Role of Primary Care Clinicians in the Management of Patients With Type 2 Diabetes and Cardiorenal Diseases

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Individuals with type 2 diabetes are at increased risk of both renal and cardiovascular events. The convergence of type 2 diabetes, chronic kidney disease, and cardiovascular disease, including heart failure, requires management by a multidisciplinary health care team. Primary care clinicians are likely to be the first and most frequent point of contact for individuals with type 2 diabetes who are at high risk of cardiorenal disease and therefore play a pivotal role in early diagnosis, establishment of effective treatment strategies, and coordination of care. This article presents a clinical perspective with multidisciplinary collaboration on a patient case representative of those seen in routine clinical practice. The authors assess reasons why patients may not receive evidence-based care and identify opportunities to initiate therapies that reduce cardiovascular and renal events in the primary care setting.

Both diabetes (present in 13% of adults in the United States, with type 2 diabetes accounting for 90% of these cases) and hypertension (present in 46% of adults in the United States) are independently associated with an increased risk of chronic kidney disease (CKD) and cardiovascular disease (CVD), including both ischemic heart disease and heart failure (HF) (1). Between 2013 and 2016, the estimated prevalence of CKD was 15% in the general U.S. population and substantially higher in people with diabetes or hypertension (37% and 31%, respectively) than in those without these conditions (1). The global prevalence of CVD in people with type 2 diabetes is estimated to be >30% and continues to increase (2). Given that people with type 2 diabetes are twice as likely to develop HF as those without type 2 diabetes (3), increased use of therapies that prevent cardiovascular events is needed.

The heart and kidneys are closely linked, and acute or chronic impairment in one organ can lead to dysfunction in the other (4). The term cardiorenal syndrome (CRS) is used to define the group of disorders that arise from this bidirectional dysfunction of the heart and kidneys (4,5). People with CRS, with or without diabetes, are at increased risk of mortality, hospitalization, and poor health-related quality of life, leading to elevated health care resource utilization (6,7). Furthermore, concomitant type 2 diabetes and CKD or HF increases the risk of adverse outcomes compared with type 2 diabetes alone. People with type 2 diabetes and CKD are at increased risk of major adverse cardiovascular events, HF, and all-cause mortality compared with those with type 2 diabetes alone (8). HF in people with type 2 diabetes has been associated with a higher 5-year absolute and relative risk of death when compared with those with type 2 diabetes but without cardiovascular or renal diagnoses (9).

The convergence of CKD, CVD, and type 2 diabetes poses a unique challenge to health care systems and requires management by a multidisciplinary team of health care practitioners. Here, we discuss the key role that primary care clinicians (PCCs) play in the management and treatment of individuals with type 2 diabetes and cardiorenal diseases. Although individuals with advanced cardiorenal diseases may be managed by cardiologists and/or nephrologists, PCCs often have long-standing relationships with these patients and see them more frequently than do specialists. In addition, PCCs

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remain crucial for maintenance of basic health needs and support.

Methods

Clinical perspectives on a patient case that is representative of those seen in routine clinical practice were gathered from a PCC, a nephrologist, and a cardiologist to assess opportunities for the earlier diagnosis and comanagement of cardiorenal diseases in individuals with type 2 diabetes. The role of PCCs in the treatment and management of individuals with CKD, HF, and type 2 diabetes was also discussed.

Case Presentation

An African American woman aged 58 years with type 2 diabetes and a BMI of 31.2 kg/m^2 was admitted to the hospital with dyspnea and fatigue. The patient had a history of hypertension, treated with lisinopril 20 mg once daily, and her blood pressure 1 month before admission was uncontrolled at 156/80 mmHg. Before admission, she was also receiving treatment with hydrochlorothiazide 25 mg once daily, metformin 1,000 mg twice daily, and glipizide 10 mg twice daily.

At admission, the patient had a blood pressure of 220/105 mmHg; a left ventricular ejection fraction of 45% (heart failure with mildly reduced ejection fraction [HFmrEF]) (10); left ventricular hypertrophy and grade 1 diastolic dysfunction; N-terminal pro-B-type natriuretic peptide (NT-proBNP) level of 2,789 pg/mL; serum creatinine level of 1.16 mg/dL (estimated glomerular filtration rate [eGFR] of 60 mL/min/1.73 m^2 [stage 2 CKD]); urine albumin-to-creatinine ratio (UACR) measurement of 80 mg/g; and normal complete blood count, electrolyte, and thyroid-stimulating hormone levels. Her A1C was 7.1%, suggesting relatively well-controlled blood glucose. Her chest X-ray showed mild cardiomegaly, bilateral infiltrates, small bilateral pleural effusions, and fluid in her pulmonary fissures. During hospitalization, the patient received treatment with intravenous furosemide, and her dose of lisinopril was increased to 40 mg daily.

The patient lost 3 kg in weight and diuresed 4 L during hospitalization, with a blood pressure of 110/70 mmHg at discharge. She was discharged feeling well, with new diagnoses of diabetic kidney disease (DKD) and HFmrEF, in addition to existing diagnoses of type 2 diabetes, hypertension, and obesity. Furosemide 40 mg once daily, metformin 500 mg twice daily, and lisinopril 40 mg once daily were prescribed at discharge, with glipizide 10 mg twice daily continued. Hydrochlorothiazide treatment was discontinued at discharge (Figure 1).

Opportunities for the Early Diagnosis and Management of Cardiorenal Diseases

Risk Factors for Cardiorenal Disease Progression in Individuals With Type 2 Diabetes

CKD is a common complication of type 2 diabetes, seen in ~40% of patients (1). Hemodynamic drivers (hypertension leading to increased intraglomerular pressure and hyperfiltration), metabolic drivers (hyperglycemia and hyperinsulinemia), and inflammatory drivers have each been shown to contribute to the development and progression of CKD in individuals with type 2 diabetes (11). In particular, hyperglycemia is associated with an increased risk of both microvascular and macrovascular complications, often leading to CVD (12,13). Individuals with diabetes have a two- to fourfold increased risk of developing CVD compared with those without diabetes (14).

With regard to HF, some studies have suggested that patients with type 2 diabetes have as much as a twofold increased risk of developing HF compared with people without type 2 diabetes (15,16). The exact mechanisms behind this increased risk remain poorly understood but are likely related to vascular disease (both macro- and microvascular), cardiovascular effects of common morbidities (e.g., hypertension, obstructive sleep apnea, and obesity), and diastolic dysfunction (17). A modest association between hyperglycemia and an increased risk of HF has been observed (18,19), and in a study of >2,500 patients with HF, the rates of hospital mortality and 30-day and 1-year mortality after hospitalization were higher in those with hyperglycemia than in those without (20). Other mechanisms such as inflammation (19), changes in myocardial substrate utilization (21), changes in mitochondrial bioenergetics (22), and increased glucotoxicity and lipotoxicity (23,24) may also increase an individual's risk of HF, making it challenging to establish the direct effect of glycemic control.

Opportunities for Earlier Diagnosis of CKD and HF in This Patient

It is recommended that annual eGFR and UACR tests to screen for CKD be performed in all individuals with type 2 diabetes irrespective of their treatment regimen (25). UACR is of particular importance given its strong association with adverse events in patients with renal disease. Individuals such as the patient in this case study, with a UACR >30 mg/g (and/or an eGFR <60 mL/min/1.73 m^2), should have their UACR and

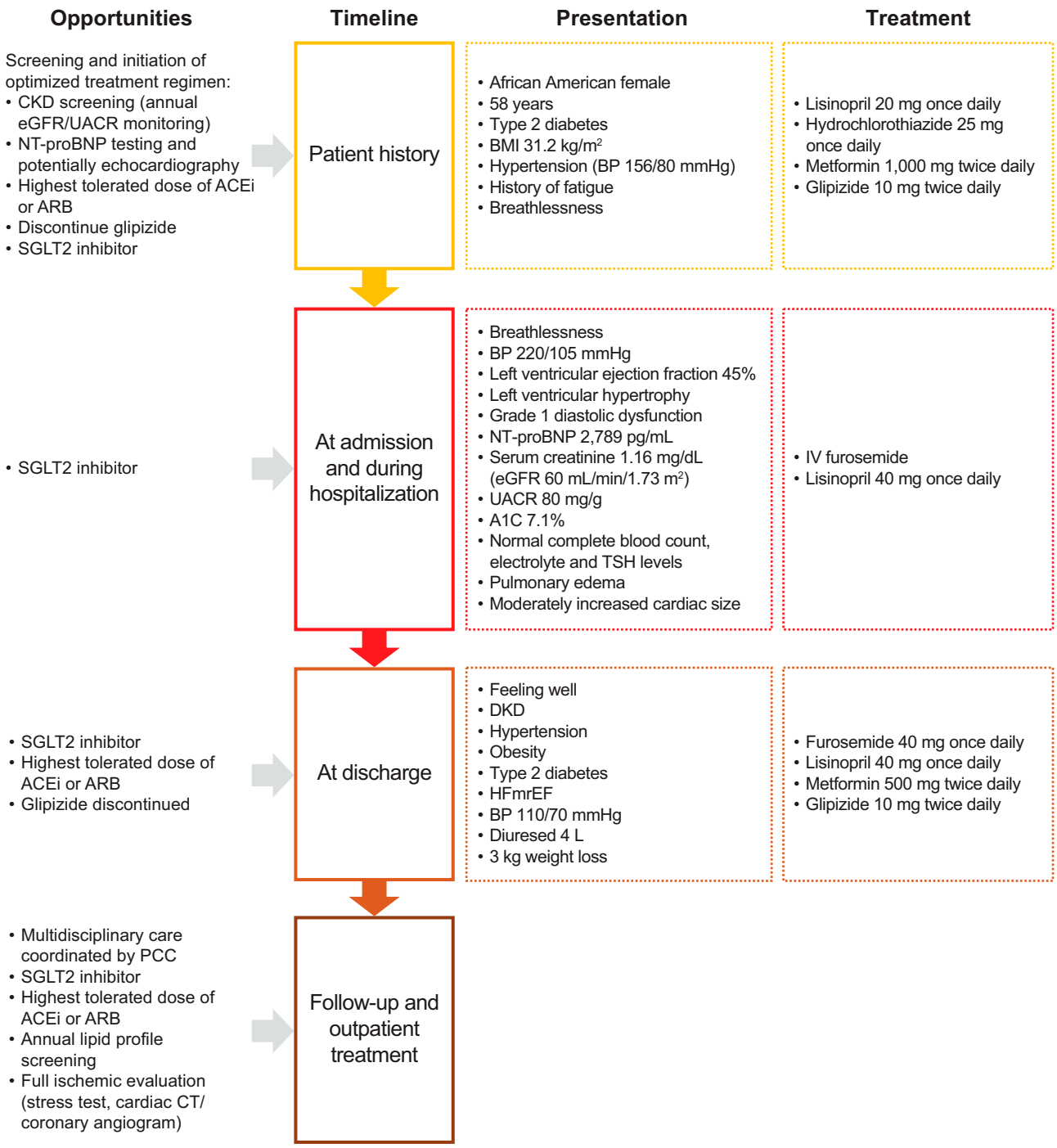

FIGURE 1 Case presentation and opportunities for earlier diagnosis and improved treatment of cardiorenal disease in a patient with type 2 diabetes. ACEi, ACE inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CT, computed tomography; IV, intravenous; TSH, thyroid-stimulating hormone.

eGFR levels monitored twice annually to guide therapy, according to American Diabetes Association (ADA) guidelines (25). Kidney Disease: Improving Global Outcomes (KDIGO) also recommends CKD screening, risk stratification, and treatment for high-risk individuals, including those with hypertension, diabetes, or CVD (26).

For many patients, the first diagnosis of HF is made during a presentation of acute decompensated HF. However, nonspecific signs (edema, swelling, and weight gain) or symptoms (shortness of breath with exertion, fatigue, paroxysmal nocturnal dyspnea, and/or orthopnea) of HF may have been present previously. Because CKD is a risk factor for HF, an earlier diagnosis of CKD

through eGFR and UACR screening in this patient, in addition to her existing diagnoses of hypertension, obesity, and type 2 diabetes, would have led to her being categorized as high risk for HF by her PCC (5,27).

Given this medical history, the patient would have been a candidate for B-type natriuretic peptide (BNP) or NT-proBNP testing, which is available to PCCs at a relatively low cost. Elevated levels (BNP ≥35 pg/mL and NT-proBNP ≥150 pg/mL) may be a sign of subclinical volume overload (28), and testing establishes a baseline for future comparison. When BNP or NT-proBNP levels are found to be elevated, an echocardiogram should be considered to evaluate cardiac function, including systolic and diastolic function, valvular heart disease, and other parameters of myocardial stress or dysfunction (29). Although access to and reimbursement of echocardiography may vary across health care settings and geographical locations, it is widely available throughout the world.

What Treatment Regimen Should This Patient Have Received?

Current evidence suggests that the treatment regimen this patient received before hospitalization was not optimized to prevent or delay the progression of cardiorenal diseases. Irrespective of their UACR measurement, patients with hypertension and diabetes should receive renin-angiotensin receptor inhibition with either an ACE inhibitor or an angiotensin receptor blocker; renin-angiotensin-aldosterone system inhibitors should be titrated to the maximal tolerated dose to reach a suggested blood pressure target of <130/80 mmHg (30,31). This target is in line with 2022 ADA guidelines for the management of CVD in type 2 diabetes (32), although an ideal blood pressure goal for patients with hypertension and diabetes has yet to be firmly established from randomized clinical trials. This patient, like many others, received a suboptimal dose of lisinopril, based on current guidelines (33). In addition, her relatively well-controlled glycemic level (A1C 7.1%), eGFR indicative of stage 2 CKD (60 mL/min/1.73 m^2), and high BMI (31.2 kg/m^2) meant that glipizide treatment was not ideal, given data demonstrating that this class of drug increases the risk of hypoglycemia and weight gain (17). It has also been suggested that treatment with sulfonylureas may exacerbate the risk of HF, although evidence is weak (34,35).

With her history of type 2 diabetes, hypertension, and obesity; new diagnosis of DKD; and the associated increased risk of HF, early treatment with a sodium–glucose cotransporter 2 (SGLT2) inhibitor would have been an ideal choice for the management of this patient's type 2 diabetes and comorbidities. Four SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin) have been approved by the U.S. Food and Drug Administration (FDA) for glycemic control, and their cardiorenal benefits have been demonstrated in randomized control trials (RCTs) (Table 1) (7,36–44). Based on these trial results, the FDA approved dapagliflozin for use in patients with either HF with reduced ejection fraction (HFrEF) (45) or CKD at risk for progression (46), regardless of their type 2 diabetes status. Furthermore, the FDA recently (August 2021) approved empagliflozin for use in patients with HFrEF (47).

Accordingly, SGLT2 inhibitors are included in the ADA's *Standards of Medical Care in Diabetes—2022* (32) and in particular were recommended for people with type 2 diabetes and established atherosclerotic CVD (ASCVD) or CVD risk factors, HFrEF, or CKD (32). SGLT2 inhibitors were also included in guidelines from the American College of Cardiology (ACC) in 2020 (48), the European Association for the Study of Diabetes in 2019 (49), the European Society of Cardiology (ESC) in 2021 (10), and KDIGO in 2020 (30) for the treatment of type 2 diabetes with CKD and/or HF.

Another class of glucose-lowering therapies, glucagon-like peptide 1 (GLP-1) receptor agonists, have also been shown in RCTs to significantly reduce cardiovascular events in people with type 2 diabetes and may slow progression of CKD (50–52). GLP-1 receptor agonists are therefore also included in the ADA's 2022 Standards of Care for people with type 2 diabetes and established ASCVD or CVD risk factors (32) or in people with CKD and increased risk for cardiovascular events (25).

Mineralocorticoid receptor antagonists (MRAs) may also be used with caution in patients with HF and type 2 diabetes to reduce the risk of mortality from HF (53–55). The FDA recently (July 2021) approved a third-generation MRA, finerenone, for the treatment of people with CKD associated with type 2 diabetes (56). Despite these new treatment options, a significant burden of CKD and CVD still exists in people with type 2 diabetes (32).

CKD is an independent risk factor for hypoglycemia (57), and concomitant use of SGLT2 inhibitors with sulfonylureas or insulin may increase the risk of hypoglycemia (58). In the case presented here, the patient's diagnosis of DKD and continuation of glipizide may

TABLE 1 Evidence of Cardiorenal Benefits of SGLT2 Inhibitors From Randomized Controlled Phase 3 Clinical Trials of SGLT2 Inhibitors Versus Placebo

Study (*N*)	Trial Population	Primary End Point(s)	Hazard Ratio (95% CI) for SGLT2 Inhibitor Versus Placebo; *P*
Dapagliflozin			
DECLARE-TIMI (*N* = 17,160) (36)	Patients aged ≥40 years with type 2 diabetes who had or were at risk for ASCVD	MACE (CV death, MI, or ischemic stroke)	0.93 (0.84–1.03); 0.17
		Composite of death from CV causes or HHF	0.83 (0.73–0.95); 0.005
DAPA-HF (*N* = 4,744) (37)	Patients aged ≥18 years with NYHA class II–IV HF with LVEF ≤40%, with or without type 2 diabetes	Composite of worsening HF (HHF or urgent visit resulting in intravenous therapy for HF) or death from CV causes	0.74 (0.65–0.85); <0.001
DAPA-CKD (*N* = 4,304) (38)	Patients aged ≥18 years with CKD (eGFR 25–75 mL/min/1.73 m^2 and UACR 200–5,000 mg/g), with or without type 2 diabetes	Composite of sustained eGFR decline >50%, ESRD, or death from CV causes	0.61 (0.51–0.72); <0.001
Canagliflozin			
CANVAS (*N* = 10,142) (39)	Patients with type 2 diabetes who were either aged ≥30 years with a history of symptomatic ASCVD or aged ≥50 years at high risk for CVD	Composite of death from CV causes, nonfatal MI, or nonfatal stroke	0.86 (0.75–0.97); <0.001
CREDENCE (*N* = 4,401) (40)	Patients aged ≥30 years with type 2 diabetes and CKD (eGFR 30–90 mL/min/1.73 m^2 and UACR 300–5,000 mg/g)	Composite of ESRD, doubling of serum creatinine level, or death from renal or CV causes	0.70 (0.59–0.82); <0.001
Empagliflozin			
EMPA-REG OUTCOME (*N* = 7,020) (41)	Patients aged ≥18 years with type 2 diabetes at high risk for CV events	Composite of death from CV causes, nonfatal MI, or nonfatal stroke	0.86 (0.74–0.99); 0.04
EMPEROR-Reduced (*N* = 3,730) (42)	Patients aged ≥18 years with NYHA class II–IV HF with LVEF ≤40%, with or without type 2 diabetes	Composite of death from CV causes or HHF	0.75 (0.65–0.86); <0.001
EMPEROR-Preserved (*N* = 5,988) (43)	Patients aged ≥18 years with NYHA class II–IV HF with LVEF >40%, with or without type 2 diabetes	Composite of death from CV causes or HHF	0.79 (0.69–0.90); <0.001
Ertugliflozin			
VERTIS CV (*N* = 8,238) (44)	Patients aged ≥40 years with type 2 diabetes and established ASCVD	MACE (composite of death from CV causes, nonfatal MI, or nonfatal stroke)	0.97 (0.85–1.11); <0.001

CANVAS, Canagliflozin Cardiovascular Assessment Study; CREDENCE, Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants With Diabetic Nephropathy; CV, cardiovascular; DAPA-CKD, A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients With Chronic Kidney Disease; DAPA-HF, Study to Evaluate the Effect of Dapagliflozin on the Incidence of Worsening Heart Failure or Cardiovascular Death in Patients With Chronic Heart Failure; DECLARE-TIMI 58, Dapagliflozin Effect on Cardiovascular Events; EMPA-REG OUTCOME, BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients; EMPEROR-Reduced, Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction; EMPEROR-Preserved, Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction; ESRD, end-stage renal disease; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; NYHA, New York Heart Association; VERTIS CV, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess Cardiovascular Outcomes Following Treatment With Ertugliflozin (MK-8835/PF-04971729) in Subjects With Type 2 Diabetes Mellitus and Established Vascular Disease.

partly explain why an SGLT2 inhibitor was not prescribed. However, used alone in DKD, SGLT2 inhibitors are not associated with a higher risk of hypoglycemia (40), and the ADA's *Standards of Medical Care in Diabetes—2022* recommended use of SGLT2 inhibitors independent of A1C level (59).

Given the evidence for the benefits of SGLT2 inhibitors on renal outcomes and the lack of equivalent evidence for the use of sulfonylureas, discontinuation of glipizide in favor of treatment with an SGLT2 inhibitor should have been considered. Although not indicated for HF in this case, the positive effect on cardiovascular outcomes seen with SGLT2 inhibitors may have offered additional benefits for this patient, who was high risk for HF.

Multidisciplinary Outpatient Management of Patients With Type 2 Diabetes and Cardiorenal Diseases

Why Is the Early Diagnosis of CKD and HF Important?

Early diagnosis and management of CKD is important for delaying CKD progression and preventing adverse clinical outcomes. In individuals >40 years of age who are otherwise healthy, there is a decline in eGFR of ~1 mL/min/1.73 m^2 per year (60). In type 2 diabetes, an accelerated annual eGFR decline of 2–3 mL/min/1.73 m^2 is often seen, even in those with relatively good glycemic control (A1C 6.5–7.0%) (61). Greater eGFR declines of 4–5 mL/min/1.73 m^2 per year occur in patients with albuminuria levels ≥900 mg/g (38,40). Severity of CKD and degree of albuminuria are multipliers of risks for cardiovascular events, progression to end-stage renal disease, and both cardiovascular and all-cause death.

Early drug therapy may also slow disease progression and improve clinical outcomes in individuals with HF, reducing their risk of hospitalization for acute heart failure (HHF). Reducing HHF is key in reducing cardiovascular-related mortality, because repeated HHF is a strong predictor of both all-cause and cardiovascular death (62). Often unrecognized, but critically important, the risk of cardiovascular death is additive, increasing with each subsequent HHF (63).

What Role Does Nutrition Play in the Management of Type 2 Diabetes and Cardiorenal Disease?

Guidelines from KDIGO for patients with type 2 diabetes and CKD and from the ACC/American Heart Association (AHA) for those with HF and/or type 2 diabetes recommend a balanced diet that is high in vegetables, fiber, legumes, nuts, plant-based protein, unsaturated fats, and whole grains and limited in phosphorus (30,64). In line with recommendations from the World Health Organization, the KDIGO guidelines also suggest a daily dietary protein intake of 0.8 g/kg body weight, a daily salt intake of <5.0 g, and at least 150 minutes of moderate-intensity physical activity per week (30,65). Importantly, diet should be tailored to each patient and result from shared decision-making between accredited dietitian nutritionists, diabetes educators, counselors, and other community health care practitioners (30).

What Was the Rationale for This Patient's Treatment Regimen?

Why Was the Patient Sent Home on Metformin?

Previously, it was suggested that metformin use in patients with HF may increase the risk of lactic acidosis, but subsequent research has not supported this relationship, and the boxed warning for metformin was removed in 2016 (66,67). The use of metformin has also been associated with hypoglycemia in patients with CKD, but guidelines now state that a dose of 1,000 mg metformin can be used safely in patients with an eGFR of ≥30–45 mL/min/1.73 m^2 (30,59,68). Given that the patient in this case had an eGFR of 60 mL/min/1.73 m^2 (stage 2 CKD), continued treatment with metformin was in line with guidelines. Furthermore, metformin use has been shown to be associated with better short- and long-term prognosis and reduced mortality in patients with HF and type 2 diabetes, suggesting that continued treatment with metformin in this case may be beneficial beyond glycemic control (66).

Should the Patient Have Been Prescribed a β-Blocker on Discharge?

Current ESC guidelines acknowledge that there is limited evidence for effective treatment of HFmrEF owing to a lack of dedicated RCTs in this group and therefore do not make strong recommendations for specific treatments. The use of β-blockers in patients with HFmrEF can be considered, particularly in patients with additional indications for a β-blocker (10). In this case, there was not a clear indication for the prescription of a β-blocker.

Why Was the Patient Not Prescribed an SGLT2 Inhibitor on Discharge?

Given her medical history and inpatient diagnosis, this patient was an ideal candidate for treatment with an SGLT2 inhibitor at discharge. However, despite the clear benefits of SGLT2 inhibitors in reducing adverse

renal and cardiovascular outcomes, there remains clinical inertia for prescription of SGLT2 inhibitors in type 2 diabetes and concomitant CKD and/or HF. This inertia is compounded by concerns regarding how to initiate the treatment safely in an inpatient setting (69). Trials testing SGLT2 inhibitors in an inpatient setting, including after a myocardial infarction and/or acute HF, are ongoing. In addition, access to SGLT2 inhibitors may vary among hospitals depending on whether they are available on inpatient formularies, which may also limit their use. Concerns remain regarding the risk of acute decline in eGFR and acute kidney injury (AKI) because of the renal mode of action of SGLT2 inhibitors. On the contrary, RCTs examining renal outcomes have shown that rates of AKI are reduced among those receiving SGLT2 inhibitors compared with placebo (70).

In this case, there may have been concerns about excessive diuresis and a perceived risk of natriuresis in the patient by combining an SGLT2 inhibitor with furosemide, because it has been suggested that the diuretic effect is a potential mechanism underlying the cardiorenal benefits of SGLT2 inhibitors (7). The RECEDE-CHF (SGLT2 Inhibition in Combination With Diuretics in Heart Failure) trial (71), a randomized, double-blind study of individuals with HF and type 2 diabetes who received a loop diuretic with either 25 mg of empagliflozin or a placebo, revealed that SGLT2 inhibition resulted in a sustained additional urine volume of about 500 mL/day throughout the 6-week trial. A 24-hour urinary sodium excretion comparison between the empagliflozin and placebo groups (71,72) suggested that concomitant treatment with a loop diuretic did not place patients at increased risk of an electrolyte imbalance. A subgroup analysis also showed that the benefits of SGLT2 inhibitors in patients with HF were similar with and without diuretic use (71).

Why Was the Hydrochlorothiazide Discontinued at Discharge?

Although combination therapies of loop and thiazide diuretics may be beneficial in individuals with diuretic-resistant edema, intensive treatment can lead to electrolyte disorders through sequential nephron blocking, increasing the risk of hypokalemia, hyponatremia, and hypotension (73,74). With this patient's diagnosis of HF and pulmonary edema and her eGFR of 60 mL/min/1.73 m^2, it is appropriate that hydrochlorothiazide was discontinued upon initiation of furosemide.

What Is the Role of PCCs in the Follow-Up Care of Patients With Cardiorenal Disease and Type 2 Diabetes?

Who Should Provide the Patient's Follow-Up Care?

AHA guidelines recommend a multidisciplinary approach to the management of individuals with type 2 diabetes and cardiorenal disease, with regular glucose, lipid, and blood pressure monitoring (7). However, patients often only have access to specialized care at a relatively late stage in their disease trajectory. PCCs are in a unique position to facilitate the early diagnosis of cardiorenal disease in individuals with type 2 diabetes, in addition to playing a key role in establishing their treatment regimen.

Primary care practices have an opportunity to coordinate the multidisciplinary management of these patients to ensure comprehensive care (7), in which the expertise of each specialty is maximized and type 2 diabetes, HF, and CKD are not treated as discrete problems. A team approach with input from nephrologists, cardiologists, endocrinologists, diabetes educators, social workers, and community support works best to manage individuals as outpatients. It is vital that a good chain of communication be established between PCCs and other specialists and that any changes to a patient's monitoring or treatment plan be made clear to the multidisciplinary team. Timely referrals to relevant specialists when appropriate are also key (Figure 2) (32,75).

What Treatment(s) Should Have Been Prescribed to This Individual as an Outpatient?

In line with recommendations from both the American Academy of Clinical Endocrinology and the ADA, this patient would have been an ideal candidate for outpatient therapy with an SGLT2 inhibitor (59,76). The renal and cardiovascular benefits of SGLT2 inhibitors have led health care professionals to question who should be responsible for their prescription—specialists such as nephrologists, cardiologists, and endocrinologists or PCCs such as primary care physicians (internal medicine and family medicine), primary care nurse practitioners, and primary care physician assistants? In a multidisciplinary team, not all providers feel comfortable prescribing a treatment originally indicated for use as a glucose-lowering therapy, despite one SGLT2 inhibitor (dapagliflozin) now having an independent indication for the treatment of CKD (46) and HFrEF (45) (FDA approvals granted in April 2021 and May 2020, respectively) in patients with and without type 2 diabetes (77).

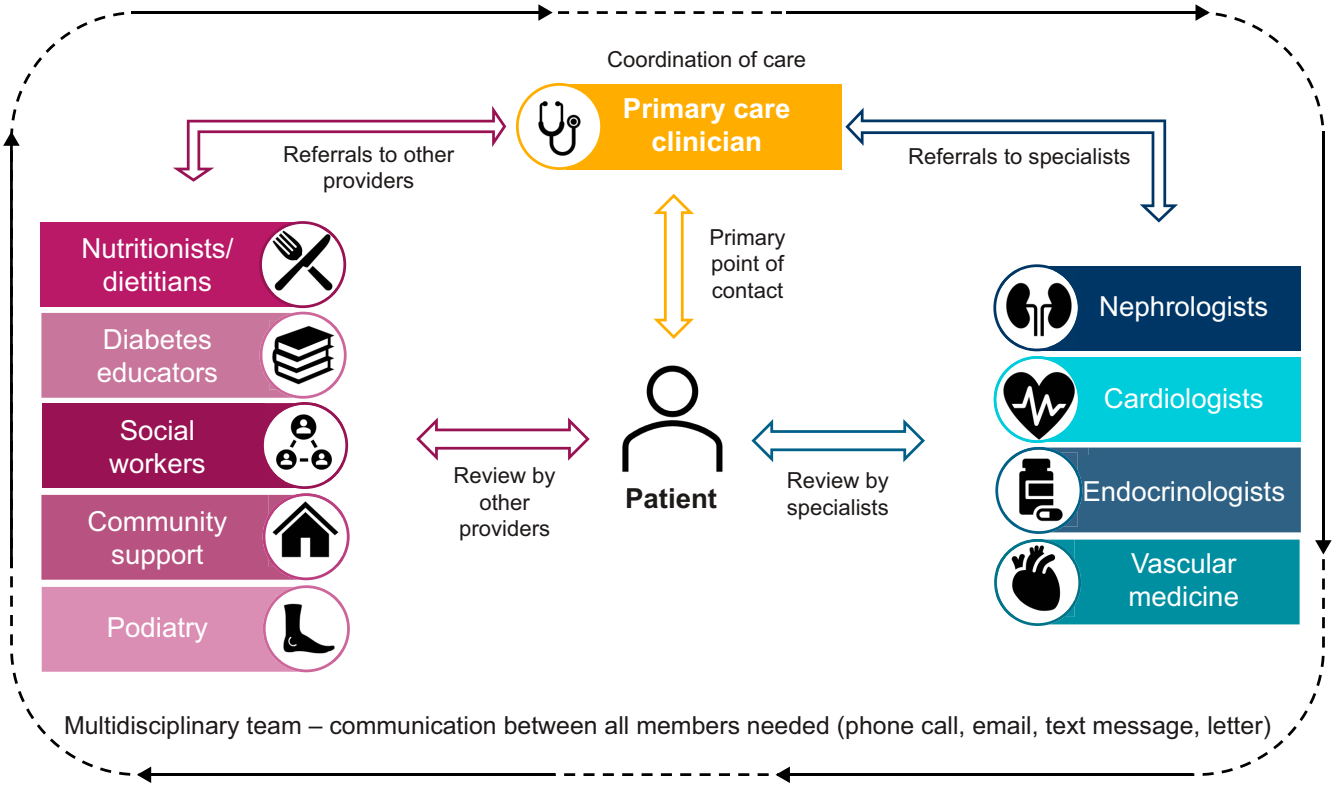

FIGURE 2 Multidisciplinary care for patients with type 2 diabetes and cardiorenal disease.

Experience and comfort with using these medications is growing, but despite the outcomes data supporting renal and cardiovascular benefits, the uptake of SGLT2 inhibitors has been slow in clinical practice. More needs to be done to ensure that all clinicians are familiar and comfortable with prescribing SGLT2 inhibitors and that cardiologists and nephrologists understand the renal and cardiovascular benefits of SGLT2 inhibitors.

Although responsibility should be shared between all clinicians, PCCs have a vital part to play in the timely prescription of SGLT2 inhibitors and the management and mitigation of potential side effects associated with their use. For example, SGLT2 inhibitor use is associated with an elevated risk of genital mycotic infections and may be associated with a slightly elevated risk of urinary tract infections (78). PCCs can play a role in mitigating these side effects by educating patients about appropriate hygiene. A transient decrease in eGFR of ~2–5 mL/min/1.73 m^2 may be observed within the first 2–4 weeks after SGLT2 inhibitor initiation (79–81). Although it is important for PCCs to be aware of this small decline in kidney function, this acute eGFR dip is largely reversible and does not have a negative effect on long-term cardiovascular and renal outcomes. SGLT2 inhibitor use may also cause transient volume depletion in the first 1–2 weeks of treatment (82), although AKI resulting from this drop can be prevented by volume status monitoring. Furthermore, there may be an increased risk of euglycemic diabetic ketoacidosis associated with SGLT2 inhibitor use, particularly in patients with restricted carbohydrate intake (83). However, these events are rare. It is important for PCCs to be aware of these potentially severe adverse events so they can monitor patients appropriately and make timely diagnoses should these events occur.

In addition to an SGLT2 inhibitor, it was appropriate that the patient in this case continue to receive treatment with an ACE inhibitor, but it should have been increased to the maximal tolerated dose (10,30), as used in studies of SGLT2 inhibitors for HF and CKD. Annual lipid profile screening and, if necessary, treatment with lipid-lowering medications per ACC/AHA guidelines (64,84,85) may also have been beneficial in this patient, given her HF diagnosis. Ideally, a full ischemic evaluation with a stress test, cardiac computed tomography scan, or coronary angiogram should have been considered. A summary of the case presentation and opportunities for improved treatment of this patient is provided in Figure 1.

What Are the Barriers to Multidisciplinary Management of Patients With Type 2 Diabetes and Cardiorenal Diseases, and How Can They Be Overcome?

Clinical inertia, or the failure to intensify treatment in a timely manner, is likely a major barrier to the multidisciplinary management of individuals with type 2 diabetes and concomitant CKD and/or HF. Clinicians and patients may be hesitant to make changes to treatment plans that appear to be working, and clinicians may overestimate how many of their patients are reaching treatment targets (86).

A lack of communication between clinicians may also prevent continuous multidisciplinary care, and more needs to be done to facilitate communication channels between clinicians, including regular contact between members of a multidisciplinary care team centered around a shared responsibility for facilitating treatment. Improving communication between clinicians and patients regarding the treatment plan is also important; regular review of medications at each visit will help to decrease the risk of polypharmacy (7).

Motivational interviewing may be beneficial for improving adherence to a complex shared treatment plan by engaging patients and establishing their motivations for change (87). As part of this effort, social determinants of health, particularly financial limitations that are prevalent in patients with type 2 diabetes, HF, and CKD, must be considered when making treatment decisions, because these can significantly affect patients' ability to adhere to treatment (31).

Conclusion

In this clinical vignette, we presented a patient with a history of hypertension, obesity, and type 2 diabetes who was hospitalized for breathlessness and discharged with a diagnosis of DKD and HFmrEF. This case is representative of many seen in clinical practice, in which earlier diagnosis of cardiorenal conditions may have prevented or delayed hospitalization.

The case highlights the key role PCCs should play in each stage of a patient's journey, from the early diagnosis of cardiorenal conditions (requiring improved risk factor recognition) to coordination of multidisciplinary care upon hospital discharge. It also shows that establishing good cross-team clinical guidelines and clear communication channels is essential for ensuring continuity of care.

In conclusion, early screening for cardiorenal conditions, adherence to current treatment guidelines, and management of patients across multidisciplinary teams provide vital opportunities to reduce the morbidity, mortality, and hospitalization rates of individuals with type 2 diabetes and cardiorenal diseases. Such efforts could reduce associated health care costs and improve patients' health-related quality of life.

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AUTHOR CONTRIBUTIONS

All authors contributed to the manuscript conceptualization, clinical content, manuscript writing, and discussion. All authors critically reviewed the manuscript and approved its final version for submission. P.R.K. is the guarantor of this work and, as such, had full access to all the data presented and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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