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Cardiovascular Medication Utilization and Adherence Among Heart Failure Patients in Rural and Urban Areas: A Retrospective Cohort Study

Gaetanne K. Murphy, MSc,[a] Finlay A. McAlister, MD, MSc,[b] and Dean T. Eurich, PhD[a]

[a] School of Public Health, University of Alberta, Edmonton, Alberta, Canada

[b] Division of General Internal Medicine, Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

ABSTRACT

Background: Rural residence is a negative prognostic factor for heart failure (HF). The objective was to explore rural and urban differences in the utilization, adherence, and persistence with medications, and mortality among incident HF patients.

Methods: Using administrative databases from Alberta (Canada), subjects > 65 years old with a first hospitalization for HF between 1999 and 2008 who survived ≥ 90 days after discharge were identified. Pharmacy claims for renin-angiotensin system (RAS) agents, β-blockers (BBs), digoxin, or spironolactone were identified. The association between rural and urban residence and medication utilization, adherence (optimal adherence defined as ≥ 80% adherence over 1 year), persistence, and 1-year mortality was assessed.

Results: The cohort included 10,430 patients, with a mean age of 80.2 (SD, 7.7) years, 47% were male, and 25% were rural residents. Rural residents were less likely to receive RAS agents (74% vs 79%, adjusted odds ratio [aOR], 0.78; 95% confidence interval [CI], 0.69-0.89) or BBs (44% vs 54%; aOR, 0.83; 95% CI, 0.73-0.93) than urban residents, but had similar use of other medications. Although < 69% of patients who received RAS agents and 53% who received BBs had optimal adherence, few differences in adherence or persistence were detected among patients in rural vs urban areas. The 1-year mortality rate was significantly lower for patients who demonstrated optimal adherence to RAS agents or BBs (aOR, 0.78; 95% CI, 0.65-0.94) with no significant differences in the first 6 months between patients residing in rural vs urban areas.

RÉSUMÉ

Introduction : La résidence en zone rurale est un facteur pronostique négatif de l'insuffisance cardiaque (IC). L'objectif était d'examiner les différences entre le milieu rural et le milieu urbain quant à l'utilisation, l'observance et la persévérance dans la prise des médicaments, ainsi que la mortalité chez les patients nouvellement atteints d'IC.

Méthodes : À l'aide des banques de données administratives de l'Alberta (Canada), les sujets > 65 ans ayant eu une première hospitalisation pour une IC entre 1999 et 2008 qui survivaient ≥ 90 jours après le congé étaient relevés. Les demandes de remboursement pour des agents agissant sur le système rénine-angiotensine (SRA), des β-bloquants (BB), de la digoxine ou de la spironolactone étaient relevées. L'association entre la résidence en zone rurale et la résidence en zone urbaine pour ce qui est de l'utilisation des médicaments, de l'observance (observance optimale définie comme étant une observance ≥ 80 % durant 1 an), de la persévérance et de la mortalité à 1 an était évaluée.

Résultats : La cohorte de 10 430 patients dont l'âge moyen était de 80,2 (écart-type, 7,7) ans comptait 47 % d'hommes et 25 % de résidents de zones rurales. Il était moins probable que les résidents de zones rurales reçoivent des agents agissant sur le SRA (74 % *vs* 79 %, ratio d'incidence approché ajusté [RIAa], 0,78; intervalle de confiance [IC] à 95 %, 0,69-0,89) ou des BB (44 % *vs* 54 %; RIAa, 0,83; IC à 95 %, 0,73-0,93) que les résidents de zones urbaines, mais l'utilisation était similaire pour les autres médicaments. Bien que < 69 % des patients qui recevaient des agents agissant sur le SRA et 53 % des patients qui recevaient des BB montraient une observance optimale, peu de

Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-receptor blockers (ARBs), hydralazine with long-acting nitrates, β-blockers (BBs), and spironolactone have all been shown to decrease morbidity and mortality in patients with heart failure (HF).[1] Despite this evidence, these medications are often underutilized because of a failure to initiate, persist with, or adhere to therapy.[2-4]

In patients with HF, medication nonadherence alters the clinical status of patients and is associated with poor outcomes.[1,2,5] Although patient-related factors, such as resources, knowledge, and attitudes are often the focus of adherence, these represent just one dimension that affects adherence behaviour. There is increasing focus on the effect of geography on utilization and adherence to drug therapies and subsequent outcomes. Previous studies have observed rural vs urban variations in HF outcomes[6] that might, at least partially, be related to barriers such as social isolation, financial constraints, lower education, limited health care facilities, distance to care, physician shortages, and lack of access to specialist care.[7,8] Although it has been speculated that these barriers would cause harm through primary underuse of evidence-based

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Corresponding author: Dr Dean T. Eurich, 2-040 Li Ka Shing Center for Health Research Innovation, University of Alberta, Edmonton, Alberta T6G 2E1, Canada. Tel.: +1-780-492-6333; fax: +1-780-492-7455.

E-mail: deurich@ualberta.ca

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Conclusions: Rural residents with HF were less likely to receive RAS agents or BBs, but few differences in adherence were noted compared with their urban counterparts. Suboptimal adherence with evidence-based HF therapy was associated with increased risk of mortality.

différences dans l'observance ou la persévérance étaient détectées entre les patients des zones rurales *vs* les patients des zones urbaines. La mortalité à 1 an était significativement plus faible chez les patients qui démontraient une observance optimale du traitement par les agents agissant sur le SRA ou les BB (RIAa, 0,78; IC à 95 %, 0,65-0,94), et ce, sans différence significative entre les patients résidant en zone rurale *vs* les patients résidant en zone urbaine au cours des 6 premiers mois.

Conclusions : Il était moins probable que les résidents des zones rurales qui souffrent d'IC reçoivent des agents agissant sur le SRA ou des BB, mais peu de différences dans l'observance étaient notées comparativement à leurs homologues des régions urbaines. Une observance sous-optimale du traitement de l'IC fondé sur des données probantes était associée à l'augmentation du risque de mortalité.

medications, it is possible that these barriers might also negatively affect patient adherence to therapies, although data to support this premise are lacking.

Previous studies have shown that lower levels of adherence to evidence-based medications among HF patients is associated with increased risk of hospitalization and death.[9,10] However, we are not aware of any studies that have evaluated potential adherence differences according to rural vs urban residence. Thus, this study was undertaken to determine if, among newly diagnosed HF patients, the utilization, adherence, and persistence with HF-specific medications differs between those living in rural and urban areas, and whether these medication use patterns could explain 1-year mortality differences.

Methods

Setting

A population-based cohort of patients with incident HF was assembled using deidentified administrative databases from Alberta Health. Alberta Health manages a single-payer government-funded health care system that provides universal access to hospital, emergency department, and physician services for all 3.7 million residents within the province of Alberta, Canada. Patient data from 5 demographic, vital statistic, and health care utilization databases were linked as described previously.[11] Briefly, the Canadian Institute for Health Information Discharge Abstract Database supplied data on hospital admission dates, most responsible diagnosis, and up to 24 secondary diagnoses. The Alberta Blue Cross Medication Database provided outpatient prescription drug utilization data for all Alberta residents 65 years of age or older. The Alberta Health Care Insurance Plan Registry file provided demographic and vital statistics data, and the Ambulatory Care and Practitioner Claims Databases were used to obtain information on emergency department visits and office-based physician visits. The Health Ethics Research Board at the University of Alberta approved this study (Pro00033827).

Study cohort

We identified all subjects $>$ 65 years of age who were discharged from hospital between April 1, 1999 and December 31, 2008 with the most responsible diagnosis of HF (International Classification of Diseases [ICD] 9 or 10 code of 428.x or I50.x).[12,13] To ensure incident HF, we excluded those with a HF-related hospitalization (ICD 9/10 HF claim code in any diagnosis field) within 5 years before the index hospitalization. Because we were primarily interested in medication usage after diagnosis, to ensure subjects had sufficient opportunity to initiate therapies, we excluded all patients who died within 90 days of hospital discharge. In addition, those with an index hospitalization length of stay $>$ 365 days, missing postal code data, and patients with no claims in any of the databases during the follow-up period were also excluded. All patients were followed until death or 365 days after discharge from their index HF hospitalization. As per previous methodology used by Statistics Canada and others,[6,14] rural and urban residence was determined according to the postal code of each patient's home address obtained from the registry file.

Outcomes

The coprimary outcomes were the proportion of patients utilizing and adherent to HF-related medications. Utilization of HF-related medications was defined as at least 1 dispensation 7 days before and up to 1 year after discharge. Seven days before discharge was used to capture new prescriptions that might have been filled during the hospital stay or while patients were transitioning to out-of-hospital care. Adherence was defined as proportion of days with medication coverage (PDC) $\geq$ 0.8 for the medications of interest (ACEI, ARB, BB, digoxin, and spironolactone). By convention, the PDC was calculated as the sum of days with medication available divided by the total days of follow-up for patients with a minimum of 2 dispensations for that drug class.[15] The primary analysis assumed medication was available on the dispensation date and for the estimated number of days supplied, based on the quantity dispensed and usual dosing frequency. An 80% adherence level has been associated with a reduced risk of death in HF[5] and is the threshold commonly used in studies of cardiovascular medication adherence. Secondarily we evaluated medication persistence at 1 year. Persistence was defined as the availability of medication for at least 1 day during a 30-day window, at 3, 6, or 12 months after the first dispensation. Patients who died before the end of follow-up had their last observation carried forward. In addition, we evaluated whether adherence to HF-related medications within the first 6 months of discharge was associated with mortality in the subsequent 6 months. All outcomes were