INTRODUCTION

1. Background

- The target hemoglobin for patients with end-stage renal disease is currently 11 g/dL, but evidence for this target is lacking.

- The National Kidney Foundation Kidney Disease Outcomes Quality Initiative recommends a target hemoglobin of 12-13 g/dL (KDOQI, 2000).

- Although several studies have shown benefits of increased hematocrit in anemic hemodialysis patients, such as increased quality of life, left ventricular hypertrophy, exercise capacity, and quality of life, most studies have shown no survival benefit.

2. Previous studies using administrative databases

- Studies examining the relationship between achieved hemoglobin and survival have relied on studies using surrogate endpoints and retrospective analysis.

- Prior epidemiological studies only measured associations, not causality and did not completely adjust for confounders.

3. Limitations of epidemiological studies

- Poor epidemiological studies only measured associations, not causality and did not completely adjust for confounders.

- There may be residual confounding effects even after adjustment for age, sex, race, presence or absence of diabetes, total number of comorbidities, and socioeconomic status.

- Data on hematocrit level and epoetin dose are available for all patients.

4. Rational for our re-analysis

- There may be a relationship between hematocrit and survival for patients with end-stage renal disease.

- Patients with higher hematocrits may be more responsive to epoetin therapy if their hematocrit is below 30% and 33%.

5. Methods

- Studies examine the relationship between achieved hemoglobin and survival.

- Hemoglobin is a time-dependent variable and most studies use only the hemoglobin in the baseline period.

- Prior epidemiological studies only measured associations, not causality and did not completely adjust for confounders.

- A well-designed randomized clinical trial can provide the best answer to the question of appropriate hematocrit target.

- If such results are to be used as evidence for selecting appropriate hematocrit targets, it is essential to adjust for potential confounders and the time-dependent relationship of epoetin dose and hematocrit of each subject.

6. Conclusions

- We have shown that both lower hematocrits and higher epoetin doses are associated with decreased survival.

- Although there may be direct adverse causal effects, such as the effect of hematocrit on cardiac function or epoetin dose on blood pressure, we find that these associations are most likely due to a common variable, disease severity, leading to higher epoetin doses and lower hematocrits.

- A well-designed randomized clinical trial can provide the best answer to the question of appropriate hematocrit target.

- In lieu of such studies, analyses of administrative databases must account for potential confounders and the time-dependent relationship of epoetin dose and hematocrit of each subject.

7. Conclusion

- Our analysis shows that both lower hematocrits and higher epoetin doses are associated with decreased survival.

- Although there may be direct adverse causal effects, such as the effect of hematocrit on cardiac function or epoetin dose on blood pressure, we find that these associations are most likely due to a common variable, disease severity, leading to higher epoetin doses and lower hematocrits.