



Factors associated with multimorbidity and its link with poor blood pressure control among 223,286 hypertensive patients



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ABSTRACT

Multimorbidity has become the norm worldwide as populations age. It remains, however, infrequently researched. This study evaluated factors associated with multimorbidity in a predominantly Chinese hypertensive population. We included all adult patients prescribed their first antihypertensive agents in the entire public sector in Hong Kong from a validated database. Multimorbidity was defined as having one or more medical conditions (cardiovascular diseases; respiratory diseases; diabetes or impaired fasting glucose; renal disease) in addition to hypertension. We studied the prevalence of multimorbidity and performed multinomial regression analyses to evaluate factors independently associated with multimorbidity. 223,286 hypertensive patients (average age of 59.9 years, SD 17.6) were included. The prevalence of having 0, 1 and ≥ 2 additional conditions was 59.6%, 32.8% and 7.5%, respectively. The most common conditions were cardiovascular disease (24.2%) and diabetes (23.0%), followed by respiratory disorders (14.6%) and renal disease (10.9%). Older age (>50 years), male sex, lower household income, receipt of social security allowance and suboptimal blood pressure control (>140 mmHg or >90 mmHg; >130 mmHg or >80 mmHg for diabetes patients; AOR = 3.38–4.49) were significantly associated with multimorbidity. There exists a synergistic effect among these variables as older (≥ 70 years), male patients receiving security allowance had substantially higher prevalence of multimorbidity (19.9% vs 7.5% among all patients). Multimorbidity is very common in hypertensive patients and its prevalence increased markedly with the presence of risk factors identified in this study. Hypertensive patients with multimorbidities should receive more meticulous clinical care as their blood pressure control tends to be poorer.

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1. Introduction

Multimorbidity, defined as the presence of more than one chronic disorder, has become the norm in many countries as populations age [1,2]. It represents a substantial challenge to physicians, patients and the healthcare systems [2–5]. Patients with multimorbidity require utilization of more health services [6], incur higher healthcare costs [7,8], present with more complicated healthcare needs [9], and are associated with poorer health outcomes including a lower quality of life [10] and increased mortality [11,12].

Hypertension is one of the most common chronic conditions in clinical practice, and carries a substantial global burden of disability and cost. Worldwide, approximately 54% of stroke and 47% of ischemic

heart disease have been attributed to hypertension alone [13]. We studied hypertensive patients in this study because of the frequency of this disorder in world populations, including both Asian and Caucasian populations. There is a tendency for risk factor clustering, wherein hypertensive patients are more prone to have concomitant comorbidities such as cardiovascular diseases, diabetes, kidney diseases, and pulmonary complications [13,14]. Multimorbidity has been recognised as a major research priority due to its high prevalence [15]; nevertheless, there have been few studies addressing the typology and the determinants of multimorbidities including patients' demographic parameters (age, sex, household income, payment status, service settings) and anti-hypertensive prescription details, in routine clinical practice. Also, the number and diversity of articles on multimorbidity have been considered insufficient to provide adequate scientific evidence to guide patient care [16]. Previous studies on multimorbidity have mainly focused on older people; are small in scale; or relied on patient self-reports [17–20]. None of the existing studies on multimorbidity has been conducted among Chinese populations based on physician diagnosed medical conditions.

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The World Health Organization (WHO) called for action to prioritise resources for worldwide care of chronic diseases in the next decade, and there is a universal consensus that the issue of multimorbidity should be a central focus of attention [21,22]. The primary objective of this study is to test the *a priori* hypothesis that multimorbidity was associated with suboptimal blood pressure (BP) control among hypertensive patients. The secondary objective is to evaluate the prevalence of multimorbidity in a large Chinese hypertensive population, and to explore the independent factors associated with multimorbidity.

2. Materials and methods

2.1. Ethics statement

The ethics clearance of the study was obtained from the Clinical Ethics Research Committee of the Hospital Authority, and the Survey and Behavioral Research Ethics Committee of The Chinese University of Hong Kong. Informed consent was not deemed necessary as all subjects were anonymized with unique identity numbers. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Data source

The computerized databases, known as electronic Clinical Management System in Hong Kong, have been previously described in detail [23–32]. We included all variables captured in these databases, including patients' demographic parameters (age, sex, household income, payment status, service settings), prescription details, and clinical diagnoses in the forms of the International Classification of Diseases (ICD-9 and ICD-10) or the International Classification of Primary Care (ICPC-2), as independent variables in the study. The database was previously validated and it demonstrated a high level of completeness with respect to socio-demographic information (100%) and prescription details (99.8%) [23]. It serves as the sole portal of data entry which allows the linkage of physician-entered information at each patient visit in all public clinical settings among different districts. All prescriptions are inputted by the attending physicians and are cross-checked by dispensers or pharmacists using standardized procedures, and any amendments to the prescriptions after the initial consultations are also recorded in the system. The present study included the entire Hong Kong population, which is more than seven million as of 2014. Hong Kong is divided into three distinct regions, namely Hong Kong Island (most urbanized); Kowloon; and the New Territories (most rural).

2.3. Patients

From the database, all patients who had a consultation at any public practice and who were prescribed their first-ever antihypertensive agents between the calendar years 2001 and 2005 (the index date) were included. Patients who received any antihypertensive medications or had known cardiovascular disease (CVD) before the index date were excluded. All patients were followed up for 5 years and the cumulative number of physician-entered disease coding at the end of the study period was evaluated.

2.4. Outcomes variables and covariates

The primary outcome variable was the presence of multimorbidity. Multimorbidity was defined and measured in different ways across a variety of studies and contexts, and there is no clear findings showing the superiority of one multimorbidity measure over another [33]. In this study, multimorbidity was defined as having concomitant comorbidities (including cardiovascular risk factors and the major complications of systematic or pulmonary hypertension, as indicated by the respective ICPC-2 or ICD-9/ICD-10 codes) in addition to hypertension, at the end of the follow-up period. We captured both systematic hypertension (occurs in the brachial artery) and pulmonary hypertension (occurs in the arteries in the lungs), and the concomitant comorbidities were categorised as: 1) Cardiovascular diseases, including coronary heart disease or stroke (ICD-9: coronary heart diseases: 410–414, heart failure: 428, cerebrovascular disease: 430–435, 437, 438; ICPC-2: cardiovascular or cerebrovascular disease: K74–K77, K84, K90, K91, K99); 2) Respiratory diseases, including chronic obstructive airway disease, asthma, pneumoconiosis and other lung diseases (ICD-9: 491–493, 495, 496, 500–508, 510–513, 516, 517.1, 517.2, 517.8, 518.1, 518.2, 518.3, 518.5, 518.8, 518.82, 518.89, 519.1, 519.4, 519.8; ICPC-2: R79, R95, R96) that are major complications of pulmonary hypertension and a complication that are commonly seen among patients on certain anti-hypertensive agents (e.g., ACE inhibitors); 3) Diabetes or impaired fasting glucose (ICD-9: 250, 648.8, 790.2; ICPC-2: T90, T901); and 4) Renal disease, including glomerulonephritis, nephritic syndrome, renal failure (ICD-9: 581–583, 585, 588.0, 588.1, 588.8, 588.9, 589, 590, 590.0, 590.2, 590.3, 590.8, 590.9, 591, 592, 592.0, 592.9, 593, 593.0, 593.1, 593.2, 593.5, 593.7, 593.72, 593.73, 593.81, 593.8, 593.83, 593.89, 593.9; ICPC-2: U14, U78, U88, Y79, Y85). Patients having multiple disease entities under any of the four categories were regarded as having one medical condition only. The variable tested for association with the presence of multimorbidity was BP control, defined as suboptimal if the systolic BP \geq 140 mmHg or the diastolic BP \geq 90 mmHg; and systolic BP \geq 130 mmHg or diastolic BP \geq 80 mmHg among patients with concomitant diabetes or chronic kidney diseases [34]. Blood pressure is routinely measured in each antihypertensive refill visit in the clinic settings by

standardized automated BP machines which are regularly calibrated. Following the methodology used in previous studies [31,32,35], we averaged all BP measurements over all visits within the study period as the outcome. The covariates included patients' age, sex, household income, payment status (recipients vs non-recipients of comprehensive social security assistance; each consultation in a primary care setting costs approximately US \$5.77, including both investigation and prescription fees), the service settings (In- or day-patient clinics; specialist outpatient clinics [SOPCs], accident and emergency departments (AEDs); general outpatient clinic [GOPC], and other clinic type), and the first antihypertensive drug class received.

2.5. Statistical analyses

For descriptive analysis, Student's *t* tests and chi-square tests of heterogeneity were used to compare continuous and categorical variables, respectively. The sociodemographic characteristics were compared among patients having 0, 1 and \geq 2 additional medical conditions, respectively. The proportions of patients having different numbers of comorbidities were presented according to patients' age, sex, and payment status. A multinomial regression model was constructed with the number of medical conditions (0, 1 and \geq 2) as the outcome variable. The predictor variable (BP control) and all the covariates listed above were entered into the regression analysis. We evaluated for multicollinearity and interactions among variables to ensure the robustness of the regression model. The Statistical Package for Social Sciences version 16.0 (SPSS, Inc, Chicago, Illinois) was used for all data analyses. All *p* values $<$ 0.05 were regarded as statistically significant.

3. Results

3.1. Participant characteristics

A total of 223,286 patients were included in the study (Table 1). Their average age was 59.9 years (SD 17.6) with 54.8% being female patients. The proportion of patients having 0, 1 and \geq 2 conditions was 59.6%, 32.8% and 7.5%, respectively. From descriptive analysis, older patients, male subjects, those with lower household income, recipients of social security allowances, patients attending day- or in-patient service settings, and those who received alpha-blockers, ACEIs and combination therapy tended to have increased multimorbidity (Table 1). The most common conditions include cardiovascular disease (24.2%), diabetes (23.0%), respiratory disorders (14.6%) and renal disease (10.9%) (Fig. 1). Among younger patients, diabetes and cardiovascular diseases were the leading coexisting conditions; whereas renal disease and diabetes predominated among older patients aged \geq 70 years.

3.2. Profiles of multimorbidity according to age, sex and socioeconomic status

The proportion of patients having \geq 1 medical condition progressively increased when any one of the factors - advanced age (\geq 70 years), male sex and the receipt of social security allowance, was consecutively added (Table 2). 69.1% of male patients aged \geq 70 years who received comprehensive social security assistance (CSSA - a scheme that provides a safety net for those who have financial hardship for supporting themselves) had at least one medical condition, when compared with 18.2% of female patients aged $<$ 50 years who did not receive CSSA.

3.3. Independent factors associated with multimorbidity

From multinomial regression analyses, older age (\geq 50 years; adjusted odds ratios [AOR] 2.17–5.47, $p <$ 0.001); male sex (AOR 0.52, 95% C.I. 0.50–0.54 for females); receipt of public assistance (AOR 1.96, 95% C.I. 1.88–2.04, $p <$ 0.001); attendance in day- or in-patients (AOR 2.21, 95% C.I. 2.02–2.42, $p <$ 0.001); and prescriptions of ACEIs, α -blockers and combination therapy as first antihypertensive medications (AOR 2.15–2.73, $p <$ 0.001) were associated with the presence of two or more conditions (Table 3). Patients with poor blood pressure control were more likely to have one (65.0% vs 35.0%, AOR 3.38, 95% C.I. 3.29–3.46, $p <$ 0.001) and \geq 2 (69.1% vs 30.9%, AOR 4.49, 95% C.I. 4.28–4.70, $p <$ 0.001) concomitant medical condition than patients with optimal blood pressure control (Table 3). Fig. 2 shows that the proportion of patients having poor blood pressure control increased from 35.0% to 65.0%

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