Association of Continuity of Health Care with Risk of All-Cause and Disease-Specific Mortality in Hypertensive Patients

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ABSTRACT

Association of Continuity of Health Care with Risk of All-Cause and Disease-Specific Mortality in Hypertensive Patients

BACKGROUND : Hypertension is an important public health concern worldwide with increasing age and better care continuity is essential for the effective hypertension management. This study was to investigate whether or not better care continuity is expected to improve patient outcome and reduce mortality among hypertensive patients.

METHODS : This study analyzed claim data obtained from collected from the National Sample Cohort 2002-2015 which is the national representative 1 million individuals sample (2% of the Korean population). A total of 152,526 newly developed hypertensive patients were identified for the final study population. Medication Possession Ratio for antihypertensive medications was considered the exposure of interest as a proxy of continuity of care for hypertension. If the total observation period was more than 6 months (180 days) and the MPR was more than 0.8, those patients were classified as High Continuity of Care group and others as Low Continuity of Care group. For outcome of interest, all-cause mortality, ischemic heart disease mortality, ischemic stroke mortality, hemorrhagic and other non-ischemic stroke mortality, hypertension related disease mortality including hypertensive heart disease and chronic kidney disease due to hypertension were used in this study.

RESULTS : 4,527 patients (8.1 per 1,000 person-year) in the High Continuity of Care group died and 10,356 patients (14.3 per 1,000 person-year) in the Low Continuity of Care group died during the observation period. Compared with patients in the Low Continuity of Care group, patients in the High Continuity of Care group had lower risks of all-cause mortality (Adjusted HR: 0.52, 95% CI: 0.51-0.54, P<.0001), ischemic heart disease mortality (Adjusted HR: 0.76, 95% CI: 0.61-0.94, P=0.013), ischemic stroke mortality (Adjusted HR: 0.47, 95% CI: 0.35-0.64, P<.0001), and hemorrhagic and other non-ischemic stroke mortality (Adjusted HR: 0.44, 95% CI: 0.35-0.55, P<.0001). There was no significant difference in hypertension related disease mortality between Continuity of Care groups (Adjusted HR: 0.87, 95% CI: 0.58-1.30, P=0.5).

CONCLUSION : The results of this study confirmed that controlling hypertension through high continuity of care decrease the risk of all-cause mortality, ischemic heart disease mortality, ischemic stroke mortality, and hemorrhagic and other non-ischemic stroke mortality. Efforts to improve and maintain care continuity may be warranted for the effective hypertension management.

Keywords: Continuity of care, Hypertension, Mortality

Ⅰ. INTRODUCTION

1. Background

The World Health Organization (WHO) defines hypertension, also known as high or raised blood pressure, as a condition in which the blood vessels have persistently raised pressure. The heart is pumped to carry blood from the heart through the vessels to all parts of the body, and blood pressure is generated by the force of blood pushing against the walls of arterial blood vessels when the heart is pumped. The higher the pressure, the harder it is for the heart to pump. Hypertension is a serious medical condition that can increase the risk of heart, brain, kidney and other diseases.

Hypertension is an important public health concern because its prevalence is high and increasing worldwide. Hypertension has an estimated 31.1% of adults (1.39 billion) worldwide in 2010.[1] The global healthcare expenditure on hypertension in 2001 had an estimate of US $370 billion or about 10% of the world's overall health-care expenditure.[1] In addition, hypertension usually clusters with other chronic disease, such as diabetes mellitus, obesity, and dyslipidemia, and even persons with normal blood pressure at age less than 65 years have a lifetime risk of developing hypertension if they survive to age more than 80 years. Globally, the prevalence of chronic diseases, including hypertension, is expected to increase rapidly over the next few years as life expectancy is extended, and as the number of people with chronic diseases increases, so does

the personal and social cost burden.[2,3] The literature suggests that proportion of total health-care resources spending on hypertension has been significantly increased in recent years as the progressive increase in life expectancy in the general population and chronic diseases in the aged population in many developed countries.[4] Increasing prevalence of chronic diseases, including hypertension, is a major cause of increased risk of cardiovascular disease and death worldwide.[5-7]

In particular, hypertension and diabetes are the most common comorbid chronic diseases seen in healthcare setting, with one patient having both diseases in general.[8,9] The number of people who have two or more diseases at the same time is increasing, and the same person has an increasing number of diseases at the same time.[10-12] Those multimorbidity is significantly associated with increased mortality and disability and a lower quality of life.[13,14] The increasing number of patients with chronic diseases, including hypertension, increases the economic burden of health care costs on the individual, as well as the social and national burdens, and increases the mortality rate from chronic diseases and related complications. In many developed countries, the prevalence of chronic diseases, such as diabetes and hypertension, is high, and the mortality rate from cardiovascular and cardiovascular disease, which is highly correlated with the prevalence of diabetes and hypertension, is increasing.[15] In addition, the prevalence of chronic diseases has increased rapidly and the mortality rate due to COPD associated with chronic diseases continues to increase in developing countries.[16] Therefore, hypertension is one of the commonest cardiovascular ailments and that health policy about hypertension management assumes more importance with increasing age. Hypertension and diabetes are the leading chronic diseases in Korea and are a major cause of the risk of cardiovascular and cerebrovascular

disease and death. According to a recent report by the Health Insurance Review and Assessment Service, the number of outpatient care for hypertension and diabetes in 2018 was 917 million, an increase of 360,000 from the previous year. The number of patients with both diseases was 1.94 million, an increase of 100,000 from the previous year. Among the patients with those diseases, 41.5% of the patients were aged 70 or older.

Although hypertension is a serious medical condition, many people with hypertension may not be aware of the symptoms and may be unaware there is a problem. This characteristic of hypertension is a major cause of delaying detecting hypertension or stopping hypertension treatment. Based on the statistics[17] of 2016 in Korea, only 65% of hypertensive populations reported to be diagnosed with hypertension from physicians and 61% of hypertensive populations were using antihypertensive medications for 20 days or more per month. Since hypertension can be managed for a lifetime by avoiding risk factors and maintaining proper blood pressure control, continuity of patient care is very important. Unlike acute disease, which can be cured, integration and comprehension of chronic disease care would be essential for better outcomes. Explicit concern for continuity in medical specialties has emerged since the late 1980s, reflecting the increased complexity of managing chronic diseases including hypertension.

Regardless of developed and developing countries, health care policy has profoundly changed into the paradigm that focuses on the management of chronic diseases in primary care rather than disease prevention. Therefore, the WHO has developed action plans to prevent four of the most prominent chronic diseases-cardiovascular diseases, cancer, chronic obstructive pulmonary disease and type 2 diabetes. Those major chronic diseases are linked by common and

preventable biological risk factors, notably high blood pressure, high blood cholesterol and overweight, and by related major behavioral risk factors including unhealthy diet, physical inactivity and tobacco use. The WHO emphasizes that action to prevent these major chronic diseases should focus on controlling these and other key risk factors in a well-integrated manner. In Korea, the quality improvement program administrated by the Health Insurance Review and Assessment service is running, specially focusing on managing hypertension and diabetes, which are the representative chronic diseases. For successive hypertension management, anti-hypertension treatment is necessary along with life style modification including diet and exercise. Therefore, better care continuity is essential for the effective hypertension management.

Hypertension cannot be cured once diagnosed, but the risk of hypertension and other related diseases can be greatly reduced with effective antihypertensive therapy. Therefore, the evaluation of efficacy of continuity of care for antihypertensive drugs may have important and broad implications for public policy. There are extensive evidences about the association between hypertension and health outcomes. However, most of epidemiological and clinical trial data have been based on lowering blood pressure, there is few researches which provide clear evidence of the value of continuity of care.[18,19] Thus, understanding whether or not the continuity of care are associated with better health outcomes is important for planing an effective health policy agenda.

2. Hypothesis and Objectives

2.1. Hypothesis

The high continuity of care decreases the risk of mortality in hypertensive patients.

2.2. Objectives

The purpose of this study was to determine whether or not better care continuity is expected to improve patient outcome and reduce mortality among hypertensive patients. The specific objectives are following.

(1) To evaluate the risk of all-cause mortality associated with high continuity of care

(2) To evaluate the risk of ischemic heart disease mortality associated with high continuity of care

(3) To evaluate the risk of ischemic stroke mortality associated with high continuity of care

(4) To evaluate the risk of hemorrhagic and other non-ischemic stroke mortality associated with high continuity of care

(5) To evaluate the risk of hypertension related diseases including hypertensive heart disease, chronic kidney disease due to hypertension mortality associated with high continuity of care

Ⅱ. LITERATURE REVIEW

1. Concept of continuity of care

The continuity of care is how one patient experiences care consistent and linked over time. It is the result of good information flow, good inter-personal skills and good care coordination. The traditional concept of care continuity was to provide high quality of care by maintaining information continuity and ensuring continuity of disease management based on the continuity of relationship with a single provider.[20] Continuity of care is conceived differently in primary care, chronic care, mental-health care but its meaning is more often presumed than defined.[18,19] However, there are two core elements and three types of continuity summarized based on the notable literature review by John Saultz[18]. The core elements are the experience of care by a single patient with his or her providers and the cae continues over time. Both elements must be present for constitute continuity. The three types of continuity are informational continuity, management continuity, and relational continuity. Informational continuity reflects the use of information on past events and personal circumstances to make current care appropriate for each individual. Management continuity is a consistent and coherent approach to the management of a health condition that is responsive to a patient's changing needs. Finally, relational continuity means an ongoing therapeutic relationship between a patient and one or more providers.

Defining continuity of care for research, policy, or quality assessment is

extremely complex because continuity of care is conceptualized in many different ways by health care professionals and researchers across communities and population. In addition, the health care environment have changed as the prevalence of chronic disease increases and the number of patients suffering from multiple diseases increases, and it is very difficult to get qualified integrated medical care from a single provider.[21,22] Patients now routinely receive care from different organizations and different disciplines. Such changes potentially fragment care and reduce all types of continuity.

There are mainly two way for gathering information about continuity of care: one is patient-reported measures data and the other is claim-based data. The strengths of using claim-based data include the ability to assess longitudinal continuity and the limitations of using claim-based data include the potential errors between the real primary provider and the provider-patient relationship. Continuity in the provider-patient relationship is especially important for patients with multiple chronic diseases.[23] In this case, patient-reported measures data may be appropreate to identify such a relationship. There are few researches using patient-reported measures data and there is also debate about whether patient-reported measures can be used to identify the true provider-patient relationship.[24,25]

Because relationship continuity is increasingly irrelevant to most patients and increasingly difficult to achieve in team based care,[26] relationship continuity has been particularly neglected by recent policy even though there are several evidences about the value of relationship continuity, especially those with chronic and complex problems.[27-30] Instead recent policy focuses on emphasizing management and informational continuity through guidelines, care pathways, and

electronic health records in terms of responding to potential fragmentation.

The basic idea of continuity of care is a patient has an on-going relationship with a physician, a physician group practice, or a clinic. There are several methods to measure continuity of care and these methods are summarized below.

1.1. Bice-Boxerman Continuity of Care Index (COC)[31]

The Bice-Boxerman Continuity of Care Index integrates both the frequency of visits to each provider and the dispersion of visits between providers into a single metric. The COC index reflects the extent to which a given individual's total number of visits for a specific time period being with a single or group of referred providers. The indices range from zero to one and a higher value corresponds with better care continuity. The COC index is able to capture 'concentration' of visits to multiple providers, but the results will be only stable for patient when the annual number of visits is more than three.

1.2. Usual Provider of Care Index (UPC)[32]

The Usual Provider of Care Index primarily focuses on the concentration of visits with the health care provider most often seen in the past year. The index reflects the "density" of care, or the extent to which visits are concentrated with a single usual provider or group of providers during an episode. It equals the number of visits to the provider or practice group with the highest number of visits divided by the total number of visits.

1.3. Sequential Continuity Index (SECON)[33]

The Sequential Continuity Index varies from the other indices in that it

considers the order of visits, not just their concentration or dispersion among providers. The index reflects sort term continuity and it equals the fraction of sequential visits pairs at which the same provider is seen.

1.4. Modified Modified Continuity Index (MMCI)[34]

The Modified Modified Continuity Index focuses on the dispersion between providers and is based on the number of caretakers and number of visits only. Index values range from 0 (each visit made to a different physician) to 1 (all visits made to a single physician).

1.5. Medication Possession Ratio (MPR)[35]

The Medication Possession Ratio is the ratio of the number of days for which a patient has medication on hand divided by the total number of days a patient was observed. This method has the advantage of a very simple calculation method that does not take into account the gap between refills and the need for continuous treatment that requires multiple prescriptions, but appropriate calibration using correlation and average would be necessary because the denominator variation can be limited in large population analysis.

Table 3. Continuity of care indices

Index	Estimation	Equation	Strengths[36,37]	Limitations[36,37]
COC	Weights both the frequency of visits to each provider and the dispersion of visits between providers	$COC = \frac{\sum_{i=1}^{k} n_i^2 - N}{N(N-1)}$ where n_i is the number of visits to provider i and N is total number of visits in a defined period	It is able to shifts in the distribution of visits among providers. Good mathematical performance which tends to have a mean of 0.5	Index value may be affected by utilization levels Index value will be stable with at least 3 annual visits
UPC	Proportion of outpatient visits that a patient has with his/her most frequent provider	$UPC = \max\left(\frac{N_i}{N}\right)$ where N_i is the number of visit to most frequent provider i and N is total number of visits in a defined period	It is able to analyze the role of other health providers in addition to physicians.	Only assesses visits with most frequent provider Index value may be affected by utilization levels
SECON	Proportion of the number of visits that an individual made to the provider that the individual saw on their most recent visit	$SECON = \frac{\phi_i + \ldots + \phi_{N-1}}{N-1}$ where N is total number of all provider visits and φ=1 when the current and subsequent visits are made to the same provider, otherwise φ=0	Sensitive to shifts in sequence of visits Useful as measure of amount of inter-provider communication necessary	Insensitive to the distribution of visits among providers if sequencing remains constant

Index	Estimation	Equation	Strengths[36,37]	Limitations[36,37]
MMCI	Dispersion between providers and is based only on the number of providers and number of visits	$MMCI = \frac{1-(\frac{K_i}{N_i+0.1})}{1-(\frac{1}{N_i+0.1})}$ where N_i is the number of visits and K_i is total number of providers seen by patient i during a defined time interval	Only needs summary utilization measures Not overly sensitive to large number of providers	Unable to capture sequential data
MPR	Ratio between the days of medication supply of all prescription fills within a time interval	$MPR = \frac{\sum_{i=0}^{k} MedDays}{ObsDays}$ where k is the end point of observation, MedDays is total number of days for medication supply, ObsDays is total number of days for observation	Easy to calculate using claim-based data	Index value may be overestimated

2. Conceptualizations of continuity of care in chronic disease

Increasing the prevalence of chronic diseases has become one of the most important challenges to be addressed in the health care system. In contrast to the traditional disease management models that focus on acute conditions, chronic disease management requires patients to play a more active role in disease management in their everyday life. This new disease paradigm requires patient-provider cooperation for effective treatment within an integrated system of collaborative care.

The essential element of effective chronic disease management is the partnership between the patient and the health care provider, which gives the patient the opportunity to participate more actively in their health care. Effective interaction with health care providers provides patients with sufficient information for disease management and encourages them to achieve healthier outcomes.[38] The patient is central to defining disease-related problems, and self-management programs help solve disease-related problems as well as build self-esteem and self-confidence to deal with the problems. As a result of effective partnerships between the patient and the health care provider, the level of continuity of care elevates and finally has a positive effect on patients' health care outcomes.

There are various models of chronic disease, and the factors considered vary from model to model. Some representative models of chronic diseases are summarized.

2.1. Chronic Care Model[39]

The Chronic Care Model (CCM) is an organizational approach of care designing

essential elements of chronic disease care. The six major elements, which are the community including organizations and resources for the patient, the health system or health organization, self-management support, delivery system design, decision support, and clinical information systems, within the model are identified as essential elements that interact to promote high quality care for patients with chronic disease. The model emphasizes the involvement of health care providers and patients themselves, with the theory that structural changes are needed to manage people with chronic diseases.

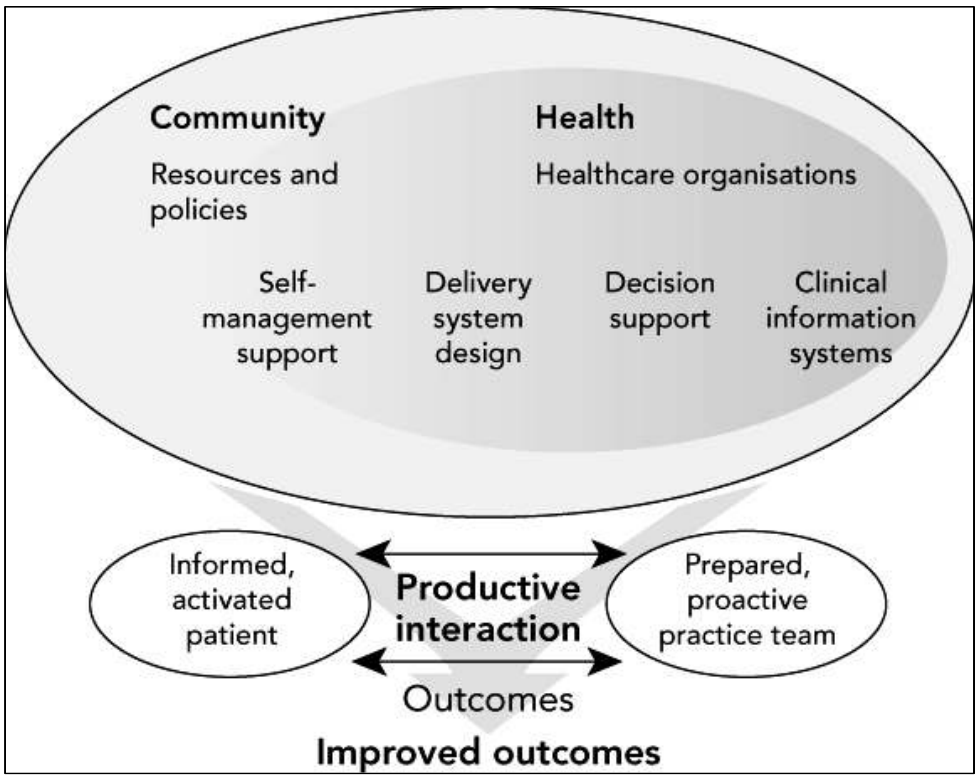

Figure 1. The Chronic Care Model (Wagner, 1996)[39]

2.2. Improving Chronic Illness Care[40]

The Improving Chronic Illness Care (ICIC) is a prolonged model from the Chronic Care Model to integrate medical science with redesigned health care delivery systems so chronic patients in any setting can receive prompt diagnoses and care. There are five addition elements which were incorporated into the existing Chronic Care Model: patient safety in health system, cultural competency in delivery system design, care coordination in health system and clinical information systems, community policies in community resources and policies, case management in delivery system design.

2.3. Innovative Care for the Chronic Conditions[41]

The Innovative Care for the Chronic Conditions (ICCC) model is an expansion of the Chronic Care Model and the model was developed by the World Health Organization in 2002. The model addresses the broader policy environment including patients, their families, health care organizations, and communities. There are eight major elements within the model: support a paradigm shift, manage political environment, build integrated health care, align sectoral policies for health, use healthcare personnel more effectively, center care on the patient and family, support patients in their communities, emphasize prevention.

2.4. Chronic Disease Self-Management Program[42]

The Chronic Disease Self-Management Program (CDSMP) is the most widely used model for self-efficacy enhancing health care intervention in patients with chronic conditions. The model was developed by Stanford University in 2012. The purpose of the program is to help participants' master six fundamental

self-management tasks including problem solving, decision making, resource allocation, forming a patient-provider partnership, and making action plans.

2.5. Transitional Care Model[43]

The Transitional Care Model is designed to ensure the coordination and continuity of healthcare by providing patients with comprehensive discharge planning and home follow-up to prevent health complications and re-hospitalizations. The comprehensive planning and coordination of care is provided by healthcare practitioners who are well-trained in the care of people with chronic conditions. The model emphasized patients' chronic care needs across time including identification of patient-specific concerns or needs, medication adherence and persistence, supporting patient's health literacy, and the utilization of remote patient monitoring for optimal condition management.

Figure 2. The Transitional Care Model [43]

3. Review previous studies

3.1. Studies of hypertension

Hypertension, one of the typical chronic diseases, is a lifelong disease that is manageable but generally not curable. In addition, hypertension has recognized as the leading risk factor contributing to premature many other diseases morbidity and mortality. There are several researches to show the relation between hypertension as a risk factor and cardiovascular disease. Zhou (2018)[44] examined whether uncontrolled hypertension increase the risk of all-cause and cardiovascular disease mortality in US adults using the National Health and Nutrition Examination Survey (1988-1994) data and uncontrolled hypertension is a major risk factor for the development of cardiovascular disease. Rosendorff (2007)[45] suggested that lowering blood pressure through treatment of hypertension decrease the risk of ischemic heart disease. Ettehad (2016)[46] showed from a meta analysis that every 10mmHg reduction in systolic blood pressure significantly reduced the risk of cardiovascular disease events, coronary heart disease, stroke, and heart failure. This study provided strong support for strong support for lowering blood pressure to systolic blood pressures less than 130mmHg and providing blood pressure lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease.

Hypertension is a major modifiable risk factor for stroke, with an estimated 51% of stroke deaths being attributable to high systolic blood pressure globally. Bowry (2014)[47] emphasized selecting appropriate blood pressure agent for effective blood pressure control for hypertensive patients with ischemic or hemorrhagic stroke, because the relationship between hypertension and stroke is dynamic and

multifaceted. Aiyagari (2009)[48] suggested that the degree of blood pressure reduction may be more important than the class of hypertensive agents although lowering blood pressure is effective for recurrent stroke prevention. Appleton (2016)[49] cautioned that high blood pressure can lead to cerebral edema, haematoma expansion or haemorrhagic transformation while low blood pressure can lead to increased cerebral infarction or perihaematomal ischemia. Wajngarten (2019)[50] examined that screening and treatment of hypertension prevents cardiovascular disease and reduces mortality in the middle-aged population. There are several studies to support that hypertension is both causes and risk factors for chronic kidney disease.[51-54]

Based on adults aged 18 years or older, hypertension is defined as a systolic blood pressure (SBP) of 140mmHg or more, or a diastolic blood pressure (DBP) of 90mmHg or more, or taking antihypertensive medication.[55] Even though people with prehypertension, those in the blood pressure range 130/80 to 139/89 mmHg, have a double risk of progression to hypertension compared to those with lower blood pressure values.[56] The prevalence of hypertension will increase even further as the population ages without an extensive and effective prevention program. According the Framingham Heart Study,[57] normotensive people at 55 years of age have a 90% lifetime risk of developing hypertension. The prevalence of hypertension was 29% and at least 11 million adults suffer from hypertension among Korean adults aged 30 years or older.[58-60] Therefore, research on hypertension is one of the most important research topics.

Previous studies have suggested that lowering blood pressure has a positive effect on health outcomes. In clinical trials,[61] lowering blood pressure through antihypertensive therapy has been associated with 20% to 39% reductions in

stroke, 15% to 28% reductions in cardiovascular events, and 19% to 20% reductions in coronary heart diseases. In a meta-analysis[62] of 61 prospective observational studies, every 10mmHg reduction in systolic blood pressure is associated a 50% to 60% lower risk of death from stroke and a 40% to 50% lower risk of death from coronary artery disease or other vascular diseases. In addition, a recent study[59] conducted in Korea suggested that uncontrolled blood pressure was significantly associated with an increased risk of death from non-cardiovascular diseases including diabetes, alcoholic liver disease, renal failure, and intestinal ischemia. In particular, because cardiovascular disease and stroke are the leading cause of premature morbidity and mortality on a global basis,[63] programs aimed to effectively manage hypertension are therefore expected to have a significant impact on the health of the world population. There are extensive evidences about the association between hypertension and health outcomes. However, most of epidemiological and clinical trial data have been based on lowering blood pressure, so there are few focusing on the efficacy of continuity of care for antihypertensive drugs. Hypertension cannot be cured once diagnosed, but the risk of hypertension and other related diseases can be greatly reduced with effective antihypertensive therapy. Therefore, hypertension is very useful as research subjects for studying the effect of disease management focusing on care continuity on health outcomes.

The pharmacological treatment strategies and patient's adherence to antihypertensive treatment are essential for effective hypertension management. Poor adherence to antihypertensive treatment correlates with the magnitude of blood pressure elevation and is resulted in the structural or functional alteration of the arterial vasculature or end organs include the brain, the heart, the kidneys, the

eyes, and central and peripheral arteries.

According to the Korea hypertension fact sheet 2018,[17] 8.9 million in 2016 made clinical visit at least once per year to receive treatment for hypertension and those antihypertensive medications included diuretics, beta-blockers, calcium channel blockers, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, aldosterone antagonists, alpha-blockers, vasodilators, and others. Among people receiving antihypertensive prescription, only 40% were prescribed single class of antihypertensive medication and the remaining 60% were prescribed combination regimen of two or more antihypertensive medication.

Figure 3. Trends in the prevalence of hypertension in Korea [17]

There are many studies to support that hypertensive patients have several common comorbidities that can affect cardiovascular risk and pharmacological treatment strategies. A strong correlation exists between hypertension and coronary artery disease and both the diffused arteriosclerosis of hypertension and the more patchy atherosclerotic lesions of epicardial coronary artery disease may have the same common pathophysiological mechanisms.[45,46] Hypertension is the most important risk factor for ischemic or hemorrhagic stroke and there is substantial evidence[47-50] to support that stroke can be largely preventable by controlling blood pressure. Commonly known hypertension comorbidities include coronary artery disease,[44-46] stroke,[49,50] chronic kidney disease,[52-54] heart failure,[45] diabetes,[8] lipid disorders,[64,65] metabolic syndrome,[66] and chronic obstructive pulmonary disease (COPD).[67]

Uncommon comorbidities include rheumatic diseases and psychiatric diseases. Several studies[68,69] showed rheumatic diseases are associated with an increased prevalence of hypertension under diagnosed and poorly controlled. Studies[70,71] have shown that the prevalence of hypertension increases in people with psychiatric disorders and especially depression. In particular, some antihypertensive medications may exhibit pharmacological interactions under antidepressants and, as a result, may affect health outcomes. Therefore, underlying diseases and concomitant medications should be adjusted for more precise research design when researching the association between hypertension management and health outcome.

3.2. Studies of continuity of care

There are several studies to show the association between continuity of care and healthcare outcome. Chen and Cheng (2011)[72] reported that higher continuity of

care was associated with fewer hospitalizations and emergency department visits. The analysis was adjusted for age, sex, low-income status, hospitalizations in previous year, and diabetes complication severity index score. The study was assessed continuity of care using 3 indices: UPC, COC, and SECON. Knight (2009)[73] suggested that high levels of continuity of care are associated with reduced hospitalizations in elderly people with diabetes. Other significant predictors of reduced hospitalizations were female sex, fewer chronic conditions, and higher income. Mainous (2004)[74] examined the relationship between continuity of care and diabetes control using the Third National Health and Nutrition Examination Survey data. The study showed that continuity of care is associated with better glycemic control among people with diabetes, however, the results do not support a benefit of having a usual provider above having a usual site of care.

Ascher-Svanum (2006)[75] examined low continuity of care was associated with poorer functional outcomes among schizophrenia patients. The continuity of care was calculated with MPR. Kabore (2014)[76] found that significant associations between self-reported adherence and MPR approaches to measuring antiretroviral therapy adherence. The associations between an objective metric (MPR) and subjective (self-reported adherence) adherence measures suggest that the latter has clinical value in monitoring antiretroviral therapy adherence. Voorham (2011)[77] showed that patients with lower MPR for antihypertensive drugs were more likely to have those medications discontinued or the dose decreased. For glucose-regulating medication, dose increases and medication additions were less likely in patients with lower adherence levels.

Atlas (2009)[78] found that being connected to a physician versus being connected to a practice significantly improved glycosylated hemogolbin (HbA1c) levels in

patients with diabetes. Atlas assessed patients' 'connectedness' with a physician or practice using a validated algorithm developed by the study authors, instead of using a previously published index of continuity to measure continuity. Lin (2009)[79] used the Fragmentation of Care Index (FCI) to assess continuity with clinic site; it did not assess individual care provider continuity. Lin reported that patients with more chronic diseases had higher fragmentation scores, which mean lower continuity, because they had more specialist appointments at different clinic sites. The study found that there was a significant association between the number of emergency department visits and the FCI. In addition, Lin (2009) reported a significant reduction in long-term complications leading to hospitalization in patients with high continuity of care compared to low continuity, but not compared to medium continuity. They did not report a significant difference in the relationship between continuity and short-term complications leading to hospitalization.

Ⅲ. METHODS

1. Study design

The conceptual framework of this study is based on the Chronic Care Model developted by Edward H. Wagner in 1996.[39] The Chronic Care Model is a system-level framework used to guide quality improvement efforts in health care. The purpose of this study is to evaluate the continuity of care on all-case mortality and disease specific mortality in hypertensive patients. Therefore, this study seek to examine whether or not high continuity of care impacts on all-cause mortality during 12 years follow-up and also ischemic heart disease mortality, ischemic stroke mortality, hemorrhagic and other non-ischemic stroke mortality, and hypertension related diseases mortality including hypertensive heart disease, chronic kidney disease due to hypertension during 5 years follow-up after adjusting confounding factors which may affect on patients' efficacy of disease management (Figure 4).

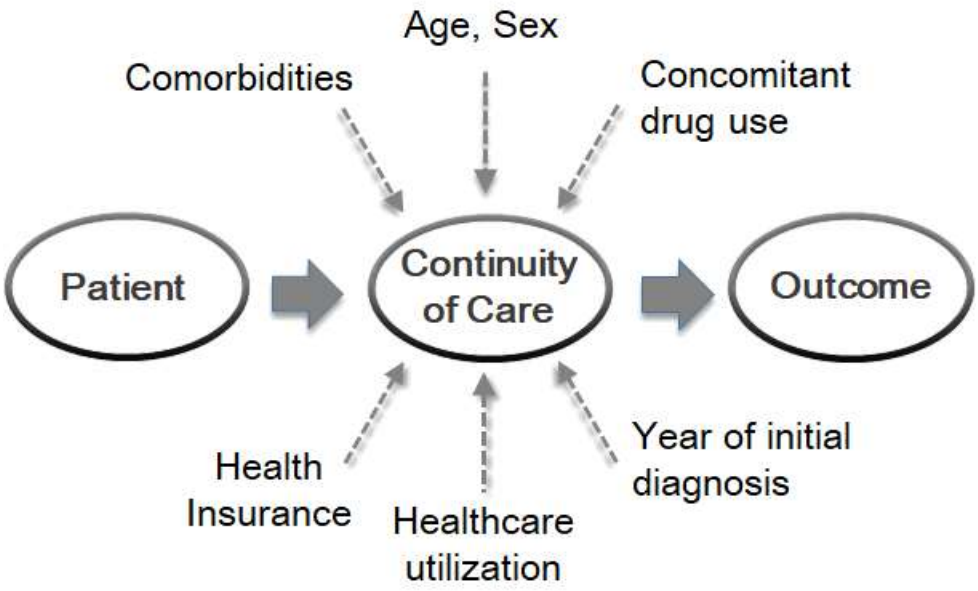

Figure 4. Framework of the study

2. Data source and study population

2.1. Data source

The study data was obtained from the National Sample Cohort 2002-2015 which was developed by the Korea National Health Insurance Service. The NHIS-NSC database, which began in 2014, is a set of claim data for the national representative 1 million individuals sample (2% of the Korean population). The first version[80] of the NHIS-NSC including prolonged follow-up durations from 2002 to 2013 was released in 2015 and the second version of the NHIS-NSC 2002-2015 was newly released in 2017. All reimbursement claims from 2002 to

2015 of these 1 million samples were included. The data include age and sex, healthcare use (clinic, hospital, and emergency department visits), diagnoses coded by International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), and prescription of medications covered by the NHIS.

2.2. Definition of hypertensive patients

The study population was defined as having newly developed hypertension if both of the following criteria met : (1) Patients had an inpatient care or an ambulatory visit with diagnosis of ICD-10 code of I10, I11, I12, I13 between 2002 through 2015. (2) Patients who have at least two ambulatory visits for prescriptions of antihypertensive agents and at least seven prescribed days of total for antihypertensive drugs prescription (except for the same date). To have a washout period, patients who received on the first hypertension related health care use during the year 2002 were excluded. Patients were aged at least 30 years on the first hypertension related health care use to be eligible for inclusion. In addition, patients who died in 3 months after hypertension diagnosis were excluded. After all, a total of 152,526 hypertensive patients were identified for the final study population (Figure 5).

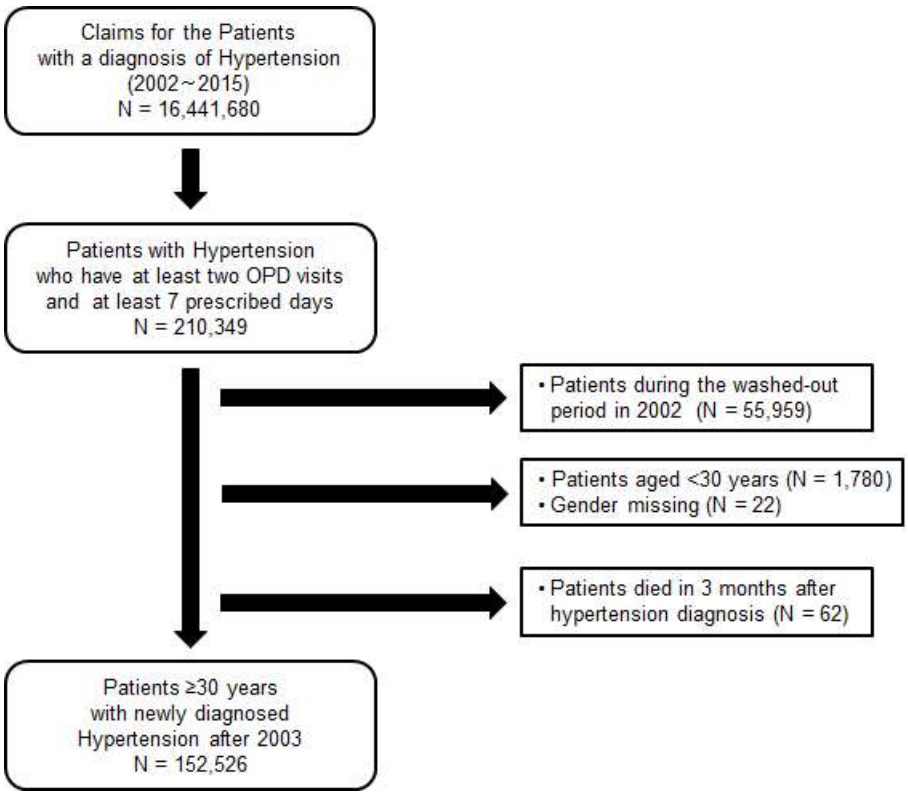

Figure 5. Flow diagram showing the process for selecting subjects

3. Measurements

3.1. Exposure of interest

Medication Possession Ratio for antihypertensive medications was considered the exposure of interest as a proxy of continuity of care for hypertension. During the time period from the first date of hypertension related health care use until the end of follow up, Medication Possession Ratio was calculated by the ratio of the number of total prescription days for antihypertensive medications divided by the total number of days a patient was observed. According to previous literatures regarding care persistency in hypertensive patients, persistence is usually defined as a categorical variable and defined as an adherence of 80% or higher.[81-83] If the total observation period was more than 6 months (180 days) and the MPR was more than 0.8, those patients were classified as High Continuity of Care group and others as Low Continuity of Care group.

3.2. Outcomes

The primary outcome of the study was all-cause mortality in 12 years follow-up. Secondary outcomes were ischemic heart disease mortality, ischemic stroke mortality, hemorrhagic and other non-ischemic stroke mortality, hypertension related disease mortality including hypertensive heart disease and chronic kidney disease due to hypertension in 5 years follow-up. Mortality and the cause of death were identified from death certificate data in the national death registry. The cause of death definition according to ICD-10 code by outcome category is summarized in the following table.

Table 4. ICD-10 codes for outcome events

Outcome	ICD-10 codes for cause of death
All-cause mortality	all
Ischemic heart disease mortality	I20-I25
Ischemic stroke mortality	I63, I65-I67
Hemorrhagic and other non-ischemic stroke mortality	I60-I62, I69
Hypertension related disease mortality : hypertensive heart disease, chronic kidney disease due to hypertension	I11-I13

Abbreviations: ICD-10, the 10th revision of the International Statistical Classification of Diseases and Related Health Problems

3.3. Co-variates

Based on the previous studies, demographic characteristics, comorbidities, Charlson comorbidity index, concomitant use of other medical drugs, initial year of hypertension diagnosis, type of health insurance, and health utilization were included as covariates in the analysis. The demographic characteristics included age, sex, and type of health insurance(national health insurnace or medical aids) were identified on the first date of hypertension related health care use. Comorbidities regarding medical history were identified using ICD-10 codes entered within one year prior to the first date of hypertension related health care use, and codes were categorized into disease groups. Charlson comorbidity index was calculated using ICD-10 codes entered within one year prior to the first date of hypertension related health care use, and index scores were categorized into two groups (CCI=0, CCI$\geq$1). Concomitant use of other medical drugs were

defined as drugs prescribed within one year prior to the first date of hypertension related health care use. Healthcare utilization was defined as any hospitalization, outpatient visit, or emergency department visit during the year prior to the first date of hypertension related health care use. The full list of co-variates is summarized in the following table.

Table 5. List of co-variates

Variables	Measures
Demographic characteristics	
Sex	Male, female (reference)
Age	Classified into 3 groups: 30-44, 45-64, over 65
Year of first hypertension	2003-2015 Classified into 13 groups : 2003(reference), 2004, 2005, ... 2015
Health insurance type	Medical aids, National Health Insurance (reference)
Charlson comorbidity index	Classified into 2 groups: 0 (reference), 1≤
Comorbidities	ICD-10 code
Diabetes	E10-14, H28.0, H36.0, M14.2, G59.0, G63.2, N08.3
Chronic heart disease	I34-37
Chronic lung disease	I27, J84, R09.2, E66.2, J43-47, J60-70, J92, J96, J98.2, J98.3
Cancer	C00-C43, C45-C97
Chronic liver disease	B18, I850, I859, I982, K70, K72-K75
Chronic kidney disease	M05-09, M30-34, M351, M353, M45
Chronic neurologic disease	G10-14, G20-26, G30-32, G35-37, G80-83
Concomitant drug use	ATC code
Antidepressant	N06A, N06CA
Anxiolytic	N05B, N05C
Dementia medication	N06DA04, N06DA03, N06DA02, N06DX01

Variables	Measures
Platelet inhibitor	B01AC
Lipid lowering agent	C10
Healthcare utilization	
Number of hospitalization	During the year prior to the initial diagnosis
Number of outpatient visit	During the year prior to the initial diagnosis
Number of emergency department visit	During the year prior to the initial diagnosis

Abbreviations: ICD-10, the 10th revision of the International Statistical Classification of Diseases and Related Health Problems; ATC, Anatomical Therapeutic Chemical Classification System

4. Statistical analysis

Baseline characteristics were compared between High Continuity of Care group and Low Continuity of Care group for all variables as follows: Frequencies and percentage of categorical variables were determined by using chi-square tests. Continous variables were determined by using t-test. Cumulative incidence rates of two groups during follow-up period were compared using Cox-proportional hazard model for single and multivariate analyses. The model 1 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, and number of emergency department visits during the year prior to the initial diagnosis. The model 2 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, Charlson comorbidity index, and 5 classes of concomitant drug use. The model 3 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, 7 categories of comorbidities, and 5 classes of concomitant drug use.

Based on the operational definition of Continuity of Care group, High Continuity of Care group included only patients with an observation period of 6 months or more, and this difference could affect the difference in mortality rates between groups. Therefore, a subgroup analysis for sensitivity test was performed excluding patients with total observation period of less than 6 months to examine the consistency of the results. In addition, subgroup analyses were conducted for entier covariates to find out the effectiveness of continuity of care stratified by covariates.

To evaluate the difference in disease-specific mortality rates between High Continuity of Care group and Low Continuity of Care group, the cumulative disease-specific death incidence in the two groups was compared using Cox-proportional hazard model for single and multivariate analyses. The model 1 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, and number of emergency department visits during the year prior to the initial diagnosis. The model 2 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, Charlson comorbidity index, and 5 classes of concomitant drug use. The model 3 was adjusted for sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, 7 categories of comorbidities, and 5 classes of concomitant drug use. In addition, subgroup analyses were conducted for entier covariates to find out the effectiveness of continuity of care stratified by covariates.

All the statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ⅳ. RESULTS

1. Characteristics of the Study Population

A total of 152,526 hypertensive patients aged over 30 years were included in the present study, of whom 69,068 (45.3% of the total) were identified as the High Continuity of Care group. The baseline characteristics of the study subjects are summarized in Table 4.

The proportion of males was slightly higher (79,862 of the total; 52.4%) than that of females. 82% of the total patients were aged over 45. Diabetes were most common comorbidity in both groups. 8,618 (12.5%) in the High Continuity of Care group and 10,897 (13.1%) in the Low Continuity of Care group had chronic lung disease. Patients in High Continuity of Care group showed slightly lower prevalence than those who in Low Continuity of Care group except for diabetes and chronic kidney diseases.

The year 2003 had more cases of hypertension than any of the other years (13.0% of the total), and there was a second peak (12.6% of the total) in 2005. Overall, patients in Low Continuity of Care group tended to be slightly younger, and showed higher healthcare utilization within the year prior to hypertension diagnosis.

Table 6. Baseline characteristics of study subjects

Variables	N(%)		P-value
	High Continuity of Care (n=69,068)	Low Continuity of Care (n=83,458)	
Demographic characteristics			
Sex			
male, n (%)	36,309 (52.6)	43,553 (52.2)	0.1346
female, n (%)	32,759 (47.4)	39,905 (47.8)	
Age, mean (range)	57 (30-94)	56 (30-94)	<.0001
30-44, n (%)	10,132 (14.7)	17,335 (20.8)	
45-64, n (%)	40,519 (58.7)	43,089 (51.6)	
over 65, n (%)	18,417 (26.7)	23,034 (27.6)	
Medical Aids, n (%)	4787 (6.9)	5440 (6.5)	0.0013
Charlson comorbidity index, mean (SD)	0.54 (0.9)	0.58 (0.9)	<.0001
Comorbidities within 1 years before diagnosis of hypertension			
Diabetes, n (%)	10,217 (14.8)	11,347 (13.6)	<.0001
Chronic heart disease, n (%)	4,741 (6.9)	5,862 (7.0)	0.2224
Chronic lung disease, n (%)	8,618 (12.5)	10,897 (13.1)	0.0007
Cancer, n (%)	1,354 (2.0)	1,839 (2.2)	0.0010
Chronic liver disease, n (%)	9,277 (13.4)	12,292 (14.7)	<.0001
Chronic kidney disease, n (%)	1,575 (2.3)	1,807 (2.2)	0.1283
Chronic neurologic disease, n (%)	3,511 (5.1)	4,506 (5.4)	0.0060
Concomitant drug use within 1 years before diagnosis of hypertension			
Antidepressant, n (%)	4,499 (6.5%)	6,408 (7.7%)	<.0001
Anxiolytic, n (%)	22,687 (32.8%)	30,032 (36.0%)	<.0001
Dimentia medication, n (%)	161 (0.2%)	299 (0.4%)	<.0001
Platelet inhibitor, n (%)	4,227 (6.1%)	4,131 (4.9%)	<.0001
Lipid lowering agent, n (%)	5,511 (8.0%)	5,216 (6.2%)	<.0001
Healthcare utilization within 1 years before diagnosis of hypertension			
Number of hospitalization, mean (SD)	0.14 (0.5)	0.17 (0.6)	<.0001
Number of outpatient visit, mean (SD)	11.90 (16.2)	11.32 (15.5)	<.0001
Number of ED visit, mean (SD)	0.07 (0.3)	0.07 (0.3)	<.0001
Year of initial hypertension diagnosis			
2003	7,815 (11.3%)	12,088 (14.5%)	<.0001
2004	6,864 (9.9%)	10,047 (12.0%)	
2005	8,503 (12.3%)	10,776 (12.9%)	
2006	6,202 (9.0%)	8,840 (10.6%)	
2007	5,513 (8.0%)	6,953 (8.3%)	
2008	5,481 (7.9%)	6,210 (7.4%)	
2009	5,328 (7.7%)	5,826 (7.0%)	

Variables	N(%)		P-value
	High Continuity of Care (n=69,068)	Low Continuity of Care (n=83,458)	
2010	4,848 (7.0%)	5,015 (6.0%)	
2011	4,549 (6.6%)	4,219 (5.1%)	
2012	4,466 (6.5%)	3,778 (4.5%)	
2013	3,993 (5.8%)	3,326 (4.0%)	
2014	3,582 (5.2%)	2,663 (3.2%)	
2015	1,924 (2.8%)	3,717 (4.5%)	

2. Continuity of Care and the number of deaths

The number of deaths among 152,526 hypertensive patients are shown in Table 5. The exact number of all-cause death during the study period is 4,527 (6.6% of total) in High Continuity of Care group and 10,356 (12.4% of total) in Low Continuity of Care group and which means the all-cause mortality rate per 1,000 person-year is 8.1 for High Continuity of Care group and 14.3 for Low Continuity of Care group, respectively. Among those, 367 (0.2%) patients died from ischemic heart disease, 229 (0.2%) patients died from ischemic stroke, 411 (0.3%) patients died from hemorrhagic and other non-ischemic stroke, and 102 (0.1%) patients died from hypertension related disease including hypertensive heart disease and chronic kidney disease due to hypertension in 5 years after hypertension diagnosis.

Among the High Continuity of Care group, deaths per 1,000 person-year of ischemic heart disease was the highest at 0.4, and among the Low Continuity of Care group, deaths per 1,000 person-year of hemorrhagic and other non-ischemic stroke was the highest at 0.8. Mortality rates per 1,000 person-year in the High Continuity of Care group, compared to the Low Continuity of Care group, were statistically significantly lower for all diseases, including all-cause mortality, except hypertension related disease.

Table 7. The number of deaths caused by outcome disease

Outcomes	High Continuity of Care (N=69,068)		Low Continuity of Care (N=83,458)		P^*
	No. of Deaths (%)	Deaths per 1,000 PY	No. of Deaths (%)	Deaths per 1,000 PY	
All-cause mortality	4,527 (6.6)	8.1	10,356 (12.4)	14.3	<.0001
Ischemic heart disease mortality in 5 years	135 (0.2)	0.4	232 (0.3)	0.6	.001
Ischemic stroke mortality in 5 years	56 (0.1)	0.2	173 (0.2)	0.5	<.0001
Hemorrhagic and other non-ischemic stroke mortality in 5 years	102 (0.1)	0.3	309 (0.4)	0.8	<.0001
Hypertension related disease mortality in 5 years	37 (0.1)	0.1	65 (0.1)	0.2	.068

* *P* value was calculated using the chi-squared test.

Abbreviations: PY, person years

3. Subgroup analysis for sensitivity test

Since the operational definition of the High Continuity of Care group was limited to patients with an observation period of more than 6 months, this could affect difference in mortality between groups. Therefore, to examine the consistency of the results, the subgroup analysis for the all-cause mortality was performed after excluding patients with total observation period of less than 6 months.

The number of total hypertensive patients was 152,526 and the number of subgroup excluding patients with total observation period of less than 6 months was 144,905. The hazard ratio (HR) of High Continuity of Care group for all-cause mortality of total patients, compared to Low Continuity of Care group, was 0.52 (95% confidence interval [CI]: 0.51-0.54, P<.0001). The incidence of all-cause mortality in patients with total observation period of more than 6 months was similar to the total patients (HR: 0.53, 95% CI: 0.51-0.55, P<.0001, Table 6).

In both whole population model and subgroup model, sex, age, year of hypertension diagnosis, medical aids, and healthcare utilization were significantly affect all-cause mortality. The degree and statistical significance of all-cause mortality for each class of concomitant drug use and comorbidities also showed consistent results in the whole population model and subgroup model. In hypertensive patients, factors associated with a higher risk of all-cause mortality included concomitant use of antidepressant, anxiolytic, dementia medication, lipid lowering agent and pre-existing conditions of diabetes, chronic heart disease, chronic lung disease, cancer, chronic kidney disease, chronic neurologic disease.

Table 8. Analysis of relationship between Continuity of Care groups and all-cause mortality in whole population and subgroup population

Variable	all-cause mortality for total patients (N=152,526)			all-cause mortality for patients with an observation period of more than 6 months (N=144,905)		
	Adjusted HR	95% CI	*P**	Adjusted HR	95% CI	*P**
Continuity of care group						
High	0.52	(0.51-0.54)	<.0001	0.53	(0.51-0.55)	<.0001
Low	1.00			1.00		
Sex						
Male	2.00	(1.93-2.07)	<.0001	2.00	(1.93-2.07)	<.0001
Female	1.00			1.00		
Age	1.10	(1.10-1.10)	<.0001	1.10	(1.10-1.10)	<.0001
Year of hypertension diagnosis	1.07	(1.06-1.07)	<.0001	1.06	(1.05-1.07)	<.0001
Medical Aids						
Yes	1.98	(1.88-2.07)	<.0001	1.98	(1.88-2.07)	<.0001
No	1.00			1.00		
Healthcare utilization						
Hospitalization	1.23	(1.19-1.26)	<.0001	1.23	(1.19-1.26)	<.0001
Outpatient visit	1.00	(0.99-1.00)	<.0001	1.00	(0.99-1.00)	<.0001
Emergency department visit	1.12	(1.05-1.18)	0.0002	1.11	(1.04-1.17)	0.0008

Variable	all-cause mortality for total patients (N=152,526)			all-cause mortality for patients with an observation period of more than 6 months (N=144,905)		
	Adjusted HR	95% CI	*P**	Adjusted HR	95% CI	*P**
Comorbidities						
Diabetes	1.35	(1.29-1.41)	<.0001	1.35	(1.29-1.41)	<.0001
Chronic heart disease	1.08	(1.02-1.15)	0.0132	1.08	(1.02-1.15)	0.0139
Chronic lung disease	1.11	(1.05-1.16)	<.0001	1.10	(1.05-1.15)	<.0001
Cancer	1.52	(1.38-1.67)	<.0001	1.47	(1.34-1.61)	<.0001
Chronic liver disease	1.01	(0.96-1.07)	0.6274	1.02	(0.96-1.07)	0.5417
Chronic kidney disease	1.16	(1.04-1.30)	0.0074	1.16	(1.04-1.30)	0.0088
Chronic neurologic disease	1.14	(1.07-1.22)	0.0001	1.15	(1.07-1.23)	<.0001
Concomitant drug use						
Antidepressant	1.17	(1.09-1.24)	<.0001	1.16	(1.09-1.24)	<.0001
Anxiolytic	0.83	(0.79-0.86)	<.0001	0.83	(0.80-0.86)	<.0001
Dementia medication	1.69	(1.39-2.06)	<.0001	1.71	(1.40-2.10)	<.0001
Platelet inhibitor	1.01	(0.93-1.09)	0.9078	1.00	(0.93-1.08)	0.9783
Lipid lowering agent	0.81	(0.75-0.88)	<.0001	0.81	(0.75-0.88)	<.0001

* *P* value was calculated using the Wald test.

Abbreviations: HR, Hazard Ratio; CI, confidence interva

4. Continuity of Care and the Risk of Disease-specific Mortality

This study was analyzed with four Cox proportional hazards models. First, crude model analysis was performed, including only the Continuity of Care group variable, which is the research interest in the model. Second, multivariate model 1 was performed including sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, and number of emergency department visits during the year prior to the initial diagnosis. Then multivariate model 2 was performed including sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, Charlson comorbidity index, and 5 classes of concomitant drug use. Finally, multivariate model 3 was performed including sex, age, year of diagnosis, health insurance type, number of hospitalization, number of outpatient visits, number of emergency department visits, 7 categories of comorbidities, and 5 classes of concomitant drug use.

4.1. Ischemic heart disease mortality

Deaths from ischemic heart disease occurred in 135 (0.2%) of those in High Continuity of Care group and 232 (0.3%) of those in Low Continuity of Care group (Table 5). The crude incidence of deaths from ischemic heart disease was significantly lower in the High Continuity of Care group (HR: 0.70, 95% CI: 0.57-0.87, P=0.001, Figure 6). In the multivariate model 3, factors associated with a higher risk of ischemic heart disease mortality included male sex, age, the older diagnostic year, medical aids beneficiaries, comorbidities with chronic heart disease, and concomitant anxiolytic or platelet inhibitor user. Based on the analysis from the multivariate model 3, the adjusted incidence of deaths from ischemic heart

disease was significantly lower in the High Continuity of Care group (HR: 0.76, 95% CI: 0.61-0.94, P=0.013, Figure 7). The results of multivariate model 1 and model 2 followed similar pattern (Table 7).

Table 9. Analysis of relationship between Continuity of Care groups and ischemic heart disease mortality

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*
Continuity of care group								
High	0.70 (0.57-0.87)	0.001	0.79 (0.64-0.99)	0.031	0.77 (0.62-0.96)	0.018	0.76 (0.61-0.94)	0.013
Low	1.00		1.00		1.00		1.00	
Sex								
Male			2.05 (1.67-2.53)	<.0001	1.95 (1.58-2.41)	<.0001	1.95 (1.58-2.41)	<.0001
Female			1.00		1.00		1.00	
Age			1.10 (1.09-1.11)	<.0001	1.10 (1.08-1.11)	<.0001	1.10 (1.08-1.11)	<.0001
Year of hypertension diagnosis			0.93 (0.90-0.96)	<.0001	0.92 (0.89-0.95)	<.0001	0.93 (0.90-0.96)	<.0001
Medical Aids								
Yes			2.23 (1.71-2.91)	<.0001	2.19 (1.68-2.86)	<.0001	2.23 (1.70-2.91)	<.0001
No			1.00		1.00		1.00	
Healthcare utilization								
Hospitalization			1.16 (1.03-1.30)	0.011	1.12 (0.97-1.28)	0.113	1.13 (0.98-1.30)	0.085
Outpatient visit			1.00 (0.99-1.00)	0.284	1.00 (0.99-1.01)	0.390	1.00 (0.99-1.01)	0.403
Emergency department visit			1.30 (1.06-1.59)	0.012	1.20 (0.95-1.50)	0.121	1.14 (0.89-1.45)	0.303
Charlson comorbidity index					1.08 (0.97-1.20)	0.163		

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Comorbidities								
Diabetes							1.24 (0.94-1.64)	0.124
Chronic heart disease							2.26 (1.67-3.07)	<.0001
Chronic lung disease							1.04 (0.79-1.38)	0.768
Cancer							0.53 (0.23-1.19)	0.123
Chronic liver disease							0.78 (0.56-1.09)	0.146
Chronic kidney disease							1.10 (0.57-2.15)	0.777
Chronic neurologic disease							1.04 (0.70-1.55)	0.843
Concomitant drug use								
Antidepressant					0.80 (0.52-1.23)	0.309	0.81 (0.53-1.25)	0.345
Anxiolytic					0.75 (0.59-0.95)	0.016	0.73 (0.57-0.93)	0.011
Dementia medication					1.21 (0.53-2.79)	0.655	1.35 (0.57-3.15)	0.493
Platelet inhibitor					1.98 (1.40-2.81)	0.000	1.53 (1.04-2.25)	0.032
Lipid lowering agent					1.14 (0.77-1.68)	0.518	1.00 (0.67-1.50)	0.984

* *P* value was calculated using the Wald test.

Abbreviations: HR, Hazard Ratio; CI, confidence interval

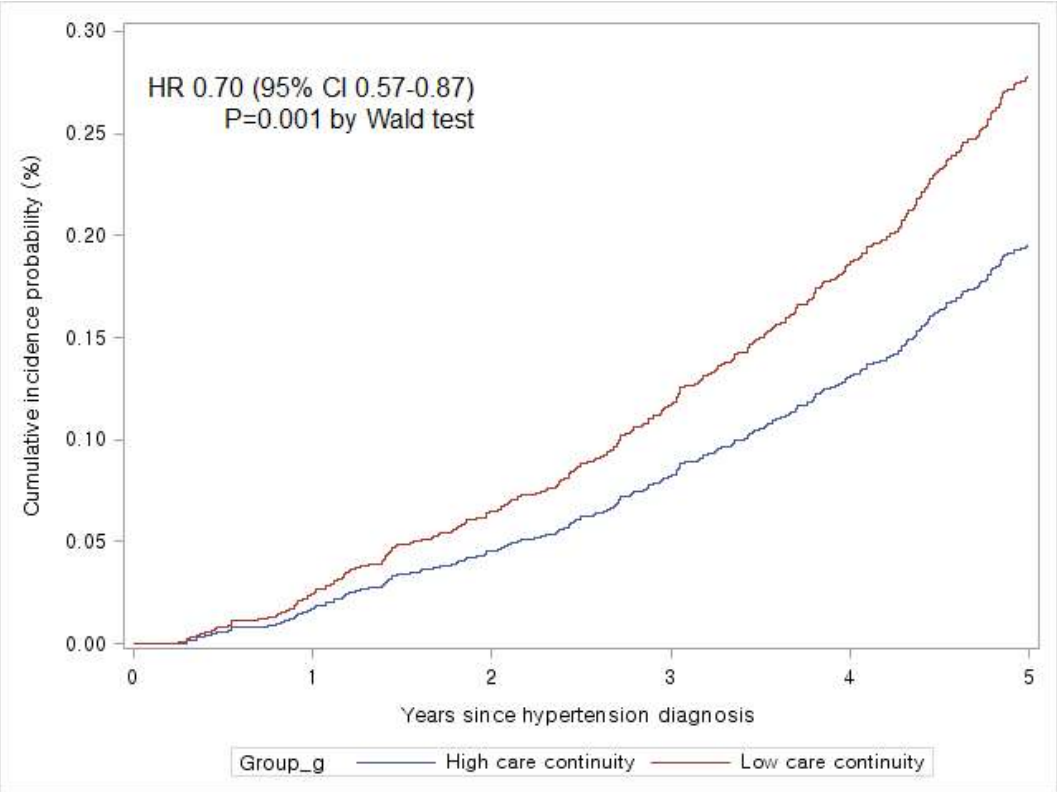

Figure 6. Time-to-event curves for crude incidence of ischemic heart disease deaths by continuity of care group

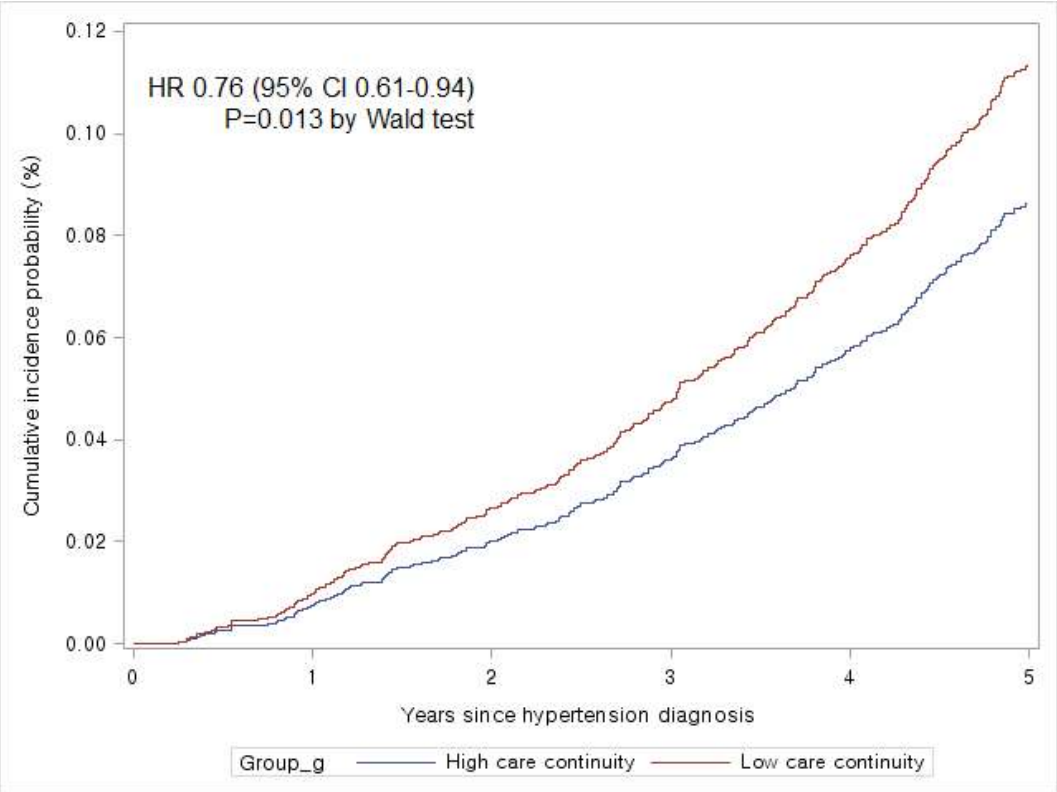

Figure 7. Time-to-event curves for adjusted incidence of ischemic heart disease deaths by continuity of care group

4.2. Ischemic stroke mortality

Deaths from ischemic stroke occurred in 56 (0.1%) of those in High Continuity of Care group and 173 (0.2%) of those in Low Continuity of Care group (Table 5). The crude incidence of deaths from ischemic stroke was significantly lower in the High Continuity of Care group (HR: 0.39, 95% CI: 0.29-0.53, P<.0001, Figure 8). In the multivariate model 3, factors associated with a higher risk of ischemic stroke mortality included male sex, age, the older diagnostic year, medical aids beneficiaries, number of hospitalization, and comorbidities with chronic neurologic disease. Based on the analysis from the multivariate model 3, the adjusted incidence of deaths from ischemic stroke was significantly lower in the High Continuity of Care group (HR: 0.47, 95% CI: 0.35-0.64, P<.0001, Figure 9). The results of multivariate model 1 and model 2 followed similar pattern (Table 8).

Table 10. Analysis of relationship between Continuity of Care groups and ischemic stroke mortality

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Continuity of care group								
High	0.39 (0.29-0.53)	<.0001	0.48 (0.35-0.65)	<.0001	0.47 (0.35-0.65)	<.0001	0.47 (0.35-0.64)	<.0001
Low	1.00		1.00		1.00		1.00	
Sex								
Male			1.51 (1.14-1.99)	0.004	1.47 (1.11-1.94)	0.007	1.51 (1.14-1.99)	0.004
Female			1.00		1.00		1.00	
Age			1.14 (1.12-1.15)	<.0001	1.13 (1.12-1.15)	<.0001	1.13 (1.11-1.15)	<.0001
Year of hypertension diagnosis			0.93 (0.90-0.97)	0.001	0.93 (0.89-0.97)	0.001	0.93 (0.89-0.97)	<.0001
Medical Aids								
Yes			2.18 (1.58-3.02)	<.0001	2.17 (1.57-2.99)	<.0001	2.18 (1.57-3.01)	<.0001
No			1.00		1.00		1.00	
Healthcare utilization								
Hospitalization			1.22 (1.08-1.38)	0.001	1.18 (1.02-1.35)	0.023	1.22 (1.07-1.39)	0.003
Outpatient visit			0.99 (0.97-1.00)	0.111	0.98 (0.96-1.01)	0.158	0.99 (0.97-1.01)	0.191
Emergency department visit			1.20 (1.84-1.70)	0.316	1.11 (0.76-1.60)	0.595	1.11 (0.76-1.61)	0.591
Charlson comorbidity index					1.10 (0.95-1.28)	0.221		

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Comorbidities								
Diabetes							1.07 (0.72-1.58)	0.750
Chronic heart disease							1.12 (0.68-1.85)	0.650
Chronic lung disease							1.01 (0.68-1.50)	0.964
Cancer							0.64 (0.23-1.77)	0.394
Chronic liver disease							0.65 (0.39-1.11)	0.113
Chronic kidney disease							0.26 (0.04-1.83)	0.177
Chronic neurologic disease							1.95 (1.30-2.93)	0.001
Concomitant drug use								
Antidepressant					1.24 (0.74-2.07)	0.417	1.20 (0.72-2.03)	0.483
Anxiolytic					0.84 (0.61-1.14)	0.259	0.85 (0.62-1.16)	0.295
Dementia medication					1.52 (0.66-3.52)	0.328	1.27 (0.55-2.95)	0.581
Platelet inhibitor					1.49 (0.96-2.31)	0.075	1.19 (0.74-1.89)	0.471
Lipid lowering agent					0.87 (0.47-1.62)	0.668	0.90 (0.48-1.69)	0.745

* *P* value was calculated using the Wald test.

Abbreviations: HR, Hazard Ratio; CI, confidence interval

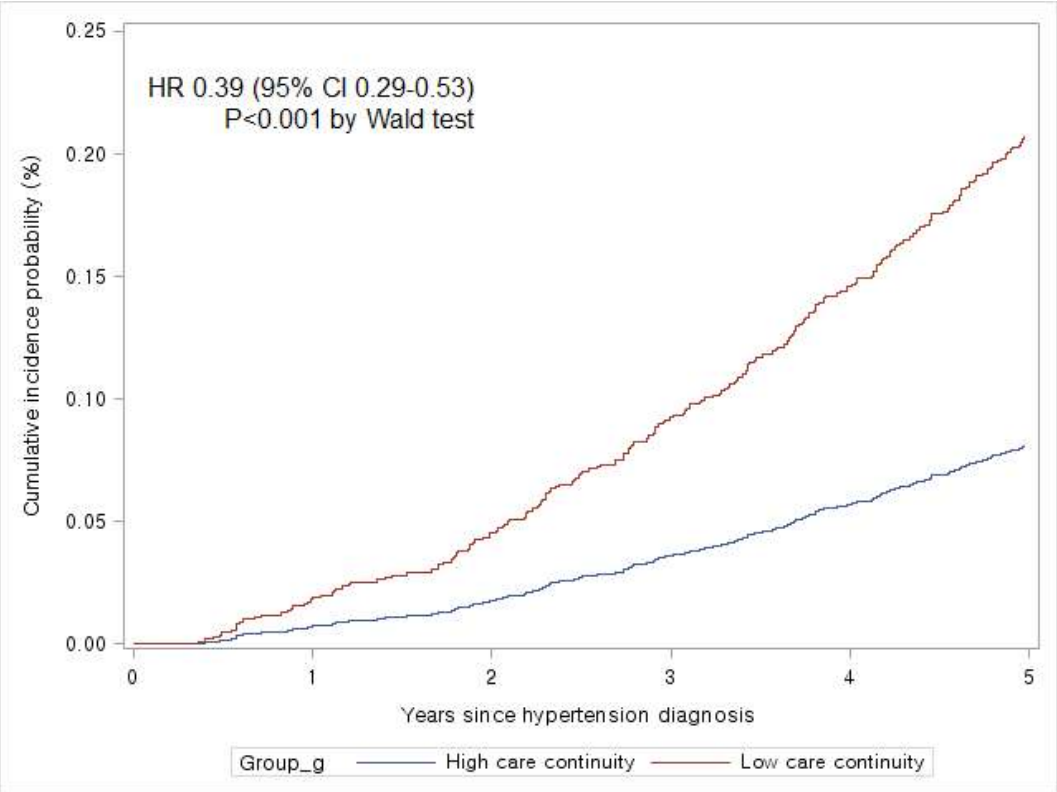

Figure 8. Time-to-event curves for crude incidence of ischemic stroke deaths by continuity of care group

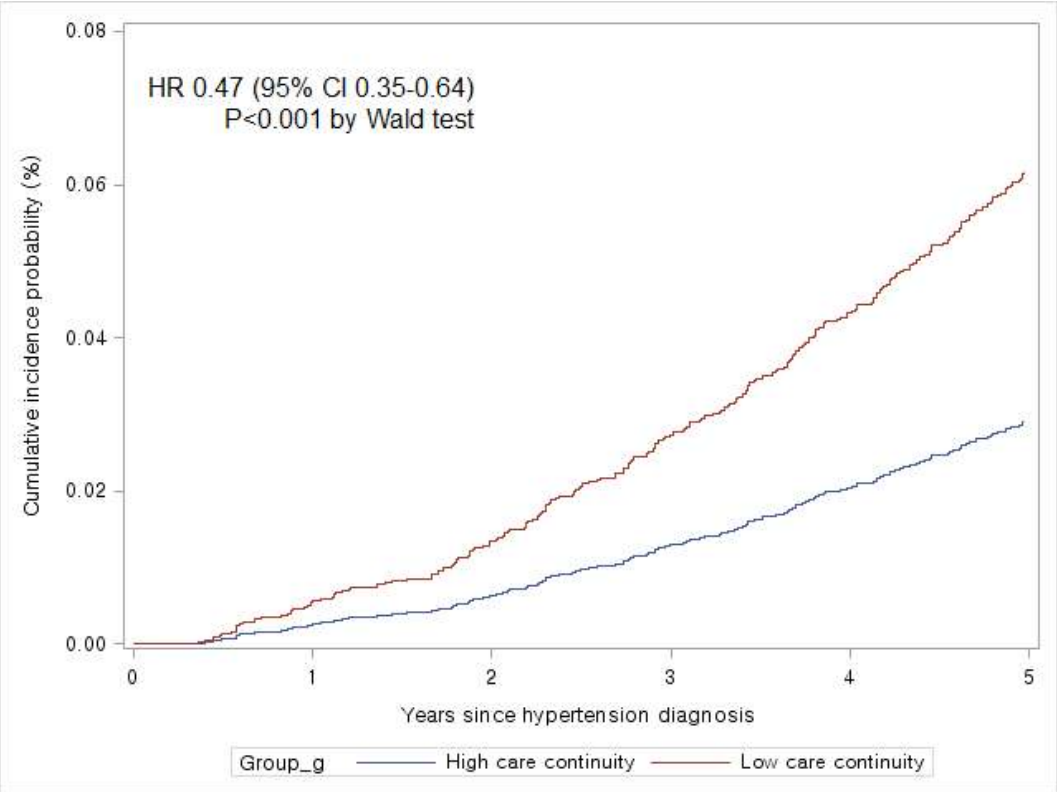

Figure 9. Time-to-event curves for adjusted incidence of ischemic stroke deaths by continuity of care group

4.3. Hemorrhagic and other non-ischemic stroke mortality

Deaths from hemorrhagic and other non-ischemic stroke occurred in 102 (0.1%) of those in High Continuity of Care group and 309 (0.4%) of those in Low Continuity of Care group (Table 5). The crude incidence of deaths from hemorrhagic and other non-ischemic stroke was significantly lower in the High Continuity of Care group (HR: 0.40, 95% CI: 0.32-0.50, P<.0001, Figure 10). In the multivariate model 3, factors associated with a higher risk of hemorrhagic and other non-ischemic stroke mortality included male sex, age, the older diagnostic year, medical aids beneficiaries, number of hospitalization, number of outpatient visit, comorbidities with chronic neurologic disease, and concomitant anxiolytic user. Based on the analysis from the multivariate model 3, the adjusted incidence of deaths from hemorrhagic and other non-ischemic stroke was significantly lower in the High Continuity of Care group (HR: 0.44, 95% CI: 0.35-0.55, P<.0001, Figure 11). Also, similar to crude analysis, the results of multivariate model 1 and model 2 showed significantly lower the risk of hemorrhagic and other non-ischemic stroke mortality in the High Continuity of Care group (Table 9).

Table 11. Analysis of relationship between Continuity of Care groups and hemorrhagic and other non-ischemic stroke mortality

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Continuity of care group								
High	0.40 (0.32-0.50)	<.0001	0.44 (0.35-0.55)	<.0001	0.44 (0.35-0.55)	<.0001	0.44 (0.35-0.55)	<.0001
Low	1.00		1.00		1.00		1.00	
Sex								
Male			1.49 (1.21-1.83)	<.0001	1.42 (1.16-1.75)	0.001	1.44 (1.17-1.78)	<.0001
Female			1.00		1.00		1.00	
Age			1.09 (1.08-1.10)	<.0001	1.08 (1.07-1.09)	<.0001	1.08 (1.07-1.09)	<.0001
Year of hypertension diagnosis			0.94 (0.91-0.96)	<.0001	0.93 (0.91-0.96)	<.0001	0.93 (0.90-0.96)	<.0001
Medical Aids								
Yes			2.07 (1.59-2.68)	<.0001	2.02 (1.56-2.62)	<.0001	2.01(1.56-2.60)	<.0001
No			1.00		1.00		1.00	
Healthcare utilization								
Hospitalization			1.27 (1.19-1.36)	<.0001	1.24 (1.15-1.33)	<.0001	1.27 (1.18-1.37)	<.0001
Outpatient visit			0.98 (0.97-0.99)	0.002	0.98 (0.96-0.99)	0.006	0.98 (0.97-1.00)	0.009
Emergency department visit			1.28 (1.07-1.53)	0.007	1.18 (0.98-1.43)	0.081	1.15 (0.94-1.41)	0.165
Charlson comorbidity index					1.09 (0.98-1.21)	0.119		

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Comorbidities								
Diabetes							1.08 (0.80-1.44)	0.624
Chronic heart disease							0.67 (0.44-1.01)	0.055
Chronic lung disease							0.91 (0.67-1.23)	0.553
Cancer							0.76 (0.38-1.51)	0.438
Chronic liver disease							0.91 (0.64-1.28)	0.576
Chronic kidney disease							0.86 (0.37-1.98)	0.716
Chronic neurologic disease							3.35 (2.51-4.48)	<.0001
Concomitant drug use								
Antidepressant					1.36 (0.95-1.94)	0.093	1.23 (0.85-1.76)	0.272
Anxiolytic					0.71 (0.55-0.91)	0.008	0.70 (0.54-0.90)	0.005
Dementia medication					1.34 (0.61-2.98)	0.467	0.88 (0.40-1.95)	0.757
Platelet inhibitor					2.00 (1.43-2.79)	<.0001	1.34 (0.94-1.91)	0.109
Lipid lowering agent					0.69 (0.43-1.12)	0.135	0.70 (0.43-1.14)	0.153

* *P* value was calculated using the Wald test.

Abbreviations: HR, Hazard Ratio; CI, confidence interval

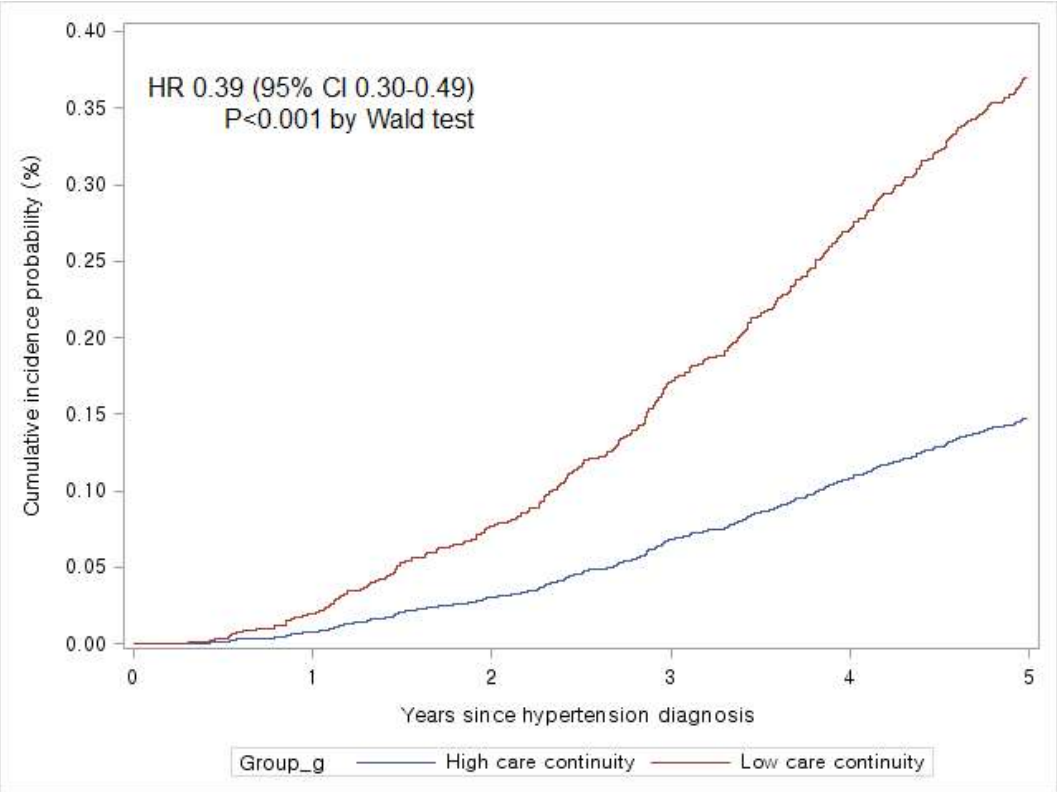

Figure 10. Time-to-event curves for crude incidence of hemorrhagic and other non-ischemic stroke deaths by continuity of care group

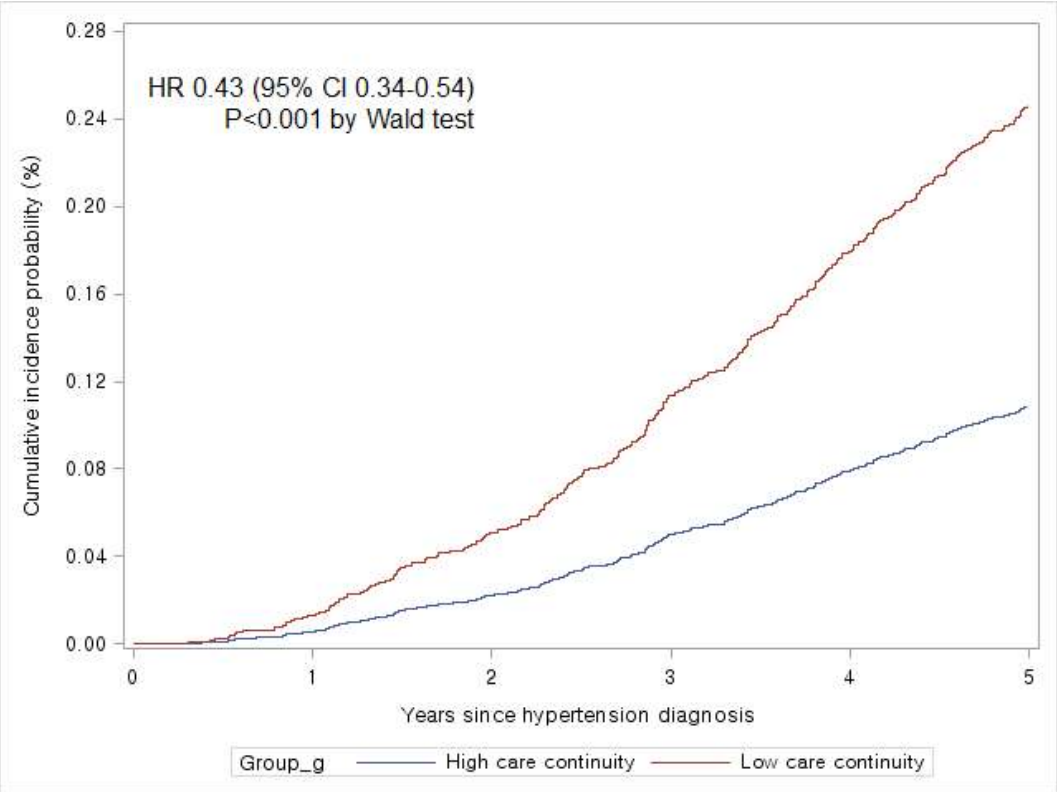

Figure 11. Time-to-event curves for adjusted incidence of hemorrhagic and other non-ischemic stroke deaths by continuity of care group

4.4. Hypertension related disease mortality

Deaths from hypertension related disease including hypertensive heart disease, chronic kidney disease due to hypertension occurred in 37 (0.1%) of those in High Continuity of Care group and 65 (0.1%) of those in Low Continuity of Care group (Table 5). There was no significant difference in the risk of hypertension related disease mortality in either the crude (HR: 0.69, 95% CI: 0.46-1.03, P=0.069, Figure 12), or the adjusted (HR: 0.87, 95% CI: 0.58-1.30, P=0.5, Figure 13) analysis from the multivariate model 3. Based on the analysis from the multivariate model 3, factors associated with a higher risk of hypertension related disease mortality included age, the older diagnostic year, medical aids beneficiaries, comorbidities with chronic heart disease and chronic kidney disease. In multivariate model 1 and model 2, there was no significant difference in hypertension related disease mortality between Continuity of Care groups (Table 10).

Table 12. Analysis of relationship between Continuity of Care groups and hypertension related disease mortality

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*	Adjusted HR (95% CI)	P^*
Continuity of care group								
High	0.69 (0.46-1.03)	0.069	0.89 (0.59-1.34)	0.568	0.89 (0.59-1.33)	0.553	0.87 (0.58-1.30)	0.500
Low	1.00		1.00		1.00		1.00	
Sex								
Male			0.88 (0.56-1.37)	0.570	0.84 (0.53-1.32)	0.452	0.83 (0.52-1.30)	0.408
Female			1.00		1.00		1.00	
Age			1.15 (1.11-1.19)	<.0001	1.15 (1.11-1.18)	<.0001	1.14 (1.11-1.18)	<.0001
Year of hypertension diagnosis			0.89 (0.83-0.96)	0.003	0.89 (0.83-0.95)	0.001	0.90 (0.83-0.97)	0.004
Medical Aids								
Yes			2.70 (1.73-4.23)	<.0001	2.58 (1.66-4.01)	<.0001	2.64 (1.70-4.09)	<.0001
No			1.00		1.00		1.00	
Healthcare utilization								
Hospitalization			1.19 (0.93-1.53)	0.171	1.21 (0.97-1.52)	0.097	1.19 (0.94-1.50)	0.151
Outpatient visit			0.99 (0.96-1.02)	0.486	1.00 (0.97-1.02)	0.934	1.00 (0.97-1.03)	0.901
Emergency department visit			1.09 (0.63-1.90)	0.754	1.11 (0.63-1.93)	0.722	1.01 (0.54-1.88)	0.975
Charlson comorbidity index					1.06 (0.83-1.36)	0.618		

Variable	Univariate		Multivariable Model 1		Multivariable Model 2		Multivariable Model 3	
	Crude HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**	Adjusted HR (95% CI)	*P**
Comorbidities								
Diabetes							1.20 (0.64-2.26)	0.572
Chronic heart disease							2.20 (1.18-4.09)	0.013
Chronic lung disease							1.22 (0.67-2.23)	0.514
Cancer							0.86 (0.20-3.64)	0.833
Chronic liver disease							0.42 (0.17-1.04)	0.060
Chronic kidney disease							3.79 (1.35-10.6)	0.011
Chronic neurologic disease							0.88 (0.35-2.22)	0.786
Concomitant drug use								
Antidepressant					0.40 (0.11-1.36)	0.141	0.39 (0.12-1.34)	0.135
Anxiolytic					0.64 (0.39-1.07)	0.089	0.62 (0.37-1.05)	0.075
Dementia medication					2.48 (0.68-9.01)	0.168	2.93 (0.79-10.8)	0.106
Platelet inhibitor					0.86 (0.33-2.22)	0.751	0.72 (0.23-2.29)	0.579
Lipid lowering agent					0.22 (0.03-1.73)	0.151	0.21 (0.03-1.53)	0.122

* *P* value was calculated using the Wald test.

Abbreviations: HR, Hazard Ratio; CI, confidence interval

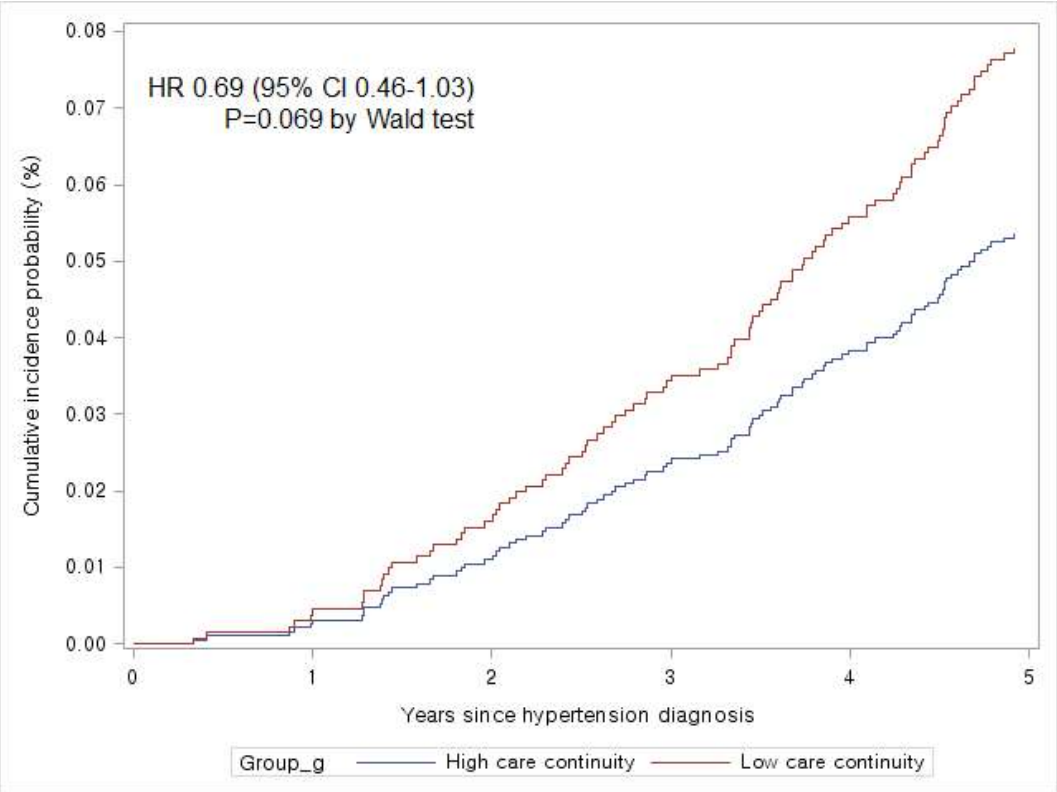

Figure 12. Time-to-event curves for crude incidence of hypertension related disease deaths by continuity of care group

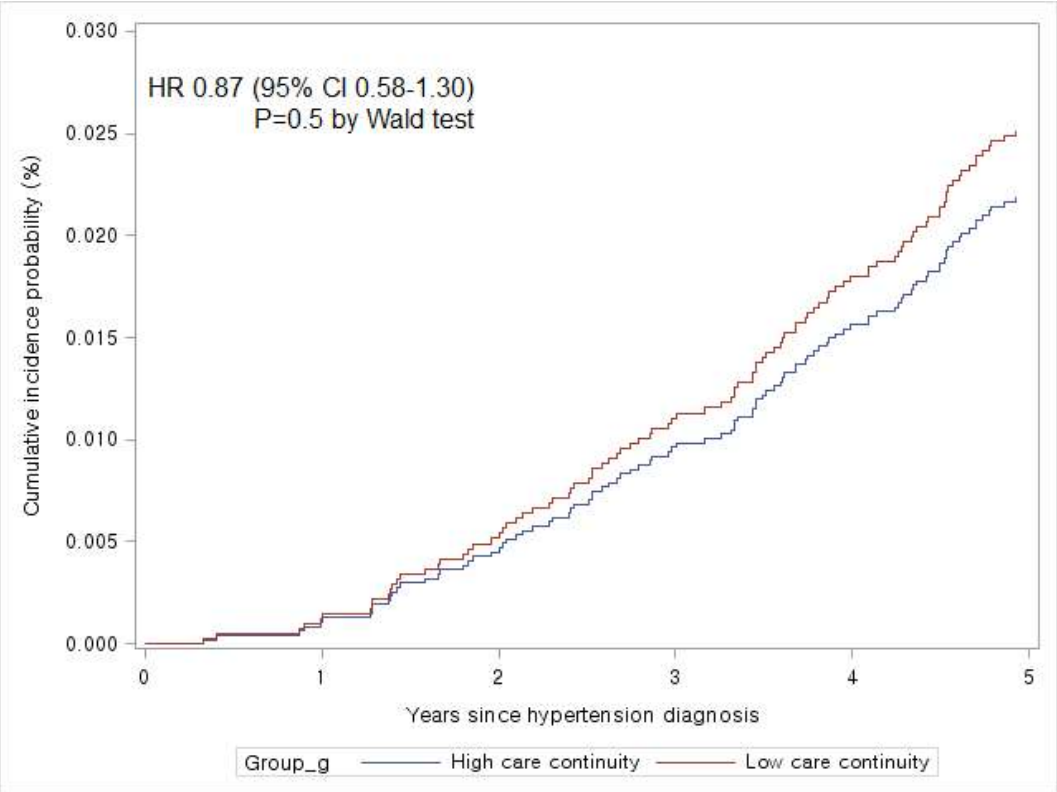

Figure 13. Time-to-event curves for adjusted incidence of hypertension related disease deaths by continuity of care group

5. Subgroup analysis of the Risk of All-Cause Mortality

This study was performed sensitivity analyses to determine whether changes in a clinically important variable would influence the effects of continuity of care on all-cause mortality in hypertensive patients. The beneficial effects of high continuity of care were maintained across most subgroups (Table 11).

Based on the results from the subgroup analysis, crude HR and adjusted HR were increased slightly in medical aids beneficiaries, patients having chronic health disease or chronic kidney disease, concomitant dimential medication, platelet inhibitor, or lipid lowering agent user. This means the beneficial effects of high continuity of care can be diminished among those subgroup patients.

Table 13. All-cause mortality in relation to High Continuity of Care or Low Continuity of Care after entry, based on various parameters in hypertensive patients

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Whole subjects	4,527	69,068	(6.6%)	10,356	83,458	(12.4%)	0.51	(0.50 -0.53)	0.52	(0.51 -0.54)
Sex										
male	2,535	36,309	(7.0%)	5,444	43,553	(12.5%)	0.53	(0.51 -0.56)	0.52	(0.49 -0.54)
female	1,992	32,759	(6.1%)	4,912	39,905	(12.3%)	0.49	(0.46 -0.52)	0.55	(0.52 -0.58)
Medical Aids										
Yes	1,056	4,787	(22.1%)	1,815	5,440	(33.4%)	0.55	(0.51 -0.59)	0.60	(0.56 -0.65)
No	3,471	64,281	(5.4%)	8,541	78,018	(10.9%)	0.49	(0.47 -0.51)	0.50	(0.48 -0.52)
Charlson comorbidity index										
≥ 1	1,845	25,420	(7.3%)	4,499	32,023	(14.0%)	0.52	(0.50 -0.55)	0.54	(0.51 -0.57)
0	2,682	43,648	(6.1%)	5,857	51,435	(11.4%)	0.51	(0.49 -0.54)	0.51	(0.48 -0.53)
Diabetes										
Yes	975	10,217	(9.5%)	1,893	11,347	(16.7%)	0.57	(0.53 -0.62)	0.57	(0.53 -0.62)
No	3,552	58,851	(6.0%)	8,463	72,111	(11.7%)	0.50	(0.48 -0.52)	0.51	(0.49 -0.53)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Chronic heart disease										
Yes	536	4,741	(11.3%)	967	5,862	(16.5%)	0.73	(0.65 -0.81)	0.72	(0.64 -0.80)
No	3,991	64,327	(6.2%)	9,389	77,596	(12.1%)	0.50	(0.48 -0.51)	0.50	(0.49 -0.52)
Chronic lung disease										
Yes	705	8,618	(8.2%)	1,792	10,897	(16.4%)	0.50	(0.46 -0.55)	0.55	(0.50 -0.60)
No	3,822	60,450	(6.3%)	8,564	72,561	(11.8%)	0.52	(0.50 -0.54)	0.52	(0.50 -0.54)
Cancer										
Yes	193	1,354	(14.3%)	443	1,839	(24.1%)	0.59	(0.50 -0.70)	0.57	(0.47 -0.68)
No	4,334	67,714	(6.4%)	9,913	81,619	(12.1%)	0.51	(0.49 -0.53)	0.52	(0.50 -0.54)
Chronic liver disease										
Yes	573	9,277	(6.2%)	1,410	12,292	(11.5%)	0.55	(0.50 -0.61)	0.55	(0.50 -0.61)
No	3,954	59,791	(6.6%)	8,946	71,166	(12.6%)	0.51	(0.49 -0.53)	0.52	(0.50 -0.54)
Chronic kidney disease										
Yes	124	1,575	(7.9%)	222	1,807	(12.3%)	0.67	(0.53 -0.83)	0.67	(0.54 -0.84)
No	4,403	67,493	(6.5%)	10,134	81,651	(12.4%)	0.51	(0.49 -0.53)	0.52	(0.50 -0.54)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic neurologic disease												
Yes	397	3,511	(11.3%)	961	4,506	(21.3%)	0.54	(0.48	-0.60)	0.56	(0.50	-0.64)
No	4,130	65,557	(6.3%)	9,395	78,952	(11.9%)	0.51	(0.50	-0.53)	0.52	(0.50	-0.54)
Antidepressant												
Yes	358	4,499	(8.0%)	948	6,408	(14.8%)	0.55	(0.48	-0.62)	0.55	(0.48	-0.62)
No	4,169	64,569	(6.5%)	9,408	77,050	(12.2%)	0.51	(0.49	-0.53)	0.52	(0.50	-0.54)
Anxiolytic												
Yes	1,496	22,687	(6.6%)	3,864	30,032	(12.9%)	0.51	(0.48	-0.55)	0.55	(0.51	-0.58)
No	3,031	46,381	(6.5%)	6,492	53,426	(12.2%)	0.51	(0.49	-0.54)	0.51	(0.49	-0.53)
Dimentia medication												
Yes	43	161	(26.7%)	120	299	(40.1%)	0.74	(0.52	-1.06)	0.67	(0.47	-0.96)
No	4,484	68,907	(6.5%)	10,236	83,159	(12.3%)	0.52	(0.50	-0.53)	0.52	(0.50	-0.54)
Platelet inhibitor												
Yes	413	4,227	(9.8%)	671	4,131	(16.2%)	0.66	(0.58	-0.74)	0.69	(0.61	-0.78)
No	4,114	64,841	(6.3%)	9,685	79,327	(12.2%)	0.50	(0.48	-0.52)	0.51	(0.49	-0.53)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Lipid lowering agent												
Yes	280	5,511	(5.1%)	418	5,216	(8.0%)	0.67	(0.57	-0.78)	0.66	(0.56	-0.77)
No	4,247	63,557	(6.7%)	9,938	78,242	(12.7%)	0.51	(0.49	-0.53)	0.52	(0.50	-0.54)

* HR was adjusted for all the other covariates.

6. Subgroup analysis of the Risk of Disease-Specific Mortality

This study was performed sensitivity analyses to determine whether changes in a clinically important variable would influence the effects of continuity of care on disease-specific mortality in hypertensive patients.

The results from the subgroup analysis of the risk of ischemic heart disease mortality are shown in Table 12. The beneficial effects of high continuity of care were maintained when there was no comorbidity except chronic lung disease. There is no beneficial effects of high continuity of care on those hypertensive patients with diabetes. And more, patients taking another medication can have no beneficial effects of high continuity of care.

The results from the subgroup analysis of the risk of ischemic stroke mortality are shown in Table 13. The beneficial effects of high continuity of care were maintained across most subgroup group except those who have any other diseases. The beneficial effects of high continuity of care were maintained among those who have chronic neurologic disease.

The results of subgroup analysis for the risk of hemorrhagic and other non-ischemic stroke mortality are shown in Table 14. Hypertensive patient with any other diseases except chronic liver disease could have no beneficial effects of high continuity of care. In addition, there is no beneficial effects of high continuity of care among those who taking another medications except anxiolytic. The beneficial effects of high continuity of care were maintaned across the group of the Charlson comorbidity index. There is no beneficial effects of high continuity of care on the risk of hypertension related disease mortality across all subgroups (Table 15).

Table 14. Ischemic heart disease mortality in relation to High Continuity of Care or Low Continuity of Care after entry, based on various parameters in hypertensive patients

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Whole subjects	135	69,068	(0.2%)	232	83,458	(0.3%)	0.70	(0.57 -0.87)	0.76	(0.61 -0.94)
Sex										
male	83	36,309	(0.2%)	121	43,553	(0.3%)	0.82	(0.62 -1.09)	0.83	(0.62 -1.10)
female	52	32,759	(0.2%)	111	39,905	(0.3%)	0.57	(0.41 -0.79)	0.72	(0.52 -1.02)
Medical Aids										
Yes	33	4,787	(0.7%)	56	5,440	(1.0%)	0.67	(0.43 -1.03)	0.69	(0.45 -1.05)
No	102	64,281	(0.2%)	176	78,018	(0.2%)	0.70	(0.55 -0.90)	0.78	(0.61 -1.00)
Charlson comorbidity index										
≥ 1	62	25,420	(0.2%)	98	32,023	(0.3%)	0.80	(0.58 -1.10)	0.88	(0.63 -1.22)
0	73	43,648	(0.2%)	134	51,435	(0.3%)	0.64	(0.48 -0.85)	0.67	(0.50 -0.89)
Diabetes										
Yes	25	10,217	(0.2%)	46	11,347	(0.4%)	0.60	(0.37 -0.98)	0.63	(0.39 -1.04)
No	110	58,851	(0.2%)	186	72,111	(0.3%)	0.72	(0.57 -0.92)	0.80	(0.63 -1.02)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic heart disease												
Yes	39	4,741	(0.8%)	31	5,862	(0.5%)	1.56	(0.97	-2.50)	1.50	(0.90	-2.49)
No	96	64,327	(0.1%)	201	77,596	(0.3%)	0.58	(0.45	-0.73)	0.63	(0.49	-0.81)
Chronic lung disease												
Yes	26	8,618	(0.3%)	38	10,897	(0.3%)	0.87	(0.53	-1.42)	0.99	(0.60	-1.63)
No	109	60,450	(0.2%)	194	72,561	(0.3%)	0.67	(0.53	-0.85)	0.71	(0.56	-0.90)
Cancer												
Yes	4	1,354	(0.3%)	2	1,839	(0.1%)	2.72	(0.50	-14.8)	2.74	(0.35	-21.6)
No	131	67,714	(0.2%)	230	81,619	(0.3%)	0.69	(0.55	-0.85)	0.74	(0.60	-0.92)
Chronic liver disease												
Yes	17	9,277	(0.2%)	25	12,292	(0.2%)	0.90	(0.49	-1.67)	0.99	(0.52	-1.89)
No	118	59,791	(0.2%)	207	71,166	(0.3%)	0.68	(0.54	-0.85)	0.74	(0.59	-0.93)
Chronic kidney disease												
Yes	3	1,575	(0.2%)	6	1,807	(0.3%)	0.57	(0.14	-2.29)	0.68	(0.14	-3.36)
No	132	67,493	(0.2%)	226	81,651	(0.3%)	0.71	(0.57	-0.88)	0.76	(0.61	-0.95)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic neurologic disease												
Yes	15	3,511	(0.4%)	24	4,506	(0.5%)	0.80	(0.42	-1.53)	0.88	(0.45	-1.71)
No	120	65,557	(0.2%)	208	78,952	(0.3%)	0.70	(0.55	-0.87)	0.75	(0.59	-0.94)
Antidepressant												
Yes	8	4,499	(0.2%)	16	6,408	(0.2%)	0.71	(0.30	-1.66)	0.81	(0.32	-2.06)
No	127	64,569	(0.2%)	216	77,050	(0.3%)	0.70	(0.56	-0.87)	0.76	(0.61	-0.95)
Anxiolytic												
Yes	44	22,687	(0.2%)	73	30,032	(0.2%)	0.80	(0.55	-1.16)	0.90	(0.61	-1.31)
No	91	46,381	(0.2%)	159	53,426	(0.3%)	0.66	(0.51	-0.85)	0.70	(0.54	-0.91)
Dimentia medication												
Yes	4	161	(2.5%)	2	299	(0.7%)	3.75	(0.69	-20.4)	3.49	(0.15	-79.6)
No	131	68,907	(0.2%)	230	83,159	(0.3%)	0.69	(0.55	-0.85)	0.74	(0.60	-0.92)
Platelet inhibitor												
Yes	23	4,227	(0.5%)	28	4,131	(0.7%)	0.80	(0.46	-1.39)	0.86	(0.48	-1.55)
No	112	64,841	(0.2%)	204	79,327	(0.3%)	0.67	(0.53	-0.85)	0.75	(0.59	-0.94)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Lipid lowering agent										
Yes	14	5,511	(0.3%)	15	5,216	(0.3%)	0.88	(0.43 -1.83)	0.95	(0.43 -2.09)
No	121	63,557	(0.2%)	217	78,242	(0.3%)	0.69	(0.55 -0.86)	0.75	(0.59 -0.93)

* HR was adjusted for all the other covariates.

Table 15. Ischemic stroke mortality in relation to High Continuity of Care or Low Continuity of Care after entry, based on various parameters in hypertensive patients

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Whole subjects	56	69,068	(0.1%)	173	83,458	(0.2%)	0.39	(0.29 -0.53)	0.47	(0.35 -0.64)
Sex										
male	25	36,309	(0.1%)	75	43,553	(0.2%)	0.40	(0.25 -0.63)	0.44	(0.27 -0.70)
female	31	32,759	(0.1%)	98	39,905	(0.2%)	0.39	(0.26 -0.58)	0.48	(0.32 -0.74)
Medical Aids										
Yes	19	4,787	(0.4%)	49	5,440	(0.9%)	0.44	(0.26 -0.75)	0.49	(0.28 -0.84)
No	37	64,281	(0.1%)	124	78,018	(0.2%)	0.36	(0.25 -0.52)	0.46	(0.32 -0.68)
Charlson comorbidity index										
≥ 1	20	25,420	(0.1%)	79	32,023	(0.2%)	0.32	(0.20 -0.52)	0.39	(0.23 -0.64)
0	36	43,648	(0.1%)	94	51,435	(0.2%)	0.45	(0.31 -0.66)	0.54	(0.36 -0.80)
Diabetes										
Yes	9	10,217	(0.1%)	23	11,347	(0.2%)	0.43	(0.20 -0.94)	0.53	(0.24 -1.18)
No	47	58,851	(0.1%)	150	72,111	(0.2%)	0.38	(0.28 -0.53)	0.47	(0.33 -0.65)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic heart disease												
Yes	5	4,741	(0.1%)	18	5,862	(0.3%)	0.34	(0.13	-0.92)	0.39	(0.13	-1.16)
No	51	64,327	(0.1%)	155	77,596	(0.2%)	0.40	(0.29	-0.54)	0.48	(0.35	-0.67)
Chronic lung disease												
Yes	10	8,618	(0.1%)	26	10,897	(0.2%)	0.49	(0.23	-1.01)	0.68	(0.32	-1.44)
No	46	60,450	(0.1%)	147	72,561	(0.2%)	0.38	(0.27	-0.52)	0.44	(0.31	-0.62)
Cancer												
Yes	3	1,354	(0.2%)	1	1,839	(0.1%)	4.08	(0.76	-21.8)	7.83	(0.54	-15.4)
No	53	67,714	(0.1%)	172	81,619	(0.2%)	0.37	(0.27	-0.51)	0.45	(0.33	-0.61)
Chronic liver disease												
Yes	3	9,277	(0.0%)	14	12,292	(0.1%)	0.28	(0.08	-0.99)	0.33	(0.10	-1.10)
No	53	59,791	(0.1%)	159	71,166	(0.2%)	0.40	(0.29	-0.54)	0.48	(0.35	-0.67)
Chronic kidney disease												
Yes	0	1,575	(0.0%)	1	1,807	(0.1%)	-					
No	56	67,493	(0.1%)	172	81,651	(0.2%)	0.39	(0.29	-0.53)	0.48	(0.35	-0.65)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic neurologic disease												
Yes	8	3,511	(0.2%)	29	4,506	(0.6%)	0.35	(0.16	-0.77)	0.37	(0.17	-0.82)
No	48	65,557	(0.1%)	144	78,952	(0.2%)	0.40	(0.29	-0.56)	0.49	(0.35	-0.69)
Antidepressant												
Yes	6	4,499	(0.1%)	15	6,408	(0.2%)	0.57	(0.22	-1.47)	0.63	(0.24	-1.60)
No	50	64,569	(0.1%)	158	77,050	(0.2%)	0.38	(0.27	-0.52)	0.45	(0.33	-0.63)
Anxiolytic												
Yes	19	22,687	(0.1%)	58	30,032	(0.2%)	0.43	(0.26	-0.73)	0.53	(0.31	-0.91)
No	37	46,381	(0.1%)	115	53,426	(0.2%)	0.37	(0.26	-0.54)	0.45	(0.31	-0.66)
Dimentia medication												
Yes	1	161	(0.6%)	5	299	(1.7%)	0.37	(0.04	-3.13)	0.00	(0.00	-0.02)
No	55	68,907	(0.1%)	168	83,159	(0.2%)	0.40	(0.29	-0.54)	0.48	(0.35	-0.65)
Platelet inhibitor												
Yes	5	4,227	(0.1%)	19	4,131	(0.5%)	0.26	(0.10	-0.69)	0.31	(0.11	-0.88)
No	51	64,841	(0.1%)	154	79,327	(0.2%)	0.41	(0.30	-0.56)	0.50	(0.36	-0.69)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Lipid lowering agent												
Yes	1	5,511	(0.0%)	10	5,216	(0.2%)	0.10	(0.01	-0.74)	0.10	(0.01	-1.02)
No	55	63,557	(0.1%)	163	78,242	(0.2%)	0.42	(0.31	-0.56)	0.50	(0.37	-0.69)

* HR was adjusted for all the other covariates.

Table 16. Hemorrhagic and other non-ischemic stroke mortality in relation to High Continuity of Care or Low Continuity of Care after entry, based on various parameters in hypertensive patients

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Whole subjects	102	69,068	(0.1%)	309	83,458	(0.4%)	0.40	(0.32 -0.50)	0.44	(0.35 -0.55)
Sex										
male	44	36,309	(0.1%)	159	43,553	(0.4%)	0.33	(0.24 -0.46)	0.34	(0.24 -0.47)
female	58	32,759	(0.2%)	150	39,905	(0.4%)	0.47	(0.35 -0.64)	0.57	(0.42 -0.77)
Medical Aids										
Yes	31	4,787	(0.6%)	66	5,440	(1.2%)	0.53	(0.35 -0.82)	0.55	(0.36 -0.85)
No	71	64,281	(0.1%)	243	78,018	(0.3%)	0.35	(0.27 -0.46)	0.40	(0.31 -0.52)
Charlson comorbidity index										
≥ 1	40	25,420	(0.2%)	126	32,023	(0.4%)	0.40	(0.28 -0.57)	0.46	(0.32 -0.66)
0	62	43,648	(0.1%)	183	51,435	(0.4%)	0.40	(0.30 -0.53)	0.42	(0.32 -0.56)
Diabetes										
Yes	21	10,217	(0.2%)	41	11,347	(0.4%)	0.57	(0.34 -0.96)	0.62	(0.36 -1.07)
No	81	58,851	(0.1%)	268	72,111	(0.4%)	0.37	(0.29 -0.47)	0.41	(0.32 -0.52)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic heart disease												
Yes	9	4,741	(0.2%)	18	5,862	(0.3%)	0.62	(0.28	-1.38)	0.73	(0.32	-1.70)
No	93	64,327	(0.1%)	291	77,596	(0.4%)	0.39	(0.30	-0.49)	0.43	(0.34	-0.54)
Chronic lung disease												
Yes	15	8,618	(0.2%)	39	10,897	(0.4%)	0.49	(0.27	-0.88)	0.63	(0.33	-1.18)
No	87	60,450	(0.1%)	270	72,561	(0.4%)	0.39	(0.30	-0.49)	0.42	(0.33	-0.53)
Cancer												
Yes	2	1,354	(0.1%)	7	1,839	(0.4%)	0.39	(0.08	-1.87)	0.46	(0.09	-2.49)
No	100	67,714	(0.1%)	302	81,619	(0.4%)	0.40	(0.32	-0.50)	0.44	(0.35	-0.55)
Chronic liver disease												
Yes	8	9,277	(0.1%)	35	12,292	(0.3%)	0.30	(0.14	-0.65)	0.32	(0.15	-0.70)
No	94	59,791	(0.2%)	274	71,166	(0.4%)	0.41	(0.32	-0.52)	0.45	(0.36	-0.57)
Chronic kidney disease												
Yes	1	1,575	(0.1%)	5	1,807	(0.3%)	0.23	(0.03	-1.96)	0.29	(0.05	-1.77)
No	101	67,493	(0.1%)	304	81,651	(0.4%)	0.40	(0.32	-0.50)	0.44	(0.35	-0.56)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic neurologic disease												
Yes	18	3,511	(0.5%)	66	4,506	(1.5%)	0.35	(0.21	-0.59)	0.39	(0.23	-0.67)
No	84	65,557	(0.1%)	243	78,952	(0.3%)	0.42	(0.32	-0.53)	0.45	(0.35	-0.58)
Antidepressant												
Yes	11	4,499	(0.2%)	26	6,408	(0.4%)	0.60	(0.30	-1.22)	0.70	(0.34	-1.46)
No	91	64,569	(0.1%)	283	77,050	(0.4%)	0.38	(0.30	-0.49)	0.42	(0.33	-0.53)
Anxiolytic												
Yes	27	22,687	(0.1%)	95	30,032	(0.3%)	0.38	(0.25	-0.58)	0.45	(0.29	-0.70)
No	75	46,381	(0.2%)	214	53,426	(0.4%)	0.40	(0.31	-0.52)	0.44	(0.34	-0.57)
Dimentia medication												
Yes	2	161	(1.2%)	5	299	(1.7%)	0.74	(0.14	-3.82)	1.43	(0.17	-12.1)
No	100	68,907	(0.1%)	304	83,159	(0.4%)	0.40	(0.32	-0.50)	0.44	(0.35	-0.55)
Platelet inhibitor												
Yes	14	4,227	(0.3%)	34	4,131	(0.8%)	0.40	(0.22	-0.75)	0.51	(0.26	-1.02)
No	88	64,841	(0.1%)	275	79,327	(0.3%)	0.39	(0.31	-0.50)	0.43	(0.34	-0.55)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Lipid lowering agent												
Yes	5	5,511	(0.1%)	14	5,216	(0.3%)	0.34	(0.12	-0.94)	0.36	(0.12	-1.04)
No	97	63,557	(0.2%)	295	78,242	(0.4%)	0.40	(0.32	-0.51)	0.44	(0.35	-0.56)

* HR was adjusted for all the other covariates.

Table 17. Hypertension related disease mortality in relation to High Continuity of Care or Low Continuity of Care after entry, based on various parameters in hypertensive patients

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Whole subjects	37	69,068	(0.1%)	65	83,458	(0.1%)	0.69	(0.46 -1.03)	0.87	(0.58 -1.30)
Sex										
male	12	36,309	(0.0%)	18	43,553	(0.0%)	0.80	(0.39 -1.66)	0.92	(0.44 -1.90)
female	25	32,759	(0.1%)	47	39,905	(0.1%)	0.65	(0.40 -1.05)	0.86	(0.53 -1.40)
Medical Aids										
Yes	15	4,787	(0.3%)	24	5,440	(0.4%)	0.71	(0.37 -1.35)	0.81	(0.40 -1.64)
No	22	64,281	(0.0%)	41	78,018	(0.1%)	0.65	(0.39 -1.09)	0.86	(0.52 -1.43)
Charlson comorbidity index										
≥ 1	14	25,420	(0.1%)	20	32,023	(0.1%)	0.88	(0.45 -1.75)	1.19	(0.60 -2.36)
0	23	43,648	(0.1%)	45	51,435	(0.1%)	0.60	(0.36 -1.00)	0.74	(0.44 -1.22)
Diabetes										
Yes	7	10,217	(0.1%)	7	11,347	(0.1%)	1.11	(0.39 -3.17)	1.36	(0.49 -3.79)
No	30	58,851	(0.1%)	58	72,111	(0.1%)	0.63	(0.41 -0.98)	0.80	(0.51 -1.25)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic heart disease												
Yes	6	4,741	(0.1%)	8	5,862	(0.1%)	0.93	(0.32	-2.67)	0.90	(0.30	-2.71)
No	31	64,327	(0.0%)	57	77,596	(0.1%)	0.66	(0.42	-1.02)	0.85	(0.54	-1.32)
Chronic lung disease												
Yes	6	8,618	(0.1%)	11	10,897	(0.1%)	0.69	(0.26	-1.86)	1.09	(0.39	-3.05)
No	31	60,450	(0.1%)	54	72,561	(0.1%)	0.69	(0.44	-1.07)	0.84	(0.54	-1.30)
Cancer												
Yes	0	1,354	(0.0%)	2	1,839	(0.1%)	-			-		
No	37	67,714	(0.1%)	63	81,619	(0.1%)	0.71	(0.47	-1.06)	0.90	(0.60	-1.35)
Chronic liver disease												
Yes	3	9,277	(0.0%)	2	12,292	(0.0%)	1.99	(0.33	-11.9)	2.12	(0.30	-14.8)
No	34	59,791	(0.1%)	63	71,166	(0.1%)	0.64	(0.42	-0.97)	0.83	(0.55	-1.25)
Chronic kidney disease												
Yes	3	1,575	(0.2%)	2	1,807	(0.1%)	1.72	(0.29	-10.3)	2.36	(0.19	-28.6)
No	34	67,493	(0.1%)	63	81,651	(0.1%)	0.65	(0.43	-0.99)	0.85	(0.56	-1.30)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR			Adjusted HR		
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)		aHR*	(95% CI)	
Chronic neurologic disease												
Yes	3	3,511	(0.1%)	4	4,506	(0.1%)	0.96	(0.22	-4.30)	2.42	(0.43	-13.7)
No	34	65,557	(0.1%)	61	78,952	(0.1%)	0.67	(0.44	-1.02)	0.83	(0.55	-1.25)
Antidepressant												
Yes	1	4,499	(0.0%)	2	6,408	(0.0%)	0.71	(0.06	-7.85)	0.77	(0.16	-3.80)
No	36	64,569	(0.1%)	63	77,050	(0.1%)	0.68	(0.45	-1.03)	0.86	(0.57	-1.30)
Anxiolytic												
Yes	9	22,687	(0.0%)	18	30,032	(0.1%)	0.66	(0.30	-1.47)	0.83	(0.38	-1.83)
No	28	46,381	(0.1%)	47	53,426	(0.1%)	0.69	(0.43	-1.10)	0.88	(0.55	-1.41)
Dimentia medication												
Yes	1	161	(0.6%)	2	299	(0.7%)	0.93	(0.08	-10.2)	1.47	(0.04	-54.0)
No	36	68,907	(0.1%)	63	83,159	(0.1%)	0.69	(0.46	-1.04)	0.87	(0.58	-1.31)
Platelet inhibitor												
Yes	2	4,227	(0.0%)	3	4,131	(0.1%)	0.65	(0.11	-3.90)	1.50	(0.07	-31.5)
No	35	64,841	(0.1%)	62	79,327	(0.1%)	0.69	(0.46	-1.05)	0.88	(0.58	-1.35)

Variables	High Continuity of Care			Low Continuity of Care			Crude HR		Adjusted HR	
	Death(N)	Total(N)	(%)	Death(N)	Total(N)	(%)	HR	(95% CI)	aHR*	(95% CI)
Lipid lowering agent										
Yes	1	5,511	(0.0%)	0	5,216	(0.0%)	-		-	
No	36	63,557	(0.1%)	65	78,242	(0.1%)	0.68	(0.45 -1.02)	0.84	(0.56 -1.26)

* HR was adjusted for all the other covariates.

V. DISCUSSION

1. Discussion of Study Methods

This study was to investigate whether or not better care continuity is expected to improve patient outcome and reduce mortality among hypertensive patients by using representative nationwide cohort data. There could be some issues raised regarding the study methods.

First, this study used the operational definition to identify hypertensive patients rather than using actual measured blood pressure values. The present study used the operational definition for having newly developed hypertension if both of the following criteria met : (1) Patients had an inpatient care or an ambulatory visit with diagnosis of ICD-10 code of I10, I11, I12, I13 between 2002 through 2015. (2) Patients who have at least two ambulatory visits for prescriptions of antihypertensive agents and at least seven prescribed days of total for antihypertensive drugs prescription (except for the same date). Most of studies used the actual measured blood pressure value as the definition of hypertension to identify patients with hypertension. When using administrative claim data, higher positive predictive values for identifying patients can be obtained with combination of ICD, procedure codes, incorporate medications or procedure codes.[84-87] Dispite these efforts, the study populations may be underestimated because of strict definition of study population.

Second, there might be a selection bias of the study sample. This study data were collected from the National Sample Cohort data rather than entire population data file. Therefore, the frequency of newly developed patient were decreased as time goes on. Therefore, the study results for recently developed patients could not be generalized.

This study has the following limitations to be considered during interpreting the results. Because this study used administrative claim-based data for the study analysis, the person who had no healthcare services but had high blood pressure might not include in the study population.

In addition, like all claims-based analyses, the risk adjustment model lacks clinical detail that may be associated with both care continuity measurement and study outcomes. Unmeasured severity of illness or adverse health outcomes could be a confounder. For example, patients with mild conditions may show lower care continuity level but show better outcomes of mortality, while patients experiencing adverse health outcomes may lead to change health care provider along with increasing visit rates but show worse outcomes of mortality.

In this study, the definition for continuity of care used the Medication Posset ion Ratio (MPR) which is about the prescription days for the study medication. If a person who were in an intensive care unit for the more fatal condition and the priority of controlling blood pressure was not high enough then the person's MPR is low and this kind of situation may not be fully captured in this study. In the study, person who died in three months right after hypertension diagnosis were excluded.

Because of many missing values in smoking, drinking, and exercise variables, the association between the variables and the outcomes of interest may not be fully captured in this study. Whether or not a patient possesses a primary healthcare provider and whether or not care other then hypertension treatment continues overtime could not be included in the analysis because of data unavailability.

2. Discussion of Study Results

With the prolonged average life expectancy, the elderly population is rapidly increasing, and hypertension is a common chronic diseases among the elderly. In particular, the prevalence of hypertension developed the risk of causing related complications and even mortality due to the characteristics of the elderly population with multi morbidity. Using the National Sample Cohort 2002-2015, this study demonstrated that hypertensive patients with high continuity of care were associated with a reduced risk of mortality in later in life.

Compared with hypertensive patients in the Low Continuity of Care group, the High Continuity of Care group showed significantly lower all-cause mortality. In addition, the High Continuity of Care group showed significantly lower mortality rates in deaths from ischemic heart disease, ischemic stroke, and hemorrhagic and other non-ischemic stroke, compared to the Low Continuity of Care group, and this finding remained even after adjusting for personal factors and behavior factors. However, there was no significant difference between the two groups in mortality rates regarding hypertension related disease including hypertensive heart disease and chronic kidney disease due to hypertension.

According to previous published reports, hypertension has been known to be a critical risk factor for the development of coronary artery disease, stroke, and chronic kidney disease. A report using the National Health and Nutrition Examination Survey (1988-1994) data showed uncontrolled hypertension increase the risk of all-cause and cardiovascular disease mortality.[44] Several studies proved strong evidence that lowering blood pressure through effective treatment of

hypertension significantly reduced the risk of cardiovascular disease events,[44,46] ischemic heart disease,[45] stroke[46-50] and heart failure.[46] Most previous studies were to compare all-cause mortality and disease-specific mortality between uncontrolled hypertensive patients and those who had not been diagnosed with hypertension.

In a study[88] conducted on patients with low risk cardiovascular disease and mild hypertension, comparison of treated and untreated hypertensive patients showed that there was no significant difference in development of cardiovascular disease and overall mortality. The study about treated and untreated hypertensive patients only followed for a median of 5.8 years. The present study provides a more accurate answer to the question of whether there is an association between hypertension management and mortality since it examined the association during a median 11 follow-up years.

Hypertension and diabetes are the leading chronic diseases in Korea and are a major cause of the risk of cardiovascular and cerebrovascular disease and death. In the present study, we expected continuity of care to have a protective effect on the time to death, the ultimate healthcare outcome. The results from our study confirmed there was a significant protective effect on the death from ischemic heart disease, ischemic stroke, and hemorrhagic and other non-ischemic stroke. Because hypertension is one of the commonest cardiovascular ailments and cardiovascular disease and stroke are major causes of death in Korea, the results would not be surprised.

However, our study results could not confirm the association between continuity of care effect and the death from hypertensive heart disease or chronic kidney disease. Majority of studies[51-54] strongly support that hypertension and chronic

kidney disease are closely interlinked pathophisiologic states and hypertension is both a cause and effect of chronic kidney disease. Therefore, hypertension management is important in patients with chronic kidney disease because sustain hypertension can lead to worsening and progressing kidney function. However, the effect of lowering blood pressure on renal failure is remain debated.[46] Similar to the previous study results, there was no association between hypertension management and mortality rates regarding hypertension related disease including hypertensive heart disease and chronic kidney disease due to hypertension in the present study. In addition, the total number of death from hypertensive heart disease or chronic kidney disease was relatively small compared to other disease-specific mortality and this might be another possible explanation about the unsignificant association between the continuity of care and the death from hypertensive heart disease or chronic kidney disease. Therefore, further research on the effects of continuity of care on hypertension related disease mortality is needed. This is especially important because thesedays health policy about hypertension management assumes more importance with increasing aged population.

In terms of the risk of ischemic heart disease mortality, the beneficial effects of high continuity of care were maintained when there was no comorbidity except chronic lung disease. And more, patients taking another medication can have no beneficial effects of high continuity of care. In addition, the beneficial effects of high continuity of care on ischemic stroke mortality and hemorrhagic and other non-ischemic stroke was slightly decrease or disappeared when those who have another diseases or take another medication. There is no beneficial effects of high continuity of care on the risk of hypertension related disease mortality across all

subgroups.

These findings can be interpreted that the beneficial effects of high continuity of care would be large in relatively mild early detected hypertensive patients who do not have any underlying disease and do not take other drugs in combination. Therefore, it suggests that it is necessary to prepare policy implementation and guidelines to increase the continuity of care for newly diagnosed patients with hypertension.

The concept of continuity of care is getting increased and it is considered as a hallmark of quality of care for chronic disease management. However, there is little researches conducted about the association between continuity of care and healthcare outcome because defining continuity of care for research, policy, or quality assessment is extremely complex because continuity of care is conceptualized in many different ways by health care professionals and researchers across communities and population. These findings could affect implications to change healthcare system and health care policy promoting continuity of care.

Ⅵ. CONCLUSION

Using national, population-based claim data, the present study investigated that the association between the level of care continuity and the outcomes of interest including all-cause mortality, ischemic heart disease mortality, ischemic stroke mortality, hemorrhagic and other non-ischemic stroke mortality, and hypertension related disease mortality. The results were consistent across analytic models adjusted for personal factors and behavioral factors which could affect the level of care continuity and the outcomes of interest. The results of this study confirmed that controlling hypertension through high continuity of care decrease the risk of all-cause mortality, ischemic heart disease mortality, ischemic stroke mortality, and hemorrhagic and other non-ischemic stroke mortality, suggesting that optimal care should support improve and maintain care continuity.

The increasing number of patients with chronic diseases, including hypertension, increases the economic burden of health care costs on the individual, as well as the social and national burdens, and increases the mortality rate from chronic diseases and related complications. Therefore, in order to effectively manage chronic diseases, it is now necessary to shift the paradigm to aggressive early detection and treatment expansion policies rather than prevention-oriented policies.

REFERENCE

1. Mills K, Stefanescu A, He J. The global epidemiology of hypertension. *Nature Reviews Nephrology*. 2020;16(4):223-237.

2. Marengoni A, Winblad B, Karp A, Fratiglioni L. Prevalence of Chronic Diseases and Multimorbidity Among the Elderly Population in Sweden. *Am J Public Health*. 2008;98(7):1198-1200.

3. de Bruin S, Heijink R, Lemmens L, Struijs J, Baan C. Impact of disease management programs on healthcare expenditures for patients with diabetes, depression, heart failure or chronic obstructive pulmonary disease: A systematic review of the literature. *Health Policy*. 2011;101(2):105-121.

4. Starfield B, Kinder K. Multimorbidity and its measurement. *Health Policy*. 2011;103(1):3-8.

5. Sarnak M, Levey A, Schoolwerth A et al. Kidney Disease as a Risk Factor for Development of Cardiovascular Disease. *Hypertension*. 2003;42(5):1050-1065.

6. Menke A, Casagrande S, Geiss L, Cowie C. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012. *JAMA*. 2015;314(10):1021.

7. Tobias D, Stuart J, Li S et al. Association of History of Gestational Diabetes With Long-term Cardiovascular Disease Risk in a Large Prospective Cohort of US Women. *JAMA Intern Med*. 2017;177(12):1735.

8. Cloutier L, Lamarre-Cliche M. Hypertension in Adults With Type 2 Diabetes: A Review of Blood Pressure Measurement Methods, Targets and Therapy. *Can J Diabetes*. 2018;42(2):188-195.

9. Cheung B, Li C. Diabetes and Hypertension: Is There a Common Metabolic Pathway?. *Curr Atheroscler Rep*. 2012;14(2):160-166.

10. Uijen A, van de Lisdonk E. Multimorbidity in primary care: Prevalence and trend over the last 20 years. *European Journal of General Practice*. 2008;14(sup1):28-32.

11. Marengoni A, Angleman S, Melis R et al. Aging with multimorbidity: A systematic review of the literature. *Ageing Res Rev*. 2011;10(4):430-439.

12. Jakovljević M, Ostojić L. Comorbidity and multimorbidity in medicine today: challenges and opportunities for bringing separated branches of medicine closer to each other. *Medicina Academica Mostariensia*. 2013;1(1):18−28.

13. Barnett K, Mercer S, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet*. 2012;380(9836):37-43.

14. Boyd C, Fortin M. Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design?. *Public Health Rev*. 2010;32(2):451-474.

15. World Health Organization. The European health report 2012. World Health Organization Regional Office for Europe. http://www.euro.who.int/__data/assets/pdf_file/0004/197113/EHR2012-Eng.pdf. Published 2013. Accessed June 16, 2020.

16. World Health Organization. Preventing chronic diseases. A vital investment. World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/43314/9241563001_eng.pdf?sequence=1. Published 2005. Accessed June 16, 2020.

17. Kim H, Cho M. Korea hypertension fact sheet 2018. *Clin Hypertens*. 2018;24(1).

18. Saultz J. Interpersonal Continuity of Care and Care Outcomes: A Critical Review. *The Annals of Family Medicine*. 2005;3(2):159-166.

19. Gulliford M, Naithani S, Morgan M. What is 'continuity of care'?. *J Health Serv Res Policy*. 2006;11(4):248-250.

20. American Academy of Family Physicians. Continuity of Care, Definition of. Aafp.org. https://www.aafp.org/about/policies/all/definition-care.html. Published 2015. Accessed June 16, 2020.

21. Haggerty J. Continuity of care: a multidisciplinary review. *BMJ*. 2003;327(7425):1219-1221.

22. Saultz J. Defining and Measuring Interpersonal Continuity of Care. *The Annals of Family Medicine*. 2003;1(3):134-143.

23. Jee S, Cabana M. Indices for Continuity of Care: A Systematic Review of the Literature. *Medical Care Research and Review*. 2006;63(2):158-188.

24. Gulliford M, Naithani S, Morgan M. Measuring Continuity of Care in Diabetes Mellitus: An Experience-Based Measure. *The Annals of Family Medicine*. 2006;4(6):548-555.

25. Uijen A, Schellevis F, van den Bosch W, Mokkink H, van Weel C, Schers H. Nijmegen Continuity Questionnaire: Development and testing of a questionnaire that measures continuity of care. *J Clin Epidemiol*. 2011;64(12):1391-1399.

26. Boyd C, Darer J, Boult C, Fried L, Boult L, Wu A. Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Comorbid Diseases. *JAMA*. 2005;294(6):716.

27. Saultz J. Interpersonal Continuity of Care and Patient Satisfaction: A Critical Review. *The Annals of Family Medicine*. 2004;2(5):445-451.

28. Nutting P, Goodwin M, Flocke S, Zyzanski S, Stange K. Continuity of Primary Care: To Whom Does It Matter and When?. *The Annals of Family Medicine*. 2003;1(3):149-155.

29. Kearley K, Freeman G, Heath A. An exploration of the value of the personal doctor-patient relationship in general practice. *Br J Gen Pract*. 2001;51(470):712-718.

30. Schers H, Webster S, van den Hoogen H, Avery A, van den Bosch W. Continuity of care in general practice: a survey of patients' views. *Br J Gen Pract*. 2002;52(479):459-462.

31. Bice T, Boxerman S. A Quantitative Measure of Continuity of Care. *Med Care*. 1977;15(4):347-349.

32. Breslau N, Haug M. Service Delivery Structure and Continuity of Care: A Case Study of a Pediatric Practice in Process of Reorganization. *J Health Soc Behav*. 1976;17(4):339−352.

33. Steinwachs D. Measuring Provider Continuity in Ambulatory Care. *Med Care*. 1979;17(6):551-565.

34. Magill M, Senf J. A new method for measuring continuity of care in family practice residencies. *J Fam Pract*. 1987;24(2):165-168.

35. Andrade S, Kahler K, Frech F, Chan K. Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiol Drug Saf*. 2006;15(8):565-574.

36. Reid R, Haggerty J, McKendry R. Defusing the confusion: concepts and measures of continuity of healthcare. Researchgate. https://www.researchgate.net/profile/Jeannie_Haggerty/publication/245856177_Defusing_the_Confusion_Concepts_and_Measures_of_Continuity_of_Health_Care/links/56c31f9308ae8a6fab59ed74/Defusing-the-Confusion-Concepts-and-Measures-of-Continuity-of-Health-Care.pdf. Published 2020. Accessed June 16, 2020.

37. Sikka R, Xia F, Aubert RE. Estimating medication persistency using administrative claims data. *Am J Manag Care.* 2005;11(7):449−457.

38. Bodenheimer T. Patient Self-management of Chronic Disease in Primary Care. *JAMA*. 2002;288(19):2469.

39. Wagner E, Austin B, Korff M. Organizing Care for Patients with Chronic Illness. *Milbank Q*. 1996;74(4):511-544.

40. Wielawski I. Improving chronic illness care. In To Improve Health and Health Care. http://www.improvingchroniccare.org/downloads/rwjf_anthology_icic.pdf. Published 2006. Accessed June 16, 2020.

41. World Health Organization. Innovative Care for Chronic Conditions: Building Blocks for Action. World Health Organization. https://www.who.int/chp/knowledge/publications/icccglobalreport.pdf. Published 2002. Accessed June 16, 2020.

42. Lorig K. Chronic Disease Self-Management Program: Insights from the Eye of the Storm. *Front Public Health*. 2015;2.

43. Naylor M, Brooten D, Campbell R, Maislin G, McCauley K, Schwartz J. Transitional Care of Older Adults Hospitalized with Heart Failure: A Randomized, Controlled Trial. *J Am Geriatr Soc*. 2004;52(5):675-684.

44. Zhou D, Xi B, Zhao M, Wang L, Veeranki S. Uncontrolled hypertension increases risk of all-cause and cardiovascular disease mortality in US adults: the NHANES III Linked Mortality Study. *Sci Rep*. 2018;8(1).

45. Rosendorff C, Black H, Cannon C et al. Treatment of Hypertension in the Prevention and Management of Ischemic Heart Disease. *Circulation*. 2007;115(21):2761-2788.

46. Ettehad D, Emdin C, Kiran A et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *The Lancet*. 2016;387(10022):957-967.

47. Bowry R, Navalkele D, Gonzales N. Blood pressure management in stroke: Five new things. *Neurology: Clinical Practice*. 2014;4(5):419-426.

48. Aiyagari V, Gorelick P. Management of Blood Pressure for Acute and Recurrent Stroke. *Stroke*. 2009;40(6):2251-2256.

49. Appleton J, Sprigg N, Bath P. Blood pressure management in acute stroke. *BMJ*. 2016;1(2):72-82.

50. Wajngarten M, Silva G. Hypertension and Stroke: Update on Treatment. *European Cardiology Review*. 2019;14(2):111-115.

51. Moore M, Epstein M, Agodoa L, Dworkin L. Current Strategies for Management of Hypertensive Renal Disease. *Arch Intern Med*. 1999;159(1):23.

52. Sinha A, Agarwal R. Clinical Pharmacology of Antihypertensive Therapy for the Treatment of Hypertension in CKD. *Clinical Journal of the American Society of Nephrology*. 2018;14(5):757-764.

53. Ku E, Lee B, Wei J, Weir M. Hypertension in CKD: Core Curriculum 2019. *American Journal of Kidney Diseases*. 2019;74(1):120-131.

54. Pugh D, Gallacher P, Dhaun N. Management of Hypertension in Chronic Kidney Disease. *Drugs*. 2019;79(4):365-379.

55. Chobanian A. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003;289(19):2560.

56. Vasan R, Larson M, Leip E, Kannel W, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. *The Lancet*. 2001;358(9294):1682-1686.

57. Vasan R, Beiser A, Seshadri S et al. Residual Lifetime Risk for Developing Hypertension in Middle-aged Women and Men. *JAMA*. 2002;287(8).

58. Lee J, Yang D, Park H et al. Incidence of Hypertension in Korea: 5-Year Follow-up Study. *J Korean Med Sci*. 2011;26(10):1286.

59. Choi J, Jang J, An Y, Park S. Blood Pressure and the Risk of Death From Non-cardiovascular Diseases: A Population-based Cohort Study of Korean Adults. *Journal of Preventive Medicine and Public Health*. 2018;51(6):298-309.

60. Kang S, Kim S, Cho J et al. Prevalence, Awareness, Treatment, and Control of Hypertension in Korea. *Sci Rep*. 2019;9(1).

61. Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. *The Lancet*. 2000;356(9246):1955-1964.

62. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *The Lancet*. 2002;360(9349):1903-1913.

63. Ezzati M, Lopez A, Rodgers A, Vander Hoorn S, Murray C. Selected major risk factors and global and regional burden of disease. *The Lancet*. 2002;360(9343):1347-1360.

64. Sever P, Dahlöf B, Poulter N et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *The Lancet*. 2003;361(9364):1149-1158.

65. Nordestgaard B. Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease. *Circ Res*. 2016;118(4):547-563.

66. Third Report of the National Cholesterol Education Program (NCEP) Expert

Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. *Circulation*. 2002;106(25):3143-3143.

67. Banach M, Aronow W, Chandy. Current perspectives on treatment of hypertensive patients with chronic obstructive pulmonary disease. *Integr Blood Press Control*. 2013:101.

68. Agca R, Heslinga S, Rollefstad S et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. *Ann Rheum Dis*. 2016;76(1):17-28.

69. Ikdahl E, Wibetoe G, Rollefstad S et al. Guideline recommended treatment to targets of cardiovascular risk is inadequate in patients with inflammatory joint diseases. *Int J Cardiol*. 2019;274:311-318.

70. Musselman D, Evans D, Nemeroff C. The Relationship of Depression to Cardiovascular Disease. *Arch Gen Psychiatry*. 1998;55(7):580.

71. Patten S, Williams J, Lavorato D, Campbell N, Eliasziw M, Campbell T. Major Depression as a Risk Factor for High Blood Pressure: Epidemiologic Evidence From a National Longitudinal Study. *Psychosom Med*. 2009;71(3):273-279.

72. Chen C, Chen S. Better continuity of care reduces costs for diabetic patients. *Am J Manag Care*. 2011;17(6):420-427.

73. Knight J, Dowden J, Worrall G, Gadag V, Murphy M. Does higher continuity of family physician care reduce hospitalizations in elderly people with diabetes?. *Popul Health Manag*. 2009;12(2):81-86.

74. Mainous A, Koopman R, Gill J, Baker R, Pearson W. Relationship between continuity of care and diabetes control: evidence from the Third National Health and Nutrition Examination Survey. *Am J Public Health*. 2004;94(1):66-70.

75. Ascher-Svanum H, Faries D, Zhu B, Ernst F, Swartz M, Swanson J. Medication Adherence and Long-Term Functional Outcomes in the Treatment of Schizophrenia in Usual Care. *J Clin Psychiatry*. 2006;67(03):453-460.

76. Kabore L, Muntner P, Chamot E, Zinski A, Burkholder G, Mugavero M. Self-Report Measures in the Assessment of Antiretroviral Medication Adherence. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2014;14(2):156-162.

77. Voorham J, Haaijer-Ruskamp F, Wolffenbuttel B, Stolk R, Denig P. Medication Adherence Affects Treatment Modifications in Patients With Type 2 Diabetes. *Clin Ther*. 2011;33(1):121-134.

78. Atlas S. Patient−Physician Connectedness and Quality of Primary Care. *Ann Intern Med*. 2009;150(5):325.

79. Lin W, Huang I, Wang S, Yang M, Yaung C. Continuity of diabetes care is associated with avoidable hospitalizations: evidence from Taiwan's National Health Insurance scheme. *International Journal for Quality in Health Care*. 2009;22(1):3-8.

80. Lee J, Lee JS, Park SH, et al. Cohort Profile: The National Health Insurance Service-National Sample Cohort (NHISNSC), South Korea. *Int J Epidemiol.* 2017;46:e15.

81. Rizzo JA, Simons WR. Variations in compliance among hypertensive patients by drug class: implications for health care costs. *Clin Ther*. 1997;19:1446-1457.

82. Degli Esposti L, Degli Esposti E, Valpiani G, et al. A retrospective, populationbased analysis of persistence with antihypertensive drug therapy in primary care practice in Italy. *Clin Ther*. 2002;24:1347-1357.

83. Esposti LD, Di Martino M, Saragoni S, et al. Pharmacoeconomics of antihypertensive drug treatment: an analysis of how long patients remain on various antihypertensive therapies. *J Clin Hypertens* (Greenwich). 2004;6(2):76-82.

84. Chung C, Rohan P, Krishnaswami S, McPheeters M. A systematic review of validated methods for identifying patients with rheumatoid arthritis using administrative or claims data. *Vaccine.* 2013;31:K41-K61.

85. Cho S, Sung Y, Choi C, Kwon J, Lee E, Bae S. Development of an algorithm for identifying rheumatoid arthritis in the Korean National Health

Insurance claims database. *Rheumatol Int*. 2013;33(12):2985-2992.

86. Macdonald K, Kilty S, van Walraven C. Development and validation of an administrative data algorithm to identify adults who have endoscopic sinus surgery for chronic rhinosinusitis. *Journal of Otolaryngology - Head & Neck Surgery*. 2017;46(1).

87. Lee C, Ha H, Oh S et al. Nationwide validation study of diagnostic algorithms for inflammatory bowel disease in Korean National Health Insurance Service database. *J Gastroenterol Hepatol*. 2019;35(5):760-768.

88. Rosenberg K. Antihypertensive Treatment Doesn't Reduce Mortality in Patients with Mild Hypertension. *AJN, American Journal of Nursing*. 2019;119(2):67.

KOREAN ABSTRACT

고혈압 환자에서 치료의 연속성과 모든 원인 사망률 및 질병별 사망률과의 관계

연구배경 : 전 세계적으로 인구의 고령화와 함께 고혈압은 중요한 보건 문제 중 하나로 효과적인 고혈압 관리를 위해서는 치료의 연속성이 매우 중요시되었다. 이 연구는 고혈압 환자를 대상으로 치료의 연속성이 환자의 치료 결과를 개선하고 사망률을 감소시키는지 평가하였다.

연구방법 : 연구에서 이용한 자료는 전체 국민의 2%에 해당하는 전국 대표 100만 명의 국민건강보험 가입자 표본으로 구성된 2002~2015년 국민건강보험공단 표본 코호트에서 수집하였다. 총 152,526명의 신규 고혈압 확진자에 대하여 분석하였다. 고혈압 치료의 연속성은 항고혈압 약물에 대한 처방 비율을 의미하는 MPR을 이용하여 총 관찰기 간이 6개월(180일) 이상이며, MPR이 0.8 이상이면 치료 연속성이 높은 집단으로, 나머지는 치료 연속성이 낮은 집단으로 분류하였다. 치료 연속성 그룹에 따른 모든 원인 사망률, 허혈성 심장 질환 사망률, 허혈성 뇌졸중 사망률, 출혈 및 기타 비 허혈성 뇌졸중 사망률, 고혈압 관련 질병 및 고혈압으로 인한 만성 신장 질환을 포함한 고혈압 관련 사망률을 결과변수로 사용하였다.

연구결과 : 치료 연속성이 높은 집단에서 4,527명 (1,000명당 8.1 명)이 사망하였고, 치료 연속성이 낮은 집단에서 10,356명 (1,000명당 14.3 명)이 관찰기간 동안 사망하였다. 치료 연속성이 낮은 집단의 환자와 비교하여 치료 연속성이 높은 집단의 환자는 모든 원인으로 인한 사망(aHR : 0.52, 95 % CI : 0.51-0.54, P

〈.0001), 허혈성 심장 질환으로 인한 사망 (aHR : 0.76, 95 % CI : 0.61-0.94, P = 0.013), 허혈성 뇌졸중으로 인한 사망 (aHR : 0.47, 95 % CI : 0.35-0.64, P 〈.0001) 및 출혈성 및 기타 비 허혈성 뇌졸중으로 인한 사망 (aHR : 0.44, 95 % CI : 0.35-0.55, P 〈.0001)에서 그 위험 정도가 유의하게 낮았다. 고혈압 관련 질병으로 인한 사망률에서는 치료 연속성 집단에 따른 유의한 차이는 없었다 (aHR : 0.87, 95 % CI : 0.58-1.30, P = 0.5).

결론 : 이 연구에서 높은 치료 연속성을 통해 고혈압을 조절하면 모든 원인으로 인한 사망률, 허혈성 심장 질환 사망률, 허혈성 뇌졸중 사망률 및 출혈성 및 기타 비 허혈성 뇌졸중 사망률의 위험이 감소함을 확인하였다. 효과적인 고혈압 관리를 위해서는 고혈압 치료의 연속성을 개선하고 유지할 수 있는 대안의 마련이 매우 중요하다.