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COMPARATIVE STUDY OF ANGIOTENSIN RECEPTOR BLOCKERS (ARBS) AND ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEIS) FOR BP REDUCTION

Hassah Batool Iftikhar and Jiang Hong, MD*

Department of Cardiology, Renmin Hospital of Wuhan University, 430060, Wuhan, Hubei Province, PR China.

*Corresponding Author: Prof. Jiang Hong

Department of Cardiology, Renmin Hospital of Wuhan University, 430060, Wuhan, Hubei Province, PR China.

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ABSTRACT

The National WHO published guidelines in the management of hypertension beyond the approach of cardiovascular risk factors addressing the scheme of ACEI and ARB comparison to requisite the lifestyle modifications in the adherence of efficacy of safety goals. The ascertainment of mono-therapy and combined therapy trial reduced the systolic-diastolic BP statistically in the effectiveness of survival rates at the all-cause cardiac events. Moreover, the symptomatic optimal dosing randomized beneficially in the measurements of highest satisfactory intervention isolatedly arranged the sequence of ascending to descending structure directing the least potency on the pathogenesis of heart failure as the long-term hemodynamic vaso-dilators.

KEYWORDS: Angiotensin Receptor Blockers: Angiotensin Converting Enzyme Inhibitors: Antihypertensive therapy: Clinical Trials: Cardiovascular side effects.

INTRODUCTION

Hypertension is a general widespread social burden in the cardiovascular health practice. It is a major risk factor for congestive heart failure in the prevalence of 3% adult community and 10% old age from decades.^[1] National Health Survey analyze hypertension in the association with cardiac world load effect the co morbid factors of gender ratio, diabetes mellitus, heart failure and myocardial infarction in correspondence to the systolic blood pressure. [2] The American Heart Association defined the classification of systolic and diastolic heart failure in the parameters of threshold ejection fraction variations uniformly challenging the worth diagnostic measurements in the gold standard of pressure filling detecting Framingham criteria of 100% sensitivity in assessment of improved epidemiological outcomes. [3,4]

The Exclusive approach of Joint Health Care Commissions (JCAHO) indicates the obscure diastolic functioning characterizes the left ventricular relaxation evolving the risk factors and intrinsic mechanism superimposes the arbitrary Heart failure syndrome. The conflicting mechanical health implications casually percept the determined etiology in proportions of lacking in control trial studies at coronary risk factors. The substantial methodology remains with a fact of diabetes enrolling 42% of under-estimating myocardial infarction severity with the parallel expectations of hypertension overtime in the large population. Therefore, the selective incidences of heart failure cases estimate the diagnosed related statistics in the subsequent distinguishable

medical reviews and data validation on the secular cardiovascular criteria. [5] The Acknowledge limitations in the awareness of entities declining the mortality rates at the population-based discrepancies link to heart failure genesis affecting the crucial congruent survival rates in the health management.

Certainly, the Multiple Risk Factor Intervention Trial (MRFIT) clinically make the experimental studies in systemic hypertension comparatively to discriminate the effectiveness of BP drop and oxidative stress in the intimation of short and long-term therapy with the pathways of renin-angiotensin-aldosterone system (RAAS) objecting the hemodynamic stability. Moreover, the asymptomatic 50% relative risk by the modes of efficacy in treating the cardiac dysfunctions compare the adjusted interpretations in the selective studies of incidence and prevalence at atherosclerosis remain an imperative underscore surveillance in the adverse socio-economic community. [6,7] The purpose of ARBs and ACEIs in controlled randomized trials according to the guidelines of European Society of Cardiology (ESC) review the observation of 2 classes clinical end points in the acceptable alternatives, We present a research trials in comparing the uncertain potency of mono-therapy versus combined therapy Excellency in the safety measures of cardiovascular benefits encountering the tolerable appropriate dosing issues in essential hypertension related heart disease.

Pharmacology

The vasodilator treatment irrespectively measures the mechanism differently by blocking the receptors pathways in the contribution of left ventricular functions, ejection fraction, myocardial flow, hypotensive episodes and diastolic –end pressure in the worsening of similar action on hemodynamic cardiac output. The two classes of medications involving angiotensin I and angiotensin II act as an optimal dosing in the hypothesis target end organs attributing the expression of renin-angiotensin system. Captopril and enalapril significantly measure the hemodynamic variations differentiating the quantitative effect of physiological responses in coronary flow, arterial pressure; capillary wedge, vascular resistance and unchangeable heart rate signal the synergistic action of electrolyte imbalance.

However, Losartan and Captopril per day lasting the effect of 30 hours make the proportional differences in BP speculating poor prognosis in terms of hypotensive effect in chronic heart failure. In the limitations of biochemical regulation withhold the unknown deterioration altering antagonist in survival rate partially activate cardiac tissues in the magnitude of duration, penetration and binding components in the clinical activities of biosynthesis. Furthermore, in the declaration of risk ratio accomplishment at persistent hypertension and congestive heart failure mildly undergo the conclusion of a cough, high ejection fraction and low systolic-diastolic BP in the correlated incidence of cardiac death.

Efficacy of ARBs and ACEIs Combined therapy

The Comparative dissimilarity between 2 groups does not bring the benefits in reducing vascular risk and sudden cardiac arrest the all-cause mortality in the priorities of coordinating the randomized concomitant treatment adding the broad spectrum of research studies lacking the interactions of potential bias agents. The importance of angiotensin II favors the higher concentration of ventricular refilling myocardial infarction neurons patho physiologically differing the mechanistic outcomes interpretation a crossing the efficacy of superiority. The outlook results initiating the extension of controlled trial treatment substituting the duration of experimental effectiveness in heart failure cases shorten the logistic analysis demonstration in the collaboration of uniformly successful mono-therapy behavior respond heterogeneity.^[8]

The Pharmacological controversy between both the drugs of ARBs and ACEIs individually reduce the BP with the unknown conduction. The Randomized Evaluation of Strategies for Left Ventricular Ejection Fraction(RESOLVED) included the unite integrated studies along with segregation of each drugs attenuating the chronic symptoms, endocrine activation, and remodeling capacity to survey the perspectives of quantitative measurement in the inhibition of tissue modifying the mortality rates. Thus the systolic and

diastolic pressure submission designate to 40% follow up re-evaluating the discontinuation of high dose titration incriminate the segment of hyperkalemia as well. Furthermore, ACEIs remained the first choice pharmaceutics in cardiological aspects contrasting the placebo- controlled observation blocking reninangiotensin-aldosterone system. Hence the intolerant ACEIs present the fundamental prolonging medication in less dosing routine making up in dropping the serum level of potassium component and surrogating LVEF of 50% deriving the risk reduction end-points of cough effect causing the heart failure hospitalization death and renal failure.

The TRINITY

Trial triple therapy in the reduction of BP 30/18mmHg and 120/80mmHg respectively distress the effect by body mass index and type 2 diabetes mellitus. And also the studies of SCOPE and TRANSCEND adjoined both the therapies of ARBs and ACEIs similarity to involve the participants with the ages of 60-70 age in terminating the premature cardiovascular events progressive to the angiotensin receptor blockers. Thus, the double blinding risk lessens 30% of a transformed modifiable characteristic in the incidence of P value 0.002 and the composite nominal involved mortality rate in the hypertensive state.

Efficacy of ARBs Monotherapy

Losartan an orally active adjuvant act advantageous alike ACEIs in the effectual of hypotension. According to the disabilities of 25 trials, the annual resuscitation of moderate cardiac arrest classify the fewer occasions of preload and afterload systolic functioning of acute myocardial infarction. The short- term administration of 25-50mg/day losartan in a smaller period of 12 weeks at claim studies reflect no normal sympathetic activation on tachycardia, capillary wedge pressure and cardiac index directing the incidence of vasodilators. [9] At the 12 weeks, studies the active 80-100mg/day titration suspect the engaged demographic values in the associated side effects causing infectious disease striking coronary artery disease in the preventions of sodium retention, vasoconstrictions, glomerular capillary hypertension, pernicious anemia and immunosuppressive therapies as shown in (figure-1) Therefore, Losartan as a specific angiotensin II receptor blocker stance a tolerable antihypertensive completely signify the changes in monitoring baseline BP, blood profiles and nonclinical lab values.

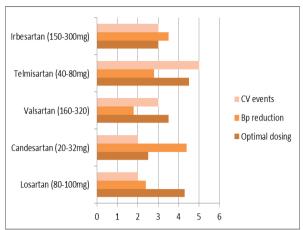


Figure 1: Graph shows the changes in mean BP reduction follow-up with the adjusted dosing of ARB mono-therapy.

Alternatively, the studies of VALIANT, CHARM and HFpEF compliance the approval of FDCs in beneficially challenging the ALLHAT scale randomizing trial in assessing the staging of hypertension and directing the heart failure with possessing chronic kidney disease. Surprisingly the exerting potent bind the organic processes safely in reducing the competitive BP emphasizing no mild changes in serum cholesterol, triglycerides, and creatinine clearance to handle the optimal regimen in absolute vasodilatation of inotropic trending cardiac risk factors every year. [12,13,14,15]

Angiotensin blockade as a mono therapeutic balanced strategy precede the further use of calcium antagonist, ACEIs, and diuretics to maximize the deleterious proteinuric effect at hyper filtrating nephrotoxicity in achieving the dual control on statistical mean calculations.[16] The theoretical phenomenon of successful isolated treatment adhere the protocols of 60% matched differences in switching the drawbacks of superiority appearing equivalent 4 times essentially at advanced trials to naïve the placebo endpoints in presenting the plasma levels record for the presolution. [17,18] in the exposure of better grading as compared to the ACEIs. Hence, at the first and second ELITE trials, the primarily follow up of half-life influence the critical results in probability of population based symptomatic heart failure by the parameters of abnormal defined clinical situations leading cause of ischemic death rate and hospitalization figuring the hazard ratios of losartan 12% as compare to Captopril 15.2% suggesting P-value 0.001 suggesting ACEIs as a ambulatory introductory antihypertensive drug selection.

Efficacy of ACEIs Monotherapy

Captopril is a paramount antihypertensive oral active angiotensin I converting enzyme inhibitor resisting the various biochemical interrupted conditions lengthening the period of BP lowering create the restrictions of receiving pharmacodynamic drugs. The Acquisition of tolerant Captopril 25-150mg/day warrants the severity of adverse reactions cumulate the dominance of early

frequent rashes, angina, fatigue, neutropenia and mouth ulcers discontinue the captopril therapy within 3-4months. The limited data support the responses of the central nervous system in satisfying the BP control necessarily moderating the miscellaneous study program of apnea, nausea and abdominal cramp extracting the pre-treatment of renovascular disease exhibit the decline of underlying progressed circumstances.

The type of RCTs and Cohort study criteria dominate the procedure of population-based chronic heart failure specifically in the sequence of nonrandom drugs crossing the protocol analysis hemodynamically the oral captopril (PT) functioning the left ventricular filling pressure precipitating the oxygen consumption accepting a vasodilator as a primary smaller dose. The included ACEIs reassure the plausible biological changes in Metaanalysis estimating the control on mortality rates yielding the efficacies in ventricular dysfunctions summarizing the over-view data of CHARM and OTIMAAL trials. The affirmation of higher incidence in Meta-regression also added the unfavorable factors of ejection fraction, mean arterial pressure (MAP), ventricular fibrillation, pulmonary edema and surgical intervention error the discrepancies impact the origin of death. Therefore, the rehospitalization effects differently consider the worst choice among the inhibitor evaluation.

The New York Heart Association classifies the simultaneous striking results obtaining the prompt factor of congestive heart failure. The standard maneuvers angiographically calculated the accordingly diagnostic hemodynamic status in hypotensive syndrome along with the disorders of artrioventricular defect, aortic and mitral combined insufficiency, ischemic heart disease and coronary sinus flow volume index to highlight the enddiastolic diameter with the dosing of 100-150mg/day Captopril probably reduce the hypovolemia in the reasonable cure ways as a prophylactic dilator. [19,20] as shown in the (figure-2) Furthermore, the correlated relations of animal and human studies symptomatically assist the readily medical signs unclear the extended hematological state, sodium depletion and the gradual titration signifying the compromising adherence of weakness, impotence, and dysuria. Therefore, the animal-based studies regulate the intra- renal glomerular sclerosis in explaining the synthesis of TGF-beta^[21] represent the treatment plan of increased 450-650mg/day captopril show a good exploration in the interference of diabetic nephropathy. The failed long term method for 1 year attest the single study intervention corresponding the efficacy with diuretics and beta blockers in noteworthy for the first six months estimation as a satisfactory without the possibility of previous biopsy reports. [22,23,24] Hence the relative acute effectiveness considers the profiles of losartan as an early regimen in systemic hypertension.

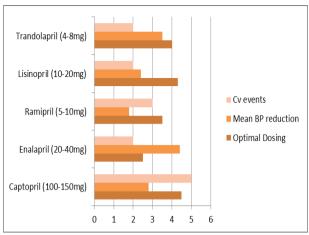


Figure-2 Graph shows the changes in mean BP reduction follow-up with the adjusted dosing of ACEI mono-therapy.

Safety of ARBs and ACEIs monotherapy

The ARB is high caliber safe and endurable three to fold since 25 years ago. The minor life-threatening cases include the bradykinin, degradation of atherosclerotic plaques and pulmonary symptoms increase the high-risk complications of myocardial infarction in activating the plasminogen inhibitor-1 in reintroducing the use of ACEIs. The immense meta-analysis inspects the statement of VALUE, LIFE and SCOPE values in the upgrades of co-morbidities, events of respiratory infection, headache and the assumed high-risk diabetes microalbuminuria definitely build a comparable study arm in enhancing the ability to manage hypertension sensitivities with placebo.

In 2001 guidelines, the publications from OPTIMAAL, CHARM and VALIANT recheck the recorded data of ARBs in 2005 to revise the particular side effect of a cough and angioedema in creating the cautious of mortality efficacy for the advisable existence of ACEIs and beta blockers therapies symptomatically inhibit the combined ACEIs treatment. The combined bedrock double-triple therapy convincingly endure an issue of appearing a spurious finding in the mandatory concerns of left ventricular volume dimensions, a hormonal consideration conferring the relative risk of 30% cardiovascular death cause events. [25]

In 2005, the European Society of Cardiology updated the A1 level of management in the regardless of converting angiotensin ATI into ATII. ACEIs inhibitors aggressively reduced the actions of circulations in cardiac as cancerous tissues, over cell growth, sodium and water retention raising the aldosterone production. Conversely, the incomplete blockade in nonenzymatic pathways^[26,27] resultant the elevation of nitric oxide levels, prostaglandin and molecules element remains a characteristic of ACEIs intolerance.^[28] The International Improvement of Congestive Heart Failure Programme received the study of SPICE converting enzyme inhibitors recount a preserved heart failure common

events^[29,30] binding the RAAS renin-angiotensinaldosterone system last distinctly in the synthesis of ACEIs independently.

In 2004, The European Heart Failure surveys registries scrutinize the pattern of hospitalized congestive heart disease symptoms revealing the uncertainties of an alternative condition. [29,31] As published the case of mayo clinic in 2012, a labeled warning spree in histology of GI endoscopy collate the clinical features in comparing the n-value with the percentage by administrating the primary care outcome at the national survey of Italian Network observing the large scale of prevalence and incidence. [32,33] And also the basic hallmark of over stimulants in blood vessel feasibility blocks the inhibitors effectiveness in the generation of positive actions at ATII. Therefore, the conserved massive heart failure occurrence for life-time further enroll the habitual left ventricular systolic dysfunction currently assess the control study in the reflection of admiring the traditional therapy recommendation in lowering sudden death. [29]

In Contrast, the appearance of ACEIs is conventional therapy proceeded with a myocardial contractility in the immediate advantage of diuretic therapy. misunderstood mechanism uniquely favor the symptoms of BP, potassium losses, cardiac output, hypokalemia, hypomagnesemia, high urea levels and the orthostatic hypotension accompany the reactions of alkalosis and elevated glucose sparing the IV volume depletion in the contribution of vasopressin and norepinephrine activating the sympathetic nervous system. Lately, the studies in the accelerating heart failure maintenance containing the anti arrhythmic agent i.e.: furosemide^[34] an emerging choice in RAAS production justify the use of diuretics and digoxin advantageous regulating system.

Subsequently, Captopril multicentre trials on refractory symptomatology participants revealed the high responses of exercise tolerance searching the other background therapies in the experience of digitalis glucoside, NSAIDs, lipid-lowering agents, insulin therapy, and nitrate isolated converse by the non pharmacological measure recognizing ACEIs is an ideal first dual step according to the clinical relief mono-therapy. [35] Hence, Captopril is a delay and sustained acting agent majorly distribute 5-10% cases a compiling vaso-dilator in the prognosis effectiveness at a smaller duration of the period. [36]

Myocardial Infarction and Heart failure

The term "Myocardial Infarction Paradox" in 2006 delineate pre-inflammatory and pre atherogenic mediators transmit the incidence of ARBs with the correlative trial of placebo to a wider symmetrical context in the predisposition of heart failure. [37,38,39] The interchangeable use of ACEIs and ARBs are exceptionally assumed head to head parallel indication of utilization in US differing the validation of pharmaceutical assistance include the selective

ascertainment of anti-platelets and PCI to prior authorize fulfillment of preceding years. Therefore, the delaying symptoms onset is influenced by ACEIs into fibrinolytic at the greater sites of myocardial infarction in making the prognostic scores at elder patients steeply risk the systolic blood pressure, heart rate, diabetes mellitus and the absolute male gender.

At the ongoing Global Key Point Studies assess the fatal and non fatal myocardial infarction condition risk the end stage organ damage under the outcome researchers (ONTARGET, TRANSCEND, NAVIGATOR, KYOTO HEART, I-PRESERVE, PROFESS and MOSES adding the secondary supplemental therapy in recurrent occurring cardiac resuscitation and worsening result the receipt of fluid therapy follow up with the means of morbidity and mortality density ratio. [40-44] Also the data from INTER HEART, LIFE and VALUE target the criteria of interventions (RCT) evaluating the extraction and quality of odd-ratio (OR), confidence interval (CI) and the credible intervals in analyzing the accurate scenarios of contrary performance domain the perception of excessive attributable effectiveness in myocardial infarction. The Editorials and analyses responded a risk of coronary heart disease in promoting the AT2-receptor stimulation pursue with fibrosis growth and hypertrophy randomizing a fixed effect towards lacking hypertension valvular heart disease. A confounding related heterogeneity varies the comparative actions of ARBs and ACEIs in the active ranges of hepatic, renal and cardiovascular disease. [45,46]

At the different distributed period, the incidence of reinfarction, 3rd AV block, cardiogenic shock and stroke increased the clinical contest on an essential trend of P value 0.003 with early ACEIs at systemic trials. The publication from circulation journal relevantly included the "Personal Communication" in consideration of overlapping pairwise and network Meta-analysis ranking the summarized treatment in determining the stability of Meta-regression differently connected to the time-based the satisfactory outcome. Hence remodeling documentation on coronary perfusion^[47] can lead to the expansion of systemic infarction under the exploratory acute myocardial infarction withdrawal in the high-risk continuation.

The overviewed collaborative agreement generally factual the approach of admitted hospitalization react the strong observation of usefulness in the apart of anterior and inferior ST elevation. In contradictory, the incremental captopril and losartan regimen account the non-inferior discordant in the apparently existing preheart failure. The inclusion of combined therapy insight a post hoc declaration on recurrent myocardial infarction and Killip I, II class in the complications of beta blockers or calcium channel blocker interactions. [48] So the contraindications of ACEIs resume the opinion of implementing a frontline use of reperfusion, thrombolytic and CABG. In result, the clarifications of

physician committee recommend the strategy of ACEIs therapy in the irrespective proportions at early few weeks of initiating high risk of tachycardia, silent ischemia and chronic heart failure in creating the preplanned identical study rate referring a vigorous long term ACEIs in postmyocardial infarction distinguish the survival advantage from multi-risk variants within first 12 hours leading to sudden death.

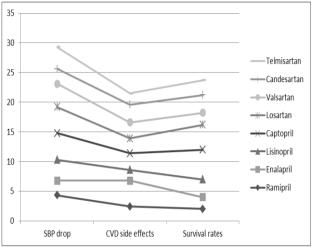


Figure-3 Trends in ACEI/ARB mono-therapy indicate the baseline characteristics of SBP effectiveness on daily regimen.

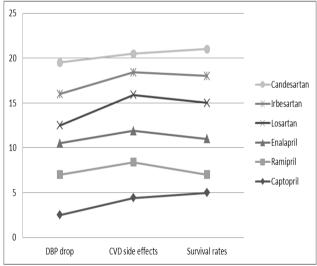


Figure-4 Trends in ACEI/ARB combined therapy indicate the baseline characteristics of DBP effectiveness on daily regimen.

CONCLUSION

The apparently observed analysis, as summarized in figure 3-4 statistically with the high-class agents in the effectiveness of co morbidities and hypertension acquire a slight proteinuria reduction ultimately by the monotherapy components. There's no clinical rationale in combined therapy for the management of adverse effects amplifying the valuable antihypertensive attributes. Apart from the stable equilibrium the selective trial programme closely adjoining the positivity of welfare

outweighs the risk factors on myocardial tissue at the huge potency of systolic and diastolic BP reduction. The medium risk factors for disability in micro-vascular and macro-vascular events the diabetic cases have the roughly poor setting of BP control.

In betray use of ACEIs and ARBs, the suppressed limits of RAAS ranking the drugs in ascending order Captopril> Enalapril> Lisinopril> Trandolapril> Ramipril versus ARBs drugs Losartan> Telmisartan> Candesartan> Valsartan> Irbesartan on single placebo trial necessitate a high quality of enormous of large sample materials with longer duration of analyses procedure in exploring the fundamental impact ratio of cardiovascular side effects and survival rates at the extremity arrhythmic re-admitted incidence. Therefore, the discern translating results in the evidence of optimal dosing weakly grounded the hypertensive previous review in the sequel of asymptomatic participants practicing ACEIs as a linear therapy affecting the diastolic BP in the negligence of contraindication beginning at the discrete situation of cardiogenic shock strongly requiring the complementary protract treatment.

Subsequently, the support of withstanding mean drugs failed end-points on high dosing greatly made a silent questionnaire on clinical medicine to compare the double blinding foremost supreme anti-hypertensive studies in promoting high procession of survival rates every year.

Competing Interests

The author declared no competing interests.

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REFERENCES

- P.A. Meredith, J. Östergen From hypertension to heart failure—is there better primary prevention strategies? Journal of the Renin–Angiotensin– Aldosterone System, 2006; 7: 64-73. Cross Ref View Record in Scopus.
- 2. J.B. Kostis, B.R. Davis, J. Cutler, *et al.* Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. SHEP Cooperative Research Group Journal of American Medical Association, 1997; 278: 212-216. Cross Ref View Record in Scopus
- 3. Di Bari M, Pozzi C, Cavallini MC, Innocenti F, Baldereschi G, De Alfieri W, Antonini E, Pini R, Masotti G, Marchionni N. The diagnosis of heart failure in the community. Comparative validation of four sets of criteria in unselected older adults: The icare dicomano study. J Am Coll Cardiol, 2004; 44: 1601–1608. [PubMed]
- 4. Tschope C, Kasner M, Westermann D, Gaub R, Poller WC, Schultheiss HP. The role of nt-probnp in the diagnostics of isolated diastolic dysfunction:

- Correlation with echocardiographic and invasive measurements. Eur Heart J., 2005; 26: 2277–2284. [PubMed]
- Psaty BM, Kuller LH, Bild D, Burke GL, Kittner SJ, Mittelmark M, Price TR, Rautaharju PM, Robbins J. Methods of assessing prevalent cardiovascular disease in the cardiovascular health study. Ann Epidemiol, 1995; 5: 270–277. [PubMed]
- Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the atherosclerosis risk in communities study) Am J Cardiol, 2008; 101: 1016– 1022. [PubMed]
- 7. Bahrami H, Kronmal R, Bluemke DA, Olson J, Shea S, Liu K, Burke GL, Lima JA. Differences in the incidence of congestive heart failure by ethnicity: The multi-ethnic study of atherosclerosis. Arch Intern Med., 2008; 168: 2138–2145. [PubMed]
- 8. Emerging Risk Factors Collaboration. Wormser D, Kaptoge S, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet, 2011; 377(9771): 1085–1095. [PubMed]
- 9. Levine TB, Olivari MT, Garberg V, Sharkey SW, Cohn JN. Hemodynamic and clinical response to enalapril, a long-acting converting enzyme inhibitor, in patients with congestive heart failure. *Circulation*, 1984; 69: 548-553. [Google Scholar] [PubMed]
- 10. Hong BK, Park CG, Kim KS, et al. Comparison of the efficacy and safety of fixed-dose amlodipine/losartan and losartan in hypertensive patients inadequately controlled with losartan: a randomized, double-blind, multicenter study. Am J Cardiovasc Drugs, 2012; 12: 189–95. [PubMed: 22462558]
- 11. Rakugi H, Ogihara T, Miyata Y, Sasai K, Totsuka N. Evaluation of the efficacy and tolerability of combination therapy with candesartan cilexetil and amlodipine besilate compared with candesartan cilexetil monotherapy and amlodipine besilate monotherapy in Japanese patients with mild-to-moderate essential hypertension: a multicenter, 12-week, randomized, double-blind, placebo-controlled, parallel-group study. Clin Ther., 2012; 34: 838–48. [PubMed: 22440192]
- Pitt B, Poole-Wilson PA, Segal R, et al. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial--the Losartan Heart Failure Survival Study ELITE II. Lancet, 2000; 355: 1582–7. [PubMed: 10821361]
- 13. Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. N Engl J Med., 2003; 349: 1893–906. [PubMed: 14610160]
- 14. Dickstein K, Kjekshus J. OPTIMAAL Steering Committee of the OPTIMAAL Study Group. Effects of losartan and captopril on mortality and morbidity

- in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan. Lancet, 2002; 360: 752–60. [PubMed: 12241832]
- Massie BM, Carson PE, McMurray, et al. I-PRESERVE Investigators. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med., 2008; 359: 2456–67. [PubMed: 19001508]
- H.J. Kloke, J.F.M. Wetzels, R.A.P. Koene, F.T.M. H uysmans Effects of low-dose nifedipine on urinary protein excretion rate in patients with renal disease Nephrol Dial Transplant, 1998; 13: 646-650 Cross Ref View Record in Scopus.
- 17. Biollaz J, Brunner HR, Gavras I, Waeber B, Gavras H. Antihypertensive therapy with MK 421: angiotensin II-renin relationships to evaluate efficacy of converting enzyme blockade. J Cardiovasc Pharmacol, 1982; 4: 966–972. [PubMed]
- 18. Rousseau MF, Konstam MA, Benedict CR, Donckier J, Galanti L, Melin J, Kinan D, Ahn S, Ketelslegers JM, Pouleur H. Progression of left ventricular dysfunction secondary to coronary artery disease, sustained neurohormonal activation and effects of ibopamine therapy during long-term therapy with angiotensin-converting enzyme inhibitor. Am J Cardiol., 1994; 73: 488–493. [PubMed]
- 19. HOCKINGS. B.E., COPE, G.D., CLARKE, G.M. & TAYLOR, R.R. Comparison of vasodilator drug prazosin with digoxin in aortic regurgitation. Br. Heart J., 1980; 43: 550-555.
- GREENBERG, B.H., DeMOTS, H., MURPHY, E. & RAHIMTOOLA, S.H. Arterial dilators in mitral regurgitation: Effects on rest and exercise haemodynamics and clinical follow up. Circulation, 1982; 65: 181-187. Google Scholar
- F.S. Shihab, W.M. Bennet, A.M. Tanner, T.F. Ando h Angiotensin II blockade decreases TGF-β1 and matrix proteins in cyclosporine nephropathy Kidney Int, 1997; 52: 660-673. Cross Ref View Record in Scopus
- Veterans Administration Co-operative Study Group on Antihypertensive Agents: Racial differences in response to low dose captopril are abolished by the addition of hydrochlorothiazide. Br J Clin Pharmacol, 1982; 14(2): 97S.
- 23. Vlasses PH, Rotmensch HH, Swanson BN, Mojaverian P, Ferguson RK: Low-dose captopril: Its use in mild to moderate hypertension unresponsive to diuretic treatment. Arch Intern Med., 1982; 142: 1098.
- 24. Smith SJ, Markandu ND, MacGregor GA: Optimal dose of captopril in hypertension. Lancet, 1982; 2: 1640.
- 25. McKelvie RS, Yusuf S, Pericak D *et al.* Comparison of candesartan, enalapril, and their combination in congestive heart failure: randomized evaluation of strategies for left ventricular dysfunction

- (RESOLVD) pilot study. The RESOLVD Pilot Study Investigators. *Circulation*, 1999; 100: 1056–1064. Google Scholar
- 26. Lopez-Sendon J, Swedberg K, McMurray J et al. Expert consensus document on angiotensin converting enzyme inhibitors in cardiovascular disease. The Task Force on ACE-inhibitors of the European Society of Cardiology. Eur Heart J., 2004; 25: 1454–1470. Google Scholar
- 27. McMurray JJ, Ostergren J, Swedberg K *et al.* Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet*, 2003; 362: 767 –771. Google Scholar
- 28. Bart BA, Ertl G, Held P et al. Contemporary management of patients with left ventricular systolic dysfunction. Results from the Study of Patients Intolerant of Converting Enzyme Inhibitors (SPICE) Registry. Eur Heart J., 1999; 20: 1182–1190. Google Scholar
- 29. Komajda M, Follath F, Swedberg K *et al.* The EuroHeart Failure Survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 2: treatment. *Eur Heart*, 2003; 24: 464–474. Google Scholar
- 30. Cleland JG, Cohen-Solal A, Aguilar JC *et al.* Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. *Lancet.*, 2002; 360: 1631–1639. Google Scholar
- 31. Cleland JG, Swedberg K, Follath F *et al.* The Euro Heart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J.*, 2003; 24: 442–463. Google Scholar
- 32. Opasich C, Tavazzi L, Lucci D *et al.* Comparison of one-year outcome in women versus men with chronic congestive heart failure. *Am J Cardiol*, 2000; 86: 353–357. Google Scholar
- 33. Rutten FH, Grobbee DE, Hoes AW. Differences between general practitioners and cardiologists in diagnosis and management of heart failure: a survey in every-day practice. *Eur J Heart Fail*, 2003; 5: 337–344. Google Scholar
- 34. Ikram H, Chan W, Espiner EA, Nicholls MG: Haemodynamic and hormone responses to acute and chronic frusemide therapy in congestive heart failure. Clin Sci., 1980; 59: 443.
- 35. The CONSENSUS Trial Study Group: Effects of enalapril on mortality in severe congestive heart failure. N Engl J Med., 1987; 3(16): 1430.
- 36. Kromer EP, Riegger AJG: Effects of the ACE-inhibitor quinapril as monotherapy in patients with congestive heart failure (CHF) NYHA class 11-111 (abstr 26). Proc Eur Soc Cardiol, 1988; 9(2).
- 37. Verdecchia P, Angeli F, Gattobigio R, Reboldi GP. Do angiotensin II receptor blockers increase the risk of myocardial infarction? Eur Heart J., 2005; 26(22): 2381–2386. [PubMed]

- 38. McDonald MA, Simpson SH, Ezekowitz JA, Gyenes G, Tsuyuki RT. Angiotensin receptor blockers and risk of myocardial infarction: systematic review. BMJ, 2005; 331(7521): 873. [PMC free article] [PubMed]
- 39. Cheung BM, Cheung GT, Lauder IJ, Lau CP, Kumana CR. Meta-analysis of large outcome trials of angiotensin receptor blockers in hypertension. J Hum Hypertens, 2006; 20(1): 37–43. [PubMed]
- Yusuf S, Teo K, Anderson C, et al. Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. Lancet, 2008; 372(9644): 1174–1183. [PubMed]
- 41. McMurray JJ, Holman RR, Haffner SM, et al. Effect of valsartan on the incidence of diabetes and cardiovascular events. N Engl J Med., 2010; 362(16): 1477–1490. [PubMed]
- 42. Sawada T, Yamada H, Dahlöf B, Matsubara H. Effects of valsartan on morbidity and mortality in uncontrolled hypertensive patients with high cardiovascular risks: KYOTO HEART Study. Eur Heart J., 2009; 30(20): 2461–2469. [PubMed]
- 43. Massie BM, Carson PE, McMurray JJ, et al. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med., 2008; 359(23): 2456–2467. [PubMed]
- Yusuf S, Diener HC, Sacco RL, et al. Telmisartan to prevent recurrent stroke and cardiovascular events. N Engl J Med., 2008; 359(12): 1225– 1237. [PMC free article] [PubMed]
- 45. Verdecchia P, Angeli F, Gattobigio R, Reboldi GP. Do angiotensin II receptor blockers increase the risk of myocardial infarction? Eur Heart J., 2005; 26(22): 2381–2386. [PubMed]
- 46. McDonald MA, Simpson SH, Ezekowitz JA, Gyenes G, Tsuyuki RT. Angiotensin receptor blockers and risk of myocardial infarction: systematic review. BMJ, 2005; 331(7521): 873. [PMC free article] [PubMed]
- 47. Ikram H, Chan W, Espiner EA, Nicholls MG: Haemodynamic and hormone responses to acute and chronic frusemide therapy in congestive heart failure. Clin Sci., 1980; 59: 443.
- 48. ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100 000 patients in randomized trials. *Circulation*, 1998; 97: 2202– 2212. Google Scholar.