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Mortality Among Patients Hospitalized with Heart Failure and Diabetes Mellitus: Results from the National Inpatient Sample 2000 – 2010

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Abstract

Background—Case-fatality and hospitalization rates for U.S. heart failure (HF) patients have steadily decreased over the past several decades. Diabetes mellitus (DM), a risk factor for, and frequent co-existing condition with, HF continues to increase in the general population.

Methods and Results—We used the National Inpatient Sample to estimate overall as well as age-, sex-, and race/ethnicity-specific trends in HF hospitalizations, DM prevalence and in-hospital mortality among 2.5 million discharge records from 2000–2010 with HF as primary discharge diagnosis. Multivariable logistic and Poisson regression were used to assess the impact of the above demographic characteristics on in-hospital mortality. Age-standardized hospitalizations decreased significantly in HF overall and in HF with DM . Age-standardized in-hospital mortality with HF declined from 2000 to 2010 (4.57% to 3.09%, p_{trend} <0.0001), while DM prevalence in HF increased (38.9% to 41.9%, p_{trend} < 0.0001) as did comorbidity burden. Age-standardized in-hospital mortality in HF with DM also decreased significantly (3.53% to 2.27%, p_{trend} <0.0001). After adjusting for year, age and comorbid burden, males remained at 17% increased risk versus females, non-Hispanics remained at 12% increased risk versus Hispanics and whites had a 30% higher mortality versus non-white minorities. Absolute mortality rates were lower in younger versus older patients although the rate of decline was attenuated in younger patients.

Conclusions—In-hospital mortality in HF patients with DM significantly decreased over the past decade despite increases in DM prevalence and co-morbid conditions. Mortality rate decreases among younger patients were significantly attenuated and mortality disparities remain among important demographic sub-groups.

Keywords

heart failure; diabetes mellitus; mortality; hospitalization

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Disclosures None.

There are nearly 5 million individuals in the United States (U.S.) with a diagnosis of heart failure (HF)¹ and HF is the principal diagnosis in >1 million hospitalizations annually². Over the past decade, overall HF hospitalization and in-hospital mortality rates have declined^{3–6}. Diabetes mellitus (DM), a disease that is increasing in prevalence^{7–9}, is a significant risk factor for the development of cardiovascular disease and amplifies the risk for the development of HF^{10–12}. In addition, HF itself is considered an insulin-resistant state and is associated with significant risk for the future development of DM^{13,14}. Given these relationships, it is not surprising that DM and HF may commonly coexist.

While the "true" population-based prevalence of DM in patients with HF (ambulatory or hospitalized) is unknown, prevalences range from 20–30% in clinical trial populations^{15,16} to > 40% in recent registries of hospitalized patients^{17–19}. What is clear is that the absolute number of individuals with HF will continue to increase world-wide²⁰ as well as in the U.S.²¹ over the next decade while the number of individuals with DM will also continue to increase world-wide²² and in the U.S.²³. Given the increasing prevalence of DM and HF and comparatively worse clinical outcomes of concomitant HF and DM in the general population^{18,24,25}, we examined trends in hospitalizations and in-hospital mortality in patients with HF and DM from 2000–2010. We also describe the factors associated with inhospital mortality with a focus on the impact of time, age, sex, race and ethnicity over this interval.

Methods

Data Source

The National Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP), is the largest all-payer inpatient database publicly available in the U.S. consisting of discharge data from over 1,000 hospitals across a majority of states and is designed to approximate a 20% stratified sample of US community hospitals²⁶.

The NIS provides discharge-level demographic and clinical characteristics that are searchable using International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) codes. Each annual release of the NIS includes patient-level hospital discharge abstracted data for 100% of discharges from the sample of hospitals in participating states. We used NIS security files to extract administratively coded comorbid conditions of patients as established by AHRQ. The study was considered exempt from formal review by the University of New Mexico institutional review board because the NIS is a public database without personal identifiers.

Data Quality

A summary data quality report is available for review for each year of the NIS²⁷. Individual reports for the years 2000–2010 were reviewed by one of the authors (WKL). With the exception of data for race and ethnicity (see below) edit check failure rates were consistently < 0.5% for other key data elements.

Study population

A total of 71 million hospital discharges were reported to the NIS from 2000 to 2010. We analyzed data for patients 18 years of age. HF hospital stays were defined as those with a primary discharge diagnosis of HF on the basis of the following ICD-9-CM codes: 402.01; 402.11; 402.91; 404.01; 404.03; 404.11; 404.13; 404.91; 404.93; and 428. We excluded any record containing an ICD-9-CM code for acute coronary syndrome or acute myocardial infarction in order to obviate the confounding issue of acute ischemia on in-hospital outcome. The total number of HF hospitalizations was calculated as the sum over all HF ICD-9-CM codes. We then obtained the proportion of HF discharges that occurred over the same time interval with a diagnosis of type 2 DM , identified by ICD-9-CM code 250.0 to 250.9 with a fifth digit of 0 or 2 since the majority of diagnosed cases of DM in adults are of type 2

Data Analysis

Figure 1 shows the sequence of data analysis. We recorded the number of records for each year and stratified these records by age group (< 60, 60–69, 70–79, and 80 years) sex, race and ethnicity. We also computed a measure of medical co-morbidities employed by HCUP in NIS datasets-the Elixhauser co-morbidity index^{28,29}.

Statistical sampling weights provided by the NIS allow extrapolation to estimate hospital discharge rates for the nation After weighting, this reflects approximately 95% of hospital discharges within the U.S. 30

Statistical Analysis

Hospitalizations are summarized as raw counts as well as counts per 100,000 adults (> 18 years of age) for that year obtained using the U.S. Census Bureau intercensal estimates for $2000-2010^{31}$. Categorical data are summarized as percents. The outcome of interest in our analysis was in-hospital mortality. In keeping with our stated objectives, exposure variables were year, age on admission, sex, the discharge-record specified race and ethnicity and the Elixhauser co-morbidity index. Survey analysis methods were employed that used hospital-level discharge weights provided by the NIS to estimate the number of HF hospitalizations and in-hospital mortality on a national level³² Direct standardization of age was performed using the average of the 2000 and 2010 NIS data sets as the standard population. Age-standardized in-hospital mortality rates for HF with DM were calculated and reported (in percent) for the overall sample and stratified by sex. All other sub-group specific mortality rates are reported as crude mortality rates (CMR). Rates were plotted and smoothed for display using a Hamming window filter.

In order to distinguish changes in population age and/or sex composition versus age/sexindependent factors driving the observed decrease in CMR over time, the method of rate decomposition was used³³. Briefly, the difference in CMR from 2000 to 2010 can be viewed as the sum of a "composition effect" (reflecting the difference in the age and/or sex composition of the sample from 2000 to 2010) and a "rate effect" (reflecting differences in the distribution of stratum-specific mortality rates from 2000 to 2010) (

CMR_{2000–2010}=composition effect+rate effect). Calculations were performed for age and sex, separately and combined.

P values are based on chi-square tests for all categorical row variables or chi-square rank based group means score statistics for continuous/ordinal row variables (equivalent to Wilcoxon tests). All such tests treat the column variable as nominal. Trends in categorical variables were tested using chi-square statistics. Multivariable logistic regression that accounted for survey methodology and hospital clustering was used to estimate the magnitude of association between clinical, temporal, and demographic covariates and inhospital mortality. Year was modeled as a continuous linear variable. An interaction term, age (group) x sex, was added to the model to test for the influence of sex on the association between age and mortality. Estimated measures of association are expressed as odds ratios (ORs) and 95% CIs. Adjusted annual rates of change in mortality were estimated from a Poisson regression model which estimated linear time trends in in-hospital mortality and included all variables used in the logistic regression model. Hospital length of stay (days) was used as the offset ("exposure") variable in the Poisson model.

A sensitivity analysis was performed in the subgroup of hospitals with >90% completion of race/ethnicity data since missing rates of the latter frequently exceeded 10% in the overall sample. Additional sensitivity analyses examining the impact of the inclusion of ICD-9-CM codes for non-acute ischemic heart disease (ICD-9-CM 412.X, 413.X, 414.X) on the associations between age, sex, race/ethnicity, time and comorbid burden and in-hospital mortality was performed. We assessed the frequency of any acute manifestation of ischemic heart disease (ICD-9-CM codes 410.0 to 410.8) using the clinical classifications software (CCS) provided by HCUP.

The study was considered exempt from formal review by the University of New Mexico institutional review board because the NIS is a public database without personal identifiers.

A p value < 0.05 was considered statistically significant. All analyses were performed using SAS (version 9.1 or higher) or STATA (version 14)..

Results

Characteristics of HF hospitalizations from 2000 to 2010

Hospitalization with a primary diagnosis of HF steadily decreased from 227,595 in 2000 to 207, 593 in 2010 and translates to a decrease from 555/100,000 U.S. adults to 460/100,000 U.S. adults ($p_{trend} < 0.0001$). (Supplemental Table 1). The overall prevalence of women was 52.5% and decreased from 55.4% in 2000 to 49.9% in 2010 ($p_{trend} < 0.0001$). The mean (\pm SD) age of the sample was 72.6 \pm 14.4 years and approximately two-thirds (65.4% in 2000 and 62.4% in 2010) were > 70 years of age. The majority were of white race (representing about 73 % in 2000 and 66 % in 2010) although non-white minority prevalence increased significantly from 27% to 34%. The prevalence of Hispanic ethnicity increased significantly from 5.3% in 2000 to 6.9% in 2010 ($p_{trend} < 0.0001$). The mean (\pm SE) Elixhauser comorbidity index increased from 3.32 \pm 0.04 in 2000 to 5.67 \pm 0.07 in 2010 ($p_{trend} < 0.0001$).

The prevalence of DM increased from 38.9% to 41.9% ($p_{trend} < 0.0001$) from 2000 to 2010 (Supplemental Table 1)..

Characteristics of HF with DM hospitalizations from 2000 to 2010

The study sample consisted of 1,014,879 hospitalizations with HF and co-existing DM which translates to an estimated weighted 5 million hospitalizations. As seen in Table 1, there was a statistically significant decrease in the prevalence of HF with co-existing DM hospitalizations from 217/100,000 U.S. adults in 2000 to 193/100,000 U.S. adults in 2010 ($p_{trend} < 0.0001$). The prevalence of females decreased from 57% in 2000 to 50% in 2010. Although the majority of the sample was > 70 years of age a significant minority was < 60 years of age and their prevalence increased over time. The prevalence of white race decreased from 68% in 2000 to 61% in 2010 ($p_{trend} < 0.0001$) whereas the cumulative prevalence of non-white minorities increased from 32% to 39% ($p_{trend} < 0.0001$). The prevalence ethnicity increased from 7.0% in 2000 to 9.2% in 2010 ($p_{trend} < 0.0001$). The annual mean Elixhauser comorbidity index significantly increased from 2.88±0.04 to 5.46±0.07 ($p_{trend} < 0.0001$).

In-hospital Mortality in HF from 2000 to 2010

There was a statistically significant decline in age-standardized in-hospital mortality from 4.57% in 2000 to 3.09% in 2010 ($p_{trend} < 0.0001$) among the 2.5 million patients in the unweighted HF sample. This trend was similar for both sexes (4.71% and 3.07% for males in 2000 and 2001, respectively; 4.48% and 3.09% for females in 2000 and 2001, respectively; 4.48% and 3.09% for females in 2000 and 2001, respectively; 6.48% and 3.09% for females in 2000 and 2001, respectively, $p_{trend} < 0.0001$). (Supplemental Figure 1). In order to better understand the driver(s) for the decrease in mortality, the method of rate decomposition (see Methods) was employed. For the entire HF population the "rate effect" was 1.4719 and the "composition effect" was 0.0006. The total, 1.4726, equals the difference in CMR from 2000 to 2010 and suggests that a change in stratum-specific risk for mortality is the main driver of the decrease in mortality and not a difference in age structure of the populations. Similar results were obtained when the analysis was limited to changes in sex distribution alone and age and sex distributions together.

In-hospital Mortality in HF with co-existing DM from 2000 to 2010

Overall and sex-specific crude and age-standardized mortality rates for HF with DM significantly decreased over this interval (Table 1, Figure 2). Rate decomposition indicated that for HF and DM the "rate effect" was 1.3511 and the "composition effect" was -0.0916. The sum of these 2 components, 1.2596, equals the difference in CMR for HF with DM from 2000 to 2010 and suggests that, as with the overall HF population, the main driver for the decrease in mortality is a change in inherent risk structure of the populations rather than a change in age structure of the populations. Similar results were obtained when the analysis was limited to changes in sex distribution alone and age and sex distributions together.

The overall decrease in in-hospital mortality was not shared equally among the selected subgroups. As seen in Figures 3 and 4, larger decreases in case fatality rates were noted in the oldest groups when compared to their younger counterparts. Women exhibited smaller decreases in mortality over time with the largest decreases noted in the oldest group. Poisson

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regression analysis indicated a lower overall mortality rate and rate of decline in younger age groups (Table 2). As seen in Figure 5 and Figure 6, declines in case fatality rates in Hispanics and non-Hispanics and whites vs. non-white minorities were noted with, however, persistent absolute differences between whites and non-white minorities.

Demographic, temporal and clinical factors associated with in-hospital death were assessed using multivariable regression (Table 3) with the results supporting significant disparities within and among our selected sub-groups. Males remained at 17% increased risk compared to females (OR, 1.17; 95% CI, 1.14 to 1.20); white populations remained at 30% higher risk compared to non-white minorities (OR, 1.30; 95% CI, 1.26 to 1.34); non-Hispanics remained at 12% increased risk compared to Hispanics (OR, 1.12; 95% CI, 1.06 to 1.19) and older patients (80 years) remained at 4 times higher risk compared to their younger counterparts <60 years (OR, 4.08; 95% CI, 3.87 to 4.29). There was no significant interaction between age and sex on the association of either with in-hospital mortality (p_{interaction}=0.19).

Analysis of the above associations for only those records containing ICD-9-CM codes specific to ischemic heart disease yielded no meaningful differences in effect size (difference in magnitude of beta coefficients < 2 %) between models. Additionally, there was minimal variation in the frequency of acute coronary syndromes coded in a secondary position with an average rate for the interval of 3.1%.

Sensitivity analysis confined to those hospitals with >90% data completion for race/ethnicity confirmed the above-mentioned significant trends in prevalences over time. As well, Poisson regression utilizing data from hospitals with >90% complete records yielded similar results to those in Table 3.

Discussion

Using a nationally representative all-payer inpatient sample of U.S. hospital admissions from 2000–2010 our observations support the following conclusions. *First*, the total number of hospitalizations with a primary diagnosis of HF decreased over this interval. *Second*, the prevalence of DM as well as a measure of the burden of co-morbidities among hospitalized HF patients increased. *Third*, despite the increased prevalence of DM and co-morbid burden there was a 36% decrease in age-standardized in-hospital mortality among HF with DM. *Fourth*, in-hospital mortality rates varied by age, sex, race and ethnicity. *Fifth*, the decrease in in-hospital mortality rate is the result of a change in the stratum-specific risk (for mortality) rather than a change in age and/or sex structure of the 2000 and 2010 samples.

Reduction in in-hospital mortality in HF patients with co-existing DM

Several studies have now documented a decrease in hospitalization rates in the U.S for patients with HF over a time interval similar to the current study^{3–6}. The inclusion of hospitalizations in all adults, i.e., greater than 18 years of age, distinguishes the current study from prior Medicare-derived data^{3,6} and the focus on the DM sub-group distinguishes the current study from prior NIS studies^{4,5}. The inclusion of patient hospitalizations with age <

Our study was limited to hospitalized patients. Nevertheless, secular changes in the management and characteristics of HF patients from 2000-2010 are relevant to these data. A decrease in HF-related hospitalization rates and in-hospital mortality was first reported from the Medicare and Medicaid population beginning in 1998³ but reflects changes beginning prior to that date. The period from 2000-2010 was a period of increasing attention to improved management strategies for all HF patients^{34,35} which would likely impact hospitalization and in-hospitality mortality rates. The observed trend in the current study is consistent with the time frame for the "diffusion" of evidence-based and clinical trial data into mainstream practice³⁶, and reflects the many changes in the timing and extent of pharmacotherapy for HF. Improved adherence to contemporary guideline-based therapies for HF and DM in conformance with national guidelines³⁷over this time interval may also have contributed to improved in-hospital outcomes in HF and DM patients. Changes in the underlying cardiovascular risk profile of patients presenting with HF and DM^{7,38}, whether a cohort effect or a true indicator of intensified risk factor recognition and treatment, is another possible explanation for the reduction in in-patient mortality- a finding supported by our rate decomposition analysis.

Similar³⁹or lower⁴⁰ in-hospital crude mortality rates in patients with HF and DM compared to those with HF without DM have been previously observed. Of note is the similarity of our current observations in hospitalized patients to trends in the U.S. population from 2005–2011³⁸In this latter study while hospitalizations and mortality rates declined in DM patients, including those with HF, decreases in event rates and mortality were lower or absent in those without DM. Thus, although hospitalized patients are a highly selected group from the general population, the above-noted secular trends may be powerful enough to beneficially impact this selected group of patients.

In-hospital mortality trends in HF with DM by age, sex, race and ethnicity

Our study also indicated that the reduction in in-hospitality mortality over time varied by age, sex, race and ethnicity. The current national focus on disparities in health care and health outcomes was the main driver for these additional analyses. Of particular concern is the lack of concordance in trends in-hospital mortality rates between younger and older age groups, notwithstanding higher event rates in the latter. Continuing increases in the incidence of obesity and DM, both contributors to the development of HF, in the young will likely further adversely impact these trajectories and could reverse much of the gain in survival noted to date. At the beginning of this study, females had higher rates of HF as well as HF with DM hospitalizations than males. However, the reverse trend was found by the end of the study period. These results are consistent with previous studies that suggested that the prevalence of HF in males is increasing in comparison to females². Age standardized inpatient HF with DM mortality rates in both sexes decreased from 2000 to 2010. However the age standardized mortality in males remained higher than females throughout the study period until around 2006 and then became more comparable to females by the end of the study period.

Concordance in trends for in-hospital mortality between Hispanic and non-Hispanics was observed- findings similar to prior reports from a national HF registry⁴¹. In the adjusted logistic regression model Hispanics were at diminished risk for in-patient mortality compared to non-Hispanics. Racial differences in in-hospital mortality persist notwithstanding overall similar declines in both white and non-white groups. Lower mortality rates in the composite non-white minority group have been observed previously and remain unexplained⁴¹ but may be of relevance as the relative proportions of whites and non-whites in the U.S. changes over the next several decades⁴².

Limitations

The NIS remains the largest publicly available database with a statistically sound sampling design allowing for accurate identification of trends in specific diseases. However, analyses and conclusions from this large administrative database have a number of caveats. Observations reflect admissions and not unique patients. Thus, the current unit of analysis is the admission. Given the inability to account for multiple admissions for a given patient in the NIS, our observations and conclusions may be confounded by the non-trivial risk for repeat hospitalization. Thus, our reported rates may be viewed as over-estimates of a per patient admission rate. Mortality rates, however, are unlikely to be affected (a patient can only die once). Misclassification (under-or over-coding) cannot be completely ruled out without more extensive and rigorous data verification although the large number of patients in the database strongly mitigates against substantial misclassification bias⁴³. Prior studies have shown excellent positive and negative predictive capability for ICD-9-CM codes for HF⁴⁴. Our analysis could be biased by "upcoding" or "Diagnosis-related group (DRG) creep," which may have resulted in over-reporting of comorbidities However, the impact of such would likely have been uniform across the groups, would be unlikely to bias CMRs, and would bias the results of comparisons toward the null if applied non-differentially It is even more unlikely that the highly statistically significant trend in hospitalizations and mortality from 2000–2010 is attributable to "downward" coding bias given the consistent trends across all sub-groups, the concordance with other published studies and the fact that there was no meaningful modification or revision of ICD-9-CM codes for HF or DM over the study interval. However, the possibility of bias against coding of comorbid or chronic conditions on discharge abstracts of patients who die is acknowledged⁴⁵Given the statistically significant and uniform increases in the prevalence of DM and the Elixhauser index over time, the extent of systematic undercoding is admittedly unquantifiable but likely small.

Data quality assessment of the NIS is performed annually and ensures the internal validity of the data. Our data are also in agreement with a report from the National Hospital Discharge Survey, a separate and independent (from NIS) analysis of hospitalization for heart failure in the U.S. over the same time interval from the Centers for Disease Control and Prevention⁴⁶.

We were only able to assess in-hospital mortality and do not have data on longer-term outcomes that may be more relevant, particularly for younger patients. Observational studies may not be able to fully adjust for residual or unmeasured confounding that might affect our estimates for the reported associations between in-hospital mortality and included

covariates. Therefore, inferences based on these observational data can only be viewed as associational and hypothesis-generating and not causal in nature. Selection (survival) bias must be considered operational in all cross-sectional studies. In the absence of a prospective cohort design it is certain that hospitalized patients represent just the fraction of all HF patients, with and without DM, that survived to hospitalization. We indeed observed such a potential source of bias in our data noting that the risk ratio for mortality in HF with DM (data not shown) declined over the age spectrum (higher ratio in the younger age groups which decreases with age), consistent with a (non-testable) hypothesis in this dataset that it is the older subjects with HF and DM who survive to hospitalization⁴⁰. The absence of specific data on pre- or in-hospital medical therapy for HF and DM in the NIS database precludes further analysis regarding the impact of prevalent treatment on outcomes. The absence of information on pre-hospitalization functional classification, e.g., NYHA Class and left ventricular function, precludes stratification on these important measures. However, modest differences in-hospital mortality between patients with preserved and depressed left ventricular function would not likely affect the observed trends or rates in the absence of large changes in the proportion of these entities over time⁴⁷.

Finally, these observations pertain to the HF population in the U.S. and may not be generalizable to other HF populations in other countries. In a recent overview of HF hospitalization on a global scale⁴⁸, it was pointed out that, at least within RCTs, there is much variability in HF hospitalization rates and that outside of the clinical trial universe, the lack of standardized, non-administrative HF-specific registries represent a major limitation to assessing and comparing HF hospitalization rates within and between countries. .Population-based and registry data from several European countries with integrated health information systems indicate a decrease in HF hospitalization rates⁴⁸ consistent with the data herein, but such trends have not been seen in other European countries.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013; 128:1810–1852. [PubMed: 23741057]
- 2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Judd SE, Kissela BM, Lackland DT, Lichtman JH,

Lisabeth LD, Liu S, Mackey RH, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Willey JZ, Woo D, Yeh RW, Turner MB. A American Heart Association Statistics, Committee Stroke Statistics, Subcommittee Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation. 2015; 131:e29–e322. [PubMed: 25520374]

- Chen J, Normand SL, Wang Y, Krumholz HM. National and regional trends in heart failure hospitalization and mortality rates for Medicare beneficiaries, 1998–2008. JAMA. 2011; 306:1669– 1678. [PubMed: 22009099]
- Blecker S, Paul M, Taksler G, Ogedegbe G, Katz S. Heart failure-associated hospitalizations in the United States. J Am Coll Cardiol. 2013; 61:1259–1267. [PubMed: 23500328]
- Chen J, Dharmarajan K, Wang Y, Krumholz HM. National trends in heart failure hospital stay rates, 2001 to 2009. J Am Coll Cardiol. 2013; 61:1078–1088. [PubMed: 23473413]
- Krumholz HM, Normand SL, Wang Y. Trends in hospitalizations and outcomes for acute cardiovascular disease and stroke, 1999–2011. Circulation. 2014; 130:966–975. [PubMed: 25135276]
- Gregg EW, Williams DE, Geiss L. Changes in diabetes-related complications in the United States. N Engl J Med. 2014; 371:286–287. [PubMed: 25014698]
- Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, Marks JS. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA. 2003; 289:76–79. [PubMed: 12503980]
- Selvin E, Parrinello CM, Sacks DB, Coresh J. Trends in prevalence and control of diabetes in the United States, 1988–1994 and 1999–2010. Ann Intern Med. 2014; 160:517–525. [PubMed: 24733192]
- Gottdiener JS, Arnold AM, Aurigemma GP, Polak JF, Tracy RP, Kitzman DW, Gardin JM, Rutledge JE, Boineau RC. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol. 2000; 35:1628–1637. [PubMed: 10807470]
- Kannel WB, McGee DL. Diabetes cardiovascular disease The Framingham study. JAMA. 1979; 241:2035–2038. [PubMed: 430798]
- Nichols GA, Hillier TA, Erbey JR, Brown JB. Congestive heart failure in type 2 diabetes: prevalence, incidence, and risk factors. Diabetes care. 2001; 24:1614–1619. [PubMed: 11522708]
- Banerjee D, Biggs ML, Mercer L, Mukamal K, Kaplan R, Barzilay J, Kuller L, Kizer JR, Djousse L, Tracy R, Zieman S, Lloyd-Jones D, Siscovick D, Carnethon M. Insulin resistance and risk of incident heart failure: Cardiovascular Health Study. Circ Heart Fail. 2013; 6:364–370. [PubMed: 23575256]
- 14. Dei Cas A, Khan SS, Butler J, Mentz RJ, Bonow RO, Avogaro A, Tschoepe D, Doehner W, Greene SJ, Senni M, Gheorghiade M, Fonarow GC. Impact of diabetes on epidemiology, treatment, and outcomes of patients with heart failure. JACC Heart Fail. 2015; 3:136–145. [PubMed: 25660838]
- 15. MacDonald MR, Petrie MC, Varyani F, Ostergren J, Michelson EL, Young JB, Solomon SD, Granger CB, Swedberg K, Yusuf S, Pfeffer MA, McMurray JJ, Investigators C. Impact of diabetes on outcomes in patients with low and preserved ejection fraction heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) programme. Eur Heart J. 2008; 29:1377–1385. [PubMed: 18413309]
- 16. Sarma S, Mentz RJ, Kwasny MJ, Fought AJ, Huffman M, Subacius H, Nodari S, Konstam M, Swedberg K, Maggioni AP, Zannad F, Bonow RO, Gheorghiade M. EVEREST investigators Association between diabetes mellitus and post-discharge outcomes in patients hospitalized with heart failure: findings from the EVEREST trial. Eur J Heart Fail. 2013; 15:194–202. [PubMed: 23059198]
- 17. Adams KF Jr, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP. ADHERE Scientific Advisory Committee Investigators Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J. 2005; 149:209–216. [PubMed: 15846257]

- Cavender MA, Steg PG, Smith SC, Eagle K, Ohman EM, Goto S, Kuder J, Im K, Wilson PW, Bhatt DL. Impact of Diabetes on Hospitalization for Heart Failure, Cardiovascular Events, and Death: Outcomes at 4 Years from the REACH Registry. Circulation. 2015; 132:923–1031. [PubMed: 26152709]
- Hsich EM, Grau-Sepulveda MV, Hernandez AF, Peterson ED, Schwamm LH, Bhatt DL, Fonarow GC. Sex differences in in-hospital mortality in acute decompensated heart failure with reduced and preserved ejection fraction. Am Heart J. 2012; 163:430–437. e3. [PubMed: 22424014]
- Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, Nodari S, Lam CSP, Sato N, Shah AN, Gheorghiade M. The global health and economic burden of hospitalizations for heart failure. J Am Coll Cardiol. 2014; 63:1123–1133. [PubMed: 24491689]
- 21. Heidenreich P, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, Ikonomidis JS, Khavjou O, Konstam MA, Maddox TM, Nichol G, Pham M, Pina IL, Trogdon JG. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013; 6:606–619. [PubMed: 23616602]
- 22. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract. 2010; 87:4–14. [PubMed: 19896746]
- 23. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988–2012. JAMA. 2015; 314:1021–1029. [PubMed: 26348752]
- From AM, Leibson CL, Bursi F, Redfield MM, Weston SA, Jacobsen SJ, Rodcheffer RJ, Roger VL. Diabetes in heart failure: Prevalence and impact on outcome in the population. Am J Med. 2006; 119:591–599. [PubMed: 16828631]
- Bertoni AG, Hundley WG, Massing MW, Bonds DE, Burke GL, Goff DC Jr. Heart failure prevalence, incidence and mortality in the elderly with diabetes. Diabetes Care. 2004; 27:699–703. [PubMed: 14988288]
- 26. Healthcare Cost and Utilization Project. [Accessed October 7, 2015] Overview of the Nationwide Inpatient Sample 2013. Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp
- HCUP Quality Control Procedures. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality. Rockville, MD: 2013 Sep. Available at: http://www.hcupus.ahrq.gov/db/quality.jsp [Accessed October 7, 2015]
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care. 1998; 36:8–27. [PubMed: 9431328]
- 29. Sharabiani MT, Aylin P, Bottle A. Systematic review of comorbidity indices for administrative data. Med Care. 2012; 50:1109–1118. [PubMed: 22929993]
- 30. Healthcare Cost and Utilization Project. [Accessed October 7, 2015] HCUP methods series. 2010. Available at: http://www.hcup-us.ahrq.gov/reports/methods/methods_topic.jsp
- Population projections of the United States by age, sex, race, and Hispanic origin: 1995 to 2050; U.S. Bureau of the Census, current population reports. Washington (DC): US Government Printing Office; 1996. Available at : http://www.census.gov/prod/1/pop/p25-1130/p251130.pdf [Accessed October 7, 2015]
- 32. Healthcare Cost and Utilization Project. [Accessed October 7, 2015] Nationwide Inpatient Sample trends supplemental files. Available at: http://www.hcup-us.ahrq.gov/db/nation/nis/nistrends.Jsp
- Kitagawa EM. Components of a difference between two rates. J Am Stat Assoc. 1955; 50:1168– 1194.
- 34. Fonarow GC, Abraham WT, Albert NM, Gattis WA, Gheorghiade M, Greenberg B, O'Connor CM, Yancy CW, Young J. Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF): rationale and design. Am Heart J. 2004; 148:43–51. [PubMed: 15215791]
- 35. Translating Research Into Practice (TRIP)-II): Fact Sheet. Agency for Healthcare Research and Quality. Rockville, MD: 2001 Mar. Available at http://archive.ahrq.gov/research/findings/ factsheets/translating/tripfac/trip2fac.html [Accessed on October 7, 2015]
- 36. Bradley EH, Webster TR, Baker D, Schlesinger M, Inouye SK, Barth MC, Lapane KL, Lipson D, Stone R, Koren MJ. Translating research into practice: speeding the adoption of innovative health care programs. Issue Brief (Commonw Fund). 2004; (724):1–12. [PubMed: 15270051]

- The Joint Commission. [Accessed October 7, 2015] Comprehensive review of hospital core measures. Available at: http://www.jointcommission.org/ comprehensive_review_of_hospital_core_measures
- 38. Desai JR, Vazquez-Benitez G, Xu Z, Schroeder EB, Karter AJ, Steiner JF, Nichols GA, Reynolds K, Xu S, Newton K, Pathak RD, Waitzfelder B, Elston Lafata J, Butler MG, Kirchner HL, Thomas A, O'Connor PJ. Who Must We Target Now to Minimize Future Cardiovascular Events and Total Mortality? Lessons From the SUPREME-DM Cohort Study. Circ Cardiovasc Qual Outcomes. 2015; 8:508–516. [PubMed: 26307132]
- 39. Greenberg BH, Abraham WT, Albert NM, Chiswell K, Stough WG, Gheorghiade M, O'Connor CM, Sun JL, Yancy CW, Young JB, Fonarow GC. Influence of diabetes on characteristics and outcomes in patients hospitalized with heart failure: a report from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure- OPTIMIZE-HF. Am Heart J. 2007; 154:277. e1-e8. [PubMed: 17643576]
- MacDonald MR, Jhund PS, Petrie MC, Lewsey JD, Hawkins NM, Bhagra S, Munoz N, Varyani F, Redpath A, Chalmers J, MacIntyre K, McMurray JJV. Discordant short-and long-term outcomes associated with diabetes in patients with heart failure: Importance of age and sex. Circ Heart Fail. 2008; 1:234–224. [PubMed: 19808297]
- 41. Vivo RP, Krim SR, Liang L, Neely M, Hernandez AF, Eapen ZJ, Peterson ED, Bhatt DL, Heidenreich PA, Yancy CW, Fonarow GC. Short- and long-term rehospitalization and mortality for heart failure in 4 racial/ethnic populations. J Am Heart Assoc. 2014; 3:e001134. [PubMed: 25324354]
- 42. Current population reports. Current Population Reports. Washington (DC): U.S. Government Printing Office; 1996. Population projections of the United states by age, sex, race, and hispanic origin: 1995 to 2050; U.S. Bureau of the Census. pdf
- Psaty BM, Delaney JA, Arnold AM, Curtis LH, Fitzpatrick AL, Heckbert SR, McKnight B, Ives D, Gottdiener JS, Kuller LH, Longstreth WT Jr. Study of cardiovascular health outcomes in the era of claims data. Circulation. 2016; 133:156–164. [PubMed: 26538580]
- 44. Saczynski JS, Andrade SE, Harrold LR, Tija J, Cutrona SL, Dodd KS, Goldberg RJ, Gurwitz JH. A systematic review of validated methods for identifying heart failure using administrative data. Pharmacoepidemiol Drug Saf. 2012; 21(Suppl 1):129–140. [PubMed: 22262599]
- Iezzoni LI, Foley SM, Daley J, Hughes J, Fisher ES, Heeren T. Comorbidities, complications and coding bias. JAMA. 1992; 267:2197–2203. [PubMed: 1556797]
- Hall MJ, Levant S, DeFrances CJ. Hospitalization for congestive heart failure: United States, 2000–2010. NCHS Data Brief. 2012:1–8.
- 47. Vaduganathan M, Fonarow GC. Epidemiology of hospitalized heart failure. Heart Failure Clin. 2013; 9:271–276.
- 48. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, Nodari S, Lam CSP, Sato N, Shah AN, Gheorghiade M. The global health and economic burden of hospitalizations for heart failure. Lessons learned from hospitalized heart failure registries. J Am Coll Cardiol. 2014; 63:1123–1133. [PubMed: 24491689]

Clinical Perspective

Given the increasing incidence and prevalence of obesity and diabetes mellitus (DM)both being risk factors for heart failure (HF)- the impact of DM on HF outcomes warrants close study. Using a nationally representative all-payer inpatient sample of U.S. hospital admissions from 2000–2010 our observations indicate that the total number of hospitalizations with a primary diagnosis of HF decreased while the prevalence of DM as well as a measure of comorbidity burden increased. Despite the increased prevalence of DM and co-morbid burden there was a 36% decrease in age-standardized in-hospital mortality among HF with DM. The decrease in in-hospital mortality was the result of a change in the stratum-specific risk for mortality rather than a change in age and/or sex structure of the 2000 and 2010 samples. However, in-hospital mortality rates varied by age, sex, race and ethnicity and emphasize the need to survey relevant strata within an overall population as well.

Study Population



Figure 1. Data Analysis Sequence

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Figure 2.

Decrease in age-standardized in-hospital mortality rate among men and women with heart failure and co-existing diabetes from 2000 to 2010. poverall $\chi^2 < 0.0001$. plinear trend < 0.0001

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Figure 3.

Decrease in crude in-hospital mortality rate among patients with heart failure and co-existing diabetes in different age groups (see text) from 2000 to 2010. p_{overall} $\chi^2 < 0.0001$. p_{linear trend} <0.0001 (for each stratum)

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Figure 4.

Decrease in crude in-hospital mortality rate among patients with heart failure and co-existing diabetes in different age groups (see text) stratified by sex, from 2000 to 2010. $p_{overall} \chi^2 < 0.0001$. $p_{linear trend} < 0.0001$ (for each stratum)

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Figure 5.

Decrease in in-hospital crude mortality rate in patients with heart failure and co-existing diabetes, by sex and ethnicity (Hispanic vs non-Hispanic), from 2000 to 2010. p_{overall} χ^2 <0.0001. p_{linear trend} <0.0001 (for each stratum)



Figure 6.

Decrease in in-hospital crude mortality rate in patients with heart failure and co-existing diabetes, by race (non-Hispanic white vs. composite non-white minority) from 2000 to 2010. poverall $\chi^2 < 0.0001$. plinear trend < 0.0001 (for each stratum)

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Table 1

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Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	Plinear trend	$\mathbf{P}_{\mathrm{overall}}$ \mathbf{X}^2
N (Sample)	88855	90786	95278	99786	97055	93189	93909	89727	89527	89685	87184		
N (Weighted)	435K	452K	460K	479K	469K	456K	459K	444K	438K	454K	436K		
HF/100,000	217	222	224	230	223	214	213	204	199	204	193	<0.0001	
Sex (%)													<0.0001
Male	43.1	43.6	44.1	44.9	46.0	47.5	47.9	48.4	49.3	49.9	50.4	<0.0001	
Female	56.9	56.4	55.9	55.1	54.0	52.5	52.0	51.6	50.7	50.1	49.6	<0.0001	
Age (%)													<0.0001
<60	18.4	18.2	19.1	19.4	19.6	19.6	20.5	20.3	19.6	20.1	20.3	<0.0001	
69-09	24.3	23.3	23.2	23.7	23.6	22.9	22.3	23.1	23.0	23.3	23.1	<0.0001	
70–79	33.7	33.5	32.8	31.5	31.2	30.3	29.6	28.9	28.5	28.2	27.2	<0.0001	
80	23.6	25.1	25.0	25.4	25.6	27.2	27.6	27.6	28.9	28.5	29.3	<0.0001	
Race (%)													<0.0001
White	68.3	67.7	64.9	62.6	63.4	67.3	61.9	61.7	63.9	63.2	60.8	<0.0001	
Black	18.7	18.5	20.7	20.5	21.6	17.4	21.2	22.2	20.6	20.6	23.6	<0.0001	
Hispanic	9.1	10.2	9.6	12.6	10.7	10.9	12.1	10.6	9.7	10.2	10.3	<0;0001	
Asian	1.6	1.6	1.9	2.0	1.9	1.7	1.9	2.1	2.1	2.1	2.2	<0.0001	
VN/IV	0.4	0.4	0.4	0.2	0.5	0.4	0.8	0.8	0.8	0.6	0.8	<0.0001	
Other	1.9	1.6	2.1	2.2	1.9	2.3	2.0	2.6	2.9	3.4	2.3	-	
Ethnicity (%)													0.0021
Non-Hispanic	92.9	92.4	92.8	90.7	92.1	92.0	90.9	92.0	92.1	91.1	90.8	< 0.0001	
Hispanic	7.0	7.6	7.2	9.3	7.9	8.0	9.1	7.9	7.9	8.9	9.2	< 0.0001	
Elixhauser comor	bidity ind	lex											
Mean (SE)	2.88 (0.04)	3.03 (0.04)	3.30 (0.06)	4.44 (0.06)	4.99 (0.07)	5.53 (0.09)	6.46 (0.10)	$\begin{array}{c} 0.50 \\ (0.09) \end{array}$	4.89 (0.06)	5.25 (0.06)	5.46 (0.07)	<0.0001	
HF = Heart Failure, /	AI/NA = A	American]	Indian/Nat	ive Alaska	an. SE = S	tandard ei	TTOF						

Table 2

In-hospital mortality in patients with heart failure and co-existing diabetes mellitus. Results from Poisson regression model

Variable	IRR	SE	p-value	95% Confidence Interval
Age 80 yr	1.00	-	-	-
Age 70–79 yr	0.58	0.01	< 0.0001	0.56-0.59
Age 60–69 yr	0.39	0.01	< 0.0001	0.38-0.40
Age <60 yr	0.27	0.01	< 0.0001	0.25-0.27
Female (vs. male)	0.81	0.01	< 0.0001	0.79–0.83
Hispanic (vs. non-Hispanic)	0.86	0.02	< 0.0001	0.82-0.89
Year (per year from 2000)	0.95	0.01	< 0.0001	0.94-0.94
Elixhauser comorbidity index (per 1 unit increase)	1.03	0.01	< 0.0001	1.03-1.04

Abbreviations: IRR, incidence rate ratio; SE, standard error

Table 3

Factors associated with in-hospital mortality in patients with heart failure and co-existing diabetes mellitus. Results from a logistic regression model.

Factor						
Tuctor	Odds Ratio	Confidence Interval (95%)				
Sex	Sex					
Male (vs. Female)	1.17	1.14-1.20				
Age (yrs)	Age (yrs)					
< 60	1.00	N/A				
60–69	1.51	1.43–1.59				
70–79	2.29	2.18-2.42				
80	4.08	3.87-4.29				
Race						
White (vs Non-White Minority)	1.3	1.26–1.34				
Ethnicity						
Non-Hispanic (vs Hispanic)	1.12	1.06–1.89				
Year	0.92	0.92–0.93				
Elixhauser comorbidity index	1.06	1.06-1.07				