Oral anticoagulants and renal failure: The mystery yet unsolved

The optimal utilization of novel oral anticoagulants (NOACs) in patients with renal failure represents an urgent, unmet, and yet unsolved need with regard to the choice of agents, duration of treatment, and potential dose/regimen adjustment. Lack of randomized trials adequately designed and powered specifically in such patients, absence of the uniformed efficacy and safety data reporting policy to the government agencies, and endless overoptimistic publications based on *post hoc* analyses of primary mega trials sometimes exaggerating benefits and hiding risks clouds the reality. In addition, triaging renal patients is problematic due to ongoing kidney deterioration, and the fact that such patients are simultaneously prone to both vascular occlusions and bleeding. Despite significant reductions in morbidity and mortality over the last half-century, residual vascular risk remains disproportionately high in this population. Our inability to assess adequately the impact of NOACs on long-term outcomes in these patients has been well recognized. Most of the evidence consists of subgroup analyses of trials, which in turn usually exclude patients with severe renal failure. Not only are the sample sizes of most renal insufficiency subgroups in such trials are woefully small, but also the definitions of are variable making cross-trial comparisons and definite conclusions difficult. In addition, many trials deliberately avoided enrolling high-risk patients, especially those with end stage renal failure or requiring dialysis or/and kidney transplantation. To make the story even more complicated, such patients are prone to both thrombotic vascular occlusions and excess bleeding makes the task of finding an optimal OA regimen a variation of “mission impossible” for such high-risk population. Regarding the impact of OA on efficacy, the scant evidence suggests some positive impact on a reduction of stroke but with uncertain effects on mortality and consistently increased bleeding rates.

Furthermore, definitions of events are constantly changing especially with respect to bleeding, with rates varying greatly depending upon the scales/classifications used. In addition, trial durations and evolving standards of care are heterogeneous making the historic comparisons even more challenging. Most experts agree that the benefits of NOACs are uncertain and may be potentially outweighed by bleeding hazards, while acknowledging several serious gaps in evidence. Hence risks may outweigh benefits among people with low annual rates of stroke including those with early stages of renal impairment, especially in patients who do not have clinically-evident vascular disease. Managing anticoagulation is tricky due to increased hemostatic activation but attenuated response to NOACs compared with patients with normal renal fuvction, even despite higher dosages. Finally, all NOACs mega trials suffer from massive double-digit incomplete follow-up rates, challenging the quality of the analyzed datasets.

Overall, the current knowledge suggests no single superior anticoagulant choice with regard to their safety and efficacy in patients with renal impairment. Further comparative randomized studies of different NOAC’s in patients with moderate and severe kidney failure are urgently needed.

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