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The association between multimorbidity and poor adherence with cardiovascular medications☆,☆☆

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ABSTRACT

Multimorbidity, defined as the presence of two or more chronic conditions, leads to a substantial public health burden. This study evaluated its association with adherence with cardiovascular medications in a Chinese population.

A proportional stratified sampling was adopted to draw a representative sample of residents living in Henan Province, China. Interviewer-administered surveys were conducted by trained researchers. The outcomes included the number of chronic medical conditions, adherence with long-term medications (MMAS-8), and depressive symptoms (CESD-20). Binary logistic regression analysis was conducted to evaluate if medication adherence was associated with the presence of multimorbidity.

From a total of 3866 completed surveys, the proportion of subjects having 0, 1 and ≥2 chronic conditions was 62.6%, 23.8% and 13.5%, respectively. Among 27.6% who were taking chronic medications, 66.6% had poor medication adherence (MMAS-8 score ≤ 6). From binary logistic regression analysis, subjects with poor medication adherence were significantly associated with multimorbidity (adjusted odds ratio [AOR]: 1.35, 95% C.I. 1.02–1.78, p = 0.037). Other associated factors included older age (AOR = 1.04, 95% C.I. 1.03–1.05, p < 0.001), smoking (AOR = 1.63, 95% C.I. 1.16–2.30, p = 0.005), family history of hypertension (AOR = 1.51, 95% C.I. 1.19–1.93, p = 0.001), and fair to poor self-perceived health status (AOR = 2.15, 95% C.I. 1.69–2.74, p < 0.001). Using medication adherence as the outcome variable, multimorbidity was significantly associated with poor drug adherence (AOR = 1.34, 95% C.I. 1.02–1.77, p = 0.037).

Multimorbidity was associated with poorer medication adherence. This implies the need for closer monitoring of the medication taking behavior among those with multiple chronic conditions.

1. Introduction

Multimorbidity is defined as the coexistence of two or more chronic diseases in an individual, and has been increasingly identified as a usual phenomenon in patients [1]. A recent epidemiology study in a database of 1.75 million patients registered at 314 practices in Scotland reported that up to 23% of all people suffered from multimorbidity [1], rising sharply with age. It presents serious challenges to patients and physicians, requiring a patient-oriented approach supported by close coordination between generalists and specialists [2,3]. Patients with multimorbidity had more complicated healthcare needs [4], incur higher healthcare costs [5], utilize more health services [6], and were associated with poor clinical outcomes [7].

The recent decade has witnessed a rising incidence of cardiovascular disease (CVD) and its risk factors, including hypertension, diabetes and dyslipidemia [8–10]. They tend to cluster with one another — and arguably patients with a single disease may easily develop into multiple conditions [11]. Persistent adherence with chronic medications according to the healthcare providers' instructions is essential to achieve optimal disease control, and it has been shown that high adherence with cardiovascular medication was associated with a 38% decreased risk of CVD events when compared with lower adherence [12].

It is currently unknown whether patients with multimorbidity may be at higher risks for poor medication adherence. Recent studies mainly focused on the impact of multimorbidity on health-related outcomes

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and health service utilization. As highlighted in some recent reviews, multimorbidity has been regarded as a major research priority [13], yet the number and diversity of evaluations on multimorbidity have been insufficient to provide robust scientific evidence in guiding patient care [14]. The WHO called for action to prioritize healthcare resources for global management of chronic diseases in the next decade, and there is a universal consensus that the topic of multimorbidity should be a central focus of attention [15,16]. We have previously conducted studies on multimorbidity [17–19] and medication adherence [20–25] among hypertensive patients, yet most of them either relied on retrospective data [17,21–24]; or were small-scaled [19,20].

The primary objective of this study is to evaluate the factors associated with multimorbidity and medication adherence in a large Chinese population. Specifically, we tested the a priori hypothesis that the presence of multimorbidity was associated with poorer medication adherence.

2. Methods

2.1. Ethics statement

The ethics clearance of the study was obtained from the Survey and Behavioral Research Ethics Committee of The Chinese University of Hong Kong. Informed consent was obtained prior to the study, and each participant was assured of survey confidentiality and anonymity. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Sampling frame and methods

This study invited participants from the resident health registry of Henan Province, China. The registry consisted of 227,021 residents aged 18 years or older, representing 92.3% of the county's entire population. All the registered individuals were classified into 12 strata, including two strata according to sex (male vs. female), and six strata according to age groups (18–24 years; 25–34 years; 35–44 years; 45–54 years; 55–64 years; and ≥65 years). Assuming the prevalence of multimorbidity and medication adherence was both 50% which would give the largest sample size, and an α value of 0.05, a total of 3800 completed surveys would give a precision level of approximately 0.01. A proportional stratified sampling method was adopted according to each stratum. A total of 5114 participants were invited, 3906 residents responded, and 3866 completed interviews were conducted. According to the above age groups, the number of study participants invited in each age stratum was 183 (4.7%), 468 (12.0%), 920 (23.6%), 954 (24.4%), 689 (17.6%) and 692 (17.7%), respectively, consisting of 1690 (43.3%) male and 2216 (56.7%) female subjects.

2.3. The survey instrument

This questionnaire consists of survey items in Chinese, including participants' sociodemographic details; family history of chronic diseases; self-perceived health status presented in a 4-point Likert scale (excellent; good; fair; poor); the Twenty-item Centre for Epidemiologic Studies Depression (CESD-20) Scale [26]; and the Eight-item Morisky Medication Adherence Scale (MMAS-8) [27]. The number of chronic conditions was recorded. There has been no standard approach to measure multimorbidity as it is partly subjective and dependent on the research setting [28]. We included morbidities recommended as core for any multimorbidity measure by a systematic review [29]. In the context of this study which focused on cardiovascular diseases, multimorbidity was defined as the presence of two or more chronic medical conditions [29]. These self-reported medical conditions included hypertension, diabetes mellitus, lipid disorder, myocardial infarction, stroke, chronic obstructive pulmonary disease, and cancer.

2.4. The interviews

Before the surveys, a territory-wide promotional initiative was promulgated by the government and the community health centers (which are the major primary care providers in China [30]) to the whole population. The importance of the survey study was highlighted, appealing for active participation by the residents. All the interviewers underwent standardized training on the proper survey procedures and relevant communication skills. The study subjects were invited by phone to attend the community health centers closest to their residence for interviewer-administered surveys.

2.5. Quality control

Before the survey study, a panel of expert consultants including epidemiologists, public health practitioners, academic professionals and physicians was set up to propose, refine and consolidate the research plan and methodology. They participated in survey design and advised on study logistics. An on-site survey team was established in each community health center, which was assigned a central coordinator. The research team members were responsible to check the completeness and accuracy of the surveys, and discussed on any problems encountered. A pilot study was conducted in two community health centers where researchers from other centers observed the interview processes to achieve standardized survey practice. To enhance survey quality, the coordinator from each center sampled 5% of all the surveys collected and reviewed the accuracy of data by communicating with the study participants. The information of all the surveys was entered into the computer in two separate rounds to reduce the risk of error due to data entry.

2.6. Outcome measures and covariates

The primary outcome measures included the presence of multimorbidity (≥2 medical conditions) and medication adherence. Three MMAS-8 survey sections asked adherence with antihypertensive agents; oral hypoglycemic agents; and lipid-lowering agents, respectively, among patients with physician diagnoses of hypertension; diabetes and lipid disorders who were also taking chronic medications for the corresponding diseases. Optimal adherence was defined as a MMAS-8 score > 6, out of a total score of 8 in all the sections, following the methodology used in our previous studies [31,32]. Hence if a patient was on an antihypertensive agent and a lipid-lowering drug, both MMAS-8 sections should each score > 6 for being defined as having optimal adherence. The covariates included age, sex, marital status, educational level, occupation, household income, smoking status, alcohol drinking habit, family history of chronic diseases, self-perceived health status, and depression measured by CESD-20 [normal: <15; minor to major depression: ≥15].

2.7. Statistical analyses

All data entry and analysis was performed by the Statistical Package for Social Sciences (SPSS) version 20.0. The characteristics of the study participants were compared according to the number of chronic conditions, by chi-square tests for categorical variables and Student's t-tests for continuous variables. A binary logistic regression model was constructed with multimorbidity as the outcome variable and all the covariates abovementioned as independent variables. In addition, among those who were taking chronic medications, adherence was used as an outcome variable and tested against each covariate consecutively in univariate analyses. Those who were tested significant ($p < 0.10$) were entered into a multivariate logistic regression equation. As an additional analysis, all covariates were included in another similar binary logistic regression model to detect the robustness of the findings. Interactions of variables were evaluated in each regression analysis. We performed sensitivity analysis using a cut-off of ≥6 in the MMAS-8 score to define optimal medication adherence, and repeated identical data analyses. A p value of <0.05 was regarded as statistically significant in the final regression model.

3. Results

3.1. Participant characteristics

From a total of 3866 participants, the proportion of having 0, 1 and ≥2 medical conditions was 62.6%, 23.8% and 13.5%, respectively (Table 1). Their average age was 50.1 years (SD 14.6), and 43.2% were male subjects. Participants in the following groups had high proportions suffering from multimorbidity: male sex (15.3% vs. 12.2%); married or cohabited (13.8% vs. 11.0%); educational level at primary or lower (22.5% vs. 12.4% and 8.2% for secondary or tertiary levels, respectively); housewives or unemployed people (15.5% vs. 10.3% for employed); smokers (16.8% vs. 12.5%); positive family history of hypertension (17.7% vs. 11.2%); self-perceived health status as fair or poor (21.0% vs. 7.3%); high CESD-20 score ≥ 15 (17.3% vs. 12.8%); and poor medication adherence (45.1% vs. 37.8%). The typology of the medical conditions was shown in Fig. 1. Among all patients, the most common chronic diseases as diagnosed by physicians included hypertension (22.5%), lipid disorders (15.8%), and diabetes (10.1%). The prevalence of these three diagnoses increased sharply as the number of medical conditions increased (Fig. 1).

3.2. Factors associated with multimorbidity

The proportion of poor medication adherence and depressive symptoms (CESD-20 ≥ 15) increased with the number of medical conditions (Fig. 2). From binary logistic regression analysis, older age (adjusted odds ratio [AOR] = 1.04, 95% C.I. 1.03–1.05, $p < 0.001$); engagement in full-time job (AOR for "others" = 0.72, 95% C.I. 0.53–0.97, $p = 0.031$), smokers (AOR = 1.63, 95% C.I. 1.16–2.30, $p = 0.005$), positive family history of hypertension (AOR = 1.51, 95% C.I. 1.19–1.93, $p = 0.001$), and health status self-perceived as being fair or