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PHYSICIAN CONNECT

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Physician Connect" which contains latest and interesting news.

This issue contains:

1. Analysis of the genetic relationship between chronic obstructive pulmonary disease and osteoporosis using the Mendelian randomization technique
2. Association of aerobic and muscle-strengthening physical activity with chronic renal disease in individuals with hypertension
3. Thyroidectomy for Euthyroid Patients with Hashimoto Disease and Persistent Symptoms: The verification of the results of Randomized controlled trial
4. Case Report on Kounis Syndrome

Should you require any article or, medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback.

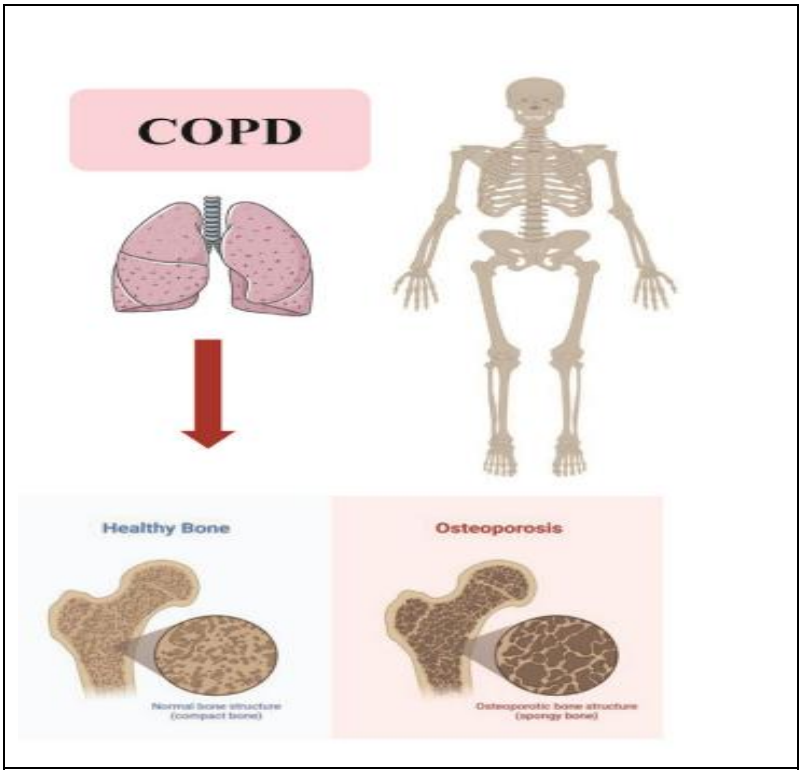
Best Regards,

Medical Team, Micro Labs Limited.

1. Analysis of the genetic relationship between chronic obstructive pulmonary disease and osteoporosis using the Mendelian randomization technique

Introduction:

Chronic obstructive pulmonary disease (COPD) is a slow-developing, incurable lung illness that causes airflow limitation and can lead to complications like pulmonary heart disease and respiratory failure. COPD is produced by a complicated interaction between genes and the environment. Cigarette smoking is the most significant environmental risk factor for COPD. COPD development is influenced by various risk factors, including age, gender, lung growth and development, exposure to particles, socioeconomic level, asthma, airway hyper-reactivity, chronic bronchitis, and infections.[1] Patients with COPD are more likely to be diagnosed with cardiovascular disease than those without COPD. They have a 2-5 times higher risk for conditions such as cardiac dysrhythmia, heart failure, pulmonary circulation disorders, and ischemic heart disease. Osteoporosis has a significant influence on worldwide public health due to fractures, which cause morbidity and mortality. Multiple studies show that COPD has systemic effects and increases the risk of osteoporosis. COPD and osteoporosis are complex diseases with various underlying causes and are becoming more prevalent worldwide. Observational studies indicated a higher prevalence of osteoporosis in COPD patients.[2] So, this study investigated the genetic association between COPD and osteoporosis by using the Mendelian randomization (MR) technique.



Osteoporosis in COPD patients

Methods:

An MR analysis model was utilized to determine the causal effect of COPD on osteoporosis. The author used a recently published GWAS database to find SNPs related to COPD. The initial screening criteria for SNPs were: (1) autosomal biallelic SNPs with a p-value $<5\times10^{-8}$ and (2) minor frequency > 1%. By grouping the 2672 SNPs with linkage disequilibrium, the selected genetic variations were found to be independent (R^2 <0.001 at a 10,000kb frame). Then, it was discovered that 108 independent SNPs were linked to COPD. The inverse variance-weighted (IVW) method was the principal technique used in this MR study. Sensitivity was measured using simple median, weighted median, penalized weighted median, and MR Egger regression analysis.

Results:

The IVW model revealed that genetically determined COPD was causally linked to an increased risk of osteoporosis (odds ratio [OR] fixed-effect, 1.010; 95% confidence interval [CI], 1.001–1.019, P=0.021; OR random-effect, 1.010; 95% CI, 1.001– 1.020, P=0.039). The association was proven to be valid across multiple techniques, including simple and weighted median, penalized weighted, MR-Egger, and MR Egger (bootstrap) (Figure 1). There was no heterogeneity in the IVW or MR-Egger analysis results (Q=131.374, P=0.061 and Q=128.895, P=0.069, respectively). MR-Egger regression demonstrated no pleiotropic influence from genetic variants (intercept, -0.0002; P=0.160). The leave-one-out sensitivity analysis revealed that no single nucleotide variation significantly affects the correlation between COPD and osteoporosis.

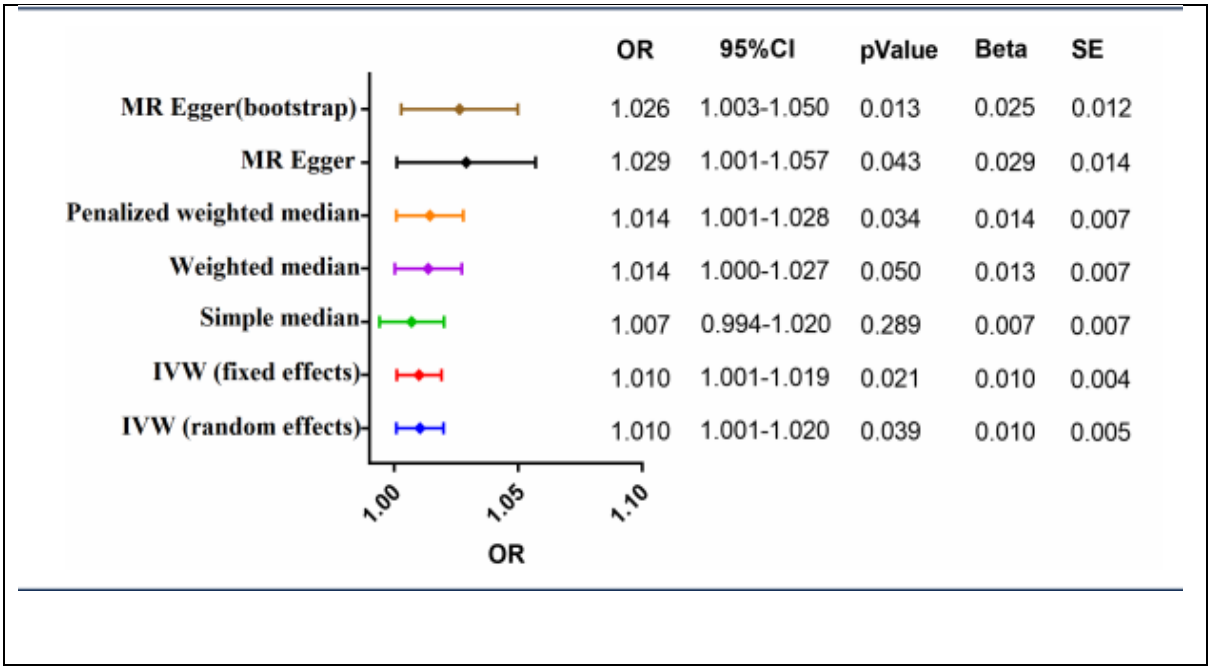


Figure 1: Genetic association Between Osteoporosis and COPD

COPD=chronic obstructive pulmonary disease; OR=odds ratio; CI=confidence interval; SE=standard error; MR=Mendelian randomization; IVW=inverse variance-weighted

Discussion:

This study examined the relationship between genetically predicted COPD and osteoporosis using a Mendelian randomization (MR) method. This MR study revealed a significant favorable influence of COPD on the risk of osteoporosis.[2] A previous study showed that the prevalence of osteoporosis was substantially higher in COPD patients than in healthy controls (40.4% versus 13%; p=0.001). Furthermore, the study discovered that a significant percentage of COPD-afflicted males (24.4%) and women (22%), respectively, had vertebral fractures.[3]

Conclusion:

This MR study revealed a significant favorable influence of COPD on the risk of osteoporosis. Further, COPD patients are more likely to experience osteoporosis recurrence, thus continuous monitoring is necessary.

This MR analysis showed a significant favourable influence of COPD on the risk of osteoporosis.

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1. Cuixue W, Jiedong Z, Wang J, Li S, Atsushi F, Junji Y, Hai T. Progress in the mechanism and targeted drug therapy for COPD. Signal Transduction and Targeted Therapy. 2020;5(1):248
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3. Graumam RQ, Pinheiro MM, Nery LE, Castro CHM. Increased rate of osteoporosis, low lean mass, and fragility fractures in COPD patients: association with disease severity. Osteoporos Int. 2018 Jun;29(6):1457-1468.

2. Association of aerobic and muscle-strengthening physical activity with chronic renal disease in individuals with hypertension

Introduction:

Chronic kidney disease (CKD) is a clinical syndrome that results from an irreversible change in the kidney's structure and/or function and is distinguished by its gradual and steady progression and irreversibility. Diabetes, hypertension, chronic glomerulonephritis, chronic pyelonephritis, long-term anti-inflammatory drug usage, autoimmune disorders, polycystic kidney disease, Alport disease, congenital abnormalities, and prolonged acute renal disease are the primary causes of CKD.[1] CKD affects more than 10% of the population worldwide. Hypertension is a serious public health concern, with a global prevalence that has more than doubled over the past 20 years. Adults with hypertension are more likely to develop CKD, affecting around 30% of the population. Adherence to physical activity (PA) recommendations, including aerobic and muscle-strengthening activities (MSA), has been shown to have advantages, but the impact on the prevalence of CKD in hypertensive individuals has not been thoroughly examined.[2] So, this study aimed to investigate the association between aerobic physical activity, MSA levels, and the prevalence of CKD in hypertension patients.

Methods:

This cross-sectional study analyzed national population-based data from 5,078 hypertensive individuals. Self-reported moderate-to-vigorous physical activity (MVPA) was used to calculate PA levels, while MSA was quantified by the number of days per week. CKD was characterized as an eGFR of <60 mL/min/1.73 m². After correcting for potential confounders, a logistic regression analysis was used to examine the relationship between meeting PA standards and CKD. A collaborative analysis was undertaken to evaluate the impact of MVPA and MSA on CKD.

Results:

The study included 5,078 participants (2,608 women), with an average age of 62.9±12.8 years. After accounting for all variables, increased MVPA was linked to a decreased prevalence of CKD. Compared to the inactive group, those with MVPA 1-149 min/week had an odds ratio (OR) of 0.80 (95% CI, 0.61-1.05), those with MVPA 150-299 min/week had an OR of 0.85 (95% CI, 0.62-1.17), and those with MVPA ≥300 min/week had an OR of 0.53. MSA alone had no significant association with CKD. In the combination analysis, those who fulfilled both MVPA and MSA standards had a lower OR of 0.54 (95% CI, 0.34-0.86) than those who did not meet either (Figure 1).

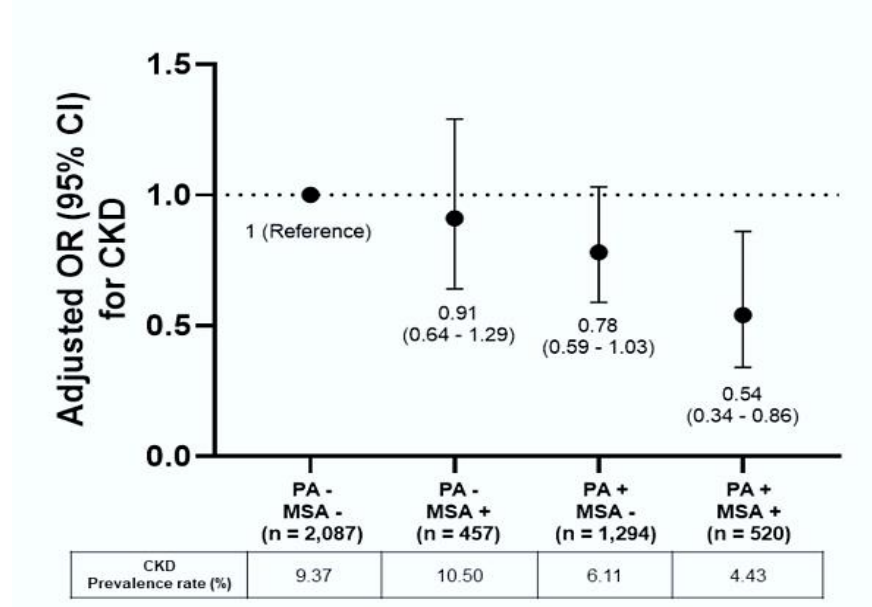

Figure 1. The joint relationships between physical activity and muscle-strengthening exercise and the odds ratios for chronic kidney disease.
OR, odds ratio; CKD, chronic kidney disease; PA, physical activity; MSA, muscle-strengthening activity.

Discussion:

This study examined the relationship between aerobic physical activity, MSA levels, and CKD in hypertensive people. Higher aerobic PA levels were linked to a decreased risk of CKD, while MSA levels were not.[2] A previous cross-sectional investigation found that higher levels of aerobic physical activity were linked to lower CKD prevalence, which was similar to the current study findings.[3]

Conclusion:

MVPA was linked to CKD in participants with hypertension but not in those with MSA alone. Compared to the non-guideline group, those who met both criteria had the lowest prevalence of CKD.

In those with hypertension, Moderate-to-vigorous PA (MVPA) was linked to the prevalence of CKD; but not in those with muscle-strengthening activities (MSA) alone.

Reference:

1. Ammirati AL. Chronic Kidney Disease. Rev Assoc Med Bras (1992). 2020 Jan 13;66Suppl 1(Suppl 1):s03-s09.

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3. Hara M, Nishida Y, Tanaka K, Shimanoe C, Koga K, Furukawa T, et al. Moderate-to-vigorous physical activity and sedentary behavior are independently associated with renal function: a cross-sectional study. J Epidemiol. 2023;33(6):285–93

3. Thyroidectomy for Euthyroid Patients with Hashimoto Disease and Persistent Symptoms: The verification of the results of Randomized controlled trial

Introduction:

Hashimoto's thyroiditis (HT), the most prevalent autoimmune thyroid disorder (AITD), is the leading cause of hypothyroidism in iodine-sufficient places around the world. Approximately 20-30% of patients have HT, which is caused by a combination of genetic predisposition and environmental factors. Loss of immune tolerance leads to an autoimmune attack on the thyroid tissue and the emergence of the disease.[1] Despite hormone replacement, certain Hashimoto disease patients may still experience persistent symptoms, suggesting an autoimmune etiology. A randomized trial utilizing patient-reported outcome measures found that complete thyroidectomy was beneficial but had major complication rates.[2] So, this study aimed to replicate the RCT results in an observational study of euthyroid patients with Hashimoto disease, persistent symptoms despite being euthyroid, and a wider range of anti-TPO antibody levels compared to the RCT.

Methods:

This was an observational post-randomization study that included 154 patients with Hashimoto disease, euthyroid with or without thyroid hormone substitution, and persisting Hashimoto-related symptoms who underwent complete thyroidectomy and were followed for 18 months following surgery. The primary outcome was the General Health (GH) dimensional score from the Short Form-36 Health Survey (SF-36). Hypocalcemia or postoperative nerve palsy that remained for more than a year were considered long-term surgical side effects.

Results:

In this study, 154 (69%) patients underwent total thyroidectomy. Eighteen months following surgery, there was a clinically significant improvement in GH levels, like the earlier RCT. Anti-TPO antibody levels decreased significantly following surgery. The multivariate logistic regression model showed that preoperative anti-TPO antibody levels did not affect the outcome in the observational groups. Three (1.9%) of 154 patients developed persistent unilateral recurrent nerve palsy, whereas six (3.9%) developed hypoparathyroidism following surgery. Preoperative anti-TPO antibody levels did not affect outcome in the multivariate logistic

regression model, even when utilizing a defined minimal clinical improvement difference (MCID) of 5.3 points (Table 1).

		GH not improved >5.3 points	GH improved >5.3 points	Univariable OR (95% CI)	Multivariable OR (95% CI)
Sex	Men (%)	3 (20.0)	12 (80.0)	1.0 (reference)	1.0 (reference)
	Women (%)	37 (29.8)	87 (70.2)	0.59 (0.16–2.21), $p = 0.431$	0.49 (0.12–2.00), $p = 0.320$
Age	Mean (SD)	51.0 (13.7)	46.8 (12.1)	0.97 (0.95–1.00), $p = 0.083$	0.97 (0.94–1.01), $p = 0.105$
Complications	No (%)	29 (27.9)	75 (72.1)	1.0 (reference)	1.0 (reference)
	Yes (%)	11 (31.4)	24 (68.6)	0.84 (0.37–1.94), $p = 0.689$	0.62 (0.24–1.56), $p = 0.305$
GH baseline	Mean (SD)	44.7 (25.5)	29.1 (23.4)	0.98 (0.96–0.99), $p = 0.001$	0.97 (0.96–0.99), $p = 0.002$
Anti-TPO ab baseline	Mean (SD)	1577.4 (1627.2)	2211.0 (2881.0)	1.00 (1.00-1.00), $p = 0.201$	1.00 (1.00-1.00), $p = 0.218$

Table 1: Multivariate logistic regression analysis of observational groups 2–5 data with 95% CIs and odds ratios (OR) to achieve a General Health (GH) score improvement of 5.3 points or more 18 months following total thyroidectomy.

Discussion:

This study found that thyroidectomy was advantageous for individuals with Hashimoto's disease, anti-TPO antibody levels greater than 1000 IU/mL, and symptoms that persisted even after proper thyroid hormone replacement for hypothyroidism. Hashimoto thyroiditis' inflammatory and fibrotic nature can increase the possibility of recurrent nerve palsy and hypoparathyroidism.[2] A prospective observational analysis of 1268 patients with Hashimoto's disease found that 0.9% had permanent nerve palsy and 1.1% had permanent hypoparathyroidism. The findings were comparable to those reported after surgery for benign goiter, with 0.8% nerve palsy and 0.9% hypoparathyroidism.[3] In the present study, there were 7 cases of persistent unilateral nerve palsy (3.1%), resulting in 1.55% per nerve at risk.[2]

Conclusion:

For those with Hashimoto's disease who continue to experience symptoms even after being kept euthyroid with or without hormone replacement therapy, a total thyroidectomy may be beneficial and long-lasting. Although there is a high rate of complications associated with the meticulous dissection thought to be necessary, the procedure might be advantageous in some cases. Anti-TPO antibody titers don't seem to be useful in the patient selection process; instead, surgery ought to be done in specialized facilities and as a component of additional, preferentially blinded studies concerning chronic symptoms.

Thyroidectomy may help relieve symptoms in euthyroid patients with Hashimoto's disease and chronic conditions.

Reference:

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4. Case Report on Kounis Syndrome

Introduction:

Kounis syndrome (KS) is an acute coronary syndrome caused by allergic or anaphylactic reactions. It has three types such as vasospastic allergic angina (type I), allergic myocardial infarction (type II), and stent thrombosis (type III). KS is not uncommon, but because of its wide range of clinical symptoms, it is usually overlooked or misdiagnosed. The diagnosis of KS relies on a combination of cardiovascular and allergic/anaphylactic symptoms, as well as laboratory, electrocardiographic, echocardiographic, and angiographic findings. ECG monitoring, cardiac enzymes, and troponin testing are required to confirm or rule out KS in patients with allergic responses.[1] Kounis and Zavras initially described KS in 1991. Allergens such as antibiotics, analgesics, and contrast media can cause KS by activating a hypersensitive reaction cascade, leading to vasospasm and plaque rupture. This type of vasospasm can occur in the coronary, cerebral, or mesenteric arteries.[2] This case report describes a possible KS secondary to ceftriaxone.

Case presentation:

A 65-year-old female with a medical history of TIA, non-obstructing kidney stone, and bilateral knee osteoarthritis arrived at the emergency department with a one-week history of dysuria, fever, and shivering. She had a social history of smoking for 45 years. At presentation, the patient denied experiencing any other symptoms such as headaches, dizziness, chest pain, or dyspnea. Additionally, they denied having any allergies. The patient was stable, attentive, awake, and oriented, with no significant physical examination findings. The patient was stable, attentive, awake, and oriented, with no significant physical examination findings. Upon arrival, her urinalysis indicated urinary tract infection, although her basic blood work was normal except for leukocytosis. A non-enhanced abdominal CT scan revealed a stable ureteral stone with no apparent renal disease. Then, the patient was admitted due to a serious urinary tract infection requiring intravenous antibiotics. After receiving IV ceftriaxone for 30 minutes, the patient experienced chest pain, shortness of breath, skin itching, and bradycardia. She also vomited twice. The patient's heart rate fluctuated between 57 and 32 beats per minute, her blood pressure was 126/78 mm Hg, and respiratory rate of 26 breaths per minute. An ECG during the incident revealed ST-segment elevation in inferior leads II, III, and aVF, with reciprocal alterations in leads V1-V2 and AVR (Figure 1). She was transferred to a monitored bed and started receiving heparin infusion and dual antiplatelet treatment. She received diphenhydramine and hydrocortisone after experiencing symptoms.

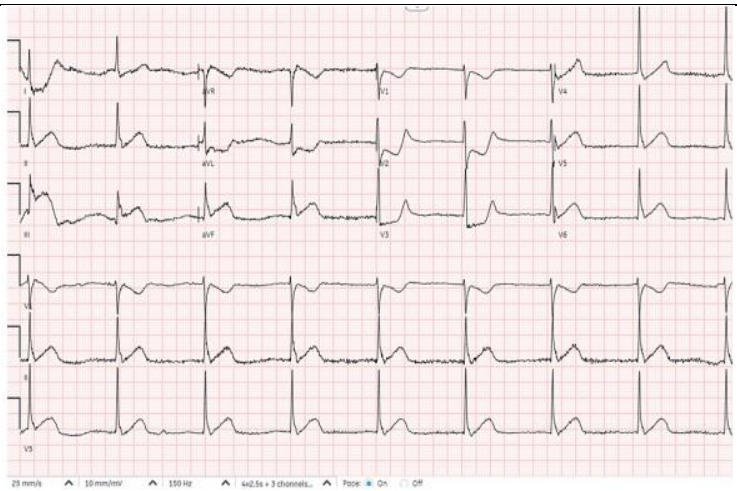

Figure 1. Initial ECG reveals ST elevation in inferior leads with reciprocal alterations.

After a few minutes, the patient's vital signs stabilized, and symptoms improved. After repeating the ECG, the patient's ST elevation was resolved (Figure 2). Her cardiac enzymes were also tested and came back negative. She was kept on cardiac monitoring with serial ECG and troponin levels. A thorough allergy history indicated that the patient previously had dyspnea, itching, and rash after receiving ceftriaxone in another hospital. The patient was allergic to ceftriaxone and was scheduled for elective cardiac catheterization the next

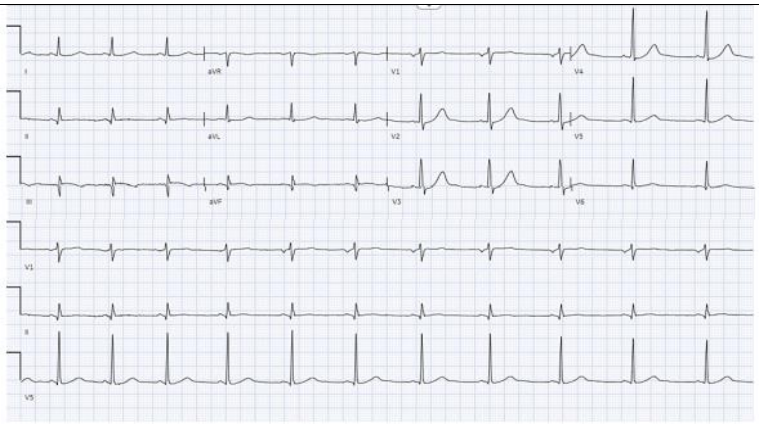

Figure 2: ECG after diphenhydramine and hydrocortisone treatment revealed resolution of previous findings.

day. However, the patient refused and was sent home against medical advice. This instance described as a potential KS from ceftriaxone.

Discussion:

Acute coronary syndrome (ACS) is an uncommon illness that develops because of allergen exposure.[2] Allergens known to cause KS include shellfish, analgesics, proton pump inhibitors, contrast media, and antibiotics, particularly penicillins, which are most commonly linked to this condition.[3] When identifying a patient with KS, a high level of clinical suspicion and extensive knowledge are essential to guide tests and treatment. A complete allergy history is crucial in preventing such a presentation.[2]

Conclusion:

KS, also known as allergic MI, is an uncommon medical disease observed in clinical practice. Guidelines for managing KS are currently inadequate, possibly due to the disease's complexity involving allergies and cardiac ischemia. The current standard of care for KS is a balanced approach that considers both disease entities and the underlying pathophysiology of all three types. Maintaining a high clinical suspicion is crucial in managing this delicate and potentially fatal illness.

References:

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3. Abdelghany M, Subedi R, Shah S, Kozman H. Kounis syndrome: A review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. Int J Cardiol. 2017 Apr 1;232:1-4.

When diagnosing KS in a patient, a high level of clinical suspicion along with thorough information is essential to guide tests and care. A complete allergy history is crucial for preventing such a presentation.