Original papers

Worsening renal failure in older chronic kidney disease patients with renal artery stenosis concurrently on renin angiotensin aldosterone system blockade: a prospective 50-month Mayo-Health-System clinic analysis*

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Summary

Background: The current US chronic kidney disease (CKD)/end stage renal disease (ESRD) epidemic, coincident with the increasing application of renin angiotensin aldosterone system (RAAS) blockade, has raised concerns of iatrogenic renal failure. The US population is an ageing one, further raising the possibility of increasing renal artery stenosis (RAS) in our patients. Current literature regarding worsening renal failure in CKD patients with RAS is based almost wholly on retrospective studies, and therefore may be poorly understood.

Aim: To prospectively examine the syndrome of worsening renal failure in CKD patients with hemodynamically significant RAS concurrently on RAAS blockade.

Design: Prospective cohort study.

Methods: Between September 2002 and February 2005, CKD patients, concurrently on RAAS blockade, with RAS >70% by magnetic resonance angiography, who presented with accelerated azotemia (≥25% increase in baseline serum creatinine) were consecutively enrolled. In addition to standard nephrology care, RAAS blockade was discontinued and renal percutaneous transluminal angioplasty (PTA)/stenting performed according to standard guidelines. Renal function as measured by MDRD-derived eGFR (estimated glomerular filtration rate) was monitored.

Results: Twenty-six Caucasian patients were enrolled—M:F = 10:16, mean age 75.3 years. Prior duration of RAAS blockade was 20.2 months. Known risk factors were absent in 15/26. Unilateral RAS with dual kidneys was common—19/26. Five patients, with higher baseline creatinine—2.1±0.6 vs. 1.5±0.4 mg/dl, P = 0.013, progressed to ESRD; 4/5 ESRD patients died after 6.3 months. Excluding the 5 with ESRD, and 2 lost to follow-up, in 19 patients, eGFR increased from 27.8±9.5 to 39.7±14.9 ml/min/1.73 m² BSA (P = 0.001), 26.4 months after stopping RAAS blockade. In these same 19 patients, mean arterial blood pressure improved from 100±9 to 92±10 mmHg.

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*This work is dedicated, first and foremost, to the memory of our dearly beloved and loving mother, mother-in-law and grand-mother, Mrs. Janet Nwofor, who passed on to the Lord in 2005. Second, this work is also dedicated to the memory of a pleasant unnamed 74-year-old white woman, with ESRD, who died suddenly at home, watching television, probably from a malignant cardiac arrhythmia, sometime in 2006.

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with 8 patients requiring additional antihypertensive substitutions. Renal PTA/stenting further improved eGFR in 7/9 patients.

Conclusions: Contrary to previous retrospective reports, we observed that renal failure/ESRD in this older CKD patient population is common in patients with unilateral RAS lesions with dual kidneys; precipitating risk factors are often absent, and progression to ESRD with increased mortality is not infrequent. Older age, higher baseline creatinine (>2.0) and/or lower eGFR (<35) predicted ESRD. eGFR improved following discontinuation of RAAS blockade, generally. Furthermore, in selected patients, renal PTA and stent placement led to additional improvements in eGFR. Our observations call for further studies.

Introduction

Since the mid 1990’s, an evidence-based consensus has emerged of enhanced renoprotection by renin angiotensin aldosterone system (RAAS) blockade with angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in diabetic chronic kidney disease (CKD) patients with microalbuminuria or overt proteinuria, as well as in nondiabetic nephropathies with proteinuria.1–5 Subsequently, the last two decades have witnessed an escalating use of RAAS blocking agents in clinical medicine here in the United States.6–8 In some surveys, nearly 80% of US diabetic patients are receiving an ACE inhibitor, an ARB or a combination of both agents.6,7

In the face of this increasing application of RAAS blocking strategies in the United States, over the past two decades, the incidence of end stage renal disease (ESRD)/CKD especially among US diabetics, had continued to rise, a rate of increase that had outpaced the rate of increase of the diabetes epidemic.9,10 Such observations and trends have led to increasing concerns regarding iatrogenic ESRD and CKD from the use of ACE inhibitors and/or ARBs in the United States.9 Moreover, Suissa et al.,11 in a population-based historical cohort analysis of 6102 diabetic patients in Canada, mean age 66 years, recently demonstrated an increased rate ratio of ESRD of 4.2 (95% CI: 2.0–9.0), after 3 years or longer of ACE inhibition. The association of accelerated renal failure in CKD patients with renal artery stenosis (RAS) on RAAS blockade is well reported and acknowledged.12–19 Nevertheless, these reports are mostly retrospective reviews, or small case series, or individual case reports.13,15–17 Furthermore, these studies suggest the need for the presence of identified risk factors to precipitate worsening azotemia, and almost always, these previous reports have implied common reversibility of the renal failure once the RAAS blocking agent(s) is withdrawn.13,15–19 Previously identified precipitating risk factors for precipitation of worsening renal failure in CKD patients with RAS on RAAS blockade include initiation of RAAS blockade, hypotension, volume depletion or dehydration, over-diuresis, infections, exposure to parenteral contrast media, exacerbated congestive heart failure (CHF), abuse of NSAIDs, dose increase of RAAS blocking agent(s) or a switch from one drug class to the other.12–19

Besides, previous reviews have indicated the necessity for the presence of bilateral RAS lesions in patients with dual kidneys, or the need for unilateral lesions in patients with single functioning kidneys to allow for the precipitation of worsening renal failure.12,14,15

Of note, the US population, like most populations in the developed world, continues to transform into an ageing population, further raising the probability of a higher incidence of RAS in our older CKD patient population. From the foregoing facts and concerns, we hypothesized that the syndrome of accelerated renal failure including ESRD, in ageing CKD patients with RAS, concurrently on RAAS blockade (ACE inhibitor and/or ARB), is poorly understood, may be under-recognized and under-diagnosed, and demands prospective examination and analysis.

Methods

Patient population

Between September 2002 and February 2005, over a 30-month period, at Luther Midelfort, Mayo Health System, Eau Claire, WI, as part of a larger cohort study, we prospectively enrolled all eligible CKD patients on RAAS blockade (ACE inhibitor, ARB, or both), who presented with accelerated worsening renal failure as defined by >25% increase in serum creatinine above baseline values, usually within the preceding 3 months or less. Standard nephrology care was administered with diagnosis-directed laboratory tests including urinalysis and culture, renal sonogram, serology testing, microbiology and toxicology as well as therapeutic interventions such as intravenous fluid repletion and antimicrobials when indicated. Diuretics were reduced or discontinued when indicated in patients with dehydration, hypotension and/or volume depletion. Gadolinium-enhanced magnetic resonance angiography (MRA), utilizing
three-dimensional gradient axial imaging was performed, when indicated by clinical guidance, and both two-dimensional and three-dimensional reformatted and reconstructed images were performed and viewed on 3D stand-alone stations to assess for the presence of RAS. Hemodynamically significant RAS was defined as the presence of unilateral or bilateral ≥70% narrowing in a major renal artery, and/or the presence of poststenotic dilatation. RAAS blockade was discontinued in all patients. Target mean arterial blood pressure (MABP) goals, according to current JNC VII guidelines were followed and additional antihypertensive substitutions with nonnephrotoxic agents were applied as necessary. Kidney function was subsequently monitored over time following withdrawal of RAAS blockade with serial measurements of serum creatinine and subsequent determination of estimated glomerular filtration rate (eGFR) by MDRD formula. Two or more weeks following discontinuation of RAAS blockade in these patients, persistence of renal failure triggered a consideration for renal percutaneous transluminal angioplasty (PTA) with stenting. Furthermore, uncontrolled hypertension (HTN) despite at least three antihypertensive medications and flash pulmonary edema were other indications for renal PTA and stenting.

We completed a 50-month review of data in November 2006, and present here the results in the patients who demonstrated the presence of hemodynamically significant RAS. IRB approval was obtained for this study.

Statistical analyses

For all continuous variables, the results are reported as means ±SD, with ranges shown in parenthesis. Differences between two means were calculated using the Student’s t-test method and a P-value of <0.05 was considered to be statistically significant. Paired t-test was used to compare differences within groups following an intervention whereas unpaired t-test was used to compare differences between groups. Baseline serum creatinine represents the previous available value, usually within 3 months or less of presentation and enrollment into the study. Enrollment serum creatinine, ≥25% increase above baseline values, represent the values at study entry. Final serum creatinine values represent the last available serum creatinine at study evaluation in November 2006. Serum creatinine values for each individual patient over time were collected, analyzed and expressed as MDRD-estimated GFR in ml/min/1.73 m² BSA. We used straight-line graphs to depict changes of eGFR in selected patients. Data was also shown in tables.

Results

Patient characteristics

Out of an estimated patient base of ~2000–3000 patients on an ACE inhibitor, an ARB, or a combination of both agents, that we have treated, 100 Caucasian CKD patients were enrolled during the 30-month enrollment period. We completed a 50-month follow-up in November 2006. There were 52 males, 48 females, mean age 71.5 (25–92) years. Of the 100 patients, MRA was available for analysis in 50 patients. Twenty-six patients had hemodynamically significant RAS, MRA was normal in 21 patients and three other patients showed minor stenotic lesions, not hemodynamically significant. We will now describe our prospective observations in the 26 CKD patients with hemodynamically significant RAS.

They include 10 males, 16 females, mean age 75.3 (63–87) years (Table 1). Seventeen of 26 (65%) patients were aged 75 years, or older. The RAS lesion was unilateral in 19 patients with dual kidneys, bilateral in six patients and unilateral in 1 patient with a single functioning right kidney following a left-sided nephrectomy more than 10 years prior to enrollment (Table 1). Medical diagnoses include HTN, diabetes mellitus (DM) and HTN, and DM alone. Eight of the patients also had diagnosis of CHF, mostly asymptomatic at study entry. Traditionally acknowledged precipitating risk factors for worsening renal failure were absent in 15 (58%) patients and present in only 11 (42%) patients. The risk factors identified in our study include initiation of RAAS blockade, administration of intravenous contrast/post acute myocardial infarction, obstructive uropathy, use or abuse of nonsteroidal anti-inflammatory drugs (NSAIDs), septicemia/pneumonia, volume depletion and switch from an ARB to an ACE inhibitor. One patient was on two ACE inhibitors, simultaneously, at enrollment. The mean duration of RAAS blockade at enrollment was 20.2 (0.5–48) months; six patients had been on RAAS blockade for more than 3 years prior to the development of accelerated renal failure. Lisinopril was the most common RAAS blocking agent in use among the cohort—12/26 patients were on lisinopril with a mean dose of 36 (5–80) mg/day. At study entry 20 out of 26 (77%) patients were on diuretics, including furosemide, hydrochlorothiazide and other diuretics. Due to hypotension or over-diuresis,
Table 1  Clinical profiles of the 26 CKD patients with renal artery stenosis

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Changes in serum creatinine, eGFR, MABP after withdrawal of RAAS blockade

In 24 patients, mean baseline eGFR prior to presentation was 41.5 ± 11.8 (20–70) ml/min/1.73 m² BSA (Table 1). Enrollment eGFR was lower at 24.3 ± 8.8 (11–47) ml/min/1.73 m² BSA (P < 0.001) (Table 1). RAAS blockade was withdrawn in all 26 patients. Antihypertensive substitutions were employed in 9/26 patients—amlodipine, hydralazine, clonidine, methyldopa, and minoxidil; 1 patient (#23 in Table 1) requiring two additional agents, amlodipine, 5 mg daily and hydralazine, 25 mg TID. The remaining 17 patients did not have antihypertensive substitutions.

Five patients (19%) progressed to ESRD despite withdrawal of RAAS blockade; 4 of the 5 (80%) patients with ESRD died 6.3 (1–11) months after starting hemodialysis (HD) and one was lost to follow-up. The causes of death are shown in Table 1. Excluding the 5 patients who progressed to ESRD, and another 2 patients lost to follow-up, in the remaining 19 patients, mean eGFR increased from 27.8 ± 9.5 (11–47) ml/min/1.73 m² BSA to 39.7 ± 14.9 (19–70) ml/min/1.73 m² BSA, (P = 0.001), 26.4 (14–38) months after withdrawal of RAAS blockade. Two of these 19 patients required temporary HD for 7 (4, 10) days (Table 1).

In the cohort, 17 patients did not undergo renal PTA and stent placement (Table 1). Of these 17 patients, 4 progressed to ESRD nevertheless, eGFR remained the same in 1 patient, but eGFR further decreased in 2 patients. In the majority, however, in 10 of 17 (59%) patients, eGFR improved from 24.7 ± 10.9 to 42.4 ± 13.9 ml/min/1.73 m² BSA, (P = 0.005), 23 (1–38) months following discontinuation of RAAS blockade.

Renal PTA with stent placement was performed in nine patients, unilateral in eight and bilateral in one (Table 1). Indications for renal PTA and stent placement include persistence of renal failure in eight patients, and symptomatic flash pulmonary edema in one. The 9 patients with renal PTA and stenting include 1 patient with single functioning kidney, 5 of 6 patients with bilateral RAS lesions and 3 of 19 patients with dual kidneys but only unilateral RAS lesions. Overall, eGFR improved in 6/9 patients following renal PTA with stenting. In all 3 of 19 patients with dual kidneys and unilateral RAS who underwent renal PTA and stent placement, eGFR improved from 36 ± 11 (25–47) to 49 ± 15.6 (31–59) ml/min/1.73 m² BSA, (P = NS) (Table 1).

Of the 5 patients with bilateral RAS who underwent renal PTA and stent placement, excluding 1 patient who progressed to ESRD, eGFR improved from 19 ± 8.1 (11–29) to 45 ± 18.2 (29–68) ml/min/1.73 m² BSA, (P = 0.04).

MABP improved following withdrawal of RAAS blockade—excluding the 5 patients who progressed to ESRD and the 2 lost to follow-up, in 19 remaining patients, MABP at presentation was 100 ± 9 (90–124) mmHg. This decreased to a lower MABP at last clinic visit of 92 ± 10 (74–111) mmHg, 22 (3–44) months after discontinuation of RAAS blockade, (P = 0.014). It must be acknowledged that in most of the patients, diuretic therapy was continued. Additional substituted antihypertensives were necessary in 9/26 patients.

Worth mentioning, 17/26 patients presented with anemia at enrollment, 16/26 with secondary hyperparathyroidism and 4/26 with hyperkalemia; most of these indices improved with better kidney function.

Of the 12 patients on lisinopril at enrollment, the average dose of lisinopril in 3 patients who developed ESRD was 41.7 (5–80) mg/day compared with an average dose of 24.4 (5–40) mg/day in the remaining 9 patients on lisinopril who did not progress to ESRD. Two of six (33%) patients with bilateral RAS developed ESRD despite renal PTA and stenting of unilateral lesions in 5 of the 6 patients; 2 died and 1 lost to follow-up (Table 1). Conversely, 3 of 19 (16%) patients with dual kidneys and unilateral renal artery stenosis developed ESRD; none of the 3 who progressed to ESRD had renal PTA and stenting and all 3 patients died (Table 1). No age difference was observed between the patients with RAS who developed ESRD and those who did not: 75.3 vs. 73 years, (P = 0.48).

Baseline serum creatinine was higher in the ESRD group, overall, when compared with the patients in the cohort who did not progress to ESRD—2.1 ± 0.6 (1.2–2.9) vs. 1.5 ± 0.4 (1.0–2.0) mg/dl (P = 0.013). Equally, baseline eGFR in the 5 patients who progressed to ESRD was lower than baseline eGFR in the 21 patients who did not: 33.0 ± 11.5 (20–48) ml/min/1.73 m² BSA compared with 43.8 ± 11.0 (27–70) ml/min/1.73 m² BSA, (P = 0.07).

Course of eGFR in one patient (#13) following drug withdrawal and subsequent left renal PTA and stent placement

Changes in eGFR, in one patient (#13 in Table 1), following withdrawal of RAAS blockade and subsequent left renal PTA with stent placement is shown graphically in Figure 1. This 67-year-old hypertensive was referred to us, in September 2004, ostensibly to start HD with symptomatic renal
failure, as serum creatinine had increased to 3.4 mg/dl, from a recent previous known baseline serum creatinine of about 2.0 mg/dl. She was anemic and hyperkalemic. She had been on lisinopril for 12 months prior to presentation with worsening renal failure. She was shown to have a small left kidney, measuring 7.9 cm together with an atretic left renal artery on MRA (Figure 2). The right kidney measured 9.7 cm with a >90% high grade RAS (Figure 2). We discontinued the lisinopril and within 2 weeks, serum creatinine had improved by more than 0.5 mg/dl. However with persistent renal failure, after 2 months, in November 2004, she underwent right renal artery PTA with placement of a 5 × 18 mm Genesis stent across the lesion. Serum creatinine promptly improved subsequently, and patient had a serum creatinine of 1.1 mg/dl, equivalent to an eGFR of 51 ml/min/1.73 m² BSA, 19 months following withdrawal of lisinopril and 17 months after right renal PTA and stent placement (Figure 1).

Discussion

We have compiled a comprehensive prospective database and follow-up of 26 older CKD patients with RAS presenting with worsening renal failure, while concurrently on RAAS blockade. We have demonstrated the behavior of renal function following discontinuation of RAAS blockade, with and without renal PTA and stenting in these patients. Our preliminary results were published previously.²¹,²² Ischemic renal disease has been previously described as an overlooked clinical entity,²³ and we believe that this syndrome is poorly understood, under-recognized and that several previously held beliefs regarding this syndrome may be out-dated or wrong. Generally, caution is advised in the use of ACE inhibitors and/or ARBs in (older) patients with hemodynamically significant RAS as acute exacerbation of renal failure may result. Clearly, however, quite often, at initiation of an ACE inhibitor and/or an ARB, the treating physician is unaware of the presence of RAS.²³

Often reversible renal failure, and rarely ESRD, associated with RAAS blockade in CKD patients with RAS, has been previously described, but mostly as retrospective reviews, or small case series, and as individual case reports.¹²–¹⁹ Previous studies often incriminated the need for precipitating risk factors to be present for renal failure to occur, and these studies also indicated common reversibility of the renal failure following withdrawal of RAAS blockade.¹²,¹³,¹⁵–¹⁸ Additionally, previous reports have stressed the necessity for bilateral RAS lesions in patients with dual kidneys, or unilateral RAS lesions in patients with single functioning kidneys to allow for the precipitation of worsening azotemia in CKD patients concurrently on RAAS blockade.¹²,¹⁴,¹⁵ Our observations from this prospective analysis appear to be different in several respects from several of these conclusions drawn earlier from previous reviews. In our cohort of 26 patients, 19 (73%) patients with dual kidneys only had unilateral hemodynamically significant RAS lesions but they still presented with accelerated renal failure. Thus, unilateral RAS lesions in patients with dual kidneys, was far more common than previously thought. Moreover, we observed that previously described precipitating risk factors such as initiation of RAAS blockade, hypotension, volume depletion or dehydration, over-diuresis, infections, exposure to parenteral contrast media, exacerbations of CHF, abuse of NSAIDs, dose increase of RAAS blocking
agent(s) or a switch from one drug class to the other, were absent in the majority (15/26) of our study patients. These observations could have significant impact and importance in the diagnosis and management of such patients when they present with accelerated renal failure to the practicing physician. Initiation of RAAS blockade, increase in dose of an ACE inhibitor or an ARB, or a change from one drug class to another have been previously implicated in the causation of renal failure in CKD patients with RAS. In contrast, our study showed that worsening renal failure was common following long periods, up to several years in some instances, of stable RAAS blockade on the same agent, and often without the need for a dose or drug change. Indeed, six patients in our cohort presented with accelerated renal failure, more than 3 years after initiation of RAAS blockade, and had remained on the same dose of the same agent all along. These new findings must be taken into consideration by treating physicians. Although lisinopril was the most common RAAS blocking agent used by the patients in our study, it must be noted, however, that this ACE inhibitor is the most commonly prescribed RAAS blocking agent in the US population, to date. Whether a particular ACE inhibitor or ARB, or any particular combination of an ACEI and an ARB, is more likely to aggravate worsening renal failure in CKD patients with RAS, remains to be demonstrated. Interestingly, one of our patients was simultaneously on two ACE inhibitors and the significance of this to precipitation of renal failure can only remain speculative.

Furthermore, the preponderance of currently available literature suggest that in most instances of worsening renal failure in CKD patients with RAS concurrently on RAAS blockade, kidney function tests almost always show a prompt normalization to baseline values following drug withdrawal. Only a few cases of irreversible ESRD have been reported heretofore. Quite the opposite, we have demonstrated progression to irreversible ESRD requiring dialysis treatment in 5 of 26 (19%) patients despite withdrawal of RAAS blockade at enrollment, followed by renal PTA and stent placement in 9/26. Four of the five (80%) patients with ESRD were dead within 7 months; one was lost to follow-up. Two additional patients, required temporary HD. Even though a direct cause–effect relationship between RAAS blockade and the observed ESRD/deaths cannot be proved from our study, we submit that renal failure associated with RAAS blockade in CKD patients with hemodynamically significant RAS could more often than previously thought, lead to irreversible ESRD and/or death and must be taken more seriously. Again, we agree with an earlier claim that ischemic renal disease is indeed an overlooked and under-diagnosed clinical entity. It is possible that earlier drug withdrawal in our cohort patients may have led to better renal and patient outcomes. ESRD occurred more frequently in 2 of 6 (33%) patients with bilateral RAS lesions vs. 3 of 19 (16%) patients with dual kidneys and unilateral RAS lesions, but clearly not exclusively so. This higher risk for ESRD among patients with bilateral RAS is even more striking given the fact that 5/6 patients with bilateral lesions vs. 2/19 patients with unilateral lesions underwent PTA and stent placement. Outstandingly, we note that our study patients, mean age of 75.3 years, are clearly older than the general outpatient population, with 17 of 26 patients (65%) aged 75 years or older and 6 of 26 (23%) were aged 80 years or older. The older patients are more likely to have significant RAS. Additionally, from our analysis, a higher dose of RAAS blockade imposed a higher ESRD risk. Also, patients with higher baseline serum creatinine (>2.0 mg/dl), or lower eGFR (<35 ml/min/1.73 m² BSA), had a higher risk for ESRD. These factors and considerations must be entertained and utilized by physicians who come across such patients in clinical practice. Clearly, as evident in 17 patients who did not have renal PTA and stent placement, significant improvement in kidney function occurred following discontinuation of RAAS blockade and application of standard nephrology care. This is evidence to implicate RAAS blockade as a causative factor in the presentation of worsening renal failure in these CKD patients with RAS. However, of note, renal PTA and stent placement, in selected patients, further improved renal and overall clinical outcomes (Figure 1). These results, although a single-center experience and a small study, call for further expanded examination and study especially in the light of current ongoing debate regarding the best treatment algorithm for symptomatic RAS – medical treatment vs. renal PTA with stent placement.

**Conclusion**

We have reported a prospective 50-month follow up of older CKD patients with hemodynamically significant RAS, who developed accelerated renal failure while concurrently on RAAS blockade and the course of kidney function as measured by eGFR following discontinuation of the ACE inhibitor, or the ARB. We identified certain characteristics of this syndrome different from conclusions drawn from several prior mostly retrospective reviews and analyses. This syndrome must be taken more seriously as irreversible ESRD and significant patient...
mortality could result from delay in stopping RAAS blockade in appropriately selected cases. Remarkably, there may or may not be precipitating risk factors present prior to onset of accelerated azotemia in these patients. The RAS lesions can, more often than previously reported, be only unilateral in patients with dual kidneys. Besides, older age, higher baseline serum creatinine (>2.0 mg/dl), or lower eGFR (<35 ml/min/1.73 m² BSA), together with higher doses of RAAS blockade appear to increase the ESRD risk. Prompt discontinuation of RAAS blockade, with or without renal PTA and stent placement, in selected patients often result in sustained renal salvage and improved patient outcomes. Our findings clearly call for larger multi-center studies especially given new concerns regarding possible iatrogenic renal failure in CKD patients on RAAS blocking agents, more so with an increasingly ageing US diabetic population.

We must conclude with a strong disclaimer here. We support current evidence-based guidelines recommending the judicious use of ACE inhibitors and/or ARBs in diabetics with microalbuminuria or overt proteinuria and in nondiabetic nephropathies with proteinuria.1–5 There is, we believe, significant evidence base for the benefits of renoprotection with these agents in these clinical settings, far beyond blood-pressure lowering.1–5 We robustly are in agreement with current guidelines which recommend that small but nonprogressive increases in baseline serum creatinine, up to 30%, following the initiation of an ACEI or an ARB should not warrant drug discontinuation as long-term benefits of renoprotection will outweigh this initial limited loss of eGFR.1,25 We propose that all patients, particularly the older patients, on RAAS blockade, should have kidney function monitored closely and indefinitely, at least every 3 months, by eGFR, and not just for the first 3 months of drug initiation. In addition, as was the case with our study cohort, the subsequent observation of progressive and/or accelerating increases in serum creatinine (falling eGFR), in CKD patients on RAAS blockade, at any time, in the absence of any other plausible explanation, may warrant trial discontinuation of RAAS blockade. We submit that such cautiously pragmatic and prudent application of RAAS blockade, particularly in the older CKD patient, will only further enhance the benefits of renoprotection.

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References


