A retrospective study on the effect of RAAS pathway Inhibitors at decreasing the risk of acute coronary syndrome in hypertensive patients with rheumatoid arthritis as compared to other antihypertensives

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Background

- Rheumatoid arthritis (RA) is a chronic multi-system inflammatory disease of which is characterized by articular and extra-articular involvement. Patients with RA have a higher risk of mortality when compared with the general population, which is due predominantly to increased cardiovascular disease. Due to the higher incidence of CVD and MI in RA patients it has been postulated that enhanced systemic inflammation plays an important role in the pathogenesis of CVD in RA patients. Previous studies have shown that anti inflammatory medication such as systemic steroids and immune blockers have been shown to decrease the risk of MI in patients with rheumatoid arthritis.

- Ace Inhibitors have long been known for their anti-inflammatory properties. Various components of the renin–angiotensin system (RAS) are expressed on immune cells, and Ang II receptors are present on lymphocytes and macrophages. Ang II elicits both its proinflammatory and pro-stress actions mainly through stimulation of AT1R. Ace Inhibitors block Angiotensin II as well as Bradykinin leading to an anti-inflammatory effect. I*n-vitro* losartan suppressed TNF-α production from inflamed human synovium in RA patients in a dose-dependent manner. Due to these data we believe Ace Inhibitors would be superior to other antihypertensives at decreasing the risk of MI due to their anti-inflammatory properties.

Objective

The goal of this study is to identify if renin angiotensin Inhibitors reduce the risk of MI in hypertensive patients with rheumatoid arthritis more than other antihypertensives.

Methods

Study period: October to December 2017-May 2023

1972 patients
With Rheumatiod arthritis and hypertension

32 patients with acute coronary syndrome with RA and hypertenion

562 patients on RAAS blockers

679 patients on other antihypertensives (betablocker, calcium channel blockers, thiazide diuretics)

Case Control study in which patients with diagnosis of rheumatoid arthritis and hypertension (inclusion criteria) who had acute coronary syndrome (outcome) are retrospectively tested to see if they had taken a RAAS blocker vs other type of antihypertensive (calcium channel blocker, thiazide diuretics or betablocker)

- **Group 1 - Cases: pts with diagnosis of rheumatoid arthritis and hypertension (inclusion criteria) who had Acute coronary syndrome (outcome)**
- **Group 2 - Controls: pts with diagnosis of rheumatoid arthritis and hypertension (inclusion criteria) who did not have acute coronary syndrome(outcome)**

Results

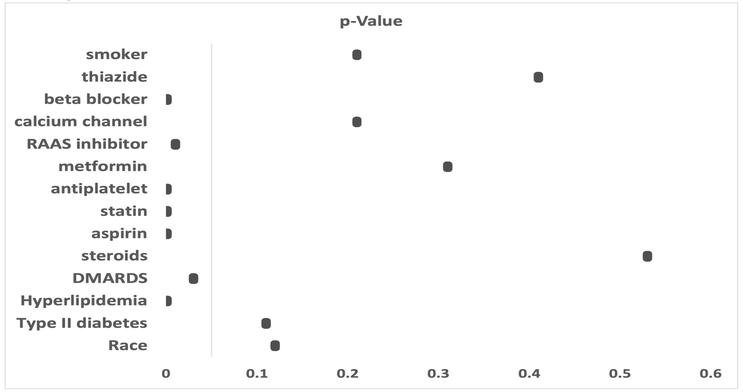
Exposures Statistics

	No Acute cornonary Syndrome	Acute coronary Syndrome
RAAS Blockers	574 (29.1%)	47 (.08%)
Thiazide/BB/Calcium channel blockers	893 (45.2%)	93 (1.0%)

Descriptive Statistics

Characteristics	Mean	Standard Deviation	Minimum	Maximum
Age (mean yr, range)	63.95	2.082)	22	90
BMI (mean, kg/m², range)	30.02	7.33	13.34	55.46
Readmit Days	28 (14%)	1 (3%)	18 (13%)	9 (32%)
LDL	89.3	34	18	192
Troponins	0.16	.041	.000	.618

•Unadjusted Data



•Adjusted Data

	Odds Ratios	Lower 95%	upper 95%	p-Value
Age	1.01	0.959	1.065	0.7
Sex M v F	2.743	0.76	9.829	0.12
BMI	0.942	0.85	1.044	0.25
nonsmoker vs smoker	0.0856	0.165	4.429	0.85
RAAS vs other hypertensives	0.607	0.156	2.356	0.47

Discussion

- RAAS inhibitors have long been known to be first line antihypertensive medication in the general population. These medications have shown to be cardio and renal protective. Guidelines do exist in the current population as when a patient should be considered to start an ace inhibitor/arb medication. Patients with rheumatoid arthritis present a special population that are known to have increased CVD and disease burden. A 1.5 times risk modifier to the Framingham Risk Score or Reynold's Risk score is required to quantify the disease burden in patients with rheumatoid arthritis. The critical gap in our knowledge is whether we should treat cardiovascular risk factors in RA patients who would not previously have fulfilled the criteria.

- This study was conducted in part to provide valuable data in answer the question if RAAS inhibitors do reduce the risk of acute coronary syndrome in patients with RA even when compared to other antihypertensives. The unadjusted data does show that there is a statistically significant reduction in the risk of ACS in patients that took Lisinopril. The adjusted data reveals that the adjusted odds ratio, and thereby can be estimated to the relative risk due to measuring rare outcomes, is 0.6 in patients who have RA developing ACS compared to patients on other antihypertensives. Unfortunately, we were not able to reach significance due to having a p value of 0.4. From the data is is clear that the study was underpowered. Predictors such as smoking vs nonsmoking on the effect they have on acute coronary syndrome did not reach significance with a p value of 0.9. We hope to present this data in an effort to have similar studies conducted with larger sample sizes to be able to conclude if RAAS inhibitors do reduce the risk of ACS in RA patients. This data can be used in the future in meta analyses to aid in showing the benefit of RAAS inhibitors in reducing ACS in RA patients. We hope this data will aid in ultimately changing guidelines for when to start RAAS inhibitors in patients with RA.

Conclusion

- This is the first study to compare RAAS inhibitors to other antihypertensives in their effects of reducing acute coronary syndrome in patients with rheumatoid arthritis. The unadjusted data reveals that Ace inhibitors reduce the risk of ACS. Additionally, the adjusted data reveals that there is a reduction of ACS in patients taking RAAS inhibitors over other antihypertensives, although the data was trending towards significance but failed to reach it due to a smaller sample size. More studies with larger sample sizes will have to be done to reach statistical significance. We hope to use this data to one day to guide treatment guidelines in the future for patients who have rheumatoid arthritis and hypertension

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