Increasing Trend in Admissions for Malignant Hypertension and Hypertensive Encephalopathy in the United States

Linnea A. Polgreen, Manish Suneja, Fan Tang, Barry L. Carter, Philip M. Polgreen

Abstract—Malignant hypertension and hypertensive encephalopathy are life-threatening manifestations of hypertension. These syndromes primarily occur in patients with a history of poorly controlled hypertension. The purpose of this study was to investigate national trends in hospital admissions for malignant hypertension, hypertensive encephalopathy, and essential hypertension. This was a retrospective cohort study that used the Nationwide Inpatient Sample. We identified all hospitalizations between 2000 and 2011, during which a primary diagnosis of malignant hypertension (ICD 9 code: 401.0), hypertensive encephalopathy (ICD 9 code: 437.2), or essential hypertension (ICD 9 code: 401.9) was recorded. Time series models were estimated for malignant hypertension, hypertensive encephalopathy, essential hypertension and also for the combined series. A piecewise linear regression analyses was performed to investigate whether there were changes in the trends of these series. In addition, we also compared the characteristics of patients with these diagnoses. The estimated number of admissions for both malignant hypertension and hypertensive encephalopathy increased dramatically after 2007, whereas discharges for essential hypertension fell, and there was no change in trend for the combined series. Costs rose substantially for patients with these diagnoses after 2007, but mortality significantly fell for malignant hypertension and mortality for hypertensive encephalopathy did not change. The dramatic increase in the number of hospital admissions for hypertensive encephalopathy and malignant hypertension should have resulted in dramatic increases in morbidity, but it did not. The change is most likely related to changes in coding related to diagnostic-related groups that occurred in 2007. (Hypertension. 2015;65:1002-1007. DOI: 10.1161/HYPERTENSIONAHA.115.05241.)

Key Words: diagnostic-related groups ■ hypertensive encephalopathy ■ malignant hypertension ■ statistical analysis ■ time series ■ trends

Hypertension is a major cause of morbidity and mortality. In general, hypertension is asymptomatic and, over long periods of time, increases the risk of strokes, cardiac disease, and chronic kidney disease. However, acute elevations of blood pressure can be symptomatic and be associated with diseases requiring urgent interventions. There are two major hypertensive emergency syndromes: malignant hypertension and hypertensive encephalopathy. Both of these syndromes are associated with a failure of the auto-regulation of blood pressure and can be life-threatening.

Malignant hypertension usually occurs in patients with long-standing hypertension and is defined as severe hypertension accompanied by retinal hemorrhages, exudates, or papilledema. Hypertensive encephalopathy also occurs with severe hypertension, but it includes cerebral edema and patients can present with changes in mental status, seizures (generalized or focal), altered mental status, visual field loss, and headache. In most cases, both malignant hypertension and hypertensive encephalopathy occur in patients with preexisting hypertension and can be associated with a recent cessation of antihypertensive therapy. These syndromes are serious and usually require hospitalization. Thus, monitoring trends in hospitalizations for these conditions may yield a convenient population-based indicator for failures related to hypertension management and patient adherence. The purpose of this study was to investigate national trends in hospitalizations for both malignant hypertension and hypertensive encephalopathy.

Methods

This was a retrospective cohort study that used the Nationwide Inpatient Sample. The Nationwide Inpatient Sample is the largest all-payer database of national discharges in the United States. The database is maintained as part of the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality and contains data from a 20% stratified sample of nonfederal acute care hospitals. These data include information about demographics, procedures, diagnoses, and total charges but not information about providers, medications, or test results. To represent the total population in the United States, we applied weights provided by the Agency for Healthcare Research and Quality.

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We identified all hospitalizations from January 2000 through December 2011 during which a primary diagnosis of either malignant hypertension (ICD 9 code: 401.0), hypertensive encephalopathy (ICD 9 code: 437.2), or essential hypertension (ICD 9 code: 401.9) occurred. We aggregated all cases by month to produce a national sample of cases of the 3 hypertension series over time. Cases were assigned to calendar month based on the date that the patient was admitted to the hospital. In a similar fashion, we extracted all hospitalizations over the same period, during which any primary diagnosis occurred, to produce the national hospital admissions series. The rate for each hypertension series was then computed as the ratio between the hypertension series and total hospitalizations.

Statistical Analysis
In addition to the series listed earlier, we formulated a fourth series with all of these codes combined. Our purpose was to determine whether each hypertension series increased during the study period and to determine whether the rate of hospitalizations assigned to these diagnoses changed at a given point during the study period. We used a piecewise linear regression model to answer both questions. The model can be written as

\[ y = \beta_0 + \beta_1 t + \beta_2 [(t - t_0) I_{cp}] + \epsilon \]

where \( y \) is the dependent outcome variable (hypertension incidence), \( t \) is the time period, \( t_0 \) is the change point, \( I_{cp} \) is an indicator variable for the change point, and \( \epsilon \sim N(0, \sigma^2) \). The indicator \( I_{cp} \) assumes a value of 1 for time periods \( t \) at or beyond the change point \( t_0 \) and assumes a value of 0 otherwise. A significant change point is detected if the change of slope parameter \( \beta_2 \) is statistically different from 0.

We fit a piecewise linear regression model based on the prespecified change point. We conducted residual diagnostics on the detrended hypertension series to investigate whether there was any autocorrelation pattern in the residuals because failure to account for such correlation may lead to incorrect inferential conclusions. The temporal correlation in the residuals were examined by the autocorrelation function and the partial autocorrelation function. The same analyses were applied to the hypertension rate series to account for the growth of total hospitalizations over time.

To inspect shifts in demographics and characteristics, the sample was divided into 2 groups based on the identified change point. For categorical outcomes (sex, mortality), comparisons of proportions were conducted using the Pearson \( \chi^2 \) test. For continuous outcomes (age, length of stay, and total charges, etc.), comparisons of means were conducted using the Wilcoxon rank-sum test.

To remove the effects of inflation, charges were adjusted by the healthcare price index reported by the Federal Reserve Bank of St. Louis.

Results
The Figure shows a plot of the 4 hypertension incidence series from 2000 to 2011. We chose January of 2007 as the change point for the investigation of the autocorrelation pattern in the residuals. This point was chosen because of changes in Medicare payments, specifically changing from diagnostic-related groups (DRGs) to medical severity DRGs. Upon inspection of the autocorrelation function and partial autocorrelation function, an autoregressive component of order 1 and
a seasonal autoregressive component of order 1 with a periodicity of 12 were used to account for the autocorrelation in the residuals.

Our final piecewise linear regression model, based on the predetermined change point, shows a significant change of slope in the number of patients admitted with a diagnosis of malignant hypertension, hypertensive encephalopathy, and essential hypertension. Malignant hypertension and hypertensive encephalopathy both showed a positive change in slope, whereas essential hypertension showed an opposite downward trend after the change point. However, a combined series featuring all the 3 different hypertensive groups together showed no significant change in slope during the study period. For illustrative purposes, the form of the fitted model without accounting for autocorrelation is shown in the Figure as a dashed line. Similar results were also observed in the hypertension rate series (results not shown).

Table 1 summarizes the model results for the 4 hypertension series illustrated in the Figure. For malignant hypertension and hypertensive encephalopathy, a significant positive change of slope \((P<0.0001)\) is found at the change point, resulting in a steeper slope after 2007. In contrast, a significant negative change of slope is detected after 2007 \((P<0.0001)\) for essential hypertension. Finally, no significant change of slope is found at the given change point for the combined hypertension series. For all of the hypertension series considered, the final models also features a significant autoregressive component of order 1, and a significant seasonal autoregressive component of order 1 with a periodicity of 12 component is found for all series except hypertensive encephalopathy, which implies the existence of strong seasonal and temporal patterns in the series.

Finally, we compared the demographics and characteristics for malignant hypertension, hypertensive encephalopathy, and essential hypertension series before and after the change point (January 2007). Tables 2–4 summarize the means and proportions for each variable considered. For malignant hypertension, there was a 36% decrease in the mortality rate (0.25% versus 0.16%, \(P=0.0153\), but there was no significant difference in mortality rate for hypertensive encephalopathy (0.67% versus 0.67%, \(P=0.9997\)) or essential hypertension (0.18% versus 0.16%, \(P=0.2061\)). A higher percentage of females were diagnosed for all hypertension series before 2007. The number of diagnoses and the adjusted average charges significantly increased after the change point for all hypertension series, although the increase in malignant hypertension and hypertensive encephalopathy was higher than that of essential hypertension. However, the length of stay significantly decreased after 2007 for all series. The mean age and number of procedures for all hypertension series were similar before and after 2007. Finally, the percentage of uninsured and self-pay patients significantly increased after the 2007 for all series.

### Discussion

Our results clearly demonstrate a gradual, steady increase in the number of hypertension-related hospitalizations in the United States from 2000 to 2011 (from \(\approx 87,000\) per year in 2000 to \(\approx 120,000\) per year in 2011). However, during this same time period, we identified a much greater rate of increase in the number of hospitalizations assigned a primary discharge
diagnosis of either malignant hypertension or hypertensive encephalopathy. For example, the yearly hospitalizations stayed stationary before 2007, but started to significantly increase at an estimated rate of 2700 per year for malignant hypertension. The estimated increase in total hospitalizations was only 364 per year before 2007, but rose to 867 per year after 2007 for hypertensive encephalopathy.

We think that there are 2 major explanations for the dramatic change in the number of patients assigned a primary diagnosis of malignant hypertension or hypertensive encephalopathy. The first possibility is that the discharge data that we report represents a true change in the epidemiology of hypertensive emergencies: the changes we report reflect a change in the true incidence of these syndromes. Such a dramatic increase would have important implications for population-based control of hypertension, as hypertensive emergencies are often caused by individuals with a pre-existing hypertension diagnosis, stopping their medications abruptly. Alternatively, these changes could be caused by changes in insurance coverage, incomes, prescribing patterns, or increased fear of side effects. There was a recession from 2007 to 2009 that led to an increase in the number of uninsured Americans. In fact, the proportion of patients in our cohort with insurance did change slightly after 2007—the percentage of uninsured and self-pay patients rose by 3 percentage points—but the uninsured were no more likely to be diagnosed with malignant hypertension or hypertensive encephalopathy than essential hypertension; this change occurred for all 3 groups, including essential hypertension. Also, we have no reason to think that providers’ treatment choices that would have influenced these findings changed substantially.

A much more likely cause of the change is that this abrupt increase was caused by a change in coding practices. In other words, the increase in both of these diagnoses reflects the assignment of administrative billing codes to these patients, rather than the disease itself. Indeed, in 2007, DRG codes were changed to medical severity DRG codes. Although we are basing our analysis on primary codes, our change coincides with a major change in billing practices that has been reported elsewhere for other diseases. Furthermore, we found a decrease in the mortality among patients diagnosed with malignant hypertension after 2007. These findings suggest that the patients before this period were different in some way—most likely they had less severe symptoms and they might have not been assigned codes associated with more severe syndromes in the era before 2007. Indeed, because the increase in malignant hypertension and hypertensive encephalopathy codes occurred at the same time as a decrease in essential hypertension codes, it seems that codes associated with more-severe symptoms were being used in place of a code associated with less-severe symptoms.

Regardless of the reason for the increase, the change in the number of patients assigned these codes has substantial implications for payers. For example, if a patient is given a diagnosis code of hypertensive encephalopathy rather than essential hypertension, costs almost double on average from $16750 to $33010. Given that hypertensive encephalopathy
and malignant hypertension diagnoses were more common after 2007, this would have led to substantial increases in costs. Although this change likely increases healthcare costs for payers, it may be the case that some of the cases before 2007 should have been assigned codes associated with hypertensive emergencies that were not billed as such: some hospitals may have been under billing. However, we think this is less likely given that the number of additional diagnoses has increased for all 3 codes that we examined: each patient received, on average, 2 additional diagnoses after 2007, whereas the average length of stay decreased for all series after 2007.

In addition, malignant hypertension and hypertensive encephalopathy are sometimes diagnosed in the same patient. For patients with a primary diagnosis of malignant hypertension, a secondary diagnosis of hypertensive encephalopathy occurs in 1.72% of the cases. For patients with a primary diagnosis of hypertensive encephalopathy, 16.39% of cases have a secondary diagnosis of malignant hypertension. However, this rate was ≈12% consistently until 2007, when it started to rise, and by the end of the series, it was above 25%. This is clearly the result of changes from DRGs to medical severity DRGs: malignant hypertension as a secondary diagnosis is one of the conditions defined as medically severe.

This work is subject to 2 major limitations. The first is that we used administrative data. No data on laboratory tests or physicians’ notes are available. Repeating this analysis at a center or multiple centers where chart reviews are possible would help confirm the observations we describe. Second, we do not know what medications patients were taking on an outpatient basis during this observation period. However, even if prescription claims data were available, we cannot determine hypertensive medication adherence. We have no evidence that more people are less adherent to therapy after 2007 than they were before 2007. However, fewer people had insurance after 2007, which may have led some patients to stop medication.

**Perspectives**

We describe a substantial shift in the assigning of principle diagnoses for malignant hypertension and hypertensive encephalopathy after 2007. Future studies could examine actual patient records to determine whether this is truly a coding phenomenon: more-granular, patient-level data are needed because the results we describe have implications for both patients and the healthcare system. Finally, our findings question the level of confidence that can be used on monitoring trends in hypertensive outcomes using administrative data.

**Disclosures**

None.

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### Novelty and Significance

#### What Is New?
- Admissions assigned a diagnosis of malignant hypertension and hypertensive encephalopathy rose after 2007, whereas diagnoses of essential hypertension fell.

#### What Is Relevant?
- These changes occurred at the same time that diagnostic-related groups were changed to medical-severity diagnostic–related groups, which suggests that changes in coding, not changes in prevalence, occurred.
- These findings suggest that administrative data should be used with caution when investigating trends in hypertension-associated diagnoses at a population level.

#### Summary
The estimated number of admissions for both malignant hypertension and hypertensive encephalopathy increased dramatically after 2007, whereas discharges for essential hypertension fell, but there was no change in trend for the combined series. The dramatic increase in the number of hospital admissions for hypertensive encephalopathy and malignant hypertension should have resulted in dramatic increases in morbidity, but it did not. It did result in increased costs. Thus, the changes observed are most likely related to changes in coding of diagnostic-related groups that occurred in 2007, rather than actual changes in disease incidence.
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