Venous and arterial coronary artery bypass grafts in a pharmacological perspective
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Changes in saphenous vein reactivity induced by experimental heart failure in rabbits

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Introduction

The condition of congestive heart failure (CHF) as the end stage of various cardiac diseases is characterised primarily by an inadequate cardiac output. Compensatory mechanisms such as activation of the sympathetic nervous (SNS) and of the renin-angiotensin-aldosterone system (RAAS) are secondary to insufficient cardiac output and oxygen supply of the various tissues. The associated elevated plasma levels of neurotransmitters and hormones are known to induce relevant alterations in the target tissues and their receptors.

Most experimental work on these changes at the receptor-level has focused on the myocardium and the arterial part of the cardiovascular system. In the myocardium mainly β-adrenoceptors are downregulated in case of CHF. In arteries the results concerning the adrenoceptors are unequivocal and depend on the model of heart failure, the state of heart failure and the vascular bed studied. In forearm plethysmographic studies in humans with CHF the α2-, and β-adrenoceptor induced responses remained intact, whereas the α1-adrenoceptor pathway was partially desensitised. However, in isolated arteries β-adrenergic relaxation was reduced while α2-adrenergic responses remained unchanged. A common finding in most human and animal heart failure studies is the attenuation of endothelium-dependent vascular relaxation.

As established in previous functional studies the saphenous vein (SV) strongly responds to vasoactive compounds both in vitro, and in vivo. Despite the importance of the contractility of the venous side of the vascular system for preload, only a few studies have reported on venous function during CHF. In isolated SV obtained from dogs with pacing-induced heart failure, a similar pattern of adrenoceptor responses was shown as demonstrated in isolated arteries. Aortocoronary bypass surgery (CABG) often involves SV autografts. Several factors may contribute to bypass graft failure, and the reactivity of the conduit is one of these factors. For example graft spasm is partially provoked by the contractile responses of the conduit to circulating vasoactive compounds. Furthermore, the characteristics of SV are affected by factors like preexisting diseases of the patient. Since more and more older and diseased patients are subjected to CABG, it seems relevant to specify the changes associated with CHF in this particular vein.

Accordingly, the SV obtained from rabbits suffering from CHF provoked by pressure-overload or myocardial infarction were investigated. Adrenoceptor-induced responses and those to angiotensin II were determined. Endothelial function was studied by muscarinic-receptor-induced vasorelaxation. We used two different experimental
models of CHF since in clinical practice CHF-patients with similar causes of the disease are subjected to CABG.

Materials

Animals
Male New Zealand White rabbits (SPF, body weight 2500-3500g) were used. For this study the guidelines were followed as presented in The Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health. The Committee on Animal Experiments of the Academic Medical Center Amsterdam approved of the protocol.

Volume- and pressure overload model of heart failure in the rabbit (CHF-PO)
A combined volume- and pressure overload model of heart failure was used, as described by Bril et al. (1991).\textsuperscript{17} CHF was provoked in two stages. The animals were subjected to general anaesthesia with a mixture of ketamine 60 mg/ml and rompun 2% (0.8 ml/kg body weight) IM and to mechanical ventilation when necessary. In the first stage volume overload was induced via insufficiency of the aortic valve. By moving a fluid filled catheter, inserted via the carotid artery, to and fro across the aortic valve the insufficiency was induced, as demonstrated by an increase in pulse pressure by more than 50%. In stage two, during a separate procedure pressure overload was induced by aortic banding. Via an abdominal incision a ligature was placed around the aorta, just above the renal arteries, until a reduction of 50% of the aortic diameter was reached.

Myocardial infarction model of heart failure in rabbit (CHF-MI)
The coronary ligation model for inducing heart failure has been described by Denvir et al. (1995).\textsuperscript{18} Accordingly, under general anaesthesia and mechanical ventilation, a left sided thoracotomy was performed. The marginal branch of the left coronary artery was ligated, and the rabbits developed myocardial infarction and subsequent heart failure during the following weeks.

Assessment of heart failure
10 to 82 weeks after the (final) operations rabbits were anaesthetised and examined for the presence of gallop rhythm. An incision was made in the neck and the left carotid artery was cannulated with a 3F-microtip-pressure transducer (Millar, Houston, Texas, U.S.A.) and passed into the left ventricle to measure left ventricular end-diastolic
pressure (LVEDP). A bolus of 5000 IU heparin was injected IV. The abdomen was opened to detect ascites, followed by a thoracotomy to excise the heart. The heart and lungs were weighed.

A 'heart failure index' as described by Vermeulen et al. (1994) was calculated as follows. One point was scored for each of the following items: heart weight relative to body weight larger than 4.6 g/kg, lung weight relative to body weight larger than 3.5 g/kg, LVEDP larger than 5 mmHg, the presence of ascites, and the presence of gallop rhythm. A minimum of three parameters was assessed in all animals. The number of variables assessed was divided by the total score and heart failure was defined as a score ≥ 0.6. Besides these parameters myocyte length and width were determined as well. Indices of heart failure are shown in Table 1.

Earlier studies using the same model of CHF have demonstrated that there is no difference between the aforementioned parameters of the SHAM operated rabbits or control rabbits. Therefore in the current study the control group consisted of rabbits which had not been subjected to surgery.

**Isolated saphenous vein preparations**

After excision of the heart and lungs, an incision was made at the lateral side of both

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**Table 1: Parameters which are characteristic for heart failure in two rabbit models**

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 6)</th>
<th>CHF-PO (n = 8)</th>
<th>CHF-MI (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bodyweight (kg)</td>
<td>4.1 ± 0.15</td>
<td>4.2 ± 0.14</td>
<td>3.9 ± 0.14</td>
</tr>
<tr>
<td>Relative heart weight (g/kg)</td>
<td>2.4 ± 0.10</td>
<td>4.7 ± 0.29*#</td>
<td>3.3 ± 0.28*</td>
</tr>
<tr>
<td>Relative lung weight (g/kg)</td>
<td>2.6 ± 0.12</td>
<td>3.9 ± 0.18*</td>
<td>4.0 ± 0.50*</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>3.0 ± 0.6</td>
<td>19.4 ± 2.0*#</td>
<td>4.3 ± 1.7</td>
</tr>
<tr>
<td>Ascites</td>
<td>-</td>
<td>2*#</td>
<td>-</td>
</tr>
<tr>
<td>Gallop rhythm</td>
<td>-</td>
<td>1*#</td>
<td>-</td>
</tr>
<tr>
<td>Myocyte length (µm)</td>
<td>129 ± 2.6</td>
<td>167 ± 2.7*</td>
<td>169 ± 4.2*</td>
</tr>
<tr>
<td>Myocyte width (µm)</td>
<td>25 ± 2.9</td>
<td>34 ± 0.6*</td>
<td>34.3 ± 1.9*</td>
</tr>
<tr>
<td>HF index</td>
<td>&lt; 0.6</td>
<td>0.7 ± 0.04*</td>
<td>0.2 ± 0.06</td>
</tr>
</tbody>
</table>

Values represent mean ± S.E.M n = 4-8 (parameters were not assessed in all control rabbits). *P < .05, CHF compared to control, #P < .05 CHF-PO compared to CHF-MI.

LVEDP = left ventricular end-diastolic pressure, CHF-MI = myocardial infarction, CHF-PO = volume- and pressure-overload.
hind limbs and the SV was identified, gently removed and immediately submerged in ice-cold Krebs-Henseleit solution. Prior to the experiments the veins were cleaned of adhesive tissue, and cut into rings of approximately 3-mm length each. For some of the experiments the endothelium was removed by gentle rubbing of the intima with a plastic, notched tube. The ring preparations were mounted between two L-shaped stainless steel hooks, in 8 ml organ baths filled with Krebs-Henseleit solution of 37°C, continuously bubbled with a carbogen mixture (pH 7.4). Each preparation was fixed, via a silk thread, to an isometric force transducer (AD Instruments, Castle Hill, Australia) and force was recorded via a MacLab/8 computer system (AD Instruments, Castle Hill, Australia). The preparations were subjected to a pre-tension of 20 mN, which was maintained throughout the experiment.

Experimental protocol
After an equilibration period of 60 minutes the SV preparations were exposed to a priming procedure. With 30 minutes’ intervals contractions were induced, respectively, twice by a KCl solution (KCl, 60 mM), followed by a phenylephrine (Phe, 0.3 mM) preconstriction and subsequent relaxation to cumulative concentrations of methacholine (MCh, 0.3 µM - 10 µM), and finally contracted by another exposure to KCl. The priming procedure was followed by another equilibration period of 60 minutes. Subsequent, by cumulative concentration-response curves were constructed for the (α/β)-adrenoceptor agonist noradrenaline (1 nM- 1 mM), the α₁-adrenoceptor agonist methoxamine (0.1 µM- 1 mM), the α₂-adrenoceptor agonist B-HT 933 (0.1 µM- 1 mM), the β-adrenoceptor agonist isoprenaline (0.01 nM- 10 µM) and angiotensin II (0.01 nM-10 µM), respectively, in separate preparations. To abolish β-adrenoceptor-mediated effects of noradrenaline, responses to NA (and methoxamine and B-HT 933 to standardise the protocol) were obtained in the presence of the non-specific β-adrenoceptor antagonist propranolol (1 µM). Ascorbic acid (1 mg.mL⁻¹) was added to prevent oxidative degradation of catecholamines. Concentration response curves to isoprenaline and angiotensin II were made in the absence of endothelium, since both agonists are known to release nitric oxide from the endothelium. To study the dilatory responses to isoprenaline the preparations were incubated for 1 hour with the non-selective α-adrenoceptor antagonist phentolamine (0.1 mM), and precontracted with the thromboxane A₂-mimetic U46619 (0.3 µM).

Drugs used
Angiotensin II, (±)-isoproterenol hydrochloride, acetyl-β-methylcholine chloride, methoxamine hydrochloride, (−)-norepinephrine bitartrate, phentolamine hydrochloride,
L-phenylephrine hydrochloride were obtained from Sigma (St. Louis, MO, U.S.A.); ascorbic acid from Merck (Darmstadt, Germany), B-HT 933 chloride from Dr. Karl Thomae GMBH (Biberach an der Riss, Germany); (±)-propranolol hydrochloride from Research Biochemicals International (Natick, U.S.A.); U46619 (1 mg.100 μL⁻¹ ethanol) from Biomol Feinchemikalien GmbH (Hamburg, Germany). All drugs were dissolved in distilled water, except norepinephrine and isoproterenol. Noradrenaline and isoproterenol were dissolved in a 0.1 mg.mL⁻¹ ascorbic acid containing solution.

Solutions used
The Krebs-Henseleit solution used for the experiments had the following composition (mM): NaCl 118.0; KCl 4.7; NaHCO₃ 25.0; MgSO₄ 1.2; CaCl₂ 2.5; KH₂PO₄ 1.1 and glucose 8.3.

For the experiments with the α-adrenoceptor agonists, propranolol (1μM) and ascorbic acid (0.1 mg.mL⁻¹) were added to the Krebs-Henseleit solution.

The KCl solution had the same composition as the Krebs-Henseleit solution used, except for the NaCl, which had been partially replaced by an amount of KCl corresponding to a concentration of 60 mM.

Statistical analysis
The data were expressed as means ± S.E.M. for n observations. The concentration-response curves for the compounds investigated were analysed by means of a computer program (Graph Pad, Institute for Scientific Informatics, San Diego, CA, U.S.A.). The pD₂-value [-log effective concentration (molar) that produces 50 % of the maximal effect (EC₅₀)], as well as the maximal effect (Eₘₐₓ) were thus obtained from the non-linear regression curve fit analysis for individual experiments. The statistical significance of the differences was analysed by means of two-sided Student’s t-test or by means of one-way analysis of variance for unpaired data, with Newman-Keuls’ post-test for multiple comparisons. Values of P < .05 were considered significant.
Results

General
The isolated SV preparations obtained either from rabbits with CHF or from control animals yielded stable functional responses throughout the experiments. Receptor-independent contractile force as provoked by KCl-induced depolarisation was similar in the three experimental groups (28.9 ± 2.2, 30.2 ± 2.2, and 36.0 ± 0.4 mN, for the control, CHF-PO, and the CHF-MI groups, respectively, n = 4-8, P = n.s.). The responses to depolarisation obtained in preparations after mechanical removal of the endothelium were equal to those found in the preparations with endothelium. The occurrence of chronic heart failure did not influence the responses to a single concentration thromboxane A2-mimetic U46619 (0.3 μM), and amounted to 44.1 ± 9.8 mN in the control preparations, compared to 38.1 ± 5.9 mN and 44.0 ± 7.7 mN in CHF-PO, and CHF-MI preparations, respectively (n = 4-6, P = n.s.). The mechanical removal of the endothelium was confirmed by a strong reduction in the dilatory response to methacholine in phenylephrine-precontracted preparations by maximally 21.5 ± 6.4 % (Figure 1).

![Figure 1](image)

**Figure 1:** The influence of CHF due to pressure overload (CHF-PO ■), or myocardial infarction (CHF-MI ▼) compared to controls (control ○) on the responses induced by methacholine (MCh) in rabbit isolated SV preparations with endothelium. Shown as well is the effect of mechanical removal of the endothelium on responses to MCh (CHF-PO □, CHF-MI ▼ and control ○). The responses are presented as percentage of the precontraction induced by phenylephrine (Phe 0.3 mM). Values are given as means ± S.E.M, n = 4-8. *P < .05
**Adrenoceptor-mediated responses**

The maximal effect of noradrenaline was increased in the SV rings obtained from rabbits exposed to pressure-overload-induced CHF (Table 2, Figure 2A). In subsequent experiments cumulative concentration response curves were constructed for the α1-adrenoceptor agonist methoxamine and the selective α2-adrenoceptor agonist B-HT 933, to investigate which α-adrenoceptor was involved in the increased response to noradrenaline. Maximal contractile responses to methoxamine were increased, whereas those to B-HT 933 were unaffected by CHF (Table 2, Figure 2A). For the sensitivity of isolated SV to α-adrenoceptor stimulation the following rank order was found: noradrenaline > methoxamine = B-HT 933. The sensitivity to the α-adrenoceptor agonists was not altered in SV from heart failure rabbits (Table 2), when compared with controls. Since the endothelial function might influence α-adrenoceptor responses, and endothelium-dependent dilation was impaired in CHF-PO animals (see endothelium-dependent relaxation), separate experiments were performed with noradrenaline in endothelium-denuded SV preparations (Figure 2B). The observed differences between CHF-PO and controls concerning the maximal effect of α-adrenergic stimulation were even more pronounced in these preparations (E\text{max} amounted 114.1 ± 5.2% of the KCl-induced responses, in SV of CHF-PO rabbits, compared to 88.6 ± 6.1% in control animals, n =4-6, P < .05). Furthermore, the concentration response curves to noradrenaline in endothelium-denuded preparations showed a significant leftward shift.

The cumulative concentration-response curves of isoproterenol in isolated rabbit SV preparations were U-shaped (Figure 3). The maximal β-adrenoceptor-induced relaxation, as

**Table 2: Responses of saphenous vein preparations to α-adrenoceptor stimulation by three different agonists**

<table>
<thead>
<tr>
<th></th>
<th>noradrenaline</th>
<th>methoxamine</th>
<th>B-HT 933</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E\text{max}</td>
<td>pD\text{2}</td>
<td>E\text{max}</td>
</tr>
<tr>
<td>control</td>
<td>80.6 ± 6.1</td>
<td>6.0 ± 0.2</td>
<td>55.7 ± 3.5</td>
</tr>
<tr>
<td>CHF-PO</td>
<td>110.3 ± 8.0*</td>
<td>5.5 ± 0.1</td>
<td>70.5 ± 4.5*</td>
</tr>
<tr>
<td>CHF-MI</td>
<td>96.2 ± 7.3</td>
<td>6.1 ± 0.4</td>
<td>60.6 ± 6.7</td>
</tr>
</tbody>
</table>

The effect of CHF due to pressure overload (CHF-PO) or myocardial infarction (CHF-MI) compared to control, on the sensitivity (expressed as negative log EC\text{50} values (pD\text{2})) and the maximal effect (expressed as E\text{max}, %), of noradrenaline, methoxamine, and B-HT 933 in isolated saphenous vein preparations. The maximal effect is presented as percentage of the maximal response to KCl. Values are given as means ± S.E.M, n = 4-10. *P < .05 for CHF-PO compared to control and CHF-MI.
Figure 2A: The effect of CHF due to pressure overload (CHF-PO), or myocardial infarction (CHF-MI) compared to control (ctrl) on the responses in rabbit isolated SV induced by noradrenaline (ctrl ■, CHF-PO □, CHF-MI ◊), methoxamine (ctrl ●, CHF-PO ○, CHF-MI *) or B-HT 933 (ctrl ▲, CHF-PO △, CHF-MI ◄), respectively.

Figure 2B: The effect of endothelium removal on the responses to noradrenaline (preparations with endothelium ctrl ●, CHF-PO ■, CHF-MI ◄, and without endothelium ctrl ○, CHF-PO □, CHF-MI ◄). The responses are expressed as % of the responses to KCl. Values are given as means ± S.E.M, n = 4-10. *p < .05
presented by the first, descending part of the curves, was decreased in SV rings obtained from CHF-PO rabbits ($E_{\text{max}}$ $14.2 \pm 3.8\%$ of the precontraction), compared to those from CHF-MI ($18.2 \pm 3.1\%$) and control rabbits ($27.3 \pm 3.7\%$) (Figure 3). The sensitivity of the SV to isoproterenol was not influenced by CHF ($\text{pD}_2$-values of $6.9 \pm 0.4$, $6.8 \pm 0.3$, and $6.9 \pm 0.4$ for the control, CHF-PO, and the CHF-MI groups of preparations, respectively, $P = \text{n.s.}$).

The presence of the $\alpha$-adrenoceptor antagonist phentolamine (0.1 mM) could not fully suppress the effect of the higher concentrations isoproterenol at the $\alpha$-adrenoceptor, as represented by the ascending part of the curve, indicating a contractile response (Figure 3). Also in this part of the curve the CHF-PO derived preparations demonstrated stronger contractions than the preparations obtained from CHF-MI and control animals, indicating a difference in $\alpha$-adrenergic properties. This observation confirms the findings for the responses to the specific $\alpha$-adrenoceptor agonists (see above).

**Angiotensin II**

Contractile responses to angiotensin II could only be obtained in endothelium-denuded SV preparations. In these isolated SV preparations angiotensin II generated small contractions. In control preparations the maximal contraction amounted to $12.6 \pm 3.9\%$ of the response induced by KCl. Nevertheless, the curve of angiotensin II-induced

![Figure 3](image)

**Figure 3:** The effect of CHF due to pressure overload (CHF-PO ■), or myocardial infarction (CHF-MI ▼) compared to control (control ○) on the responses induced by isoproterenol in rabbit isolated SV preparations. The responses are presented as percentage of the precontraction induced by U46619 (0.3 $\mu$M). Values are given as means ± S.E.M, $n = 4-6$. *$P < .05$
contractions in animals with pressure-overload provoked CHF was shifted to the right, as presented in Figure 4. The pD2-values of the responses to Ang II in CHF-PO animals was increased to 8.2 ± 0.08, compared to 8.7 ± 0.2 in SV rings from control animals (n = 4-7, P < .05). SV obtained from CHF-MI animals demonstrated no changes in contractions provoked by angiotensin II.

Endothelium-dependent relaxation

The relaxation caused by the muscarinic-receptor agonist methacholine showed clear differences between the three experimental groups of preparations. In SV rings obtained from animals with CHF due to pressure overload the endothelium-dependent relaxation to methacholine was reduced to 68.7 ± 10.5% of the precontraction, compared to 91.8 ± 5.0% in the preparations obtained from control rabbits (P < .05) (Figure 1). However, the responses found in rings from CHF-MI animals (Emax 84.6 ± 5.8%) were not different from control or CHF-PO rabbits.
Discussion

Hearts of rabbits subjected to either volume-and pressure overload or myocardial infarction developed left ventricular hypertrophy according to the myocyte characteristics obtained. The relative lung weight of both groups of heart failure rabbits was raised compared to controls. In the group of animals with pressure overload the increase in heart weight and LVEDP was more pronounced than in the myocardial infarction group. Furthermore, in the last group we observed no signs of gallop rhythm or ascites. The heart failure index assessed was positive in the pressure-overload and not significant in the myocardial infarction group. Accordingly, heart failure in the animals subjected to coronary ligation is obviously less pronounced than in the rabbits exposed to volume-and pressure overload. This might explain why the changes observed in SV from rabbits subjected to volume-and pressure overload were absent in the same preparations obtained from animals that underwent coronary ligation. Another explanation might be the underlying mechanism of heart failure. In a study comparing patients with idiopathic and ischemic cardiomyopathy, also no changes were observed in the group with ischemic cardiomyopathy. The severity of heart failure as indicated by the LVEDP was less pronounced in the ischemic group as well.20

In the present study, isolated SV obtained from rabbits exposed to volume-, and pressure overload (CHF-PO) showed an increase in the contractile, and a decrease in the dilatory responses. The enhanced contractile response was observed for the combined α-adrenergic stimulation, and also found to be so for the selective stimulation of the α1-adrenoceptor, but not for the α2-adrenoceptor. In contrast to the enhanced contractile response, relaxation to β-adrenoceptor activation was reduced.

In patients with congestive heart failure the SNS-activation results in high local and systemic levels of catecholamines.1 The exposure to elevated levels of catecholamines is known to influence vessel responsiveness in heart failure. The observation that α-adrenergic responses in isolated vein increase, as in the present study, has been described for other models of heart failure as well. However, α-adrenergic reactivity in CHF according to literature data for arteries and veins are inconsistent and differ per model and vascular bed.1-9 Globally, the literature data point towards a normal/enhanced α-adrenergic responsiveness of peripheral blood vessels and a normal/decreased reactivity of blood vessels supplying vital organs.

The demonstrated increase in α-adrenergic responses might be the result of limited inhibition of the contractile response by the endothelium.6 However, after mechanical denudation of the SV preparations the differences between heart failure and normal animals were even more pronounced. The endothelium-denuded preparations
demonstrated greater sensitivity in response to the \( \alpha \)-agonists. Thus, endothelial function appears to be involved, but does not fully explain the observed changes in \( \alpha \)-adrenoceptor responses in heart failure in the current study. The responses to isoproterenol are mediated via \( \beta \)-, \( \alpha_1 \)-, and \( \alpha_2 \)-adrenoceptors, and they are partially endothelium-dependent.\(^{14,21}\) The role of the endothelium and \( \alpha \)-adrenoceptor stimulation in the results obtained with respect to the \( \beta \)-adrenoceptor are negligible, an \( \alpha \)-adrenoceptor antagonist was present in denuded preparations. Therefore, the limited effectiveness of isoproterenol in SV from pressure-overload rabbits must be the result of changes at the level of the \( \beta \)-adrenoceptor. In the myocardium it has been demonstrated by means of radioligand binding studies that the number of \( \beta \)-adrenoceptors decreases during heart failure.\(^7\) The present results in isolated SV may also be explained on this basis.

Severe congestive heart failure is known to be accompanied by activation of the RAAS.\(^{22}\) In spite of this, the effect of angiotensin II in CHF on isolated vessels has been sparsely investigated. The reason might be the strong heterogeneity of angiotensin II-induced contractions in isolated vessel preparations. Therefore, although the response to angiotensin II in rabbit isolated SV was small and somewhat variable, it seems important to report these results, and even more so since the potency of angiotensin II was diminished in SV from CHF-PO rabbits. In functional and binding studies, evidence for a reduction in the number of AT1-receptors in CHF was obtained, and an increased/unchanged response provoked by angiotensin II was observed.\(^{20,23-26}\) Hypothetically, a downregulation of AT1-receptors in the presence of a receptor reserve, or a shift towards another subpopulation of AT1-receptors might explain our observations.

In patients with congestive heart failure the endothelial capacity to produce vasodilator substances, like nitric oxide (NO) and the effect of NO appears to be decreased.\(^{10,11,27}\) The present observation of a decreased vasodilation in response to methacholine stimulation might reflect endothelial dysfunction in SV from rabbits with CHF-PO. However, this conclusion can be drawn with caution only since a multitude of other factors might influence the results, like for example muscarinic receptor abnormality, impaired smooth muscle responsiveness to NO or reduced L-arginine availability.\(^{28}\) From the present findings we conclude that in heart failure relevant changes occur in venous responsiveness, as demonstrated in saphenous vein from rabbits subjected to pressure-overload induced heart failure. Due to CHF contractile responses to \( \alpha \)-adrenergic compounds are even more pronounced, independent of endothelial function, whereas dilatory reactions such as endothelium- and \( \beta \)-adrenoceptor-dependent relaxation are impaired. Saphenous vein autografts are susceptible to spasm and graft
failure due to endothelial injury and the subsequent higher responsiveness to vasoconstrictors. Therefore, the demonstrated enhanced contractility may have consequences for the patency of venous grafts and subsequently the peri-operative management of CHF patients subjected to CABG.

Acknowledgement

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References


