Original article

Multimorbidity and predictors of mortality among patients with cardiovascular disorders admitted to an intensive care unit: a retrospective study

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Abstract

Background: Prevalence of cardiovascular risk factors is reported to be increasing in Ethiopia. Multimorbidity of these risk factors is more likely to lead cardiovascular disease (CVD) with increased hospital admission, premature death, and poor quality of life and increase health care expenditure. There is little evidence regarding magnitude and outcome of CVD multimorbidity, particularly in the African setting. The aim of this study was to examine the magnitude of multimorbidity and predictors of mortality in patients with cardiovascular disease admitted to the Medical Intensive Care Unit of St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.

Methods: A five-year retrospective study was conducted from 01 November 2015 to 01 January 2016. A total of 362 patients with cardiovascular disease who were admitted to the Medical Intensive Care Unit participated in the study. The primary endpoint was death from any cause in the Medical Intensive Care Unit while the secondary was a cardiovascular composite. For baseline characteristics and survival analysis we classified patients according to their level of multimorbidity. We used Cox proportional hazards models to evaluate the prognostic effect of the level of risk factors or multimorbidity at admission while controlling for confounding variables.

Results: A total of 71 (19.6%) patients had a diagnosis of multimorbidity. The most common cases of cardiovascular admission were heart failure, 137 (37.8%), acute myocardial infarction, 83 (22.9%), hemorrhagic stroke, 95 (26.2%) and ischemic stroke, 24 (6.6%).There were 162 (45%) deaths. Myocardial infarction (COR 0.3; 0.18-0.53), hemorrhagic stroke (COR 3.3; 2.0-5.5) and age groups 55-64 years (COR 2.7; 1.2-6.1) and 65-74 years (COR 2.6; 1.1-6.1) were significantly associated with mortality.

Conclusions: There is a significant proportion of multimorbidity in our study population. Multimorbidity may be used as a criterion to prioritize and improve the management of patients. Measures to prevent cardiovascular disease in people who already have hypertension, diabetes or underlying causes of heart failure in primary care settings need to be emphasized. At higher levels of care, capacity building is key to addressing the management of patients who present with acute cardiovascular diseases. [*Ethiop. J. Health Dev.* 2018;32(4):215-221]

Keywords: Cardiovascular disease, multimorbidity, mortality, intensive care

Introduction

Multimorbidity – the simultaneous coexistence in individuals of more than one disease state – has become increasingly common in health care settings (1, 2). Patients who have multimorbidity are more likely to be admitted to hospital, experience premature death or the loss of physical functioning, and have a poor quality of life (3).

There is a scarcity of evidence in relation to appropriate interventions for patients with multimorbidity, as they are usually excluded from clinical trials (4). This limits the applicability of some research findings to patient groups that have multimorbidity (5, 6).

Established cardiovascular disease (CVD), hypertension and diabetes are common diagnoses. These conditions often coexist and have increased prevalence with age. In patients with established CVD, both hypertension and diabetes are associated with a significantly increased risk of cardiovascular mortality (7-11).

The significance of improving the care of patients with multimorbidity alongside CVD has been highlighted in earlier reports (10, 12).However, there is little evidence regarding the magnitude of multimorbidity, its prognosis, and predictors of mortality in patients with cardiovascular disease, particularly in the African setting.

Knowledge of the magnitude of multimorbidity, clarifying cumulative effects on the outcomes of patients and identifying predictors of mortality in patients with CVD may help to inform the development of organized approaches to risk factor management and improve processes and outcomes for patients admitted to hospital settings. It also has implications on proper health care utilization and health care costs.

The current study used a historical cohort of patients admitted to a medical intensive care unit (MICU) with a diagnosis of CVD. The study examined the magnitude of multimorbidity, whether a relationship

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exists between the level of multimorbidity and cardiovascular mortality, and predictors of mortality among patients with CVD.

Methods

Study design and setting: From 01 November 2015 to 01 January 2016, ahospital-based retrospective study was conducted on patients who were admitted to the Medical Intensive Care Unit (MICU) of Saint Paul's Hospital Millennium Medical College (SPHMMC) between 11 September 2009 and 10 September 2014. The hospital has 364 beds and provides outpatient and inpatient treatment services. The MICU is a six-bed general intensive care unit, staffed by full-time intensive care doctors (pulmonary and critical care specialists, interns and anesthesiologists) and nurses.

Study population: The study included all patients who were admitted to the MICU of SPHMMC with a diagnosis of CVD during the study period and whose case notes were available in the hospital registration archive. The study sample consisted of 362 patients with CVD who were admitted to the MICU and whose data were complete. The power of the study to detect statistical significance for the primary endpoint was 82.4%.

Patients were defined to have cardiovascular disorder if they were admitted to the MICU with a diagnosis of myocardial infarction, angina, heart failure, stroke, deep vein thrombosis, pulmonary thromboembolism, arrhythmia or pericarditis. The diagnosis of the cardiovascular disorders was based on what physicians registered on the medical record.

Data were collected from registry and patients' medical records. Data were included on outcome variables such as socio-demography, confirmed admission diagnoses, duration of hospital stay in hours, treatment and outcomes, including discharge with improvement or transfer to ward, referral to other hospitals and death. These variables were examined alongside primary diagnoses using data from a review of patient case notes and then sorted using a national health management information system (HMIS) disease classification (13). Patient case notes with incomplete information were excluded from the study.

Outcomes: The primary endpoint was death from any cause in the MICU. The secondary endpoint was a cardiovascular composite that included either myocardial infarction or stroke.

Statistical analysis: For analysis of baseline characteristics and survival rates, patients were classified according to their level of multimorbidity. Baseline characteristics were analyzed with the use of mean, standard deviation, interquartile range for continuous variables and a chi-square for categorical variables. We used Cox proportional hazards models to evaluate the prognostic effect of the level of risk factors or multimorbidity at admission while controlling for confounding variables. Adjusted hazard ratios, categorized according to the level of multimorbidity in instances of death from any cause and the cardiovascular composite endpoint, were determined while adjusting for all other significant confounding variables. All statistical test values were two-sided, and a P-value of less than 0.05 was considered to indicate statistical significance. Analysis was carried out using SPSS (version 20.0) statistical software.

Ethical clearance: Before starting data collection, a letter of support was obtained from the SPHMMC Ethical Review Committee. Written consent was obtained from the hospital administration, and confidentiality of information was ensured in the collection of data by using codes rather than the names of patients.

Results

Baseline characteristics: A total of 362 patients were admitted to the MICU with CVD from 11 September 2009 to 10 September 2014. About 53% were male. The mean age was 50 years (SD 18.4) and 281 (77.6%) were urban residents. The median length of stay in the MICU was 5.5 hours. Table 1 shows the baseline characteristics of the patients admitted to the MICU. Among the cardiovascular causes of admission, the most common were heart failure in 137 (37.8%), acute myocardial infarction in 83 (22.9%), hemorrhagic stroke in 95 (26.2%) and ischemic stroke in 24 (6.6%).

Table 1: **Baseline characteristics of CVD admissions, January 2016**

Variable	n (%), mean (standard deviation)
Sex	
Male	193 (53.3)
Female	169 (46.7)
Age (years)	
Mean	50.0 (18.4)
Location	
Urban	281 (77.6)
Rural	81 (22.4)
Median length of ICU stay in hours (interquartile range)	5.5 (4-12)
Cardiovascular causes of admission	
Heart failure	137 (37.8)
Stroke	119 (32.9)
Hemorrhagic stroke	95 (26.2)
Ischemic stroke	24 (6.6)
Acute myocardial infarction	83 (22.9)
Arrhythmia	19 (5.2)
DVT/PTE	17 (4.7)
Pericarditis	3 (0.8)
Co-morbidity	
Hypertension	71 (19.6)
Diabetes mellitus	27 (7.5)

Table 2 shows the characteristics of patients with CVD admitted to the MICU according to the level of cardiovascular multimorbidity. A total of 291 (80.4%) patients had CVD only; 44 (12.2%) had CVD and hypertension; 13 (3.6%) had CVD and diabetes; and 14 (3.9%) had CVD, hypertension and diabetes. Of the 95 patients aged 65 years or older, 23 (24.2%) were found to have multimorbidity. Stroke was highest in patients who had hypertension, while myocardial infarction and heart failure were found to be highest in diabetic patients.

Table 2: **Characteristics of patients with cardiovascular disease according to level of cardiovascular multimorbidity, January 2016**

Characteristic	CVD only (n = 291)	CVD and HTN (n= 44)	CVD and DM (n = 13)	CVD, HTN and DM (n = 14)
Mean age in years	48.8 (18.9)	52.5 (15.3)	58.1 (15.7)	61.5 (12.2)
Female, %	137 (47.1)	25 (56.8)	5 (38.5)	2 (14.3)
Specific CVD event				
Myocardial infarction, %	60 (20.6)	10 (22.7)	7 (53.8)	6 (42.9)
Stroke, %	86 (29.6)	27 (61.4)	–	6 (42.9)
Heart failure*, %	119 (40.9)	9 (20.5)	6 (46.2)	3 (21.4)
Thromboembolism: DVT, PTE, %	17 (5.8)	–	–	–
Arrhythmia, %	19 (6.5)	–	–	–
Pericarditis, %	3 (1.0)	–	–	–
Medication				
Aspirin, %	89 (30.6)	12 (27.3)	11 (84.6)	8 (57.1)
Beta blocker, %	62 (21.3)	6 (13.6)	3 (23.1)	3 (21.4)
Lipid lowering agent, %	32 (11.0)	4 (9.1)	2 (15.4)	4 (28.6)
ACE inhibitor, %	50 (17.2)	11 (25.0)	1 (7.7)	6 (42.9)

Total number of patients = 362; ACE = angiotensin-converting enzyme; HTN = hypertension; CVD = cardiovascular disease; DVT = deep vein thrombosis; PE = pulmonary embolism; DM = diabetes mellitus.
* Some patients had more than one diagnosis

Outcomes: A total of 162 (45%) patients died, 98 (27%) patients improved, and 91 patients (25%) were transferred to other centers. Heart failure as a cause for ICU mortality showed a decreasing trend as the age of patients increased, while the other causes of ICU mortality increased with increasing age (Figure 1). The risk of death from any cause (log-rank/Mantel-Cox 19.11, p= 0.002) was significantly increased in patients with stroke, myocardial infarction and heart failure (Figure 2). Of the cardiovascular admissions to the MICU and their risk factors, those that were significantly associated with mortality were stroke and myocardial infarction (Table 3).

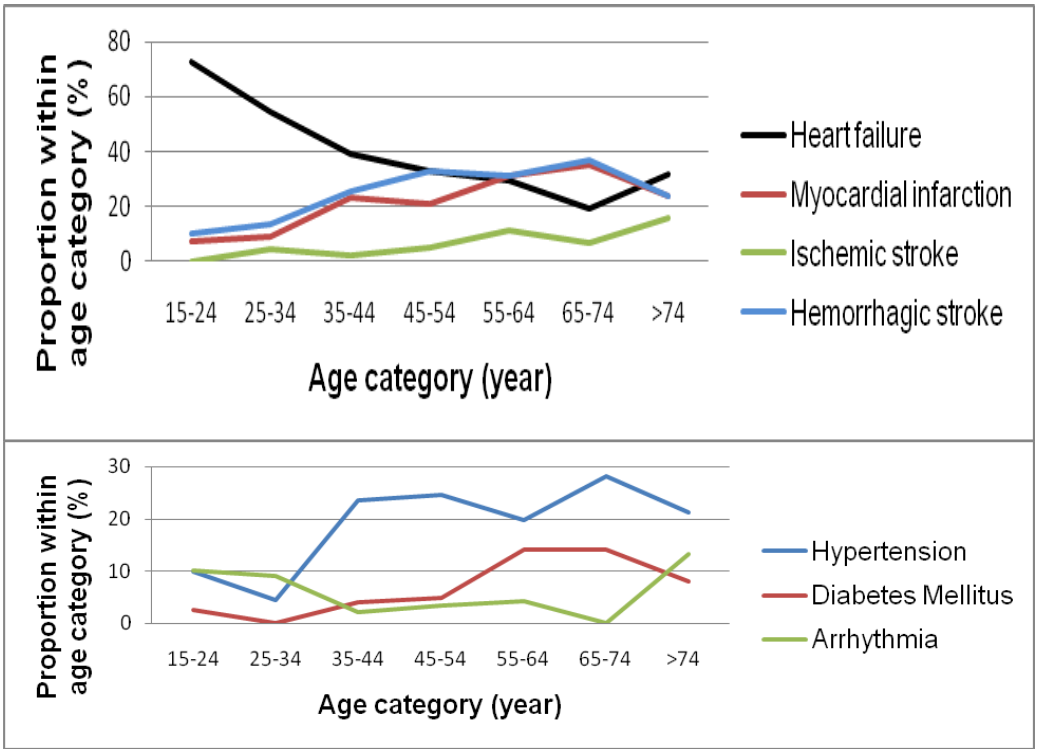

Figure 1: **Age distribution of causes of ICU death. SPHMMC, January 2016**

Table 3: **Frequency and association of confirmed diagnosis with ICU mortality, January 2016**

Diagnosis	n = 162 (%)	p (95% CI)
Stroke	76 (46.9)	< 0.0001 (2.04-5.10)
Heart failure	54 (33.3)	0.11 (0.46-1.09)
Hypertension	30 (18.5)	0.64 (0.52-1.5)
Myocardial infarction	20 (12.3)	< 0.0001 (0.18-0.53)
Diabetes mellitus	11 (6.8)	0.66 (0.38-1.86)
Arrhythmia	6 (3.7)	0.24 (0.2-1.5)

Bivariate analysis showed that factors that were significantly associated with mortality were age 55-64 years (COR 2.7; 95% CI: 1.2-6.1, p =0.02), age 65-74 years (COR 2.6; 1.1-6.1, p= 0.03), myocardial infarction (COR 0.3; 0.18-0.53, p< 0.0001), and hemorrhagic stroke (COR 3.3; 2.0-5.5, p < 0.0001) – see Table 4.

Table 4: **Bivariate analysis of age group, MI, ischemic stroke and hemorrhagic stroke with ICU mortality, January 2016**

Age (years)	n (%)	COR (95% CI), p
< 25	12 (7.4)	1.00
25-34	21 (13.0)	2.1 (0.9-5.2),0.1
35-44	18 (11.1)	1.3 (0.5-3.1), 0.6
45-54	28 (17.3)	2.0 (0.9-4.6),0.11
55-64	38 (23.5)	2.7 (1.2-6.1), 0.02
65-74	30 (18.5)	2.6 (1.1-6.1), 0.03
> 74	15 (9.3)	1.5 (0.6-3.9),0.38
Death from myocardial infarction		
No	63 (75.9)	1.00
Yes	20 (24.1)	0.3 (0.18-0.53), < 0.0001
Death from hemorrhagic stroke		
No	32 (33.7)	1.00
Yes	63 (66.3)	3.3 (2.0-5.5), < 0.0001
Death from ischemic stroke		
No	11 (45.8)	1.00
Yes	13 (54.2)	1.5 (0.7-3.4), 0.34
Death from myocardial infarction or stroke		
Female	44 (45.8)	1.00
Male	52 (54.2)	1.05 (0.66-1.67), 0.85

In the examination of the relationship between the secondary outcomes and the level of risk factors or multimorbidity while controlling for confounding variables, patients with no hypertension and no diabetes were used as the reference group (see Table 2). The confounding variables available for inclusion in the Cox proportional hazards model were age groups and sex. The adjusted hazard ratios (AHRs) for the secondary outcomes according to the level of risk factors or multimorbidity are given in Table 5. The estimated risk of the cardiovascular composite (secondary) endpoint, when compared with patients with no diabetes mellitus and no hypertension, was 1.61 (95% CI: 1.12-2.32) for patients with hypertension. This compares with 1.96 (95%CI: 0.91-4.21) for patients with diabetes; and 1.31(95%CI: 0.72-2.39) for patients with both diabetes and hypertension.

Table 5: **Adjusted hazard ratios for secondary endpoints among patients according to presence of risk factors or multimorbidity, January 2016***

Level of cardiovascular risk factor	Secondary endpoint: cardiovascular composite	
	p-value	AHR (95% CI)
No hypertension and no diabetes mellitus	–	1.00
Hypertension	0.01	1.61 (1.12-2.32)
Diabetes mellitus	0.09	1.96 (0.91-4.21)
Hypertension and diabetes mellitus	0.38	1.31 (0.72-2.39)

Total number of patients = 362
*Cox proportional hazards model used in the above analysis adjusted for the covariates age and sex

When modelling the cardiovascular composite endpoint, there was evidence of a significant interaction between diabetes and myocardial infarction (AHR 4.33; 95% CI: 1.96-9.58, p< 0.0001) and between hypertension and hemorrhagic stroke (AHR 2.27; 95% CI: 1.42-3.63, p = 0.001). There was also evidence of a significant interaction between heart failure and diabetes (AHR 3.31; 95% CI: 1.43-7.68, p = 0.005) and between heart failure and hypertension (AHR 0.50; 95% CI: 0.25-0.99, p = 0.046).

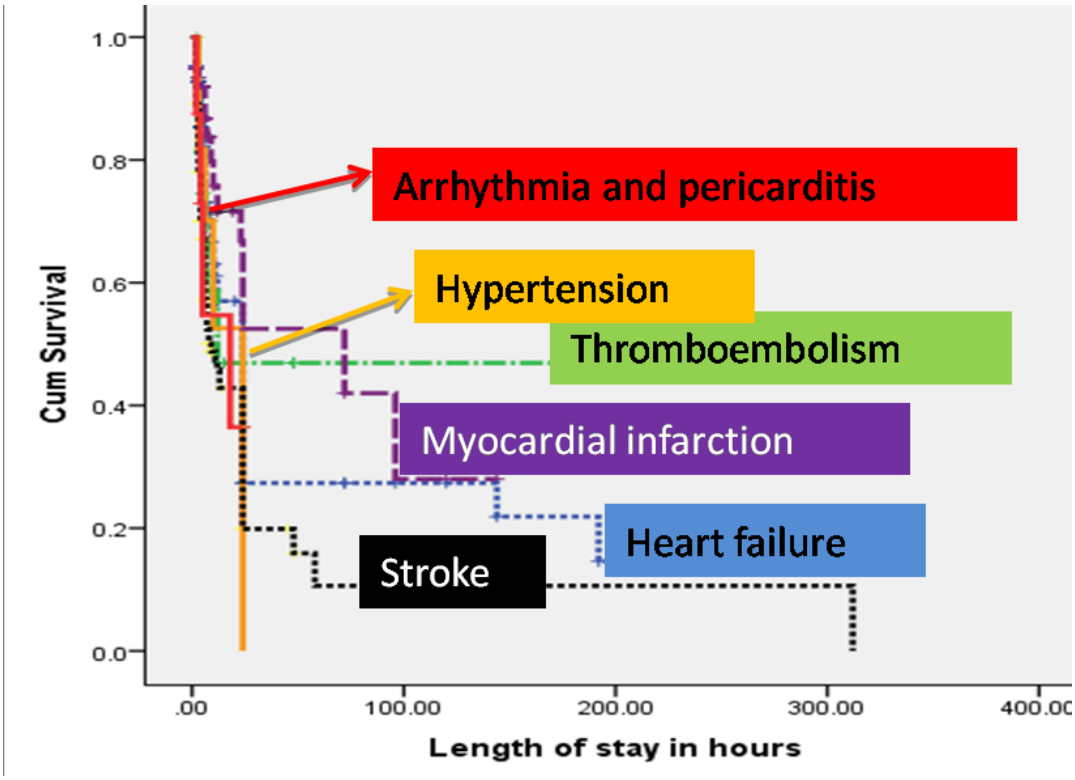

Figure 2.**Kaplan–Meier survival plots for risk of 'death from any cause' according to CVD admission diagnosis, January 2016**

Discussion

This study of patients admitted to the MICU of SPHMMC with CVD revealed the presence of a significant proportion of cardiovascular multimorbidity. About 20% of the patients admitted with CVD had diabetes mellitus, hypertension or both. The prevalence of cardiovascular multimorbidity in this study population is probably an actual estimate for the specific study group, particularly in light of the proportion of patients with hypertension and diabetes compared with other populations in Ethiopia (14-17). But it is lower than other population surveys that suggest up to 30% of adults suffer from more than one non-communicable disease (18-20).

In our study, the presence of multimorbidity appears to be a significant risk factor for mortality and cardiovascular morbidity. The overall mortality in the MICU was significantly higher in the age groups 55-74 years, and in those with hemorrhagic stroke. While heart failure was the most common cause of ICU mortality in younger patients, stroke and myocardial infarction were predominant in older age groups.

Unlike other studies that found a strong association between baseline CVD (i.e., a history of stroke or MI) and reduced survival for men compared to women, in our study there is no significant difference in mortality from MI or stroke between males and females (21).

The greatest proportion of deaths in our study was from cerebrovascular accidents or stroke, rather than from heart failure or ischemic heart disease. This concurs with Morrish *et al.*'s follow-up study (22) of the WHO Multinational Study of Vascular Disease in Diabetes, which found that, across 10 centers throughout the world, cerebrovascular deaths were more common than deaths from ischemic heart disease among people with Type 2 diabetes in Tokyo and Hong Kong, those with Type 1 diabetes in Zagreb, and men with Type 1 diabetes in Hong Kong. This study also reported that ischemic heart disease accounted for the greatest proportion of CV deaths in all other centers (23).

Patients with diabetes have an increased risk of myocardial infarction and heart failure contributing more to ICU morbidity, while those with hypertension have an increased risk of heart failure and hemorrhagic stroke that was found to be the strongest risk factor for ICU mortality in these patients. Other studies reveal that, following myocardial infarction, diabetes appears to predict mortality and increased adverse outcomes (10-19).

Conclusion

In this study we found a significant proportion of multimorbidity in patients admitted to MICU with a CVD diagnosis. The risk of death from any cause was higher in patients with stroke, myocardial infarction, heart failure, and among those in the 55-74 years age group. The strongest predictors of mortality in the MICU were 55-74 years age group, and admission with hemorrhagic stroke.

Multimorbidity may be used as a tool to prioritize the management of patients with or without CVD. This is of particular interest in light of the planned focus on the prevention and management of non-communicable diseases by the World Health Organization (22).

Our results emphasize the importance of measures to prevent CVD in people who already have hypertension, diabetes, or underlying causes of heart failure in primary care settings. On the other hand, at higher levels of care, strategies for preventing hypertension and diabetes in people who already have CVD and capacity building, to enable early management of patients presenting with acute CVD, is indispensable to improve patients' survival, physical functioning, and quality of life. Moreover, prevention of the risk factors to reduced CVD multimorbidity has a considerable impact on health care utilization and health care costs.

Limitations of the study

This study had a number of limitations. First, because the data were collected retrospectively, information bias is a limitation, as the records were not complete and we had no control over the quality of previously recorded data. In addition, the cohort was a cardiovascular population in which multimorbidity was then identified, and not a *de novo* population with multimorbidity. Although the presence of hypertension and diabetes appear to discriminate prognosis between patients with established CVD, it is difficult to identify the different elements of this association, as the confounding factors addressed in this study are limited and sample size is underpowered to detect significant differences for the secondary endpoint. Another limitation is that the study sample was from a single-center MICU, although it is reasonable to assume that the results are fairly generalizable to other similar facilities in Ethiopia. As this is the first in Ethiopia to report on the comparative risks associated with multimorbid conditions in patients admitted to MICU with CVD, it needs to be verified by prospective multisite studies.

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