ORIGINAL ARTICLE

Impact of hypertension, smoking and liver affection on endothelial dysfunction and subsequent vascular damage in Saudi middle aged males

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Summary

Endothelial dysfunction is one of the mechanisms linked to an increased risk of cardiovascular disease. To assess the impact of hypertension, smoking and past history of schistosomiasis on endothelial dysfunction and vascular damage in Saudi middle aged males who don't exercise regularly, the levels of soluble adhesion molecules E-selectin, ICAM-1 and VCAM-1, biomarkers of the activation of inflammatory cascades during the development of vascular injury, were determined. Plasma levels of sVCAM-1, sICAM-1 and sE-selectin were found to be elevated as a result of hypertension and/or cigarette smoking compared to normal counterparts. These results demonstrated that hypertension and cigarette smoking had the strongest direct associations with these biomarkers which are a reflection of their effect on endothelial dysfunction and subsequent vascular damage, while a past history of schistosomiasis had very little association with these biomarkers. These results also suggest that sVCAM-1 may be useful in assessing the impact of liver affliction, (as a result of schistosomiasis) on endothelial dysfunction.

Keywords: schistosomiasis – endothelial dysfunction – VCAM-1 – ICAM-1,E-selectin

INTRODUCTION

Vascular diseases are conditions which affect the blood vessels. Endothelial cell dysfunction is considered to be an early event which subsequently leads to vascular wall disorders. Under normal physiological conditions the endothelium constitu-

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tes a barrier to the efflux of plasma proteins into the extracellular tissues, serves to maintain an anti-coagulant environment and forms a platform upon which many important biological processes take place. Alteration of the balance of these functions by inflammatory mediators and cytokines leads to the formation of a pro-coagulant environment, fluid leakage and increased adhesivity of the endothelium for neutrophils and lymphocytes. Both neutrophils and lymphocytes have the capacity to damage the endothelium directly, by the release of oxygen radicals, enzymes and other cytotoxic molecules, or indirectly by the release of cytokines which may alter the biological properties of endothelial cells, in a process called endothelial activation (Savage and Cooke 1993).

Endothelial cell adhesion molecules (ECAMs) play a key role in leukocyte-endothelial interaction and are classified into three groups according to their structure: selectins, integrins and members of the immunoglobulin gene superfamily (Albelda et al. 1994). E-selectin is a member of the selectin family that is cytokine inducible and largely restricted to endothelial cells (Montgomery et al. 1991). It mediates the adhesion of various leukocytes, including neutrophils, monocytes, eosinophils, natural killer cells, and a subset of T cells, to activated endothelium (Bevilacqua and Nelson 1993). Intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) are two members of the Ig-like supergene family of adhesion molecules that are normally expressed by endothelial cells. Cytokine activation up-regulates dramatically their expression on the cell surface where they support the interaction of leukocytes and endothelial cells (Carlos and Harlan 1994). In addition to being expressed on the cell surface, soluble forms of adhesion molecules have been detected in circulating blood and have been shown to retain their functional ability (Gearing et al. 1992).

Leukocyte-endothelial adhesion is an early step in many inflammatory disorders including atherosclerosis (Steinberg 1987). Adhesion of leukocytes to endothelial cells is mediated by endothelial cell adhesion molecules, (ECAMs) such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin, (Dustin et al. 1986, Bevilacqua et al. 1989, Budak et al. 1998). The transcription and cell surface mobilization of ECAMs are induced by pro-inflammatory stimuli including cytokines, endotoxin, oxidized lipoproteins, and reactive oxygen metabolites (Cybulsky and Gimbrone 1991, Marui et al. 1993, Weber et al. 1994, Khan et al. 1995, Read et al. 1995, Roebuck et al. 1995). Soluble forms of these molecules may be released to the circulation, where their increased serum levels may indicate endothelial dysfunction (Austgulen et al. 1997). Not only is endothelial dysfunction thought to be the initial step in atherosclerosis (Ross 1999), it may also play a role in the propagation of the disease (Chong et al. 2003). Hence, assessment of endothelial function is likely to be a key to modifying risk factors of cardiovascular disorders and their sequel.

Risk factors of vascular diseases include hypertension, hyperlipidaemia, lack of exercise, obesity, and smoking as well as diabetes. Other factors that cannot be controlled include family history of the disease, age over 55, race and gender. Hypertension is probably the single most important predisposing factor to heart disease. Overweight, excessive sodium intake and lack of exercise contribute to an increase in blood pressure. Although physical activity raises the blood pressure at the time of activity due to increased oxygen and metabolic demands, there is strong evidence to suggest that the sense of well-being which exercise promotes leads to a longer term lowering of blood pressure. In contrast, physical inactivity is likely to lead to obesity and the development of hypertension in some individuals.

As for smoking, it is one of the most important avoidable causes of cardiovascular diseases worldwide (Teo et al. 2006), with arterial stiffness as one of the underlying pathophysiological mechanisms (Mahmud and Feely 2003, Li et al. 2006). Patients with myocardial infarction may experience as much as a 50% reduction in risk of re-infarction, sudden cardiac death, and total mortality if they quit smoking (Critchley and Capewell 2003). Recently, it was found that young adults who were exposed to smoke during gestation had a higher atherosclerosis burden as determined by increased carotid artery intima-media thickness (CIMT), putting them at higher risk of MI and stroke (Uiterwaal et al. 2007).

The aim of the present study was to assess the impact of hypertension, smoking and past history of schistosomiasis on vascular damage in Saudi middle aged males who don't exercise regularly. In view of the role of the endothelium in the initiation and propagation of vascular wall injury, the levels of markers of inflammation and endothelial dysfunction, soluble vascular cell adhesion molecule-1 (sVCAM-1), inter-cellular adhesion molecule-1 (sICAM-1) and E-selectin (sE-selectin), were evaluated as predictors of the activation of inflammatory cascades during the development of vascular injury.

MATERIALS AND METHODS

Subjects
The study involved 80 Saudi middle aged male volunteers, (mean age 47.8±2.6 years) in eight non-overlapping categories, ten persons each, of either normotensive subjects, smokers and non-smokers, with or without past history of schistosomiasis or hypertensive subjects, smokers and non-smokers, with or without past history of schistosomiasis. All subjects received no medications for the previous three months, and were subjected to the taking of a full medical history; a general individual medical check was performed to exclude those who were non-fit for the study.

Blood samples and assays of soluble adhesion molecules
Peripheral venous blood samples were collected in sterile tubes containing ethylenediamine-tetraacetic acid (EDTA). Blood samples were centrifuged at 1200 x *g* for 15 min and the supernatant was stored

in 200 μl aliquots at -70 °C. Plasma levels of VCAM-1, ICAM-1 and E-selectin were measured by commercial enzyme-linked immunosorbent assay, (R&D Systems, Heidelberg, Germany) according to the manufacture's instructions. Samples were checked by serial dilution, and measurements were performed at least in duplicate.

Statistical Analysis
Data analyses were performed using a PC with the Statistical Package for the Social Sciences, (SPSS version 13.0). Results were expressed as a mean ± standard deviation (SD). The Student t-test was used at the significance level $2\alpha=0.05$.

RESULTS

The plasma concentrations of soluble adhesion molecules, E-selectin, ICAM and VCAM are shown in Tables 1, 2 and 3, respectively. From table 1, it is clear that the level of sE-selectin was significantly higher, in general, for smokers than for non-smokers regardless of the association of high blood pressure or past history of schistosomiasis. However, the statistical significance was more pronounced in the case of normotensive compared to hypertensive patients. Moreover, the level of sE-selectin was significantly higher for all hypertensive subjects compared to their normotensive counterparts, regardless of whether they had a past history of schistosomiasis or not, with the statistical significance being more pronounced in the case of the non-smoking subject groups compared to the smoking subject ones. The level of sE-selectin was also significantly higher for all smoking hypertensive subjects compared to their non-smoking normotensive counterparts, regardless of whether they had a past history of schistosomiasis or not. In contrast, plasma levels of sE-selectin were not different statistically for all equivalent subject groups that differed only in their prior history of schistosomiasis. Likewise, there was no statistically significant difference between the levels of sE-selectin in case of smoking normotensive and non-smoking hypertensive subjects, regardless of whether they had a past history of schistosomiasis or not.

From table 2, it is clear that the plasma level of sICAM-1 was significantly higher, in general, in smokers than in non-smokers regardless of the association of high blood pressure or past history of schistosomiasis. However, the statistical significance in the case of normotensive subjects was somewhat more pronounced compared to that in the hypertensive subjects. The level of sICAM-1 was significantly higher for all non-smoking hypertensive subjects compared to all their non-smoking normotensive counterparts, regardless of

whether they had a past history of schistosomiasis or not. In contrast, there was no statistically significant difference between the levels of sICAM-1 in the case of smoking hypertensive and smoking normotensive subjects, regardless of whether they had a past history of schistosomiasis or not. On the other hand, the level of sICAM-1 was significantly higher for all smoking hypertensive subjects compared to their non-smoking normotensive counterparts, regardless of whether they had a past history of schistosomiasis or not. In contrast, there was no statistically significant difference between the levels of sICAM-1 in smoking normotensive and non-smoking hypertensive subjects, regardless of whether they had a past history of schistosomiasis or not. Equally, plasma levels of sICAM-1 were not different statistically for all equivalent subject groups that differed only in their prior history of schistosomiasis.

As for sVCAM-1 levels, (Table 3) the mean value was significantly elevated for smokers who were normotensive compared to their non-smoker counterparts regardless of the involvement of a past history of schistosomiasis. In contrast, the mean value for sVCAM-1 was significantly elevated for smokers who were hypertensive compared to their non-smoker counterparts only in association with a past history of schistosomiasis while there was no statistically significant difference between both levels in the absence of a past history of schistosomiasis. The level of sVCAM-1 was significantly higher for all non-smoking hypertensive subjects compared to all their non-smoking normotensive counterparts, with the significance being more pronounced when comparing subjects who did have a past history of schistosomiasis with those who did not. Nevertheless, plasma levels of sVCAM-1 were not different statistically for all equivalent subject groups that differed only in their prior history of schistosomiasis. Furthermore, there was no statistically significant difference between the levels of sVCAM-1 in the case of smoking hypertensive subjects and smoking normotensive ones, regardless of whether or not they had a past history of schistosomiasis. On the other hand, the level of sVCAM-1 was in general significantly higher for all smoking hypertensive subjects compared to their non-smoking normotensive counterparts, regardless of whether or not they had past history of schistosomiasis. However, the difference was highly significant when comparing smoking hypertensive subjects who had a prior history of schistosomiasis with non-smoking normotensive subjects who had no history of schistosomiasis. Finally, there was no statistically significant difference between the levels of sVCAM-1 in smoking normotensive and non-smoking hypertensive subjects, regardless of the involvement of a past history of schistosomiasis.

Table 1. **Plasma soluble E-selectin (µg/ml), in the studied groups, (mean ± SD, n = 10).**

Normotensive		Hypertensive	
Non-Smokers −ve PHS 46.85 ± 13.1	Non-Smokers +ve PHS 55.86 ± 13.9 Smokers −ve PHS 86.89 ± 20.7 * Smokers +ve PHS 96.21 ± 22.1 *	Non-Smokers -ve PHS 85.14 ± 20.1	Non-Smokers +ve PHS 94.37 ± 22.8 Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *
Non-Smokers +ve PHS 55.86 ± 13.9	Smokers −ve PHS 86.89 ± 20.7 * Smokers +ve PHS 96.21 ± 22.1 *	Non-Smokers +ve PHS 94.37 ± 22.8	Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *
Smokers −ve PHS 86.89 ± 20.7	Smokers +ve PHS 96.21 ± 22.1	Smokers -ve PHS 109.01 ± 23.6	Smokers +ve PHS 121.17 ± 24.2
Non-Smokers −ve PHS 46.85 ± 13.1		Non-Smokers −ve PHS 85.14 ± 20.1 * Non-Smokers +ve PHS 94.37 ± 22.8 * Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *	
Non-Smokers +ve PHS 55.86 ± 13.9		Non-Smokers −ve PHS 85.14 ± 20.1 * Non-Smokers +ve PHS 94.37 ± 22.8 * Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *	
Smokers −ve PHS 86.89 ± 20.7		Non-Smokers −ve PHS 85.14 ± 20.1 * Non-Smokers +ve PHS 94.37 ± 22.8 Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *	
Smokers +ve PHS 96.21 ± 22.1		Non-Smokers −ve PHS 85.14 ± 20.1 * Non-Smokers +ve PHS 94.37 ± 22.8 * Smokers −ve PHS 109.01 ± 23.6 * Smokers +ve PHS 121.17 ± 24.2 *	

* = statistically significant, +ve PHS = with past history of schistosomiasis, −ve PHS= without past history of schistosomiasis

Table 2. **Plasma soluble ICAM-1, (µg/ml) in the studied groups, (mean ± SD, n = 10).**

Normotensive		Hypertensive	
Non-Smokers −ve PHS 132.38 ± 46.2	Non-Smokers +ve PHS 144.71 ± 34.1 Smokers −ve PHS 210.84 ± 60.1* Smokers +ve PHS 231.76 ± 62.3*	Non-Smokers -ve PHS 175.98 ± 52.6	Non-Smokers +ve PHS 188.55 ± 59.7 Smokers −ve PHS 231.37 ± 65.8* Smokers +ve PHS 246.69 ± 69.7*
Non-Smokers +ve PHS 144.71 ± 34.1	Smokers −ve PHS 210.84 ± 60.1* Smokers +ve PHS 231.76 ± 62.3*	Non-Smokers +ve PHS 188.55 ± 59.7	Smokers −ve PHS 231.37 ± 65.8* Smokers +ve PHS 246.69 ± 69.7*
Smokers −ve PHS 210.84 ± 60.1	Smokers +ve PHS 231.76 ± 62.3	Smokers −ve PHS 231.37 ± 65.8	Smokers +ve PHS 246.69 ± 69.7
Non-Smokers −ve PHS 132.38 ± 46.2		Non-Smokers −ve PHS 175.98 ± 52.6* Non-Smokers +ve PHS 188.55 ± 59.7* Smokers −ve PHS 231.37 ± 65.8* Smokers +ve PHS 246.69 ± 69.7*	
Non-Smokers +ve PHS 144.71 ± 34.1		Non-Smokers −ve PHS 175.98 ± 52.6* Non-Smokers +ve PHS 188.55 ± 59.7* Smokers −ve PHS 231.37 ± 65.8* Smokers +ve PHS 246.69 ± 69.7*	
Smokers −ve PHS 210.84 ± 60.1		Non-Smokers −ve PHS 175.98 ± 52.6* Non-Smokers +ve PHS 188.55 ± 59.7 Smokers −ve PHS 231.37 ± 65.8 Smokers +ve PHS 246.69 ± 69.7*	
Smokers +ve PHS 231.76 ± 62.3		Non-Smokers −ve PHS 175.98 ± 52.6* Non-Smokers +ve PHS 188.55 ± 59.7* Smokers −ve PHS 231.37 ± 65.8* Smokers +ve PHS 246.69 ± 69.7	

Symbols as in Table 1

Table 3. **Plasma soluble VCAM-1 (μg/ml), in the studied groups, (mean ± SD, n = 10).**

Normotensive		Hypertensive	
Non-Smokers −ve PHS 351.57 ± 68.7	Non Smokers +ve PHS 379.04 ± 70.1 Smokers −ve PHS 469.2 ± 81.0* Smokers +ve PHS 491.05 ± 98.6*	Non-Smokers -ve PHS 425.34 ± 77.4	Non-Smokers +ve PHS 456.73 ± 79.1 Smokers −ve PHS 483.41 ± 93.7 Smokers +ve PHS 543.83 ± 109.2*
Non-Smokers +ve PHS 379.04 ± 70.1	Smokers −ve PHS 469.2 ± 81.0* Smokers +ve PHS 491.05 ± 98.6*	Non-Smokers +ve PHS 456.73 ± 79.1	Smokers −ve PHS 483.41 ± 93.7* Smokers +ve PHS 543.83 ± 109.2*
Smokers −ve PHS 469.2 ± 81.0	Smokers +ve PHS 491.05 ± 98.6	Smokers −ve PHS 483.41 ± 93.7	Smokers +ve PHS 543.83 ± 109.2
Non-Smokers −ve PHS 351.57 ± 68.7		Non-Smokers −ve PHS 425.34 ± 77.4* Non-Smokers +ve PHS 456.73 ± 79.1* Smokers −ve PHS 483.41 ± 93.7* Smokers +ve PHS 543.83 ± 109.2*	
Non-Smokers +ve PHS 379.04 ± 70.1		Non-Smokers −ve PHS 425.34 ± 77.4* Non-Smokers +ve PHS 456.73 ± 79.1* Smokers −ve PHS 483.41 ± 93.7* Smokers +ve PHS 543.83 ± 109.2*	
Smokers −ve PHS 469.2 ± 81.0		Non-Smokers −ve PHS 425.34 ± 77.4* Non-Smokers +ve PHS 456.73 ± 79.1 Smokers −ve PHS 483.41 ± 93.7 Smokers +ve PHS 543.83 ± 109.2*	
Smokers +ve PHS 491.05 ± 98.6		Non-Smokers −ve PHS 425.34 ± 77.4* Non-Smokers +ve PHS 456.73 ± 79.1* Smokers −ve PHS 483.41 ± 93.7* Smokers +ve PHS 543.83 ± 109.2	

Symbols as in Table 1

DISCUSSION

Endothelial dysfunction and inflammation are believed to be implicated in the initiation and progression of vascular disorders (Ross 1999, Tesfamariam and DeFelice 2007). Indeed, in the presence of cardiovascular risk factors endothelial dysfunction could be detected before there is any

angiographic evidence of disease (Nishimura et al. 1995, Schachinger and Zeiher, 2001). Endothelial dysfunction indicates a generalized alteration in endothelial cell function and is characterized by an abnormal vasodilatory response, increased production of vasoconstrictor substances, impaired endothelial control of fibrinolysis and inflammation, and altered expression of adhesion molecules.

In this study, the plasma concentration of sE-selectin was significantly higher among hypertensive subjects in all tested groups compared to their normotensive counterparts Nevertheless, the statistical significance of the elevation in sE-selectin in association with hypertension was much higher when comparing non-smoking subjects than when comparing smoking ones. This result can be explained by a background elevation in sE-selectin concentration as a result of cigarette smoking within the latter groups.

Moreover, a similarly significant increase in sE-selectin was observed for all smoking subjects compared to their non-smoking counterparts. However, the statistical significance of the increase in sE-selectin in association with cigarette smoking was much higher when comparing normotensive than when comparing hypertensive subjects which also reflects a background elevation of sE-selectin as a result of hypertension within the later groups. Interestingly, the elevation in sE-selectin concentration as a result of either hypertension or cigarette smoking was somewhat comparable which suggests that they both probably use similar mechanisms to mediate such elevation. Furthermore, the association of both hypertension and cigarette smoking significantly boosted the levels of sE-selectin above that observed with either one alone.

In contrast, there were no statistical differences in the levels of sE-selectin among all subjects as a result of a past history of schistosomiasis alone. However, a past history of schistosomiasis boosted the statistical significance of the increase in sE-selectin concentration, for hypertensive subjects, as a result of cigarette smoking. These results are in agreement with prior reports demonstrating that sE-selectin is raised in patients with hypertension and septic shock (Blann et al. 1994, Blann and Taberner 1995, Blann and Waite 1996). It is however unclear how, or under which conditions, it is actively or passively shed from the cell membrane, or cleaved by a pathological process (Blann and Taberner, 1995).

As for the immunoglobulin superfamily adhesion molecules, circulating levels of sICAM-1 were significantly elevated among all smokers, compared to their non-smoker counterparts, while that of sVCAM-1 were significantly elevated for all smokers except those who were hypertensive and had no history of schistosomiasis. In both cases, the

statistical significance of the increase, in association with cigarette smoking, was at least an order of magnitude higher when comparing normotensive subjects than when comparing hypertensive ones, which reflects a background elevation of sICAM-1 and sVCAM-1 as a result of hypertension within the hypertensive groups. As for the impact of hypertension, there was a significant increase in the levels of both sICAM-1 and sVCAM-1 in association with hypertension, compared to their normotensive counterparts, only among non-smokers but not smokers (c.f. sE-selectin).

Moreover, unlike sE-selectin, the level of increase in circulating sICAM-1 and sVCAM-1 that was observed in association with hypertension alone was less than that observed in association with cigarette smoking alone, which might reflect a difference in the mechanism of elevation. Furthermore, the association of both hypertension and cigarette smoking significantly boosted the levels of sICAM-1 and sVCAM-1 above that observed with either one alone. In contrast, there were no statistical differences in the levels of sICAM-1 and sVCAM-1 among all subjects as a result of past history of schistosomiasis alone. However, a past history of schistosomiasis for normotensive subjects boosted the statistical significance of the increase in sICAM-1 as a result of cigarette smoking. As for sVCAM-1, a past history of schistosomiasis boosted the statistical significance of the increase in sVCAM-1 concentration as a result of hypertension, cigarette smoking in hypertensive subjects or a combination of both hypertension and cigarette smoking.

These results are consistent with epidemiological data suggesting a significant association between an increasing concentration of ICAM-1 and the risk of future cardiovascular events and myocardial infarction in apparently healthy men and women (Haught et al. 1996, Ridker et al. 1998, Porsch-Oezcueruemez et al. 1999, Ridker et al. 2000). Moreover, some studies suggested that circulating VCAM-1 levels may be used to determine the stage of atherosclerosis (De Caterina et al. 1997, Peter et al. 1997).

There is ample evidence that the measurement of adhesion molecules detects endothelial dysfunction in hyperlipidaemia, arterial hypertension, smoking and diabetes, all of which are considered major cardiovascular risk factors (Schachinger and Zeiher 2001).

The endothelial dysfunction could be as a result of local release of inflammatory cytokines and chemokines that activate endothelial cells to upregulate soluble adhesion molecules, activate neutrophils and generate reactive oxygen species which serve to amplify the initial inflammation leading to dysregulated apoptosis, secondary necrosis and overt vascular injury lesions (Tesfamariam and DeFelice 2007). Many of the

cardiovascular risk factors, including hyperlipidaemia, hypertension, diabetes and smoking, are associated with overproduction of reactive oxygen species or increased oxidative stress, both of which reduce vascular nitric oxide bioavailability and promote cellular damage (Tomasian et al. 2000).

Nitric oxide production plays a central role in modulating endothelial function (Moncada et al. 1991) and evidence suggests that endogenous nitric oxide modulates vascular stiffness probably by vascular tone modulation and vascular remodelling (Kinlay et al. 2002, Wang and Fitch 2004). Hence, increased oxidative stress is considered to be a major mechanism involved in the pathogenesis of endothelial cell dysfunction and may serve as a common pathogenic mechanism of the effect of risk factors on the endothelium (Cai and Harrison 2000, Tomasian et al. 2000, Tesfamariam and DeFelice 2007).

Chronic smoking has been shown to be associated with increased arterial stiffness in healthy subjects (Mahmud and Feely 2003, Li et al. 2006) and data indicates that lipid-soluble smoke particles, but not nicotine, cause damage to arterial endothelium and reduce the endothelium-dependent dilatation in man and rat (Zhang et al. 2006). However, data are lacking in an untreated hypertensive population, since arterial stiffness is an independent predictor of events in hypertensive patients (Laurent et al. 2001, Boutouyrie et al. 2002). Yet, a recent report demonstrates that in untreated hypertensive patients, a population characterized by already stiff vessels, chronic smoking further increases arterial stiffness independent of blood pressure. The authors concluded that the effects of hypertension and smoking on the vascular wall may be cumulative (Jatoi et al. 2007). These observations are in line with the results of this study showing that association of both hypertension and cigarette smoking significantly boosts the levels of markers of endothelial dysfunction above that observed with either one alone.

In conclusion, this study evaluated the impact of hypertension, smoking and past history of schistosomiasis on endothelial dysfunction and subsequent vascular damage. Plasma levels of biomarkers of inflammation and endothelial dysfunction, sVCAM-1, sICAM-1 and sE-selectin, were elevated as a result of hypertension and/or cigarette smoking compared to normal counterparts. Hypertension and cigarette smoking had the strongest direct associations with these biomarkers while past history of schistosomiasis had very little association with these biomarkers. Nevertheless, sVCAM-1 may be useful in assessing the impact of liver affliction (as a result of schistosomiasis).

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