The impact of empagliflozin on eGFR and albuminuria: results from the ABCD nationwide empagliflozin audit

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Introduction

Following the launch of Association of British Clinical Diabetologists (ABCD) audit programmes for dapagliflozin and canagliflozin, the ABCD nationwide empagliflozin audit was launched in March 2017. A recent expansion to include anonymised datasets from clinical commissioning groups (CCGs), the primary care groups responsible for commissioning care in the United Kingdom, has vastly increased the number of patients included, as well as allowing the inclusion of new data to expand analyses or look at some aspects in more detail. The recent addition of albuminuria concentrations has facilitated this analysis.

What we know so far

Evidence from the phase III EMPA-REG outcome trial demonstrated reductions in the rates of progression of diabetic nephropathy with empagliflozin use compared to placebo (HR 0.61, 95% CI 0.53-0.7)[1]. Similar beneficial effects on slowing decline in renal function have been demonstrated by EMPEROR-reduced[2]. The ongoing EMPA-Kidney trial is deisgned specifically to assess renal and cardiovascular outcomes in people with pre-existing renal disease both with and without diabetes and is expected to complete in 2022[3].

Methods

Data were collated via the ABCD nationwide audit programme. Patients with sufficient data for eGFR and/or albuminuria at baseline and follow-up were included in the analysis. Change in eGFR levels and albuminuria levels from baseline were analysed.

Stratified sub-group analyses by baseline eGFR and albuminuria were performed using groups. For eGFR this was done as follows:

Group CKD1 – eGFR ≥90mL/min/1.73m^2 (n=3,842)
Group CKD 2– eGFR 60-89mL/min/1.73m^2 (n=2,920)
Group CKD3+ – eGFR <60mL/min/1.73m^2 (n=137)

For albuminuria , by albumin creatine ratio (ACR), this was done as follows:

Group normoalbumnuria – ACR <30mcg/mg(n=6225)
Group microalbuminua – ACR 30-300mcg/mg (n=610)
Group macroabluminuria – ACR >300mcg/mg (n=64)

Data were analysed using paired t-tests and analysis of variance where the distribution was normal. For non-normally distributed variables (albumin creatinine ratios) Wilcoxon-Signed Rank tests and Kruskal-Wallis tests were used. Analysis was performed in Stata SE 16.

Results

6,899 patient datasets were included, with baseline characteristics as outlined in **Figure 1.**

Across the population as a whole albumin creatinine ratios decreased by a median of 0.1mg/mmol (P<0.0001, 95% CI 0, 0.2) (mostly due to excessive skew towards zero). Stratified by baseline albuminuria levels those with microalbuminuria (30-300mcg/mg) or macroalbuminuria (>300mcg/mg) had significant improvements in urine albumin levels at 12-months (9-18 months) follow-up, with respective median changes of -34.75mcg/mg (P<0.0001; 95% CI -28.9, -39.4) and -331.2mcg/mg (P<0.0001; 95% CI -212.4, -506.7).

Population wide reductions in eGFR were observed at 6-months (2.75ml/min/1.73 m$^{3;}$ P<0.0001; 95% CI -2.3, -3.2) before stabilising. Stratified by baseline eGFR, those with mildly reduced renal function (eGFR 60-90) trended towards improved eGFR at 12-months, following initial reductions, whilst those with eGFR<60 had increases in eGFR at both intervals. When stratified by albuminuria, all groups had an initial dip in eGFR, most profound in the macroalbuminuric group, which subsequently stabilised or return to baseline by 12-months. **See figures 2 and 3.**

Fig 1. Table showing the baseline characteristics of those included in this analysis of the ABCD empagliflozin audit

Characteristic	n=6899
Age, years ± SD	60.6 ± 10.4
Male, %	62.0
Median diabetes duration, year (IQR)	8.4 (4.7-12.7)
Mean Hba1C, % ± SD	9.28 ± 1.56
mmol/mol ± SD	77.9 ± 17.0
Mean BMI, kg/m2 ± SD	33.9 ± 6.7
Mean weight, kg ± SD	98.0 ± 21.3
Mean serum creatinine, umol/L ± SD	73.0 ± 16.3
Mean eGFR, mL/min/1.73m^2 ± SD	95.4 ± 22.6
Mean systolic BP, mmHg ± SD	133.1 ± 14.1
Mean diastolic BP, mmHg ± SD	78.3 ± 9.2
Median albuminuria, mcg/mg, by group (IQR)	
Normal - <30mcg/mg (n=6225)	2.5 (1.1-7)
Microalbuminuria – 30-300mcg/mg (n=610)	57.7 (40-97.5)
Macroalbuminuria - >300mcg/mg (n=64)	569.3 (417.4-843.4)

BMI, body mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; IQR, interquartile range; SD, standard deviation

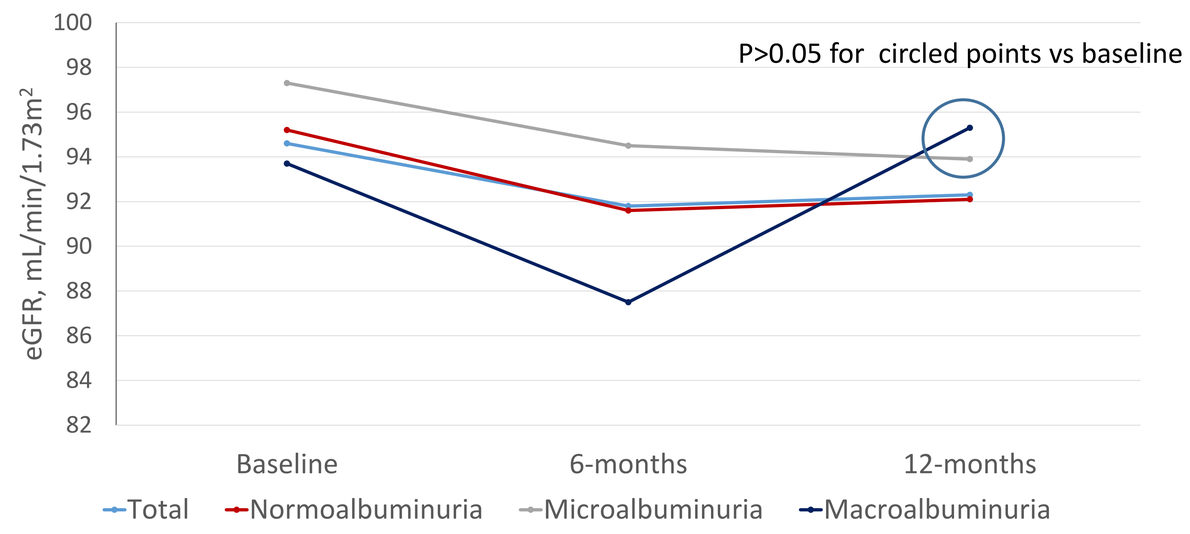
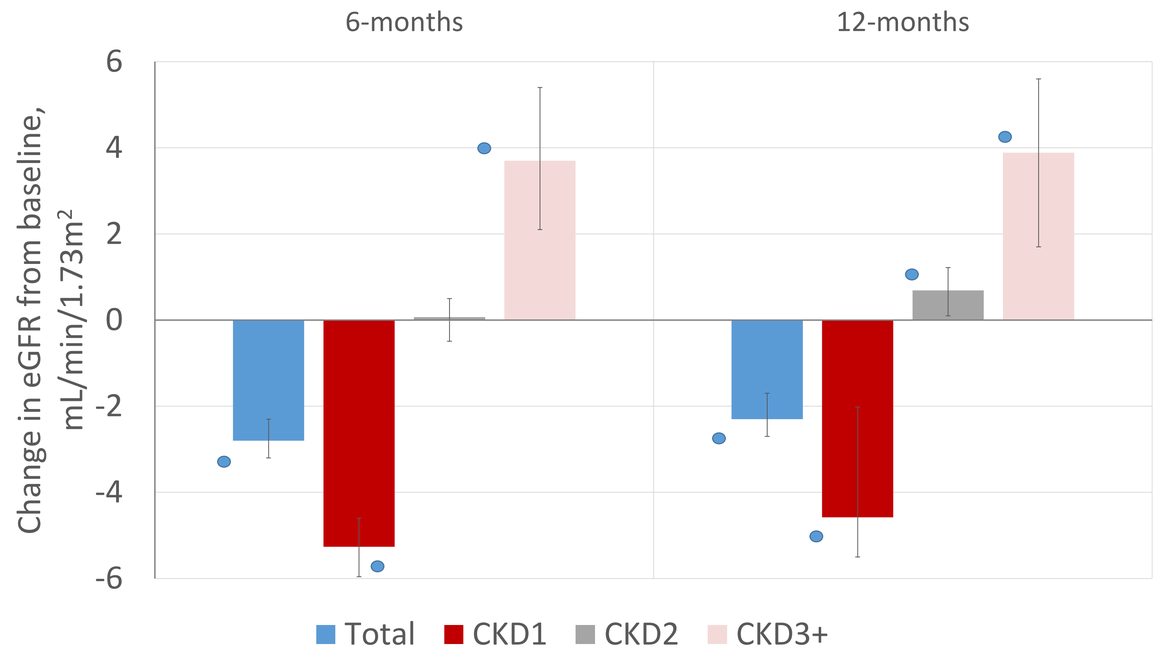


Figure 2. (above) Line chart showing eGFR levels at baseline, 6-months, and 12-months when stratified by baseline urinary albumin creatinine ratios following empagliflozin use

Figure 3. (below) Bar chat showing change in eGFR from baseline at 6- and 12-months following empagliflozin, stratified by baseline eGFR. Error bars showing 95% confidence intervals. P<0.05



Conclusion

Our results demonstrate that, in a real-world cohort of patients, empagliflozin use is associated with reduction in urinary albumin, more profound in those with elevated ACR at baseline.

eGFR tends to decrease across the population as a whole prior to stabilising but in those with decreased eGFR at baseline, improvements in eGFR rather than decreases were observed.

Further evidence is needed and we await with interest the results of EMPA-kidney in 2022.

References

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