-associated comorbidities with a very small percentage were renal diseases (10.3%), lung diseases (9.5%), and neurological diseases (7.4%) (**Figure 1**).

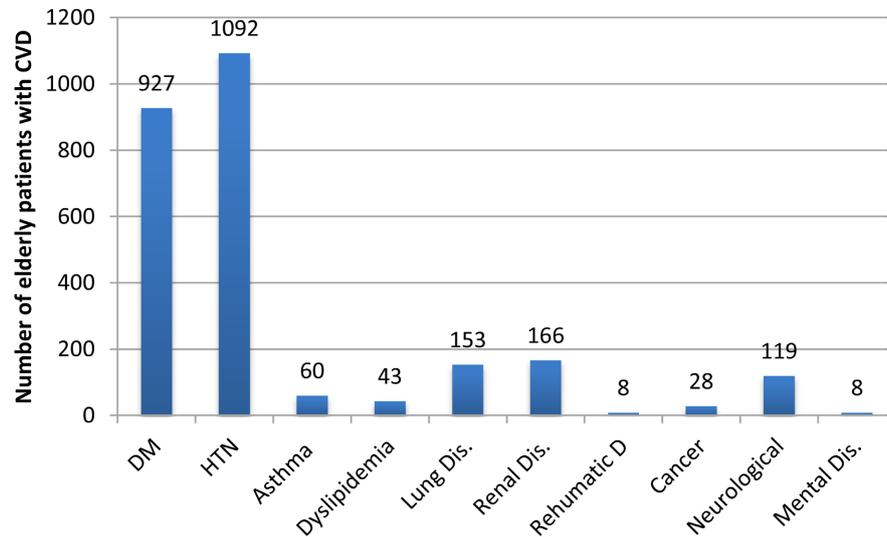
The profile for the average number of CVD-associated comorbidities started with 2.49 comorbidities at 65 years old and slightly increased to 2.75 from 75 to 85 years old. Then, the curve declined, reaching 2.48 comorbidities at 90 years old and above.

Therefore, the number of older patients with CVD declined as age progressed. Almost 95.2 patients were reduced every 5 years of age progression.

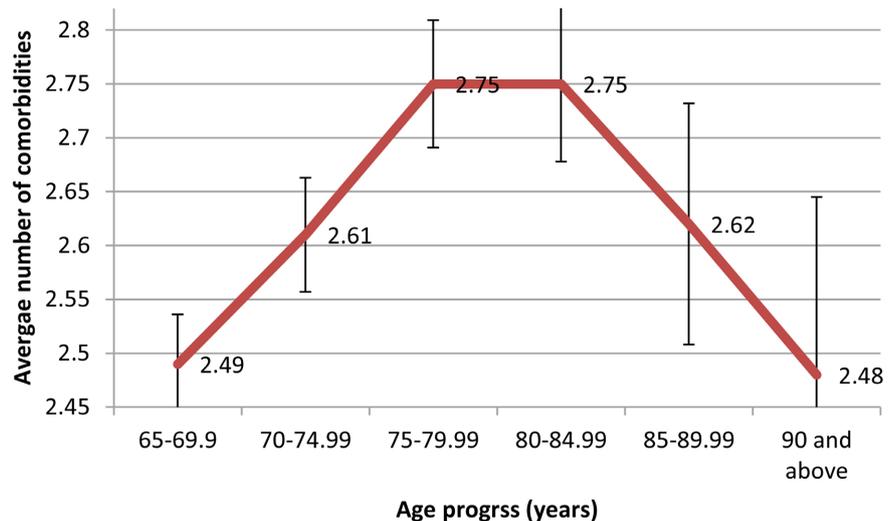
One-third (33.1%) of the patients with CVD are aged between 65 and 70 years. The average of comorbidities started with an average of 2.49 diseases during the age of 65 - 70 years and increased to reach an average of 2.75 associated diseases during age of 75 - 85 years, then became declining to reach an average of 2.48 diseases as the age progressed, as shown in **Figure 2**. Moreover, results showed

**Table 1.** Frequency and percentage of the associated diseases in all subjects with cardiovascular diseases and the differences in male and female.

FREQUENCY (%)	All	Male	Female
<b>Cardiovascular disease</b>	1614 (100%)	1044 (64.7%)	570 (35.3%)
<b>Diabetes mellitus</b>	927 (57.4%)	586 (63%)	341 (37%)
<b>Hypertension</b>	1092 (67.7%)	678 (62%)	414 (38%)
<b>Asthma</b>	60 (3.7%)	31 (52%)	29 (48%)
<b>Dyslipidemia</b>	43 (2.7%)	27 (63%)	16 (37%)
<b>Lung diseases</b>	153 (9.5%)	79 (52%)	74 (48%)
<b>Renal disease</b>	166 (10.3%)	108 (65%)	58 (35%)
<b>Rheumatic disease</b>	8 (0.5%)	4 (50%)	4 (50%)
<b>Cancer</b>	28 (1.7%)	17 (61%)	11 (39%)
<b>Neurological disease</b>	119 (7.4%)	77 (65%)	42 (35%)
<b>Mental disease</b>	8 (0.5%)	3 (38%)	5 (63%)



**Figure 1.** Number of older patients with cardiovascular disease and associated comorbidities.

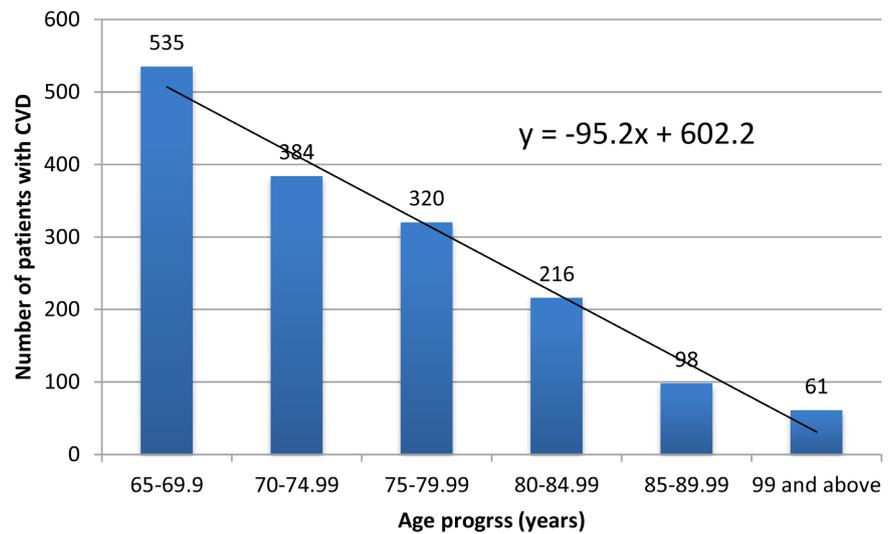


**Figure 2.** Average number of comorbidities along with age progression in older patients with cardiovascular disease.

a linear decline in the number of elderly patients with cardiovascular diseases. It showed that more than 600 patients were losing every five years as presented in **Figure 3**.

## 5. Discussion

This study showed that 1614 older patients (aged 65 years old and above) were diagnosed with CVD, with or without associated comorbidities. Males accounted for two-thirds of these patients (64.7%). HTN is the most highly prevalent CVD-associated comorbidity (67.7%), followed by DM (57.4%), thereby considered as the main comorbidities associated with CVD. Less frequent comorbidities only accounted for 10% or less; among them were renal disease (10.3%) and



**Figure 3.** Declining the number of older patients with cardiovascular disease along with age progress showing a slop with 602 patient's loss every five years.

lung disease (9.5%). The older population is expected to increase in number; thus, the physiological changes in their cardiovascular system need to be considered in addition to disabilities, the possible side effects, and pharmacodynamics and/or pharmacokinetic changes, which increase their risk of developing other comorbidities and even death [17].

HTN and DM are related to CVD, considering that HTN increases the cardiac workload, inducing structural and functional changes in the myocardium, and also considering that DM induced CVD as one of the main complications. In the last 5 years, around 50,000 articles found in PubMed reported the association between CVD and DM and almost 45,000 articles reported the association between CVD and HTN. Research studies regarding comorbidities in the older population have shown a significant impact for future investigations. HTN is proven to be the most extensively prevalent condition among older patients and might be greatly associated with other diseases [18].

This study found that the patients with CVD were associated with up to six comorbidities. However, other comorbidities showed a very small percentage. For example, only 8 (0.5%) of the 1614 patients with CVD had rheumatic disease, as well as psychiatric problems.

### 5.1. Association of HTN with CVD in Older Patients

The prevalence of HTN in older patients increases with age, affecting 65% of those over 60 years old and above [19]. HTN in older patients is a major risk factor for CVD mortality and morbidity. It could lead to stroke, left ventricular hypertrophy, congestive heart failure, coronary, and peripheral artery diseases, vision impairment, end-stage renal disease, cognitive impairment, and dementia [20].

Our study showed that CVD-associated HTN accounted for 67.7% of all older patients, with the prevalence in males almost doubled that in females (62% vs.

38%).

### 5.2. Association of DM with CVD in Older Patients

Older patients with DM, particularly type 2 DM, are highly likely to be at risk for CVD, HTN, abnormal cholesterol levels, hypertriglyceridemia, obesity, physical inactivity, and poorly controlled blood glucose levels [21]. The prevalence of DM also increases with age. DM associated with CVD occurring in older individuals strongly predicts cardiovascular and DM complications. Inflammation and oxidative stress appear to have a role in the mechanisms of DM and CVD-associated DM; however, the age-associated risk is still poorly understood [22].

In our study, CVD-associated DM accounted for 57.4% of all older patients, with a higher prevalence in males than in females (63% vs. 37%).

### 5.3. Association of Pulmonary Diseases and Asthma with CVD in Older

On average, 60% of patients with chronic obstructive pulmonary disease (COPD) and lung fibrosis are more likely to die after developing heart failure as compared with those without lung disease; thus, these conditions are considered significant risk factors for increased mortality [23]. Age is another risk factor. In our study, 9.5% of older patients with CVD have associated lung diseases, such as COPD and lung fibrosis. Meanwhile, asthma was less prevalent in these older patients with CVD (3.7%). Males and females had equal percentages for asthma and lung diseases. The involvement of lung diseases in CVD can be explained by the physiological interaction between the cardiovascular and respiratory systems. Normally, the respiratory system delivers oxygen throughout the body tissues, including the heart and blood vessels, and excretes carbon dioxide from the body [24].

### 5.4. Association Dyslipidemia with CVD in Older Patients

Dyslipidemia is a major risk factor for CVD and atherosclerosis. Although its prevalence appears higher in older patients (76%) [25], our study showed a relatively small percentage (2.7%). In addition, dyslipidemia was more prevalent in males than in females 27 (63% vs. 37%). In addition to changes in the physiological and nature (elasticity), the coexistence of both CVD and dyslipidemia could increase mortality as age progresses [26].

### 5.5. Association of Renal Diseases with CVD in Older Patients

The prevalence of renal diseases is also increasing in the older population, affecting approximately 10% of the general population. However, in this study, only 10.3% had renal diseases associated with CVD, with a higher prevalence in males than in females (65% vs. 35%). In older patients with CVD-associated renal diseases, the risk for cardiovascular events or even death is higher than the risk for progression to end-stage renal disease [27].

## 5.6. Association of Other Diseases (Cancer, Neurological, and Mental Diseases) with CVD in Older Patients

The coexistence of CVD and depression is quite frequent in older individuals, owing to biological and behavioral practices; however, the impact of psychosocial factors on depression in older patients with CVD remains unclear [28]. In our study, only eight patients (0.5%) with CVD suffered from mental disorders. Embolic stroke or chronic cerebral hypoperfusion may explain the increased risk for cognitive impairment and dementia in older patients with CVD [29].

Our study also had few cases of CVD-associated neurological diseases (7.4%). Diagnosing neurological disease in older patients could be very challenging because of the difficulty of obtaining their clinical features and history and to interpret the neurological signs and symptoms [30].

Meanwhile, a U-shaped relationship exists between the insulin-like growth factor-I level and mortality, with the increased mortality rate in older patients with CVD considered the most critical outcome [31]. In this study, the prevalence of cancer was very low (1.7%). Additionally, the cancer prevalence in males doubled that in females (61% vs. 39%).

Our results showed that the average number of comorbidities associated with CVD was 2.61 ( $\pm 1.1$ SD), with a higher average in males than in females. Up to six CVD-associated comorbidities were found, mostly with three comorbidities in 632 patients (39.2%), followed by two comorbidities in 330 patients and one comorbidity in 329 patients (20.4% each).

Interestingly, the frequency of older patients with CVD started to decline at the age of 65 - 70 years and then declined with 95 patients reduced every 5 years, reaching only 66 patients at 90 years and above. In addition, the average number of comorbidities associated with CVD started at the age of 65 years and then declined at the age of 90 years and above, with a slight increment starting from 75 to 85 years of age.

This study observed biological variations between males and females; these sex differences are caused by gene expression from the sex chromosomes. Raised awareness in improving behaviors, environment, lifestyle, and nutrition could have the ability to reach optimal treatment of CVD [32]. In this study, the prevalence of males doubled that of females, inconsistent with a previous study showing that females were more affected by CVD than males [33]. This previous study justified that the body weight may be increased as the visceral fat increases after the first year of menopause and that body fat distribution changes from a gynoid to an android pattern. However, estrogen offers females more protection from CVD even after menopause [34].

Identifying the risk of developing associated comorbidities in older patients with CVD is important to plan for preventive measures and to make guidelines on how to avoid such risks in the future [35].

## 6. Conclusion

Comorbidities in older patients have a significant impact on further investiga-

tions. The average number of comorbidities associated with CVD was 2.61, with up to six comorbidities found in each patient. Males accounted for two-thirds of older patients with CVD in this study. HTN and DM were the main CVD-associated comorbidities in this age group. Moreover, the number of older patients with CVD declined by almost 95.2 every 5 years of age progression.

### Acknowledgements

The authors acknowledged all respondents to our questionnaire for their input. Also, the authors would like to thank the research and innovation center for their assistance and contribution to this project.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

### References

- [1] Roth, G.A., Mensah, G.A., Johnson, C.O., *et al.* (2020) Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update from the GBD 2019 Study. *Journal of the American College of Cardiology*, **76**, 2982-3021. <https://doi.org/10.1016/j.jacc.2020.11.010>
- [2] World Health Organization (2017) Cardiovascular Disease. [http://www.who.int/cardiovascular\\_diseases/en/](http://www.who.int/cardiovascular_diseases/en/)
- [3] Kennedy, C. (2013) The Importance of Drug Discovery for Treatment of Cardiovascular Diseases. *Future Medicinal Chemistry*, **5**, 355-357. <https://doi.org/10.4155/fmc.13.20>
- [4] Centers for Disease Control and Prevention (2019) Chronic Kidney Disease in the United States, 2019. US Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta.
- [5] Gluckman, T.J., Wilson, M.A., Chiu, S.T., *et al.* (2020) Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction during the Coronavirus Disease 2019 Pandemic. *JAMA Cardiology*, **5**, 1419-1424. <https://doi.org/10.1001/jamacardio.2020.3629>
- [6] Shrivastava, S.R., Shrivastava, P.S. and Ramasamy, J. (2018) HEARTS Package for the Management of Cardiovascular Diseases. *Saudi Journal of Medicine & Medical Sciences*, **6**, 45-46. [https://doi.org/10.4103/sjmms.sjmms\\_128\\_17](https://doi.org/10.4103/sjmms.sjmms_128_17)
- [7] Alsuwaidan, A., Almedlej, N., Alsabti, S., *et al.* (2019) A Comprehensive Overview of Polypharmacy in Elderly Patients in Saudi Arabia. *Geriatrics*, **4**, Article No. 36. <https://doi.org/10.3390/geriatrics4020036>
- [8] Cheitlin, M.D. (2003) Cardiovascular Physiology—Changes with Aging. *The American Journal of Geriatric Cardiology*, **12**, 9-13. <https://doi.org/10.1111/j.1076-7460.2003.01751.x>
- [9] North, B.J. and Sinclair, D.A. (2012) The Intersection between Aging and Cardiovascular Disease. *Circulation Research*, **110**, 1097-1108. <https://doi.org/10.1161/CIRCRESAHA.111.246876>
- [10] Pfeilschifter, J. and Beck, K.F. (2011) Oxidative Stress Injury in Glomerular Mesangium. In: Miyata, T., Eckardt, K.U. and Nangaku, M., Eds., *Studies on Renal Disord-*

- ers, Humana Press, Totowa, 3-23. [https://doi.org/10.1007/978-1-60761-857-7\\_1](https://doi.org/10.1007/978-1-60761-857-7_1)
- [11] Jackson, C.F. and Wenger, N.K. (2011) Cardiovascular Disease in the Elderly Enfermedad Cardiovascular en el Anciano. *Revista Española de Cardiología (English Edition)*, **64**, 697-712. <https://doi.org/10.1016/j.rec.2011.05.003>
- [12] Coyle, D., Shahid, M., Dunford, E., et al. (2021) Estimating the Potential Impact of Australia's Reformulation Programme on Households' Sodium Purchases. *BMJ Nutrition, Prevention & Health*, **4**, 49-58. <https://doi.org/10.1136/bmjnph-2020-000173>
- [13] Vermond, R.A., Geelhoed, B., Verweij, N., et al. (2015) Incidence of Atrial Fibrillation and Relationship with Cardiovascular Events, Heart Failure, and Mortality: A Community-Based Study from the Netherlands. *Journal of the American College of Cardiology*, **66**, 1000-1007. <https://doi.org/10.1016/j.jacc.2015.06.1314>
- [14] Mureddu, G.F., Agabiti, N., Rizzello, V., et al. (2012) Prevalence of Preclinical and Clinical Heart Failure in the Elderly. A Population-Based Study in Central Italy. *European Journal of Heart Failure*, **14**, 718-729. <https://doi.org/10.1093/eurjhf/hfs052>
- [15] Lee, J.H., Lim, N.K., Cho, M.C. and Park, H.Y. (2016) Epidemiology of Heart Failure in Korea: Present and Future. *Korean Circulation Journal*, **46**, 658-664. <https://doi.org/10.4070/kcj.2016.46.5.658>
- [16] Ingle, G.K. and Nath, A. (2008) Geriatric Health in INDIA: Concerns and Solutions. *Indian Journal of Community Medicine*, **33**, 214-218. <https://doi.org/10.4103/0970-0218.43225>
- [17] Ribera-Casado, J.M. (1999) Ageing and the Cardiovascular System. *Zeitschrift für Gerontologie und Geriatrie*, **32**, 412-419. <https://doi.org/10.1007/s003910050138>
- [18] Alsuwaidan, S., Algharbi, A., Alyami, S., Almukhlifi, N. and Alsalamah, S. (2021) Prevalence of Comorbidity among Elderly. *Global Journal of Aging & Geriatric Research*, **1**, Article ID: 000518.
- [19] Wu, C.Y., Hu, H.Y., Chou, Y.J., Huang, N., Chou, Y.C. and Li, C.P. (2015) High Blood Pressure and All-Cause and Cardiovascular Disease Mortalities in Community-Dwelling Older Adults. *Medicine*, **94**, e2160. <https://doi.org/10.1097/MD.0000000000002160>
- [20] Rigaud, A.S. and Forette, B. (2001) Hypertension in Older Adults. *The Journals of Gerontology: Series A*, **56**, M217-M225. <https://doi.org/10.1093/gerona/56.4.M217>
- [21] Panfoli, I., Puddu, A., Bertola, N., Ravera, S. and Maggi, D. (2021) The Hormetic Effect of Metformin: "Less Is More"? *International Journal of Molecular Sciences*, **22**, Article No. 6297. <https://doi.org/10.3390/ijms22126297>
- [22] Halter, J.B., Musi, N., McFarland Horne, F.M., Crandall, J.P., Goldberg, A., Harkless, L., et al. (2014) Diabetes and Cardiovascular Disease in Older Adults: Current Status and Future Directions. *Diabetes*, **63**, 2578-2589. <https://doi.org/10.2337/db14-0020>
- [23] Wang, B., Zhou, Y., Xiao, L., Guo, Y., Ma, J., Zhou, M., et al. (2018) Association of Lung Function with Cardiovascular Risk: A Cohort Study. *Respiratory Research*, **19**, Article No. 214. <https://doi.org/10.1186/s12931-018-0920-y>
- [24] Shostak, E., Ameer, R., Gruden, J. and Jessurun, J. (2019) A Diagnostic Conundrum: Progressive Tubular Lung Mass in Asymptomatic Young Woman. *CHEST*, **155**, e131-e135. <https://doi.org/10.1016/j.chest.2019.02.318>
- [25] Rosada, A., Kassner, U., Weidemann, F., König, M., Buchmann, N., Steinhagen-Thiessen, E., et al. (2020) Hyperlipidemias in Elderly Patients: Results from the Berlin Aging Study II (BASEII), a Cross-Sectional Study. *Lipids in Health and Disease*, **19**, Article No. 92. <https://doi.org/10.1186/s12944-020-01277-9>

- [26] Félix-Redondo, F.J., Grau, M. and Fernández-Bergés, D. (2013) Cholesterol and Cardiovascular Disease in the Elderly. Facts and Gaps. *Aging and Disease*, **4**, 154-169.
- [27] Carracedo, J., Alique, M., Vida, C., *et al.* (2020) Mechanisms of Cardiovascular Disorders in Patients with Chronic Kidney Disease: A Process Related to Accelerated Senescence. *Frontiers in Cell and Developmental Biology*, **8**, Article 185.  
<https://doi.org/10.3389/fcell.2020.00185>
- [28] Xu, M., Chen, R., Liu, B., Chai, Y., Boer, D.D., Hu, P., *et al.* (2018) Psychosocial Determinants of Depression in the Community of the Elderly with Cardiovascular Disease. *Psychiatry Research*, **268**, 123-130.  
<https://doi.org/10.1016/j.psychres.2018.03.008>
- [29] Abete, P., Della-Morte, D., Gargiulo, G., Basile, C., Langellotto, A., Galizia, G., *et al.* (2014) Cognitive Impairment and Cardiovascular Diseases in the Elderly. A Heart-Brain Continuum Hypothesis. *Ageing Research Reviews*, **18**, 41-52.  
<https://doi.org/10.1016/j.arr.2014.07.003>
- [30] Stanton, B.R. (2011) The Neurology of Old Age. *Clinical Medicine Journal*, **11**, 54-56. <https://doi.org/10.7861/clinmedicine.11-1-54>
- [31] van Bunderen, C.C., van Nieuwpoort, I.C., van Schoor, N.M., Deeg, D.J., Lips, P. and Drent, M.L. (2010) The Association of Serum Insulin-Like Growth Factor-I with Mortality, Cardiovascular Disease, and Cancer in the Elderly: A Population-Based Study. *The Journal of Clinical Endocrinology & Metabolism*, **95**, 4616-4624.  
<https://doi.org/10.1210/jc.2010-0940>
- [32] Garcia, M., Mulvagh, S.L., Merz, C.N., Buring, J.E. and Manson, J.E. (2016) Cardiovascular Disease in Women: Clinical Perspectives. *Circulation Research*, **118**, 1273-1293. <https://doi.org/10.1161/CIRCRESAHA.116.307547>
- [33] Maas, A.H. and Appelman, Y.E. (2010) Gender Differences in Coronary Heart Disease. *Netherlands Heart Journal*, **18**, 598-602.  
<https://doi.org/10.1007/s12471-010-0841-y>
- [34] Robertson, R.M. (2001) Women and Cardiovascular Disease: The Risks of Misperception and the Need for Action. *Circulation*, **103**, 2318-2320.  
<https://doi.org/10.1161/01.CIR.103.19.2318>
- [35] Kannel, W.B. and D'Agostino, R.B. (1995) The Importance of Cardiovascular Risk Factors in the Elderly. *The American Journal of Geriatric Cardiology*, **4**, 10-23.