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Original Article

The relationship between serum endocan levels with the presence of contrast-induced nephropathy in patients undergoing coronary angiography

Koroner anjiyografi uygulanan hastalarda serum endokan düzeyleri ile kontrast kaynaklı nefropati varlığı arasındaki ilişki

Gamze ASLAN* , Onur BAYDAR

Koc University School of Medicine and Hospital, Department of Cardiology, Istanbul/TURKEY

Abstract

Aim: Contrast-induced nephropathy (CIN) is associated high mortality and morbidity risks in the patients undergoing coronary angiography (CAG).Endocan, a new endothelial dysfunction biomarker, could be a potential immunoinflammatory biomarker for CIN.We investigated the possible association between serum endocan levels and CIN in the patients undergoing CAG.

Material and Methods: We prospectively enrolled 92 patients undergoing CAG.For each patient, serum endocan levels were assessed at hospital admission before CAG.Contrast-induced nephropathy was defined as an increase in serum creatinine 25% or 0.5 mg/dl from baseline in the first 48 - 72 hours.

Results: Overall, 32 cases (34.8%) of CIN were diagnosed.There were no significant differences between the two groups (CIN and without-CIN) in demographic data and general risk factors. 38 patients (41%) were performed percutaneous coronary intervention. Patients with CIN had higher serum endocan levels (3.68 ng/dl;IQR, 0.78-17.3 vs 1.81 ng/dl;IQR, 0.19-17.4, p:0,002) than patients without CIN. Additionaly; basal glomerular filtration rate, contrast volume, serum endocan level and left ventricle ejection fraction were detected as independent risk factors of CIN (p= 0.014, B:0.94, CI: 0.89-0.98, p= 0.024, B:2.55, CI:1.13-5.77, p= 0.026, B:2.45, CI:1.11-5.42, p= 0.044, B:0.91, CI:0.83-1.43, respectively).

Conclusion: In patients undergoing CAG, high serum endocan levels could be associated with an increased risk for CIN.

Keywords: endocan; contrast-induced nephropathy; endothelial dysfunction.

Corresponding author*: Gamze ASLAN, Koc University School of Medicine and Hospital, Department of Cardiology, Istanbul/TURKEY
E-mail: gaslan@kuh.ku.edu.tr
Orcid ID: 0000-0003-4000-3292
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ÖZ

Amaç: Kontrast kaynaklı nefropati (KİN), koroner anjiyografi (KAG) uygulanan hastalarda yüksek mortalite ve morbidite ile ilişkilidir. Yeni bir endotelyal disfonksiyon biyomarkeri olan Endocan, KİN için potansiyel bir immünoenflamatuar biyobelirteç olabilir. KAG uygulanan hastalarda, serum endokan düzeyleri ile KİN arasındaki olası ilişkinin araştırılması amaçlandı.

Gereç ve Yöntemler: KAG yapılan 92 hasta çalışmaya alındı. KAG öncesinde, hastane başvurusunda her hastanın serum endokan düzeyleri değerlendirildi. Kontrast kaynaklı nefropati, maruziyetten 48-72 saat sonrasındaki kreatinin düzeyinin başlangıç serum kreatinin düzeyine göre % 25 veya 0.5 mg / dl artış olması olarak tanımlandı.

Bulgular: Toplam 32 hastada (%34.8) KİN saptandı. KİN olan ve olmayan 2 grup arasında demografik veriler ve genel risk faktörleri açısından anlamlı fark saptanmadı.38 hastaya (%41) perkutanöz koroner girişim yapıldı. KİN saptanan hastalarda serum endokan düzeyleri (3.68 ng/dl;IQR, 0.78-17.3 karşı 1.81 ng/dl;IQR, 0.19-17.4, p: 0,002) KİN olmayan hastalara göre daha yüksek bulundu. Ek olarak; bazal glomerüler filtrasyon hızı, kontrast volümü, serum endokan ve sol ventrikül ejeksiyon fraksiyonu KİN için bağımsız risk faktörü olarak saptandı (p= 0.014, B: 0.94, CI: 0.89-0.98, p= 0.024, B: 2.55, CI: 1.13-5.77, p= 0.026, B: 2.45, CI: 1.11-5.42, p= 0.044, B: 0.91, CI: 0.83-1.43, sırasıyla).

Sonuç: KAG yapılan hastalarda, yüksek serum endokan seviyeleri KİN oluşma riski ile ilişkili olabilir.

Anahtar kelimeler: endokan; kontrast ilişkili nefropati; endotelyal disfonksiyon.

Introduction

It was known that coronary angiography (CAG) and percutaneous coronary intervention reduce ischemic complications and improves survival in patients with coronary artery disease (CAD). However, contrast agents used for performing cardiovascular interventions are potential risks for contrast-induced nephropathy (CIN). CIN could cause renal dysfunction, longer hospital stay, increased cardiovascular events and mortality [1]. So many factors such as hypovolemia, contrast volume, some drugs (diuretics etc.) and baseline glomerular filtration rate (GFR) may contribute to the development of CIN [2]. Because of these, identifying the risk of CIN is important in patients performed CAG.

First study about Endocan was in 1996 [3]. It was cloned from human umbilical vein endothelial cell cDNA library. Endocan is a proteoglycan and produced from vascular endothelial cells (ECs) and plays as a regulator role in vascular proliferation, migration and adhesion processes [4]. Endocan has shown as a novel mediator for ECs dysfunction and inflammation in the previous studies [5,6]. Additionally, it was found to associate with cardiovascular diseases [7,8], cancer [9], sepsis [10], chronic kidney disease [11,12] and acute rejection of renal transplantation [5].

Oxidative stress, endothelial dysfunction, and apoptosis were described as pathophysiologic mechanisms for the development of acute kidney injury due to contrast administration [13]. Additionaly, previous studies have shown that endocan is a potential immunoinflammatory marker that may be linked to CIN and is highly expressed in glomeruli, and especially increases by glomerular damage and by the deterioration of glomerular filtration rate, its clearance decreases and its levels raise to higher extents [12,14].

According to these pathological mechanisms, testing novel biomarkers in the patients undergoing CAG may help determination of potential risks for acute kidney injury and may reduce the development of CIN. Therefore, we aimed to evaluate the relationship between serum endocan levels and the risk of CIN in the patients undergoing CAG.

Methods

We prospectively observed 92 consecutive patients undergoing CAG at the Cardiology Department. CAD was defined according to the current guidelines [15]. According to power analysis based on these data (alpha 0.05, power 95%), minumum a total of 87 patients were planned to be included in the study. We excluded the patients with a severe valvular heart disease, severe or decompensated heart failure, acute coronary syndromes, end stage kidney disease, severe liver disease, connective tissue disease and patients undergoing urgent cardiac surgery for revascularization. We

included the patients with angina pectoris who had positive stress test (exercise ECG, myocardial perfusion imaging or stress echocardiography). Serum creatinine concentration levels were observed at hospital admission, every following day and at hospital discharge. Glomerular filtration rate (eGFR) was calculated using the modified formula of Levey et al [16]. Contrast-induced nephropathy was defined as an increase in creatinine 25% or 0.5 mg/dl from the baseline value within the 48- 72 hour period following CAG [17]. In all patients, serum endocan levels were assessed at hospital admission. Endocan (Cloud-Clone Corp., Houston, USA), concentrations in patients' sera were analyzed using sandwich enzyme-linked immunosorbent assays (ELISA) according to the manufacturer's instructions. Values were normalized to standard curve. The intra-assay and interassay variances for serum endocan was <10% and <12%, respectively. A nonionic, low-osmolality contrast agent (iopromide) was used for performing CAG. In the cases who had heart failure and chronic kidney disease, for preventing the development of CIN, saline infusion (intravenously at a rate of 1 mL/(kg h) (0.5 mL/[kg h]) was applied during the periprocedural period. Also, in these cases, for preventing the development of CIN, the use of the nephrotoxic drugs such as non-steroid anti-inflammatory drugs, metformin, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and diuretics were stopped at least 48 hours prior to the procedure. Transthoracic echocardiography was performed for all patients (Epiq 7; Philips Ultrason System, Amsterdam, Netherlands) and left ventricle ejection fraction (LVEF) was measured using the Simpson method.

Hypertension [16] was defined as blood pressure> 140/90 mm Hg or being on treatment with antihypertensive medications. Also, diabetes mellitus (DM) was defined as fasting glucose levels >126 mg/dL or being on treatment with oral antidiabetic drugs or insulin. Finally, hyperlipidemia (HL) was defined by the references of the current guidelines [18]. The study was approved by the Local Ethics Committee (2015.096.IRB.036) and informed consent was taken from all participants. This article does not contain any studies with human participants or animals performed by any of the authors.

Statistical analysis

The statistical analysis was performed by using SPSS version 22 for Windows (SPSS Inc, Chicago, Illinois). Numerical variables were expressed as mean (standard deviation) (SD) and nominals as percentages. All variables were evaluated by Kolmogorov Smirnov Test to determine the normality of distribution. Parametric variables were compared using the Student-T test. The Mann Whitney U-test was used for the evaluation of nonparametric variables. The chi-square test was used to compare categorical data. Correlations were studied by the Pearson's correlation test. ROC analysis was performed to determine the sensitivity and specificity values of serum endocan. To evaluate the effects of various factors on CIN development, multivariate regression analyses were performed by using the backward Logistic Regression method. All p values less than 0.05 were accepted as statistically significant.

Results

92 patients were included in this study and 32 (34.8%) of them had CIN. There were no significant differences between the two groups in terms of age and gender. General risk factors, hypertension, diabetes mellitus, previous history of CAD, smoking and family history of CAD were same in both groups. Additionally, previous medications, contrast volume and coronary angiography findings did not differ between two groups. Only, GFR basal and LVEF were significantly lower in patients with CIN. Additionaly, C-reactive protein (CRP) was higher in patients with CIN. The baseline clinical and procedural characteristics of patients were shown in Table 1. Patients with CIN had higher admission serum endocan levels (3.68 ng/dl; IQR, 0.78-17.3 vs 1.81 ng/dl; IQR, 0.19-17.4, p:0,002) than patients without CIN (Figure 1). Additionally, log10 endocan parameters (0.58 ± 0.38 ng/dl vs 0.27 ± 0.44 ng/dl, p:0,001) were found higher in the patients with CIN than patients without CIN.

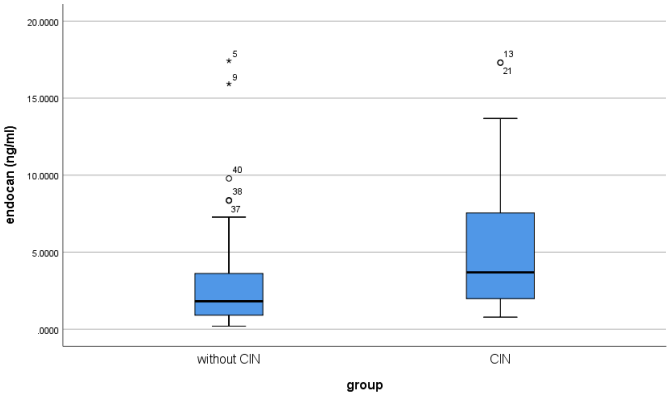

Figure 1. Serum endocan levels with and without CIN patients.

{Values more than three IQR's from the end of the box are labeled as extreme, denoted with an asterisk (*). Values more than 1.5 IQR's but less than 3 IQR's from the end of the box are labeled as outliers (<)}.

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Table 1. Baseline and laboratory characteristics of the study population.			
Clinical characteristics	CIN group (n=32)	Non-CIN group (n=60)	p
Age (years)	69.3 ± 9.4	66.3 ± 6.7	0.074≠
Gender (Male/Female)	75/25	62/38	0.250¶
Hypertension (%)	81	68	0.224¶
Diabetes Mellitus (%)	56	35	0.076¶
Family history of CAD (%)	40	28	0.251¶
Previous history of CAD (%)	34	23	0.257¶
Smoking (%)	50	38	0.376¶
Previous medication			
Angiotensin-converting-enzyme inhibitors (%)	28	21	0.489¶
Angiotensin II receptor blockers (%)	37	20	0.129¶
Calcium canal blockers (%)	40	32	0.390¶
Beta-blockers (%)	53	40	0.228¶
Diuretics (%)	18	10	0.142¶
Alpha-blockers (%)	12	13	0.910¶
Nitrates (%)	10	5	0.418¶
Lipid lowering drugs (%)	50	35	0.162¶
Antiaggregant treatment (%)	50	33	0.119¶
Metformin (%)	25	15	0.239¶
Other oral antidiabetics (%)	34	27	0.439¶
Insulin (%)	18	7	0.076¶
Coronary angiography findings			
Number of patients with obstructed coronary arteries (>%50)	18	28	0.381¶
Number of patients without obstructed coronary arteries (<%50)	9	21	0.409¶
Number of patients with normal coronary arteries (n)	5	11	0.744¶
Obstructed arteries (n)	2 (0-3)	2 (0-3)	0.426*
Left main coronary artery obstruction percentage (%)	0 (0-60)	0 (0-60)	0.458*
Left anterior decending artery obstruction percentage (%)	80 (0-100)	70 (0-100)	0.088*
Circumflex artery obstruction percentage (%)	60 (0-100)	55 (0-100)	0.806*
Right coronary artery obstruction percentage (%)	80 (0-100)	40 (0-100)	0.184*
Coronary stent implantation (%)	47	38	0.507¶
Coronary bypass surgery (n, patient)	3	5	0.344¶
Laboratory and echocardiographic findings			
Left ventricle ejection fraction (%)	51.2 ± 10.7	56.5 ± 8.1	0.011≠
Fasting glucose (mg/dl)	137.6 ± 55.8	123.7 ± 30.3	0.155≠
BUN basal (mg/dl)	29.9 ± 16.7	21.8 ± 10.0	0.005≠
Creatinine basal (mg/dl)	1.21 ± 0.3	1.09 ± 0.3	0.045≠
GFR basal (ml/dk/1.73m2)	57.7 ± 19.3	67.0 ± 16.1	0.016≠
Contrast volume $ (ml)	170 (25-600)	127.5 (40-600)	0.218*
BUN (post contrast) (mg/dl)	39 ± 21.5	21.3 ± 8.7	<0.001≠
Creatinine (post contrast) (mg/dl)	2.01 ± 1.0	1.13 ± 0.3	<0.001≠
GFR (post contrast) (ml/dk/1.73m2)	37.6 ± 16.8	65.4 ± 16.9	<0.001≠
Sodium (mmol/l)	139.9 ± 3.7	140.9 ± 3.3	0.172≠
Potassium (mmol/l)	4.3 ± 0.4	4.4 ± 0.5	0.367≠
Uric acid (mg/dl)	7.06 ± 2.23	7.09 ± 1.92	0.950≠
C-reactive protein (mg/l)	16.1 ± 16.5	8.8 ± 8.2	0.026≠
Hemoglobin (g/dl)	12.2 ± 2.1	13.0 ± 2.1	0.125≠
Leukocytes (K/ul)	7.0 (4.2-10.2)	7.4 (4.2-10.7)	0.448*
Serum endocan (ng/ml)	3.68 (0.78-17.3)	1.81 (0.19-17.4)	0.002*
Log10endocan	0.58 ± 0.38	0.27 ± 0.44	0.001≠

NS indicates non-significant; BUN, blood urea nitrogen; CAD, coronary artery disease; CIN, Contrast induced nephropathy; GFR, glomerular filtration rate; $ iopromid (0.769 g/ml).
The median (interquartile range) or frequency counts (percentages)' as appropriate.
≠ t test; *Mann-Whitney U test; ¶ Chi-square test

In Pearson correlation analysis, CRP levels correlated positively with uric acid (r = 0.44, p < 0.0005). Also, serum endocan concentrations correlated negatively only with serum sodium (r = - 0.30, p = 0.004).

In ROC analysis, the cut-off value of endocan for CIN patients in this study was > 3.04 ng/ml, with 60% sensitivity, 40% specificity (AUC: 0.70, 95% CI: 0.59-0.81, p=0.002) (Figure 2). There were 19 (59%) patients in CIN group and 22 patients (36%) in nonCIN group whose serum endocan levels were exceeding the standard upper value of 3.04 ng/ml.

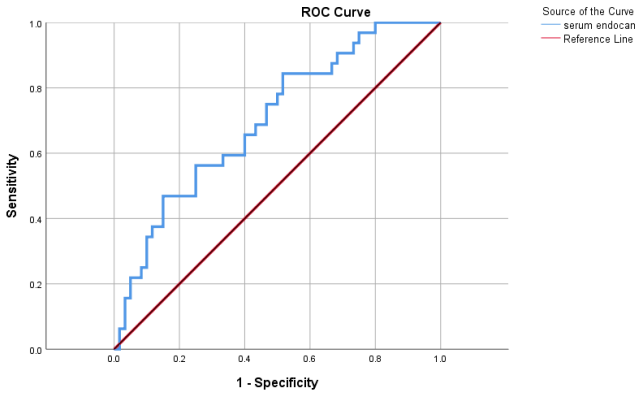
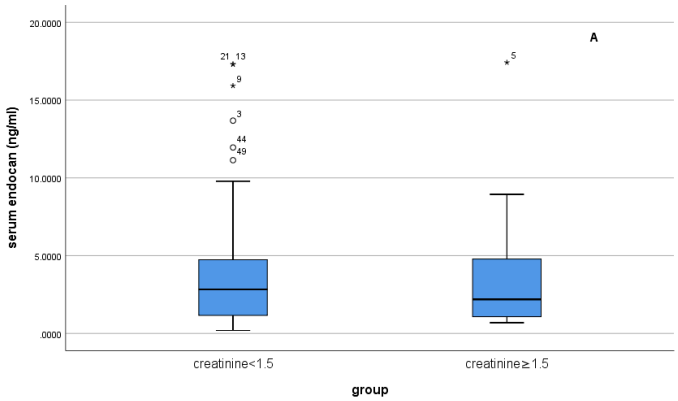


Figure 2. ROC curve analysis for values of serum endocan [3.04 ng/ml, with 60% sensitivity, 40% specificity (AUC: 0.70, 95% CI: 0.59-0.81, p=0.002)].

To analyze the associations of endocan with the potential confounder of creatinine, the study participants were divided into two groups according to creatinine<1.5 mg/dl and creatinine ≥ 1.5 mg/dl. Serum endocan levels did not differ between the creatinine<1.5 mg/dl and creatinine ≥ 1.5 mg/dl groups (2.83 ng/ml; IQR, 0.19-17.31 ng/ml vs 2.19 ng/ml; IQR, 0.68-17.40 ng/ml, p = 0.862) (Figure 3A). Additionally, serum endocan levels were analyzed in the patients with presence or absence of obstructed coronary arteries (>%50). There was not any differences between these groups (2.81 ng/ml; IQR, 0.68-17.40 ng/ml vs 2.84 ng/ml; IQR, 0.19-17.31 ng/ml, p = 0.160) (Figure 3B).



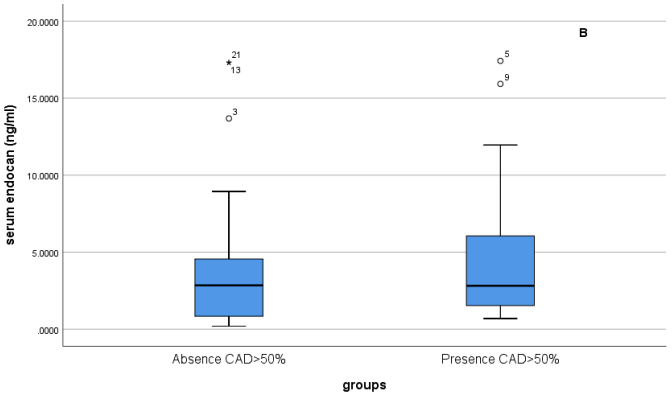


Figure 3. A) Serum endocan levels according to creatinine levels (creatinine <1.5 mg/dl compared to creatinine ≥1.5 mg/dl). **B)** Serum endocan levels according to presence or absence of obstructed coronary arteries (>%50).

{Values more than three IQR's from the end of the box are labeled as extreme, denoted with an asterisk (*). Values more than 1.5 IQR's but less than 3 IQR's from the end of the box are labeled as outliers (<)}.

Additionaly; basal GFR (p= 0.014), contrast volume (p= 0.024), serum endocan level (p= 0.026) and LVEF (p= 0.044) were detected as independent risk factors of CIN in logistic regression analysis (r2= 0.66, p= 0.00, odds ratio= 0.554 for model) (Table 2).

Table 2. The contrast induced nephropathy associated with variables according to binary stepwise logistic regression.

Variables	Logistic regression analysis Method: Backward stepwise (R2: 0.66, p: 0.00)		
	Exp (B)	% 95 CI	p
Hypertension	0.36	0.01-9.91	0.550
Uric acid	0.89	0.55-1.44	0.654
C-reactive protein	0.94	0.86-1.03	0.221
Left ventricle ejection fraction	0.91	0.83-0.99	0.044
Glomerular filtration rate (basal)	0.94	0.89-0.98	0.014
Contrast volume	2.55	1.13-5.77	0.024
Endocan	2.45	1.11-5.42	0.026

CI, confidence intervals.

4 patients from the contrast induced nephropathy group needed HD. Only one time HD was performed for these patients. Hydration therapy was applied to the other patients. All of the patients with CIN healed and their renal function came back to the previous values.

Discussion

CIN is a common cause of hospital acquired acute kidney injury. Because of CIN effects on morbidity and mortality, identifying the risk of CIN is important. Some conditions such as previous history of CAD, diabetes, dehydration, advanged age, use of diuretics, repeated contrast exposure, use of high osmolar contrast agent are related with CIN development [19]. After the contrast exposure, endothelial dysfunction and deterioration in the balance of the vasoconstrictor and vasodilator factors could cause renal hypoxia and injury [20].

In the general population, the incidence of CIN is estimated to be 1% to 6%. However, the risk may be as high as 50% in some patient subgroups (diabetes, chronic kidney disease, other comorbidities) [21]. In this study, 32 patients (34.8%) had CIN. This finding might be related with lower basal GFR and LVEF values than non-CIN group .

In our study, we found that CIN rate was significantly increased in patients with high endocan levels and also demonstrated that the endocan levels were independently associated with CIN. Endocan is also a useful biomarker for evaluation of renal injury. Gunay et al. showed high endocan levels in patients with acute kidney injury [22]. In addition, serum endocan levels were found inversely correlated with estimated GFR [14]. Yılmaz et al. reported that raised endocan levels could predict all-cause mortality and cardiovascular events in patients with chronic kidney disease [12]. Li et al. reported in the renal transplantation patients that serum level of endocan signifies the degree of endothelial cell injury and it has the potential to show glomerular/endothelial cell injury as a highly sensitive and specific biomarker [23]. Therefore, evaluation of serum endocan levels may help the clinicians for the early detection of CIN.

The amount and the type of the contrast volume is important for the patients undergoing coronary angiography because of the CIN risk, especially if these patients had chronic kidney disease [24]. Thus, contrast agent dose optimization and periprocedural hydration are very important. Therefore, we tried to use a relatively small amount of contrast in this study, and the dose of contrast used was not found different between the patients with and without CIN [25]. However, according to logistic regression analysis diabetes mellitus, contrast volume, serum endocan level and LVEF were independent risk factors of CIN in this study. Serum endocan levels may be a possible significant biomarker for development of CIN together with the known risk factors in this study. High serum endocan levels detected in this study could reflect endothelial dysfunction which is associated with inflammation. Serum endocan levels can be measured easily at the preprocedural period and intravenous hydration, sodium bicarbonate, and N-acetylcysteine for prophylactic prevention of CIN may be applied before the procedure. Thus, in comparison to other available CIN risk stratification tools, serum endocan evaluation is a simple test and therefore may be easily applied to the daily practice.

This study had some limitations. First, it was a single-center study. Second, this study's cohort was relatively small. Third, neither serum endocan levels nor urine endocan levels were not evaluated after the procedure.

Conclusion

Serum endocan levels could be associated with a increased risk for CIN in the patients undergoing CAD and it can be used as a new, simple, and reliable test to predict CIN in patients who underwent urgent CAG.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. Marenzi G, Lauri G, Assanelli E, Campodonico J, De Metrio M, Marana I, Grazi M, Veglia F, Bartorelli AL. Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. Journal of the American College of Cardiology 2004; 44: 1780-5.
2. Nakamura T, Ako J, Kadowaki T, Funayama H, Sugawara Y, Kubo N, Momomura S. Impact of acute hyperglycemia during primary stent implantation in patients with ST-elevation myocardial infarction. Journal of Cardiology 2009; 53: 272-7.
3. Lassalle P, Molet S, Janin A, Heyden JV, Tavernier J, Fiers W, Devos R, Tonnel AB. ESM-1 is a novel human endothelial cell-specific molecule expressed in lung and regulated by cytokines. The Journal of Biological Chemistry 1996; 271: 20458-64.
4. Bechard D, Scherpereel A, Hammad H et al. Human endothelial-cell specific molecule-1 binds directly to the integrin CD11a/CD18 (LFA-1) and blocks binding to intercellular adhesion molecule-1. Journal of Immunology 2001; 167: 3099-106.
5. Lee YH, Kim SY, Moon H et al. Endocan as a marker of microvascular inflammation in kidney transplant recipients. Scientific Reports 2019; 9: 1854.

6. Zhao T, Kecheng Y, Zhao X, Hu X, Zhu J, Wang Y, Ni J. The higher serum endocan levels may be a risk factor for the onset of cardiovascular disease: A meta-analysis. Medicine 2018; 97: 13407.
7. Wang XS, Yang W, Luo T, Wang JM, Jing YY. Serum endocan levels are correlated with the presence and severity of coronary artery disease in patients with hypertension. Genetic Testing and Molecular Biomarkers 2015; 19: 124-7.
8. Balta S, Mikhailidis DP, Demirkol S, Ozturk C, Kurtoglu E, Demir M, Celik T, Turker T, Iyisoy A. Endocan--a novel inflammatory indicator in newly diagnosed patients with hypertension: a pilot study. Angiology 2014; 65: 773-7.
9. Liu N, Zhang LH, Du H, Hu Y, Zhang GG, Wang XH, Li JY, Ji JF. Overexpression of endothelial cell specific molecule-1 (ESM-1) in gastric cancer. Annals of Surgical Oncology 2010; 17: 2628-39.
10. Palmiere C, Augsburger M. Endocan measurement for the postmortem diagnosis of sepsis. Legal Medicine 2014; 16: 1-7.
11. Lee HG, Choi HY, Bae JS: Endocan as a potential diagnostic or prognostic biomarker for chronic kidney disease. Kidney International 2014; 86: 1079-81.
12. Yilmaz MI, Siriopol D, Saglam M et al. Plasma endocan levels associate with inflammation, vascular abnormalities, cardiovascular events, and survival in chronic kidney disease. Kidney International 2014; 86: 1213-20.
13. Persson PB, Tepel M. Contrast medium-induced nephropathy: The pathophysiology. Kidney International Supplement 2006: 8-10.
14. Su YH, Shu KH, Hu CP, Cheng CH, Wu MJ, Yu TM, Chuang YW, Huang ST, Chen CH. Serum Endocan correlated with stage of chronic kidney disease and deterioration in renal transplant recipients. Transplantation Proceedings 2014; 46: 323-7.
15. Hamm CW, Bassand JP, Agewall S et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal 2011; 32: 2999-3054.
16. Levey AS, Beto JA, Coronado BE et al. Controlling the epidemic of cardiovascular disease in chronic renal disease: what do we know? What do we need to learn? Where do we go from here? National Kidney Foundation Task Force on Cardiovascular Disease. American Journal of Kidney Diseases : The Official Journal of The National Kidney Foundation 1998; 32: 853-906.
17. Thomsen HS. European Society of Urogenital Radiology (ESUR) guidelines on the safe use of iodinated contrast media. European Journal of Radiology 2006; 60: 307-13.
18. Expert Panel on Detection E, Treatment of High Blood Cholesterol in A: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama 2001; 285: 2486-97.
19. Toprak O, Cirit M. Risk factors for contrast-induced nephropathy. Kidney Blood Press Res 2006; 29: 84-93.
20. Pan HC, Wu XH, Wan QL, Liu, Bh, Wu XS. Analysis of the risk factors for contrast-induced nephropathy in over-aged patients receiving coronary intervention. Experimental Biology and Medicine 2018; 243: 970-5.
21. Parfrey P. The clinical epidemiology of contrast-induced nephropathy. Cardiovascular and Interventional Radiology 2005; 28: 3-11.
22. Gunay M, Mertoglu C. Increase of endocan, a new marker for inflammation and endothelial dysfunction, in acute kidney injury. Northern Clinics of Istanbul 2019; 6: 124-8.
23. Li S, Wang L, Wang C, Wang Q, Yang H, Liang P, Jin F. Detection on dynamic changes of endothelial cell specific molecule-1 in acute rejection after renal transplantation. Urology 2012; 80: 731-8.
24. Ando G, de Gregorio C, Morabito G, Trio O, Saporito F, Oreto G. Renal function-adjusted contrast volume redefines the baseline estimation of contrast-induced acute kidney injury risk in patients undergoing primary percutaneous coronary intervention. Circulation Cardiovascular Interventions 2014; 7: 465-72.
25. Abu El-Asrar AM, Nawaz MI, De Hertogh G, Al-Kharashi AS, Van den Eynde K, Mohammad G, Geboes K. The angiogenic biomarker endocan is upregulated in proliferative diabetic retinopathy and correlates with vascular endothelial growth factor. Current Eye Research 2015; 40: 321-31.