Cost-utility of urinary C-C motif chemokine ligand 14 biomarker (CCL14) in predicting persistent severe acute kidney injury (PS-AKI)

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Introduction

Acute kidney injury (AKI) is staged according to disease severity. Some patients with stage 2 or 3 AKI recover their kidney function in 2 to 3 days of AKI onset. In others, kidney dysfunction persists for up to 7 days and may progress to acute kidney disease (AKD, 7–90 days) or CKD (>90 days).

Persistent severe AKI (PS-AKI), defined as either stage 3 AKI lasting ≥3 days or with death in ≤3 days, or stage 2 or 3 AKI with dialysis in ≤3 days, occurs in 25% of hospitalized patients with stage 2 or 3 AKI [1]. PS-AKI leads to worse outcomes and higher costs [1, 2]. Identifying patients at risk for PS-AKI could provide clinicians with information to help guide evaluation and management strategies to reduce the risk of further kidney damage and associated poor outcomes.

The urinary C-C motif chemokine ligand 14 (CCL14) biomarker predicts PS-AKI in patients with stage 2 or 3 AKI [3], allowing the implementation of interventions to prevent PS-AKI, which may improve clinical and economic outcomes.

Objective

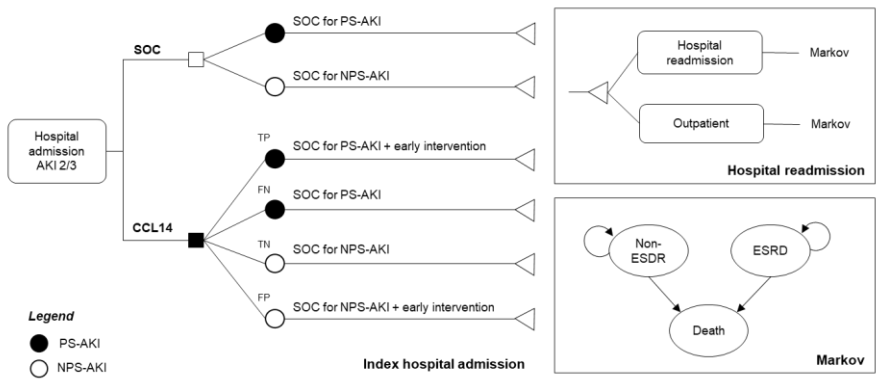
To explore the cost-effectiveness of in-hospital CCL14 testing in addition to standard serum creatinine and urinary output monitoring, compared to standard of care (SOC) alone, from a US third-party payer perspective.

Methods and Materials

The analysis combines a decision tree using CCL14 operating characteristics to identify patients predicted to have PS-AKI and modeled 90-day clinical outcomes, with a Markov cohort estimating lifetime costs and quality-adjusted life years (QALYs) (**Figure 1**).

It was assumed that patients requiring dialysis at 30-day follow-up would be dialysis dependent for life (ESRD) with the remaining patients completely recovering from AKI (non-ESRD). The Markov model used 90-day cycles (decision tree duration) and half-cycle correction.

Figure 1
Economic model structure



Acronyms: AKI, acute kidney injury; ESRD, end-stage renal disease; FN, false negative test FP, false positive test; NPS, non-persistent severe; PS, persistent severe; SOC, standard of care; TN, true negative test; TP, true positive test

The modeled population consists of 66-year-old patients admitted to a US hospital, 50% females, and AKI by serum creatinine stage 2 (53%) or stage 3 (47%) [1].

The rate of true positives (TP) was informed by CCL14 sensitivity (0.91 [95% confidence interval 0.84 to 0.96]), and true negatives (TN) by the test specificity (0.51 [0.44 to 0.57]) at the 1.3 ng/ml CCL14 concentration cutoff [3].

US lifetables [4] and USRDS data [5] informed mortality in the absence or presence of ESRD, respectively.

The probability of critical care requirements, 30-day readmission, out-patient care requirements, dialysis dependence, and death were informed by the analysis of a large retrospective cohort (n=126,528) of adult patients discharged between 01/01/2017 and 31/12/2019, covering one-fifth of all US hospital admissions [1].

There is no consensus about the most efficacious intervention for preventing PS-AKI, therefore, the base case assumed an early hypothetical intervention would be only 10% efficacious in reducing all clinical and cost consequences of PS-AKI in TP patients.

Length-of-stay and costs were sourced from a published analysis of PINC AI Healthcare data [2]. Costs of dialysis used the base rate for renal dialysis services ($266) assuming 3 weekly sessions over 52 weeks [6]. Costs were reported as 2023 US dollars.

The cost of CCL14 testing was assumed to be $0 as there is currently no market price for CCL14 in the US. It was assumed that a hypothetical intervention would have the same cost in both comparators but would be implemented earlier in people testing positive for PS-AKI.

Utilities were sourced from published UK and US economic evaluations of renal therapies.

Incremental cost and QALYs accrued over the index admission, 30-day readmission, critical care use, dialysis dependence, and death in the CCL14 and SOC arms were calculated and synthesized as incremental cost-effectiveness ratios (ICER) (**Equation 1**).

Equation 1 $$ICER = (Costs\_CCL14 - Costs\_SOC)/(QALY\_CCL14 - QALY\_SOC)$$

Uncertainty surrounding a hypothetical intervention's efficacy and cost and CCL14 cost was explored in two-way sensitivity analyses (TWSA). Input uncertainty was explored in deterministic (**figure 2**) and probabilistic sensitivity analyses (PSA). Costs/effects were discounted at 3% annually.

Results

In the base case, assuming the intervention would avoid 10% of PS-AKI complications in AKI stage 2 or 3 patients identified as TP resulted in 0.07 additional QALYs and a $486 reduction in in-patient and dialysis costs per capita (CCL14 dominates) (**Table 1**).

Table 1
Base case results

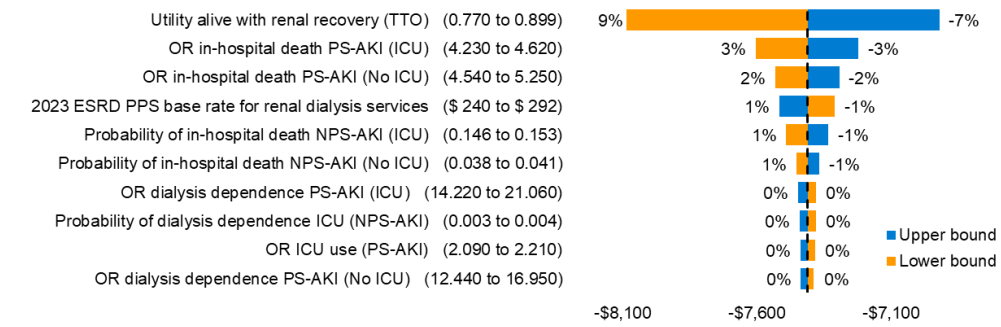
	Outcomes	CCL14	SOC	Incremental
Costs	Index Hospitalization (no ICU)	$10,053.25	$10,052.75	$0.49
	Index Hospitalization (ICU)	$21,152.23	$21,574.75	-$422.52
	Hospital readmission	$2,884.90	$2,881.15	$3.75
	Total Inpatient costs	**$34,090.37**	**$34,508.65**	**-$418.27**
	Outpatient visits	$395.20	$393.24	$1.96
	Dialysis	$1,057.72	$1,127.63	-$69.91
	Total Lifetime Costs	**$1,452.92**	**$1,520.87**	**-$67.95**
	Total costs	**$35,543.30**	**$36,029.52**	**-$486.22**
Effects	Life-years on dialysis	0.026	0.027	-0.002
	Life-years	11.118	11.040	0.078
	QALYs	9.282	9.216	0.066
	ICER ($/QALY)	**CCL14 Dominates**		**-$7,410.45**

Acronyms: CCL14, C-C motif chemokine ligand 14 biomarker; ICER, Incremental cost-effectiveness ratio; ICU, intensive care unit; QALY, quality-adjusted life-year; SOC, standard of care

When varying costs and efficacy of a hypothetical intervention and CCL14 cost in TWSA, the model predicted that adding CCL14 to better inform clinical actions was associated with lower costs and more QALYs (dominating) or was cost-effective at a willingness to pay of $50,000 to $100,000/QALY (**Figure 3**).

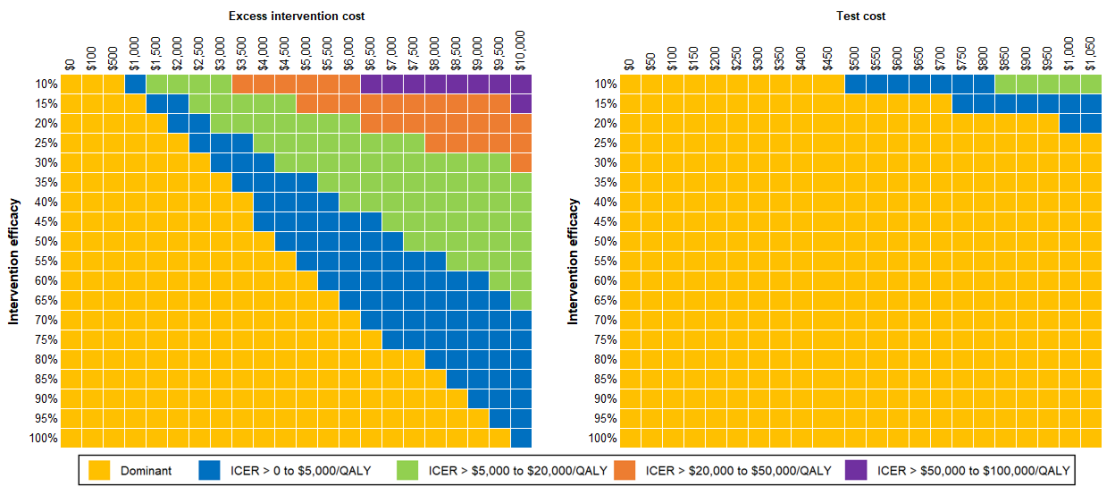
PSA results were very similar to the base case (ICER -$7,446, 95% credible interval -$8,103 to -$6,944). Using CCL14 in addition to standard of care practices was associated with a 100% probability of being cost-effective at any willingness to pay. The results were robust to substantial variation of costs and efficacy of the intervention, and CCL14 costs.

Figure 2 One-way sensitivity analyses results



Acronyms: ESRD, end-stage renal disease; ICU, intensive care unit; NPS-AKI, non-persistent severe acute kidney injury; PPS, Prospective Payment System; PS-AKI, persistent severe acute kidney injury; OR, odds ratios; TTO, time-trade off.

Figure 3 ICERs resulting from TWSA varying efficacy and cost of an early intervention, and CCL14 costs



Acronyms: C-C motif chemokine ligand 14; ICER, incremental cost-effectiveness ratio QALY, quality-adjusted life year.

Discussion

Strengths: (1) Modelling is aligned with previous peer-reviewed publications; (2) model inputs were informed by analysis of large US dataset capturing one-quarter of all hospitalized patients; (3) thorough exploration of uncertainty in scenario and sensitivity analyses.

Limitations: (1) 30-day readmissions to hospitals outside the database network were not captured; (2) lack of evidence for the assumption underlying the 10% efficacy of a hypothetical intervention in preventing PS-AKI; (3) cost and adverse events of hypothetical intervention equal for CCL14 and SOC; (4) cost of testing was $0; (5) 30-day dialysis used as proxy for lifetime dialysis dependence. These limitations were extensively explored in sensitivity and scenario analyses.

Assuming that an early intervention can reduce progression to PS-AKI, the model is supportive of CCL14 cost-effectiveness in identifying patients at risk of PS-AKI to guide clinical practice.

Conclusions

These findings suggest CCL14 is likely to represent a cost-effective use of resources in the presence of an efficacious intervention such as the consistent implementation of the Kidney Disease Improving Global Outcomes (KDIGO) bundle [7].

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