Myogenic reactivity and resistance distribution in the coronary arterial tree: a model study

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1Faculty of Design, Engineering and Production, Mechanical Engineering and Marine Technology, Man Machine Systems and Control Group, Delft University of Technology, 2628 CD Delft; and 2Department of Medical Physics, Cardiovascular Research Institute Amsterdam, Academic Medical Center, University of Amsterdam, 1100 DE Amsterdam, The Netherlands

Cornelissen, Annemiek J. M., Jenny Dankelman, Ed VanBavel, Henk G. Stassen, and Jos A. E. Spaan. Myogenic reactivity and resistance distribution in the coronary arterial tree: a model study. Am J Physiol Heart Circ Physiol 278: H1490–H1499, 2000.—The objectives of this study were to evaluate the myogenic behavior of blood vessels and their interaction within the coronary arterial tree and to evaluate the possible role of the myogenic response in autoregulation. The model consists of 10 compartments in series, each representing a class of vessel sizes. Diameter and resistance in each class are determined by their value at full dilation (dp, Rp) and by the myogenic response. Three distributions of Rp and three distributions of myogenic strength, M, (slope of pressure-diameter curve, range −0.05 to −0.4%/mmHg) were evaluated (9 cases). It was found that larger vessels attenuate the myogenic activity of smaller vessels and that myogenic responsiveness is sufficient to achieve autoregulation. When M has a maximum in vessels of 84 µm, the maximum effect of perfusion pressure on active diameter occurs in vessels between 123 and 181 µm, depending on the distribution of Rp. Distribution of resistance and control mechanisms in the coronary arterial tree are important for interpretation of individual vessel responses as observed in vivo.

coronary circulation; myogenic response; autoregulation; mathematical model

MYOGENIC CONSTRICTION of the smooth muscle cells in the arterial wall due to a rise in pressure is thought to be one of the mechanisms involved in coronary autoregulation, i.e., a relative constant flow despite changes in arterial pressure. Myogenic responsiveness in isolated resistance arteries is well documented (6, 16–20, 23, 26). However, the position of a resistance vessel in the arterial tree determines how effective the response can be. As Johnson (9, 10) argued in 1980, myogenic constriction of proximal arterioles due to arterial pressure elevation may limit the increase in pressure that is transmitted to the more distal vessels.

Studies in isolated vessels generally demonstrate heterogeneous myogenic responsiveness with the stronger myogenic reactivity in the smaller arterioles (4, 22).

For example, in isolated porcine coronary arteries and arterioles with active diameters ranging from 37 to 180 µm, arterioles of ~62 µm were shown to exhibit the strongest myogenic reactivity (19). This agrees well with the observations of only a moderate responsiveness in porcine arteries of 180 µm (26) and an absence of myogenic responsiveness in porcine arteries of 223 µm (23). Therefore, on the basis of isolated vessel studies, one would expect that the smaller arterioles form the primary site for myogenic flow control.

Several studies report on the diameter changes of small arteries with diameters varying between 50 and 400 µm in the epicardial vascular bed in vivo, supporting the concept of diameter-dependent myogenic response (2, 12). However, since all these vessels are part of a network, it is not clear how the response of a single vessel under observation is determined by the other vessels in the tree.

The first aim of this study was to evaluate myogenic behavior of single coronary segments within a network and their interaction. The second aim was to evaluate the possible role of myogenic tone in autoregulation. We used a simple theoretical model with 10 resistance compartments in series. This is a strong simplification, since it has been shown that heterogeneity of branching has to be taken into account to achieve a good prediction of pressure distribution as a function of the vessel diameter (27). However, the complexities of such a heterogeneous model obscure the role of the distribution of resistance with respect to our specific aims. In our compartmental model, we evaluated three different resistance distributions, which covered the range of pressure distributions that can be found in literature, either as measured (3) or as estimated from the coronary branching structure (13, 14, 27).

METHODS

The model consists of 10 resistance compartments in series. The first nine compartments are applied to mimic the resistance distribution of the arterial tree. Nine compartments are used because this is approximately the number of Strahler orders of the vessels in the coronary arterial tree covering diameters ranging from 10 to 500 µm (15, 27). The resistance of capillaries and venules are assumed to be constant and are lumped in the 10th compartment. Passive and active pressure-diameter relations of vessels with certain diameter determine the resistance behaviors of each of the

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first nine compartments. Therefore, we assume that each of these compartments, \(i\), represent \(N_i\) identical vessels in parallel. Hence, according to Poiseuille, the resistance can be written as

\[
R_i = \frac{128\eta_i L_i}{N_i\pi d_i^4} \Rightarrow R_i = \frac{128K_i}{\pi d_i^4} \quad i = 1, 2, \ldots, 9 \quad (1)
\]

where \(\eta_i\) is the viscosity constant; \(L_i\) is the length of the vessel; \(N_i\) is the number of parallel vessels in the compartment; and \(d_i\) is the diameter of the vessel. Since \(K_i\) includes the length and number of vessels as well as the viscosity constant in each compartment, it represents anatomical and rheological data. We assume \(K_i\) in each compartment independent of pressure and independent of diameter variations induced by myogenic response or pressure variations directly. The Fahraeus-Lindqvist effect is taken into account insofar as the viscosity in the reference condition is considered. Hence, according to Poiseuille, the resistance can be calculated as

\[
P_i = \frac{P_{in,i} + P_{in,i+1}}{2} \quad \text{for} \quad i = 1, 2, \ldots, 9 \quad (2)
\]

The flow through each compartment, \(Q_i\), can be calculated as follows

\[
Q_i = \frac{P_{in,i} - P_{in,i+1}}{R_i (P_i)} \quad \text{for} \quad i = 1, 2, \ldots, 9
\]

\[
Q_{10} = \frac{P_{in,10}}{R_{10}}
\]

Since the flows through all compartments \((Q_1, Q_2, \ldots, Q_9)\) must be equal, the local pressures in the vessels can be calculated providing the parameters \(K_i\) and relations \(d_i(P_i)\) are known as well as the inlet and outlet pressures of the 1st and 10th compartment, respectively.

In this study, the outlet pressure of the 10th compartment is kept constant and equal to zero. Furthermore, it is assumed arbitrarily that the flow equaled 1 ml/s when the inlet pressure equals 90 mmHg at full dilation. All normalized passive pressure-diameter relations (see below) are taken to be identical for all compartments. For the resistance of the most distal compartment \((R_{10})\), it is assumed that the inflow pressure \(P_{in,10}\) equals 30 mmHg at a perfusion pressure of 90 mmHg at full vasodilation. Since the present model ignores the heterogeneity in topology of the coronary tree, it is not possible to estimate \(K_i\) from observed arteriolar length, density, and viscosity distributions. Therefore, a set of \(K_i\) values has been determined from a given pressure distribution in the coronary tree at full vasodilation, as explained below.

Three different pressure distributions are considered, given by the dashed lines in Fig. 1. These three curves in Fig. 1 result in three different resistance distributions at full dilation as given in Fig. 2. We will further refer to these distributions as: 1) distal dominant resistance, 2) gradual resistance distribution, and 3) proximal dominant resistance. As is clear from Fig. 1, our distal dominant and proximal dominant resistance distributions form an upper and lower bound for measured pressure distributions (1, 3), while the gradual resistance distribution forms an intermediate case. Without an evaluation of best fit, this gradual resistance distribution is considered the most realistic case of the three.

**Passive Pressure-Diameter Relations**

Figure 3A shows data on passive pressure-diameter relations observed by various authors on isolated coronary vessels. The anatomical diameter of these vessels at 100 mmHg varied from 65 to 260 \(\mu\)m. As can be seen, the normalized passive pressure-diameter data from the different studies are rather similar over this range of vessel diameters. The function as provided by Liao and Kuo (19) is used to fit through these data points

\[
\frac{d_i}{d_{anat,i}} = d_0 + (d_{\max} - d_0) \frac{P_i/P_{0.5}}{1 + P_i/P_{0.5}} \quad i = 1, 2, \ldots, 9
\]

with \(d_{\max} = 1.07\), \(d_0 = 0.7\) and \(P_{0.5} = 22.7\) mmHg where \(d_{anat,i}\) equals the anatomical diameter defined as the passive diameter at local pressure of 100 mmHg. In contrast to Liao and Kuo (19), the passive pressure-normalized diameter relations are taken equal for all vessel orders. This curve is depicted by the solid line in Fig. 3A. To obtain the different pressure-diameter curves in each compartment, the anatomical diameters \(d_{anat,i}\) need to be chosen.

Fig. 1. Definition of pressure distribution as function of vascular diameter. Dashed lines provide the pressure profiles for the fully dilated tree at a perfusion pressure of 90 mmHg. Solid lines provide the passive pressure-diameter relations for the 9 compartments. Local pressure \((P_i)\) and diameter \((d_i)\) in compartments with distal dominant (○), gradual (▲), and proximal dominant (●) resistance distribution. Data from Chilian et al. (3) measured in coronary arterioles of the beating cat epicardium, dilated with dipyridamole (○) or in control conditions (□). Interpolation of data measured by Chilian (1) in coronary subendocardium (○) and subepicardium (▲) arterioles of an isolated porcine heart.
Estimation of $K_i$ and $d_{anat,i}$ in the Compartments

Since it is assumed that the control of flow takes place in vessels with diameters ranging from 20 to 400 µm, we chose $d_{anat,1} = 400$ µm and $d_{anat,9} = 20$ µm. According to the application of Strahler ordering to topological findings, $\log(d_i)$ should be linear related to $i$ (27). This determines the values of $d_{anat,i}$ for $i = 1, 2, \ldots, 8$. Figure 1 provides the passive pressure-diameter relations for the vessels with different values of $d_{anat,i}$ over the relevant pressure range, with $P_i$ on the y-axis and $d_i$ on the x-axis (vertical running solid curves). The values for $d_i$ at $P_i = 100$ mmHg are indicated along the top axis of Fig. 1 and in Table 1. The intercepts of these pressure-diameter relations with the pressure distribution curves provide the actual diameter at full dilation of all compartments when the inlet pressure of the first compartment equals 90 mmHg. From these intercepts the values of $K_i$ for a given pressure distribution can be calculated when the flow is defined. For the three resistance distributions, the three sets of $K_i$ values are reported in Table 1.

Active Pressure-Diameter Relations

Besides a standardized passive pressure-diameter relationship we also need a standardized active pressure-diameter relationship. This is implemented as shown in Fig. 3B. Up to a pressure of 5 mmHg the vessel is assumed to behave passively. For higher pressures the active pressure-diameter relationship is assumed to be a straight line with negative slope crossing the passive pressure-diameter relation at 5 mmHg. The magnitude of the slope represents the strength of the myogenic response. In Fig. 3B, the two extremes for myogenic strength used in this study are depicted. The active pressure-diameter relationship is calculated as follows

$$d_i(P_i) = d_i(5) - \frac{M_i}{100} d_{anat,i} P_i \quad \text{for} \quad P_i > 5 \text{ mmHg}$$

where $M_i$ is the myogenic strength in percent per millimeter Hg.

Three different distributions of myogenic strength over the compartments are studied. Two distributions are homogeneous.
Simulations

84 µm passive diameter. The three different distributions are dependent on the anatomical diameter, with a maximum at illustrated in Fig. 5, which is stopped when the flows (Q

For the calculations, an iterative procedure is used, as illustrated for perfusion pressures ranging from 5 to 140 mmHg.

Distributed homogeneously, but with different strengths; the weak and strong homogeneous distributions correspond to the two extremes in Fig. 3B. In the third distribution, myogenic strength is dependent on the anatomical diameter, with a maximum at 84 µm passive diameter. The three different distributions are depicted in Fig. 4.

Simulations

The diameters of the vessels, the local pressures in the vessels, and the resistances of the compartments are calculated for perfusion pressures ranging from 5 to 140 mmHg. For the calculations, an iterative procedure is used, as illustrated in Fig. 5, which is stopped when the flows (Q values) in all compartments are equal with an accuracy of 10⁻¹² m/s.

RESULTS

Autoregulation Curves

Figure 6 shows the pressure-flow relations for the three resistance distributions at full dilation and 90 mmHg. The passive pressure-flow relations are nearly identical; at equal pressure, flow differs only by 0.2% maximal between the different resistance distributions. The slight curvature of the passive pressure-flow line reflects the distensibility of the vessels in the first nine compartments. When the myogenic response is distributed homogeneously, the resistance distribution is hardly affecting the autoregulation curves. However, for the diameter-dependent myogenic response, the three different resistance distributions result in quite different autoregulation curves. When resistance is proximal dominant and myogenic tone diameter dependent, the autoregulation is weak due to the fact that distal vessels having the high myogenic strength hardly contribute to the total resistance.

Individual Diameter Responses in the Networks

Figure 7 shows the normalized diameter distribution as a function of the perfusion pressure when resistance is gradually distributed, and the different distributions in myogenic strength. Although quantitatively different, comparable results are found when resistance is dominant in the proximal compartments or in the distal compartments (results not shown). In the low perfusion pressure range, the diameters of the vessels in the different compartments increase with pressure when local pressure is smaller than 5 mmHg. At higher perfusion pressures the myogenic reduction in diameter emerges. The slope of the perfusion pressure-diameter relation at 90 mmHg is defined as the sensitivity of the myogenic response to changes in perfusion pressure. This sensitivity is provided for the nine compartments in Fig. 8, which relates to the three resistance distributions. In case of homogeneously distributed myogenic response (Fig. 7, left and middle, and Fig. 8), the strongest diameter reduction is always in the most proximal compartment. However, when myogenic reactivity is diameter dependent (Fig. 7, right; and Fig. 8), the strongest diameter reduction is in smaller vessels with the diameter of highest response dependent on the resistance distribution at full vasodilation. Maximal sensitivity of diameter to perfusion pressure is found at 123, 181, or 181 µm for the distal dominant, gradual distributed, or proximal dominant resistance distribution, respectively.

Distributed Response of Resistance

Figure 9 provides the dependence of total resistance (top) and resistances of the compartments (bottom) on perfusion pressure for the case of gradual resistance distribution, reflecting the different distributions in myogenic strength. Despite quantitative differences, the two other resistance distributions resulted in comparable changes in resistance in the compartments as a function of perfusion pressure (results not shown). The sensitivity of resistance to perfusion pressure determined at 90 mmHg is demonstrated in Fig. 10 for all three resistance distributions.

The myogenic activity of a compartment should result in an increase of resistance with perfusion

![Fig. 4. Assumed distributions of myogenic strength, as defined in Fig. 3B, along the arterial tree: ■, strong response, homogeneously distributed; ○, weak response, homogeneously distributed; ▲, myogenic strength is varying with diameter between the weak and the strong case, having a maximum at an anatomical diameter of 84 µm.](http://ajpheart.physiology.org/)

### Table 1. Assigned diameters of the dilated vessels at 100 mmHg in the different compartments and the $K_i$ values in each compartment

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Anatomical Diameter, µm</th>
<th>Distal dominant</th>
<th>Gradual distributed</th>
<th>Proximal dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>400</td>
<td>174</td>
<td>4,053</td>
<td>13,032</td>
</tr>
<tr>
<td>2</td>
<td>268</td>
<td>65</td>
<td>797</td>
<td>1,546</td>
</tr>
<tr>
<td>3</td>
<td>181</td>
<td>24</td>
<td>161</td>
<td>191</td>
</tr>
<tr>
<td>4</td>
<td>123</td>
<td>9.31</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>84</td>
<td>3.55</td>
<td>7.23</td>
<td>3.31</td>
</tr>
<tr>
<td>6</td>
<td>58</td>
<td>1.36</td>
<td>1.59</td>
<td>0.46</td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>0.52</td>
<td>0.36</td>
<td>0.067</td>
</tr>
<tr>
<td>8</td>
<td>28</td>
<td>0.20</td>
<td>0.08</td>
<td>0.010</td>
</tr>
<tr>
<td>9</td>
<td>20</td>
<td>0.08</td>
<td>0.02</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Values are assigned diameters of dilated vessels at 100 mmHg in the different compartments (anatomical diameter) and the $K_i$ values in each compartment for the distal dominant, gradual distributed and proximal dominant resistance, tuned to obtain the prescribed pressure distributions and a flow of 1 ml/s.

![Table 1](http://ajpheart.physiology.org/)
The importance of resistance distribution becomes apparent when considering the homogeneously distributed cases. When resistance is proximal dominant (Fig. 10, right), the resistance increase occurs mainly in the proximal compartments and annihilates the myogenic rise in resistance of the more distal compartments. When resistance is gradually distributed (Fig. 9, left and middle; and Fig. 10, middle), the myogenic resistance increase becomes more distributed as well, but the effect remains dominant in the proximal compartments. When resistance is distal dominant (Fig. 10, left), the strongest myogenic rise in resistance occurs at intermediate diameters notwithstanding the homogeneous distribution of myogenic strength.

For diameter-dependent myogenic strength (peak strength at 84 µm), maximal sensitivity of active resistance to perfusion pressure is found at 84, 123, or 268 µm for the distal dominant, gradual distributed, or proximal dominant resistance distribution, respectively (Fig. 9, right; Fig. 10).

**DISCUSSION**

Our results demonstrate that myogenic activity of the large resistance vessels in the arterial tree attenuates the myogenic stimulus of the small vessels during changes in perfusion pressure. The more proximal the resistance, the stronger this effect. Hence, in flow control, the distribution of resistance is important for the role of myogenic behavior of individual vessels within the coronary network. This is most clearly demonstrated in the model with diameter-dependent myogenic tone. Peak myogenic tone was assumed here to occur in vessel segments with a passive diameter of 84 µm. However, in the network, peak myogenic diameter alterations to a change in perfusion pressure shifted to vessels with passive diameters in the range of 123 to 181 µm.

The model with homogeneously distributed resistance in combination with a diameter-dependent myogenic response seems to be the most realistic of the cases studied. It describes best the experimental data on pressure distribution in the dilated coronary bed (3) and diameter dependence of myogenic response of isolated vessels (19). However, coronary vascular trees show heterogeneous branching, and therefore resistance distributions along various paths may well be quite different, sometimes more closely resembling...
either the proximal dominant case or the distal dominant case. Hence, the different resistance distributions chosen provide insight into the importance of heterogeneity of the coronary tree in relation to physiological measurements. Obviously, the more local the measurement, e.g., diameter of individual in vivo vessels vs. pressure-flow lines in arteries, the more important heterogeneity will be.

Limitations of the Model

The model consists of nine compartments, which corresponds to the number of Strahler orders established for porcine coronary subtrees starting with a vessel of 400–500 µm in diameter (13, 27). A model consisting of a series of resistances can be rationalized as the equivalent of a symmetrical dichotomous branching tree. In that case, resistance of each compartment corresponds to the equivalent value of all vessels with a certain diameter and length in parallel. However, when applying the Strahler order vs. vessel diameter relation and the vessel diameter vs. length relation as reported by VanBavel and Spaan (27), the pressure distribution follows the top dashed curve of Fig. 1 (resistance dominant in the distal compartments). This curve deviates from experimental data on pressure-diameter relations in vivo, as is demonstrated in Fig. 1 as well. It has been shown that the artificial steep pressure drop at the smallest vessel diameter disappears when heterogeneity in branching characteristics is taken into account (27). To arrive at more realistic pressure distributions for our serial model, we changed the value of $K_i$ for each compartment, which can be interpreted either as modifying the length ($L_i$) or changing the number of parallel vessels ($N_i$). Also, changing the viscosity ($h_i$) in the compartment can modify $K_i$. Note that we did not alter the passive and active local pressure-diameter relations of the vessels representative for the compartments.

Two rheological effects are not accounted for in our model but may have an impact since viscosity may change with diameter change. As has been described by Pries et al. (24), apparent viscosity may decrease with increasing diameter for diameters lower than 40 µm, whereas for larger diameters, viscosity will increase. The latter effect is known as the Fahraeus-Lindqvist effect, whereas the former effect in apparent viscosity may relate to an endothelial surface layer (25, 29). However, for both rheological phenomena, it holds that their influence depends on the relative diameter variation of the vessels and the sensitivity of the apparent viscosity to these diameter changes. We calculated the variations in apparent viscosity based on diameter variation induced by a change in $P_{in,1}$ from 140 to 10 mmHg predicted with constant $K_i$. The maximal effect occurs in the case of the distal dominant resistance.
distribution and strong homogeneous myogenic strength. In this case, most of the diameter variation is limited to the first compartment, and apparent viscosity does change by 20%. For the gradual resistance distribution and diameter-dependent myogenic response, the maximal viscosity change is 8.5% and occurs in the 4th compartment. These changes are all due to the Fahraeus-Lindqvist effect. The other effect hardly plays a role, because vessels in the relevant compartments do not change much in diameter.

Especially at low pressures, there may be differences in the normalized passive pressure-diameter relationships between vessels of various caliber. However, for the sake of simplicity, these relations were taken independent of the size of the vessel. We also assumed myogenic characteristics of each compartment to be represented by a linear myogenic pressure-diameter relation above 5 mmHg. The current simplifications do not, however, influence the basic conclusions of our study, since myogenic strengths applied to the model cover the experimentally observed pressure-diameter relations found in isolated vessel studies, as is shown in Fig. 3B. In the case of diameter-dependent myogenic tone, the peak strength was taken for vessels with 84 µm in passive diameter at local pressure of 100 mmHg, which is in agreement with Liao and Kuo (19).

Our model does not contain an element describing metabolic vasodilation. Hence, the predictions by the model should be considered to be at a constant metabolic rate. Furthermore, possible other control mechanisms, including flow-dependent dilation, were purposely not taken into account to study the effect of myogenic response per se. Obviously, these modifications should be taken into account in a more comprehensive model. Griffith et al. (8) reported that the inhibition of endothelium-derived relaxing factor (EDRF) changes the resistance distribution in the microvascular network of a rabbit ear. Therefore, in vivo an interaction between flow-dependent dilation and the myogenic mechanism exists. Since the flow-dependent mechanism is generally assumed to be active in the larger vessels, the effect of myogenic constriction of these vessels on attenuation of local pressure changes in the smaller vessels may have been overestimated in the present study.

Previous Model Studies

Liao and Kuo (19) used a model approach similar to ours to investigate the potentiating effect of shear-dependent dilation by adenosine. That study used four compartments in series. Each compartment exhibited myogenic responsiveness as well. Granger (7) used a series-coupled model with three compartments to investigate the interaction of myogenic control, metabolic control, and flow-dependent dilation in the arterial tree. However, neither study gave special attention to the interaction between myogenic strength and resistance distribution over the compartments.

Model Predictions and Experimental Observations

Autoregulation curves. The pressure-flow lines show quite good autoregulation and support the notion that the myogenic response contributes to this phenomenon (5). To compare the slopes of our predicted autoregulation curves with in vivo observations, we may apply the correlation between flow (Q) on the one hand and
pressure (P_{in,1}) and oxygen consumption (MV_O2) on the other hand, as provided by Vergroesen et al. (28)

\[ Q = aP_{in,1} + bMV_O2 + c \]  

(6)

where \( a \) equals the sensitivity of flow to \( P_{in,1} \), and \( b \) indicates the sensitivity of flow to \( MV_O2 \); \( c \) is the rest term. These authors calculated the relative sensitivity, \( a^* \), which equals the ratio of the slopes of the autoregulation curve (a) and of the pressure-flow curve at maximal dilation. They reported values for \( a^* \) between 0.041 and 0.202. Our simulations are at constant \( MV_O2 \), and therefore \( a^* \) can be directly calculated from the slopes of the autoregulation curve and the fully dilated pressure-flow curve. These slopes, determined by linear regression between 60 and 120 mmHg, are shown in Table 2. Table 2 indicates that the pressure-flow lines with distal dominant and gradual resistance distribution and with the strong and diameter-dependent myogenic strength are within the range of the experimental found pressure-flow lines. When resistance is proximal and myogenic strength is diameter dependent, predicted autoregulation is too strong, whereas in the other combinations autoregulation is too weak. It should again be stressed that in in vivo studies, other control mechanisms are active as well, and therefore comparing quantitative results should be done with care.

Our model demonstrates flow reserve at pressures lower than actually found in experimental studies, where the dilated and the active pressure-flow lines start to diverge beyond 35 mmHg (21). However, coronary isolated vessel studies demonstrate myogenic tone at low pressures. This discrepancy could be due to either metabolic vasodilation at low perfusion pressure in the whole heart, vessel selection for isolated vessel studies, or alterations in vessel properties due to isolation or cannulation.

The current study demonstrates the difficulty of drawing conclusions with respect to myogenic tone and resistance distribution from coronary arterial pressure-flow lines. For example, for both the strong and the weak myogenic response, the pressure-flow line is independent of the resistance distribution (Fig. 6), notwithstanding quite large differences in the distribu-

<table>
<thead>
<tr>
<th>Resistance Distribution</th>
<th>Weak</th>
<th>Strong</th>
<th>Diameter Dependent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal dominant</td>
<td>0.33</td>
<td>0.045</td>
<td>0.095</td>
</tr>
<tr>
<td>Gradual distribution</td>
<td>0.33</td>
<td>0.043</td>
<td>0.125</td>
</tr>
<tr>
<td>Proximal dominant</td>
<td>0.33</td>
<td>0.023</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Values indicated with ‘+’ are too high, with ‘−’ too low, and with ‘&’ reasonable, compared with data of Vergroesen et al. (28).

Fig. 11. Diameter variation induced by maximal vasodilation and pressure steps. A: diameter variation induced by maximal vasodilation, with data of Chilian and Layne (2) (○) obtained in anesthetized open-chest dogs by intracoronary infusion of adenosine while perfusion pressure was kept constant at ~96 mmHg. Solid symbols show the simulated results for the different combinations in resistance distribution and myogenic strength. Relative diameter change from myogenic constriction to maximal dilation, [d_{\text{pas}}(90) - d_{\text{act}}(90)]/d_{\text{act}}(90), was calculated at a constant perfusion pressure of 90 mmHg. d_{\text{pas}}(90) values are the passive diameters for each compartment according to Eq. 4, with P_{in,1} = 90 mmHg; d_{\text{act}}(90) values are the active diameters for each compartment according to Eq. 5, with P_{in,1} = 90 mmHg. In B, open symbols are relative diameter changes measured by Chilian and Layne (2) (○) and Kanatsuka et al. (12) (△) in anesthetized open-chest dogs after reductions in perfusion pressure from approximately 90 mmHg to 30 mmHg. [d_{\text{act}}(40) - d_{\text{act}}(90)]/d_{\text{act}}(90). Solid symbols show the results of simulating this pressure step for the different combinations in resistance distribution and myogenic strength.
suka et al. (11) infused adenosine intravenously, and the pressure caused full dilation, is also shown in Fig. 11A. The percentage dilation predicted with the three resistance distributions and diameter-dependent myogenic tone was a factor of 3 in the experiments and was a factor of 4 for our prediction applying the gradual resistance distribution. For a given flow demand, the distributed myogenic response is consistent with both experimentally found diameter changes and the course of the pressure-flow line. Hence, the myogenic response is sufficient to explain autoregulation, notwithstanding the fact that other control mechanisms have their own role in flow control. Therefore, the myogenic response obscures the in vivo study of other mechanisms mediating autoregulation by its potential for flow control. This study emphasizes the importance of knowledge of the distribution of resistance and control mechanisms when studying vessels in the coronary tree.

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