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| **Table 1**. Major studies and related findings |
| Author, year | Study design | Study population | Study aim | Major findings |
|  Mehta, 2020[18] | Prospective cohort study | 666 asymptomatic individuals and 4184 patients with coronary artery disease (CAD).  | To assess the impact of sex on association of suPAR with all-cause mortality in patients with CAD using multivariable-adjusted Cox models. | Women had 10% higher suPAR levels compared to men. Elevated sex-specific plasma suPAR levels are equally predictive of risk of adverse events in both sexes. |
| Isola, 2020[25] | Prospective study | 326 individuals (healthy controlls, patients with coronary heart disease and periodontitis) | To assess the impactof gingival health, periodontitis and CHD on plasma and saliva suPAR and to evaluate the role of suPAR as abiomarker of periodontitis and CHD. | Patients with periodontitis and with periodontitis + CHD had higher plasma and salivary suPAR levels compared to CHD patients and healthy controls. In this studied population, suPAR was a valuable prognostic biomarker of periodontitis and CHD. |
| Mima, 2020[21] | Prospective study | Patients with stable coronary artery diseases and patients with one or more cardiovascular risk factors | Assessment of plasma levels of novel biomarkers that reflect different pathophysiological pathways (sST2: mechanical strain, IGF-BP2: metabolic pathways, suPAR and GDF-15: inflammatory processes) in patients undergoing physical exercise | From the assessed biomarkers, 4 weeks of high-intensity exercise training resulted in a statistically significant change in the plasma level of sST2 and IGF-BP2. 8 months of intensive exercise resulted in a significant increase of IGF-BP2. Plasma suPAR concentrations did not show a significant change  |
| Frary, 2020[24] | Prospective study | 1951 subjects included in the 10-year follow-up of the MONICA study, between 1993 and 1994. | To examine the prognostic value of hs-CRP, NT-proBNP and suPAR in predicting cardiovascular morbidity and mortality beyond traditional risk factors in healthy individuals | Hs-CRP, suPAR, and particularly NT-proBNP predicted cardiovascular death and may enhance prognostication beyond traditional risk factors in apparently healthy people |
| VJ van den Berg , 2019[31] | Prospective study | 263 patients with chronic heart failure during a median follow-up of 2.2 years | Associations between temporal biomarker PAI-1, tPA, uPA and suPAR patterns during follow-up and a cardiac event were investigated | Fibrinolytic factors PAI-1, uPA, and suPAR were strongly associated with adverse cardiac events during the course of chronic heart failure |
| Sörensen, 2019[14] | Prospective study | suPAR levels were determined in 1314 patients presenting to the ED with suspected AMI. Patients were followed up for 12 months to assess all-cause mortality | To evaluate the predictive value of suPAR levels for 1-year mortality in patients with suspected AMI | suPAR levels reliably predicted mortality in patients with suspected AMI. The prognostic value for 6-month mortality for suPAR was comparable to an established risk prediction model, the Global Registry of Acute Coronary Events (GRACE) score |
| Sörensen, 2019[15] | Prospective study | 1220 patients with suspected MI presented in the ED | Evaluation of the diagnostic potential of suPAR on top of hs-TnI in a cohort of patients with suspected AMI | Circulating levels of suPAR on top of hs-TnI do not improve the early diagnosis of AMI |
| Wlazel, 2019[12] | Prospective study | 139 patients enrolled and 1 –year follow up | Assessment of the diagnostic power of suPAR and its predictive value for adverse cardiac events in patients with first MI undergoing primary PCI  | suPAR levels appear to be an independent biomarker for the prediction of major adverse cardiac events (myocardial infarction, revascularization, stroke and death) early after first myocardial infarction |
| Mima, 2018[45] | Prospective study | 79 patients with severe aortic valve stenosis undergoing TAVI and analysis of plasma concentrations of GDF-15, H-FABP, fetuin-A, galectin 3, sST2 and suPAR  | Evaluation whether TAVI is followed by a change in the plasma levels of novel cardiovascular biomarkers including suPAR | The initial increase of suPAR could indicate an inflammatory stimulus |
| Wu, 2018[26] | Prospective study | 99 adult hemodialysis patients | The occurrence of cardiovascular events and all-cause mortality during 6-year follow-up  | suPAR was associated with the coronary artery calcification (CAC) score and was found to be a risk factor for new-onset CVD in patients undergoing hemodialysis |
| Jirak, 2018[29] | Prospective study | 51 patients with peripheral artery disease (PAD) and 55 control patients with excluded coronary and peripheral artery disease  | Evaluation of the correlation of biomarker levels and PAD after assessment of plasma samples for sST2 (hemodynamics and inflammation), galectin-3 (fibrosis and remodeling), GDF-15 (remodeling and inflammation), suPAR (inflammation), and fetuin-A (vascular calcification) | Circulating plasma levels of sST2, suPAR, galectin-3, and GDF-15 were significantly elevated in patients with PAD  |
| Westin, 2018[39] | Registry-based cohort study | suPAR was analyzed in 14,764 patients admitted to ED for a 2-year period | If plasma suPAR levels could predict new-onset atrial fibrillation (AF) in con-secutively admitted ED patients during long-term follow-up | suPAR was independently associated with a subsequent new-onset of AF in a population of recently hospitalized patients, but adding suPAR to baseline risk markers did not improve AF prediction |
| Hodges, 2018[43] | Study stems from the larger Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study | 411 patients who underwent AVR surgery during follow-up  | Evaluation of whether early measurement of suPAR could predict risk of postoperative complications in initially asymptomatic patients with mild-moderate aortic stenosis (AS) undergoing aortic valve replacement (AVR) surgery | Higher baseline suPAR levels were associated with increased risk for postoperative complications and mortality in patients with mild-moderate, asymptomatic AS undergoing later AVR surgery |
| Huang, 2017[20] | Prospective study | 196 consecutive (age ≤ 55 years) patients with CAD and 188 age-matched non-CAD individuals as control | Investigation of the role of suPAR in young Chinese patients with coronary artery disease (CAD) | suPAR was an independent risk factor for CAD as its levels were significantly correlated with age, smoking, body mass index, and high-sensitivity C-reactive protein |
| Samman Tahhan, 2017[30] | Prospective study | 5810 patients with obstructive coronary artery disease (CAD) undergoing cardiac catheterization | To assess whether suPAR levels are associated with peripheral arterial disease (PAD) and its adverse outcomes  | Plasma suPAR levels were 22.5% higher in those with PAD compared to non-PAD patients. Plasma suPAR level was predictive of prevalent PAD, PAD-related events and of cardiovascular incidents  |
| Ichihara, 2017[37] | Retrospective study | 426 patients enrolled, 310, 62, and 54 with diagnosis of sinus rhythm, PAF, and NPAF, respectively | Investigation of the potential association between suPAR and the prevalence of atrial fibrillation (AF) when analyzed patients with sinus rhythm, paroxysmal atrial fibrillation (PAF), or non-paroxysmal atrial fibrillation (NPAF) | After multivariate logistic regression analysis, plasma suPAR was associated with AF, particularly NPAF |
| Fujita Shu-Ichi, 2017[38] | Retrospective study | 242 patients, admitted to Cardiology Department  | Investigation of association between suPAR and left ventricular ejection fraction (LVEF), left ventricular mass index (LVMI), and plasma B-type natriuretic peptide (BNP) among cardiac inpatients | Plasma suPAR levels were associated with low LVEF and elevated BNP, but not with left ventricular hypertrophy, independent of CRP, renal function, and use of diuretics  |
| Schernthaner, 2017[15] | Retrospective analysis  | 61 STEMI patients, 57 NSTEMI patients and 76 with excluded coronary artery disease  | The role of biomarkers soluble suppression of tumorigenicity (sST2), growth-differentiation factor-15 (GDF-15), suPAR, heart-type fatty acid-binding protein (H-FABP) and plasma fetuin A in blood of patients with AMI  | Among the studied biomarkers, sST2, GDF-15, H-FABP and suPAR were significantly elevated and fetuin A was inversely downregulated in patients with AMI. Several significant correlations between these biomarkers and various clinical parameters were found |
| Fujisaka, 2017[33] | Prospective study | 291 patients who had sinus rhythm and a left ventricular ejection fraction (LVEF) of ≥50% (8.9% of them were considered to have diastolic dysfunction | Investigation of the potential association between suPAR and left ventricular diastolic dysfunction among patients with preserved LVEF and sinus rhythm | Among cardiac patients with preserved LVEF, suPAR was associated with diastolic dysfunction independent of confounding factors. ROC analysis showed that the utility of suPAR as a biomarker for diastolic dysfunction was limited from the clinical point of view |
| Lichtenauer, 2017[36] | Prospective study  | 65 patients with DCM and 59 patients with ICM were enrolled in the study | Investigation of the role of novel cardiovascular biomarkers sST2, GDF-15, suPAR and H-FABP in patients with ischaemic (ICM) or dilative cardiomyopathy (DCM) | Amomg several biomarkers, suPAR may be considered a precise diagnostic tool in patients with ICM and DCM  |
| Koller, 2017[32] | Prospective study  | 319 patients in outpatient department with CHF for heart failure and 346 patients with CHF for validation. | Evaluation of the predictive value suPAR in patients with chronic heart failure (CHF). | suPAR was found to be a strong and independent predictor of mortality in CHF patients |
| Ghasemzedah, 2017[22] | Study based on subjects recruited from the Emory Cardiovascular Biobank in Emory Healthcare hospitals between 2003-09. | CRP, fibrin degradation product, heat shock protein-70, and suPAR were measured in 3278 patients undergoing coronary angiography | Whether suPAR is an independently predictive factor of adverse outcomes, and its addition to a 3-BRS can improve risk reclassification | suPAR was an independently predictive factor of adverse outcomes, and its addition to a 3-BRS score comprising C-reactive protein, fibrin degradation product, and heat shock protein-70 improved patients’ risk reclassification |
| Hodges, 2016[42] | Prospective study | 1503 who were recruited in the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study | The prognostic value of suPAR in asymptomatic patients with aortic stenosis (AS) | In patients with mild-moderate AS, suPAR was independently associated with the incidence of ischemic cardiovascular events and mortality, and all-cause mortality. |
| Theilade, 2016[34] | Observational study | suPAR levels were measured in 318 patients with type 1 diabetes without known heart disease and with normal left ventricular ejection fraction (LVEF). These patients had a conventional, tissue Doppler and speckle tracking echocardiography | Investigation whether suPAR is associated with early myocardial impairment, assessed with conventional, tissue Doppler and speckle tracking echocardiography | suPAR is associated with early myocardial impairment, also both suPAR and advanced echocardiography were useful diagnostic tools for identifying patients with diabetes at risk of future clinical heart disease |
| Rasmussen LJ, 2016[17] | Nested case-control study | 55 HIV-1-infected patients with verified first-time MI and 182 HIV-1-infected controls with no known cardiovascular disease (CVD) | Evaluation of suPAR as a predictive biomarker of MI in HIV-1-infected patients | suPAR could predict first-time MI in HIV patients, as elevated levels were associated with increased risk of MI even years before the event. |
| Rundgren, 2015[40] | Pilot sudy  | 55 patients were included and 33 of them were alive after 6 months | Aim of the study was the evaluation of suPAR levels in relation to outcome after cardiac arrest (CA) and mild induced hypothermia | suPAR levels at 6 and 36 hours after CA were significantly higher in patients who did not survive, however, the overlap in suPAR levels between the outcome groups was substantial, reducing the prognostic value |
| Mekonnen, 2015[28] | Cross-sectional study | 66 patients with predisposing factors for coronary disease were enrolled in the study | To investigate the relation between suPAR and coronary flow reserve (CFR) in patients with non-obstructive coronary artery disease | suPAR was found an independent predictor factor of coronary microvascular function |
| Eapen, 2014[16] | Study based on participants recruited from the Emory Cardiology Biobank across 3 Emory Healthcare sites between 2003 and 2009 | 3367 subjects (67% with CAD) and adverse cardiovascular (CV) outcomes over a foolow up period of mean 2.1±1.1 years were noticed | To assess the role of suPAR in the prediction of the presence and severity of coronary artery disease (CAD) and the incident of myocardial infarction (MI) and death in patients with suspected CAD | suPAR elevated levels were associated with the presence and severity of CAD and were independent predictors of death and MI in patients with suspected or known CAD |
| Sørensen, 2014[27] | Cross-sectional study | 1126 randomly sampled middle-aged individuals | To investigate the relation between suPAR and hs-CRP and coronary artery calcification (CAC) score detected by cardiac computed tomography (CT) scan | Only suPAR was related to CAC score independently of the Systematic Coronary Risk Evaluation (SCORE) |
| Jalkanen, 2014[41] | A pre-determined substudy of the prospective FINNRESUSCI study | 287 ICU patients after out of hospital cardiac arrest (OHCA) | To evaluate if ischaemia/reperfusion injury after OHCA increases plasma suPAR concentrations, also the prognostic value of suPAR regarding 90-day mortality and the 12-month neurological outcome | suPAR elevated levels were associated with poor outcome in OHCA ICU patients. suPAR alone had inadequate predictive value for poor outcome and not related to 12-month neurological outcome |
| Kruger, 2014[44] | Study formed part of the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trial | 374 patients with mild to moderate AS at baseline and in a follow-up after 1 and 4 years of treatment with Simvastatin and Ezetimibe or placebo | To evaluate the role of Fibulin-1 and suPAR and mild to moderate aortic valve stenosis (AS) | Increased fibulin-1 levels were independently associated with higher suPAR levels and NT-proBNP especially in patients with lower aortic valve area index (AVAI) |
| Borné, 2014[35] | Prospective study | 4530 subjects who participated in the Malmö Diet and Cancer study during 1991–1996 | The association of suPAR and incident of HF and AF in a population-based cohort | suPAR was associated with elevated levels of NT-proBNP and incidence of HF, but not with AF among middle-aged subjects |
| Persson, 2014[47] | Prospective cohort study | 5166 individuals, participating in the Malmö Diet and Cancer study with a mean follow-up of 15 years for ischemic stroke and CAD  | The relationships among suPAR, carotid plaque, and incidence of ischemic stroke and coronary artery disease (CAD) events | suPAR was associated with high occurrence of carotid plaque and incidence of ischemic stroke and CAD  |
| Lyngbæk, 2013[11] | Prospective single center study | 449 consecutive chest pain patients  | The long-term prognostic value of suPAR in chest pain patients admitted on suspicion of non-ST-segment elevation acute coronary syndrome NSTEACS | suPAR was a strong predictor of adverse long-term outcomes and improved the risk stratification in chest pain patients admitted with suspected NSTEACS |
| Intzilakis, 2013[46] | Observational study | 596 healthy individuals | Evaluation of heart rate variability (HRV) and its determinants in non-diabetic individuals vs. impaired fasting glucose, insulin resistance, lipidaemia and markers of inflammation and immune activation including suPAR | A low HRV was related to the immune and inflammatory markers suPAR and CRP and plasma triglyceride |
| Kruger, 2013[19] | Cross-sectional study | 117 black and 116 white men | Assessment of associations between a marker of cardiac strain, the NT-proBNP, and inflammation markers in a bi-ethnic South African cohort | A low-grade inflammatory state possibly contributed to higher cardiovascular risk in black men, as NT-proBNP, CRP and suPAR levels were higher in black compared to white men |
| Lyngbæk, 2013[23] | Prospective study | 2315 generally healthy Danish people who were followed for median of 12.7 years for the composite outcome of IHD, stroke and CVD mortality  | The prognostic value of suPAR and CRP combined with Framingham Risk Score (FRS) | suPAR provided better prognostic information of CVD risk and improved risk prediction when combined with CRP  |
| Lyngbæk, 2012[10] | Prospective study | 296 consecutive patients with ST-segment elevation myocardial infarction admitted for primary PCI | The prognostic capability of suPAR, its temporal course, and its relation to CRP in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous intervention (PCI) | suPAR was found to be a stable plasma biomarker after ST-segment elevation myocardial infarction treated with primary PCI predicting all-cause mortality and recurrent MI |
| Sehestedt, 2011[48] | Prospective study | 2038 individuals, aged 41, 51, 61 and 71 years, without diabetes, prior stroke or myocardial infarction and not receiving related medications | To assess if suPAR was associated with markers of subclinical organ damage | suPAR was associated with the subclinical organ damage, but predicted cardiovascular events independent of subclinical organ damage, traditional risk factors and hsCRP |