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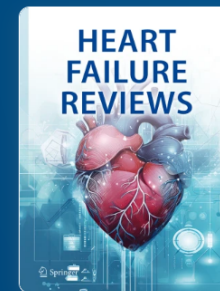
The heart failure burden of type 2 diabetes mellitus—a review of pathophysiology and interventions

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27% of the study population in both trials had T2DM with no heterogeneity in the results [22]. The Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial explored the effect of spironolactone on a primary outcome of CV death, aborted cardiac arrest and hospitalization for HF in a population with EF \geq 45% of which approximately 30% had DM, with no significant effects on the primary outcome [81]. One discussed explanation for the neutral effect was the regional differences observed with higher event rates and significant effect in patients included in the Americas and lower event rates and no treatment effect in those included in Russia/Georgia, potentially caused by different practice patterns and use of hospitalization [8]. Three other smaller pilot studies with digoxin, perindopril, and carvedilol in HFpEF also failed to show any beneficial impact on survival or HF hospitalizations [82,83,84]. Sacubitril/valsartan (ARNI) is a new treatment option which combines an ARB with a neprilysin inhibitor and now is being studied in patients with symptomatic HFpEF (EF \geq 45%) in the “Prospective comparison of ARNI with ARB Global

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