Increased expression of monocytic angiotensin-converting enzyme in dialysis patients with cardiovascular disease

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Abstract

Background. Patients with chronic renal disease suffer from accelerated atherogenesis, which is promoted by inflammation and oxidative stress. Tissue angiotensin converting enzyme (ACE) exerts proinflammatory and prooxidative effects by producing angiotensin II. Monocytes are strongly involved in the pathogenesis of atherosclerosis. They express ACE, which might contribute to their atherogenic potency. We hypothesize that dialysis patients have increased monocytic ACE expression, and that ACE expression on circulating monocytes is associated with prevalent cardiovascular disease.

Methods. In 74 dialysis patients, ACE expression on total monocytes and monocyte subsets was measured flow-cytometrically in a whole-blood assay. A subpopulation of 22 dialysis patients was compared to an age- and gender-matched control group with intact renal function. Cardiovascular risk factors and the prevalence of cardiovascular disease were assessed. In a subgroup of patients (n = 8), monocytic ACE activity was measured in vitro and correlated with monocytic ACE expression.

Results. Dialysis patients had an increased expression of monocytic ACE compared to controls. Monocytic ACE expression was higher in dialysis patients with prevalent cardiovascular disease than in those without cardiovascular disease. This association remained significant after correction for classical cardiovascular risk factors. Among monocyte subsets, CD14++CD16+ monocytes had the highest ACE expression. Monocytic ACE activity correlated with ACE surface expression.

Conclusions. The finding of increased ACE expression on monocytes of dialysis patients with cardiovascular disease links monocytes to the activated renin–angiotensin system. ACE expression was found highest among CD14++16+ monocytes, which is in accordance with a prominent role of these proinflammatory cells in atherogenesis.

Keywords: angiotensin converting enzyme; cardiovascular disease; dialysis; monocytes; monocytic ACE

Introduction

Patients with chronic renal disease have an extraordinarily high risk for cardiovascular disease (CVD) [1], which at least in part results from accelerated atherogenesis [2] and which is the cause of premature death in more than 50% of dialysis patients [3]. The accelerated atherogenesis is not fully explained by a high prevalence of traditional cardiovascular risk factors [4,5]. Instead, the so-called non-traditional risk factors essentially contribute to the development of CVD in patients with chronic renal disease [6,7].

Among such non-traditional risk factors, inflammation and oxidative stress are of major importance, and their impact on premature atherogenesis in chronic renal patients has recently been reviewed [8].

Inflammation and oxidative stress both may in part be mediated by an activated renin–angiotensin system (RAS). Activation of the RAS is under control of the angiotensin converting enzyme (ACE), which cleaves the C-terminal dipeptide from angiotensin I to produce angiotensin II. Angiotensin II itself augments oxidative stress and increases endothelial cytokine formation and leukocyte adhesion to the vessel wall [9,10].

Even though ACE may be detected in plasma, the major part of ACE exists on the endothelial lining of the body’s vasculature, in non-endothelial parenchymal cells, and on circulating leukocytes, mainly on
Monocytic ACE expression in dialysis patients

Monocytes, as reviewed recently [9]. Monocytes have been identified as major constituents of the atherosclerotic plaque, and chronic renal failure induces a state of preactivation of monocytes [11,12]. Recently, it has been reported that ACE expression on monocyte-derived cells may contribute to local RAS activation at sites of vessel wall lesions and to subsequent progression of the atherosclerotic plaque [10].

We hypothesize that patients with end-stage renal disease have increased expression of monocytic ACE compared to individuals with intact renal function. In addition, patients with end-stage renal disease and prevalent CVD should have higher ACE expression than patients without prevalent CVD.

Subjects and methods

Seventy-four unselected patients with end-stage renal disease undergoing haemodialysis (HD) \(n = 64\) or peritoneal dialysis \(n = 10\) treatment were included in a cross-sectional study. The patients suffered from chronic renal disease due to diabetic nephropathy \(n = 23\), glomerulonephritis \(n = 16\), autosomal dominant polycystic kidney disease \(n = 6\) or other diagnoses \(n = 21\). The underlying renal disease was unknown in eight patients. Patients were on dialysis treatment for 4.7 ± 6.1 years. All HD patients were treated with synthetic membranes (polyamide or polysulfone). Patients receiving ongoing immunosuppressive medication, or with any acute medical complications necessitating hospitalization were excluded.

Among our cohort of dialysis patients, a subpopulation of 22 dialysis patients was chosen for whom age- and gender-matched controls with normal kidney function and no history of kidney disease were available from the department of ophthalmology, University of Saarland. This subgroup of 22 dialysis patients did not differ from the initial cohort of 74 patients with regard to age, gender, diabetic and lipid profile as well as blood pressure, ACE inhibitor (ACE-I) or angiotensin receptor blocker (ARB) comedication. Informed consent was obtained from all study subjects and the study was registered prior to a dialysis session in HD patients or during an outpatient clinic appointment in peritoneal dialysis patients. Mean arterial pressure was defined as

\[
RR_{\text{dia}} = (RR_{\text{sys}} - RR_{\text{dia}})/3.
\]

All patients completed a questionnaire that provided information about smoking habits, history of diabetes mellitus and family history of premature CVD (myocardial infarction or stroke of one first degree relative before the age of 65 years). Residual kidney function was defined as urine output ≥ 500 ml/24 h.

Laboratory data

Blood was drawn before the start of a haemodialysis session in HD patients, at least 48 h after the last haemodialysis session had been performed. In peritoneal dialysis patients, blood was drawn during an outpatient clinic appointment. In individuals with intact renal function, blood was drawn in the morning under standardized conditions.

Flow cytometry

Expression of monocytic ACE was flow-cytometrically analysed in a whole blood assay using 70 μl of heparin anti-coagulated blood. Soluble plasma ACE was removed from the samples by extensive washing of cells in phosphate buffered saline containing 5% foetal calf serum (Seromed, Berlin, Germany), 2.5% bovine serum albumin (Fraction IV, Serva, Heidelberg, Germany) and 0.07% sodium azide (Serva, Germany). Subsequently, cells were stained by monoclonal antibodies (as listed below) and analysed by flow cytometry (FACSCalibur, BD Biosciences, Heidelberg, Germany) using the Cell Quest software. Monocytes were defined by expression of CD86 and by cell size and granularity in the forward/side scatter. According to the surface expression pattern of the LPS receptor CD14 and the Fcγ receptor CD16, monocytes were divided into different subpopulations (CD14++CD16−, CD14++CD16+, CD14+CD16+, CD14−CD16+, CD14(+)CD16−, Figure 1). Apart from the classical population of CD14 positive monocytes, CD14−CD16+CD86+ cells can be

Clinical data

Comorbidity was assessed by review of the medical charts as well as by standardized interviews with the patients. Coronary artery disease was diagnosed in patients and controls who had either had a myocardial infarction or had undergone coronary artery bypass surgery or coronary artery intervention. In patients who had had a stroke or had undergone carotid endarterectomy or carotid stenting, cerebrovascular disease was diagnosed. Finally, in patients who had undergone peripheral bypass surgery, non-traumatic lower extremity amputation, lower limb artery angioplasty or stenting, peripheral artery disease was diagnosed. Patients were defined as having CVD if they had coronary artery disease, cerebrovascular disease or peripheral artery disease.

Systolic \(\left( RR_{\text{sys}} \right)\) and diastolic \(\left( RR_{\text{dia}} \right)\) blood pressure was registered prior to a dialysis session in HD patients or during an outpatient clinic appointment in peritoneal

![Fig. 1. Monocyte subsets. Monocytes were defined as CD86 positive cells, and differentiated according to their surface expression pattern of the LPS receptor CD14 and the Fcγ receptor CD16](https://academic.oup.com/ndt/article-abstract/21/6/1596/1890318/fig1)
defined as monocytes as they express characteristic monocytic antigens (CD86), and do not express markers of T-cells (CD3−), of B-cells (CD19−) and of NK-cells (CD56−). In a forward/side scatter (FSC/SSC) dotplot, CD14−CD16+ are characterized as small monocytes (low FSC signal) which have few granules (low SSC signal), and they are accordingly found in the lower left region of the monocyte population. Flow-cytometrical data are presented as median fluorescence intensity (MFI).

The following antibodies were used: CD86 (HA5.2B7) (Beckman-Coulter, Krefeld, Germany), CD143 (9B9 Serotec, Düsseldorf, Germany), CD16 (3G8, Caltag, Hamburg, Germany), CD3 (SK7), CD19 (SJ25C2), CD11 (ICRF44), CD56 (MOPC21-NS1), CD14 (Mφ9) (all BD Biosciences, Heidelberg, Germany). Cells stained with isotype control mouse anti-rat IgG1 (Serotec) were used as negative controls.

**Fluorimetric determination of monocytic ACE activity**

For measurement of monocyctic ACE activity, peripheral blood mononuclear cells (PBMCs) were isolated from heparinized blood of eight HD patients by Ficoll centrifugation. These eight patients were arbitrarily chosen from our cohort of dialysis patients according to their monocytic ACE expression including four patients with high and four patients with low ACE expression, respectively. To minimize putative influencing variables for ACE expression, the patients were matched for age, gender and the prevalence of diabetes. Using 24 well plates, 5×10⁶ PBMCs were seeded in 24 well plates (Greiner, Frickenhausen, Germany) and monocytes were obtained by plastic adherence (1 h of incubation at 37°C, subsequent removal of the supernatants). Adherent cells (purity >80%) were tested for ACE activity using a fluorimetric assay as described before [13]. In brief, monocytes were incubated with 200 μl of 5 mM Z-Phe-His-Leu substrate solution (Bachem, Heidelberg, Germany) for 2 h at 37°C. ACE activity was measured on a Victor™ fluorimeter (Wallac-ADL GmbH, Freiburg, Germany). Fluorimetric measurement of ACE activity assay was validated by measurement of ACE serum standards, and by inhibition experiments, in which co-incubation of 10 μl serum with the ACE-I Captopril (50 μM; Sigma, Deisenhofen, Germany) resulted in a significant decrease of ACE activity.

**Effect of ACE inhibitor-/angiotensin receptor blocker medication on monocytic ACE expression**

PBMCs from six healthy controls were incubated for 20 h with either vehicle (dimethyl sulfoxide, DMSO), captopril (10 μM) or telmisartan (10 μM, Boehringer Ingelheim, Ingelheim, Germany). ACE expression on total monocytes was analysed using flow-cytometry as described earlier.

**Clinical laboratory parameters**

Albumin, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, calcium, phosphate and HbA1c were determined by routine methods. Serum ACE activity was measured by a convenient spectrophotometric (UV kinetic) method utilizing the synthetic substrate N-FAPGG (normal range: 8–52 U/l). In order to account for intra-individual variations in CRP levels, median CRP values were calculated from six consecutive CRP measurements which were routinely performed once a month [14]. Low-density lipoprotein (LDL) cholesterol was calculated according to the Friedewald formula. The calcium–phosphorus product (Ca–P, mg²/dl²) was calculated as serum calcium (mmol/l) × serum phosphorus (mg/dl) × 2.5. Diabetes mellitus was defined as either self-reported diabetes, a diagnosis of diabetes mellitus in the medical charts, the intake of oral antidiabetic drugs or insulin, a non-fasting plasma glucose of >200 mg/dl, a fasting plasma glucose of >126 mg/dl or a HbA1c of >6.2%. ACE genotyping was performed as described earlier [15].

**Statistics**

Results are expressed as mean±SD unless otherwise indicated. All continuous variables were analysed for normality of distribution using the Kolomogorov–Smirnov test. Normal distribution of median CRP was generated by log transformation. Categorical variables were compared by chi-square test, and, if normally distributed, continuous data were compared by Student’s t-test (paired test for comparison of dialysis patients vs controls, and for comparison of dialysis patients with high vs low ACE expression; unpaired test for dialysis patients with prevalent CVD vs patients without CVD).

For analysis of ACE surface expression among leukocytes and monocyte subsets, as well as for comparison of monocytic ACE expression and ACE serum levels between patients with the DD, ID and II ACE genotype, one-way ANOVA with post-hoc Bonferroni test was performed.

Finally, a binary logistic regression model (backward stepwise logistic regression model) was applied, which included the prevalence of CVD as dependent variable, and median fluorescence intensity of monocytic ACE expression, as well as classical cardiovascular risk factors, as independent variables (age, total cholesterol, gender, HbA1c, mean arterial pressure as continuous variables and smoking habits as categorical variable). The good fit of the model was assessed by the Hosmer–Lemeshow test. All calculations were carried out using the SPSS 11.5 (SPSS Inc., Chicago, USA) statistical software.

**Results**

**Monocytes express more membrane-bound ACE than other leukocyte subsets**

Higher ACE expression (isotype-corrected MFI) was found on monocytes (MFI:47.3±10.6) compared to other leukocyte subpopulations (granulocytes [CD11b+/CD16+]: 17.2±5.1, B lymphocytes [CD19+]: 1.8±1.5, T lymphocytes: 0.8±1.2 [CD3+], monocytes vs granulocytes, P<0.01; monocytes vs T, B cells P<0.001) in healthy controls (n=5).

Monocytes comprise a heterogeneous cell population which is characterized by its expression pattern of the receptors CD14 and CD16 (see ‘Subjects and
Monocytic ACE expression significantly differed among these subpopulations in controls as well as in dialysis patients. Among all monocyte subsets, CD14++CD16+ monocytes had the highest ACE surface expression (CD14++CD16+ vs all other subsets: controls: P < 0.01; dialysis patients: P < 0.001, compare Figure 2).

ACE expression on total monocytes did not significantly differ between HD patients (MFI 35.7±22.3) and peritoneal dialysis patients (MFI 34.2±21.9). The differences in ACE expression between monocyte populations could be confirmed in both HD and peritoneal dialysis patients.

Monocytic ACE is elevated in dialysis patients compared to subjects with intact renal function

To compare the expression of monocytic ACE between patients with end-stage renal disease and non-uraemic controls, 22 dialysis patients were paired to age- and gender-matched subjects. The prevalence of diabetes as well as smoking habits were not different between the two groups. The intake of ARB and the prevalence of CVD were more frequent in dialysis patients in comparison to subjects with intact renal function (Table 1).

Surface expression of monocytic ACE was significantly elevated in dialysis patients. This held true throughout the different monocyte subpopulations with the exception of CD14−CD16+ cells (Figure 2).

Association between monocytic ACE and classical cardiovascular risk factors

While there was no association of monocytic ACE expression with smoking, diabetes, residual renal function, LDL, HDL, total cholesterol or blood pressure, we found a significant inverse relationship with triglyceride levels (Pearson r = −0.25, P = 0.032) and a weak inverse correlation with albumin levels (Pearson r = −0.21, P = 0.077). We did not find any difference in monocytic ACE expression between patients taking ACE-I/ARB or not (patients receiving ACE-I/ARB: MFI 37.7±21.1 vs patients not receiving ACE-I/ARB: 35.2±22.4, P = 0.75). Therefore, ACE-I and ARB medication do not seem to have a major impact on monocytic ACE expression. These findings are also supported by in vitro data showing that neither the ACE inhibitor captopril nor the angiotensin receptor blocker telmisartan had any significant influence on monocytic ACE expression (vehicle, MFI: 26.8±14.2; captopril MFI 26.5±12.7; or telmisartan, MFI 25.6±11.5).

Monocytic ACE expression significantly differs between dialysis patients with and without CVD

Prevalent CVD was diagnosed in 29/74 patients, who suffered from coronary artery disease (n = 18), cerebrovascular disease (n = 8), and/or peripheral artery disease (n = 10). The baseline characteristics of dialysis patients with and without CVD are summarized in Table 2.
Patients with CVD had a higher prevalence of classical atherosclerotic risk factors and were significantly older than patients without CVD.

Monocytic ACE expression differed significantly between dialysis patients with and without CVD ($P = 0.03$). This difference was found among all monocyte subsets (Figure 3).

To identify the variables independently associated with CVD among our dialysis patients, a logistic regression model was applied which integrated monocytic ACE expression and classical atherosclerotic risk factors (age, gender, smoking habits, mean arterial pressure, HbA1c, total cholesterol). In the backward stepwise regression analysis, active smoking, HbA1c, total cholesterol and monocytic ACE expression were independent predictors of prevalent CVD (Table 3).

Monocytic ACE activity was evaluated in eight HD patients who were not receiving ACE-I or ARB medication, four of whom had high monocytic ACE expression, and four low ACE expression.

There was no correlation between serum ACE activity and monocytic ACE expression. Monocytic ACE activity was significantly increased in the high-ACE expression group compared to the low-ACE expression group (Table 4). The results remained significant after adjustment for absolute monocyte counts.

As cellular and serum ACE levels are partly under genetic control, we investigated whether monocytic ACE expression is determined by the I/D polymorphism of the ACE gene. Of our dialysis patients 41.9% were genotyped as having DD, 44.6% as ID, and 13.5% as II ACE genotype. Serum ACE activity was significantly higher in DD patients

| Table 2. Characteristics of dialysis patients with or without prevalent CVD |
|-----------------|-----------------|--------|
|                  | Non-CVD (n = 45) | CVD (n = 29) | P-value |
| Age (years)      | 61.1 ± 16.2     | 71.7 ± 8.5  | 0.002  |
| Gender% (male/female) | 44/56         | 62/38    | 0.139  |
| Active smoker (%) | 27             | 3        | 0.010  |
| Familiar history of CVD (%) | 16          | 21       | 0.571  |
| Residual kidney function (%) | 44         | 45       | 0.974  |
| Intake of ACE Inhibitor (%) | 13         | 10       | 0.147  |
| Mean arterial pressure (mmHg) | 95.7 ± 15.1 | 96.9 ± 15.0 | 0.743 |
| Diabetes mellitus (%) | 44           | 66       | 0.095  |
| Time on dialysis (years) | 4.7 ± 6.1     | 4.9 ± 6.2 | 0.546  |
| HbA1c (%)         | 5.8 ± 1.0      | 6.5 ± 1.3 | 0.011  |
| Total cholesterol (mg/dl) | 163.4 ± 43.9 | 148.0 ± 34.7 | 0.115 |
| Triglyceride (mg/dl) | 162.8 ± 89.9 | 190.1 ± 99.9 | 0.226 |
| HDL cholesterol (mg/dl) | 48.8 ± 15.8   | 41.7 ± 9.2 | 0.032  |
| LDL cholesterol (mg/dl) | 89.6 ± 31.9   | 77.1 ± 28.6 | 0.093  |
| Serum ACE (U/l)   | 27.7 ± 21.6    | 30.8 ± 20.0 | 0.539  |
| Ca–P product (mg2/dl2) | 53.5 ± 15.3  | 55.4 ± 16.1 | 0.614  |
| Albumin (g/l)     | 37.8 ± 4.2     | 36.6 ± 3.1 | 0.180  |
| Median CRP (mg/l) | 11.2 ± 16.0    | 8.9 ± 7.8  | 0.476  |

Monocyte ACE surface expression correlates with cell-associated with ACE activity but not with serum ACE activity

The association between monocytic ACE expression with different cardiovascular risk factors was investigated by using binary logistic regression analysis (backward stepwise logistic regression model). Variables included in step 1 were: age, gender, HbA1c, mean arterial pressure, total cholesterol, monocytic ACE expression and smoking habit. Mean arterial pressure was eliminated at step 2, gender at step 3, and age at step 4 of the analysis.

<table>
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<th>Table 3. Logistic regression model</th>
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<tr>
<td>Regression-coefficient B</td>
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<tr>
<td>HbA1c</td>
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<tr>
<td>Smoker</td>
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<tr>
<td>Monocytic ACE</td>
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<td>Cholesterol</td>
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<td>Constant</td>
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Fig. 3. Higher monocytic ACE expression in dialysis patients with cardiovascular disease (CVD, white box plots) in comparison to patients without CVD (gray box plots). Monocytic ACE expression of dialysis patients with CVD is significantly elevated in all monocytes subsets (*$P < 0.05$ for all subsets with exception of CD14(+)CD16−; **$P < 0.01$), Student’s t-test for paired samples. Box plots at the left-hand side indicate overall monocytic ACE expression. Data (median fluorescent intensity) are presented as box plots extending from the 25th to the 75th percentile with a horizontal line at the median.
Monocytic ACE expression in dialysis patients

Table 4. Determination of monocytic ACE activity

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Monocytic ACE (MFI)</th>
<th>ACE activity (arbitrary units)</th>
<th>Leukocytes (µl)</th>
<th>Monocytes (µl)</th>
<th>P-value</th>
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<td>(n = 4)</td>
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<tr>
<td>69.5 ± 13.0</td>
<td>65.8 ± 21.3</td>
<td>10697 ± 1849</td>
<td>7233 ± 1467</td>
<td>635.1 ± 177.2</td>
<td>0.821</td>
</tr>
<tr>
<td>29.7 ± 7.0</td>
<td>3.3 ± 1.3</td>
<td>4877 ± 1542</td>
<td>7730 ± 3339</td>
<td>927.7 ± 519.2</td>
<td>0.005</td>
</tr>
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(36.5 ± 21.0 U/l) compared to ID (24.4 ± 18.9 U/l, P < 0.01 vs DD patients) and II patients (21.7 ± 21.6 U/l, P < 0.05, respectively). Monocytic ACE expression, however, was not associated with the I/D polymorphism (DD patients: MFI 31.5 ± 19.9; ID patients: MFI 40.0 ± 24.4; II patients: MFI 30.9 ± 21.3, NS [not significant]).

Discussion

Activation of the RAS has major adverse effects on the cardiovascular system. Initially, scientific interest mainly focused on the haemodynamic effects of ACE, which converts angiotensin I to the potent vasoconstrictor Ang II. In the recent years, the importance of tissue ACE and its local production of Ang II have gained major attention [16]. Monocyte-derived cells express membrane-bound ACE (CD143), which may promote the progression of atherosclerotic plaques [10].

In accordance, current evidence suggests that a significant part of the vasculoprotective effects of ACE inhibitors may be due to inhibition of tissue ACE rather than due to haemodynamic effects.

In vascular lesions, endothelial ACE may be upregulated in response to endothelial injury. Local Ang II induces the generation of superoxide anions and hydrogen peroxide, thus augmenting oxidative stress [17]. In addition, Ang II contributes to endothelial dysfunction. Ang II reduces the generation of nitric oxide (NO) and other endothelium-derived vasodilators, and induces the production of the vasoconstrictor endothelin-1 and of plasminogen activator inhibitor [18]. Both oxidative stress and endothelial dysfunction, result in an increased propensity for inflammation because of increased cytokine formation and leukocyte recruitment [19]. These effects contribute to myocardial and vascular hypertrophy and remodelling as well as to plaque growth and rupture.

The benefits of therapeutic intervention of the RAS have clearly been demonstrated in two large clinical trials among high-risk cardiovascular or diabetic patients without apparent heart failure [20,21]. Interestingly, both trials used high tissue-affinity ACE inhibitors, namely ramipril and perindopril.

Monocytes and monocyte-derived macrophages play important roles in atherosclerosis [22]. It is noteworthy that ACE expression is upregulated (up to 150-fold) during differentiation of monocytes to macrophages and dendritic cells, and there is some speculation of the physiological importance of ACE in the functioning of these cells [23]. We found that dialysis patients have a significantly higher ACE expression on monocytes compared to age- and gender-matched healthy controls. As shown by in vitro analysis, monocytic ACE expression is directly linked to cell-associated ACE activity. Upregulation of monocytic ACE expression may be the consequence of a generalized activation of proinflammatory and proliferative cascades caused by uraemia, and its effect might be the enhancement of oxidative stress and endothelial dysfunction at the site of vascular lesion.

We found a weak correlation of ACE expression on monocytes with low triglyceride levels and hypoalbuminaemia. This finding fits well with the fact that hypoalbuminaemia reflects chronic inflammation and low triglycerides are associated with the malnutrition–inflammation–atherosclerosis-syndrome (MIA-syndrome) [24]. Therefore, elevated expression of monocytic ACE seems to be a part of the chronic inflammatory activation of monocytes that is associated with the MIA-syndrome.

It is noteworthy that we found neither a difference in monocytic ACE expression when stratifying patients according to ACE I/D genotype polymorphisms, nor a correlation between monocytic ACE expression and serum ACE levels. In contrast, Costerousse and coworkers [25] earlier reported higher ACE levels in lymphocytes from subjects who are homozygous for the deletion genotype of the ACE polymorphism, and a significant correlation between lymphocytic and plasma ACE levels. These observations point to different ACE activation pathways among leukocyte subsets, which merit further study [25].

Monocytes are characterized by a significant heterogeneity [26]. Dialysis patients have an elevated frequency of proinflammatory CD14++16+ monocytes [27], which have recently been associated with coronary atherosclerosis [28,29]. To the best of our knowledge, we are the first to show that CD14++16+ monocytes predominantly express an Ang II generating system which most probably acts as an enhancer of the proinflammatory cycle in renal failure patients.

Conclusions

Monocytic ACE expression is increased in dialysis patients compared to individuals with intact renal function. In addition, monocytic ACE expression is significantly associated with prevalent CVD even after adjusting for classical cardiovascular risk factors. Monocytic ACE expression differs among monocyte subsets. A higher expression of ACE on CD14++16+
monocytes is in line with a prominent role of these cells in atherosclerosis. A follow-up analysis of our study cohort will have to show how far monocyteic ACE expression predicts further cardiovascular events.

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Conflict of interest statement. None declared.

References