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MINERALOCORTICOID RECEPTOR ANTAGONISTS IN HEART FAILURE

Exploring the gap between guideline-directed medical therapy and real-world practice

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Akademisk avhandling

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Abstract
Heart failure is a complex clinical syndrome with a prevalence of 1-2% in the adult population and has a 5-year all-cause mortality of about 50%. The triad of Angiotensin-Converting Enzyme Inhibitor (ACEI) or Angiotensin II Receptor Blocker (ARB), Beta-blockade (BB) and Mineralocorticoid Receptor Antagonist (MRA) are recommended in all patients with heart failure with reduced ejection fraction (HFrEF). Despite that MRAs showed a 15-30% risk reduction of all-cause mortality in patients with HFrEF in landmark clinical trials, not even half of all eligible patients received MRA treatment. The aims of this thesis were to explore the pattern of MRA use in a real-world heart failure population and the reasons for MRA underuse.

With an observational retrospective study design, patients were included if they had a heart failure diagnosis and had at least one visit at the Heart Centre or Department of Internal Medicine between 2010 and 2018. All data were collected from medical records. Index data were collected at the time of diagnosis, and follow-up data were collected by the journal entry closest to the end of the data collection period (2016-2018). In the heart failure population, 45% of the patients with HFrEF were prescribed and remained on MRAs but we estimated that about 60% of the patients with HFrEF would tolerate MRA treatment in the long-term. From the medical record content analysis, we found that contraindications including renal dysfunction, hypotension and hyperkalemia were the most common reasons for not receiving treatment with MRAs. However, almost half of those patients did not meet the guideline-recommended contraindications. After excluding patients with contraindications, one out of ten patients that were eligible for MRAs were not treated with MRAs. These patients had been hospitalized for heart failure to a much lesser extent while one-third did not have any follow-up at the cardiology clinic. The most common reasons for MRA discontinuation were renal dysfunction and elevated serum-potassium; but again, a majority did not meet the guideline-recommended levels for dose reduction or discontinuation of MRAs. Patients who discontinued MRAs had an increased adjusted risk of all-cause mortality. Nearly half of all patients with HFrEF had at least moderately impaired renal function, and of these, treatment with MRAs did not impact the risk of developing worsening renal function or the risk of all-cause mortality. Since renal dysfunction is common, estimating glomerular filtration rate (eGFR) is an important factor in the management of the medical treatment in heart failure. We showed that none of the exclusively creatinine-based equations for eGFR were accurate in predicting measured GFR. All creatinine-based eGFR equations overestimated the renal function.

Our findings suggest that more accurate methods are needed for determining eGFR in patients with heart failure since overestimation causes an unnecessary risk of serious adverse effects and may lead to patients not receiving optimal medical therapy. There seems to be substantial avoidable underuse with MRAs, especially for elderly patients that are admitted to the hospital for other reasons than heart failure and in patients with moderately impaired renal dysfunction with mildly increased serum-potassium. These findings contribute to the understanding of the underlying reasons behind the gap between the guideline-directed use of MRAs and real-world practice.

Keywords
Heart failure, mineralocorticoid receptor antagonists, renal dysfunction, estimated glomerular filtration rate, hyperkalemia, worsening renal function, real-world population

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