Lasting Improvement of Renovascular Hypertension by Transluminal Dilatation of Atherosclerotic and Nonatherosclerotic Renal Artery Stenoses

A Follow-up Study

FELIX MAHLER, M.D., PETER PROBST, M.D., MICHAEL HAERTEL, M.D., PETER WEIDMANN, M.D., AND ALEX KRNETA, M.D.

SUMMARY Sixteen consecutive patients with renovascular hypertension were treated by transluminal dilatation and observed during 6–39 months (mean 21.8 months). Poststenotic renal artery pressure increased ($p < 0.001$) and the renal arteries were patent on angiograms taken immediately after dilatation. In 13 patients, angiography was repeated 2–9 months later; at that time the selective renal vein renin ratio had decreased ($p < 0.001$). At the end of the follow-up, blood pressure was improved or normal in 14 cases. One of the eight patients with atherosclerosis was normotensive without treatment, compared with five of six patients with fibromuscular dysplasia ($p < 0.05$). The results in two cases with vasculitis are uncertain. The four patients with relapses, one after intimal catheter dissection, were treated successfully by redilatation. Thus, renovascular hypertension can be improved by transluminal dilatation in patients with atherosclerosis and in patients with fibromuscular dysplasia with lasting success and a low morbidity rate.

THE APPLICATION of percutaneous transluminal dilatation in patients with renovascular hypertension is the most recent use for this method, which was initially used in peripheral and then in coronary arteries.\(^1\)\(^-\)\(^4\) Although the initial results and the data from short-term follow-up studies are encouraging,\(^2\)\(^,\)\(^3\)\(^,\)\(^6\)\(^-\)\(^8\) the beneficial effects should be shown to be persistent before propagating the method further. We report our experience in 16 consecutive cases, including patients with atherosclerosis, fibromuscular dysplasia (FMD) and vasculitis, observed for 6–39 months.

Patients and Methods

Patient Evaluation

Nineteen stenosed renal arteries were treated by transluminal dilatation in a group of 16 consecutive patients (table 1). Eight patients had renal artery stenosis regarded by radiologic criteria\(^16\),\(^17\) as due to atherosclerosis; in one (patient 7), this was found in three renal arteries. Six other patients showed angiographic signs of FMD, in one case the intimal and in five the medial type of FMD. Systemic vasculitis was suspected in two patients: in one man because of multilocular vascular lesions, including bilateral renal artery stenoses, the histologic aspect of a popliteal artery biopsy and a high erythrocyte sedimentation rate, and in one woman because of progressive bilateral renal artery stenosis, associated with lupus erythematosus discoides. Only case 15, who had vasculitis, was treated systemically (prednisone 30 mg/day).

In all patients, renal vein renin was determined by radioimmunoassay.\(^18\) Selective renal vein blood samples were taken before and after dilatation after renin stimulation by daily ingestion of furosemide (120 mg) given 3 days before the examination. Beta-blocking drugs were discontinued for at least 2 weeks. Ischemic/contralateral kidney renin ratios ranged from 1.56–3.35 before dilatation. The patients were examined before and immediately after dilatation and every 3 months thereafter. In 13 patients, renal arteriography and selective renal vein renin determinations were repeated 2–9 months after dilatation. In patients 3, 4 and 14, no late follow-up angiograms were performed. The patients were classified as either cured, when they were normotensive (150/90 mm Hg or less) without antihypertensive treatment, or as improved, when systolic and diastolic pressures were at least 15% lower than control or in the normal range while under constant or reduced antihypertensive therapy.\(^7\),\(^14\),\(^17\),\(^19\)

The follow-up blood pressures were compared with control values by using a paired \(t\) test after a one-way analysis of variance; renin ratio and renal artery pressure were compared by using a paired \(t\) test, and the cure rates by applying a chi-square test in a 3 \(\times\) 2 contingency table.

Transluminal Dilatation

We used a coaxial catheter system\(^2\)\(^-\)\(^4\),\(^16\) inserted percutaneously through the femoral or, in one instance, through the axillary artery. In 15 patients the intervention was done under local and in one under general anesthesia. The system consists of a curved catheter (2.7-mm o.d.), guiding an insertable dilatation catheter to the orifice of the renal artery. The dilatation catheter carries a preshaped, inelastic balloon segment (5-mm diameter in inflated state, 12 mm long) approximately 10 mm from the tip, that can be inflated through one of the two lumens with a pressure of 5–6 atm (500–600 kPa). Through the other lumen

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TABLE 1. Patient Description and Clinical Results Before and After Transluminal Dilatation of Renal Artery Stenoses

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Type of lesion</th>
<th>Follow-up (months)</th>
<th>Data before dilatation</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial dilat.</td>
<td>Repeat dilat.</td>
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<tr>
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<td>1</td>
<td>46</td>
<td>M</td>
<td>AS-L</td>
<td>33</td>
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<tr>
<td></td>
<td>2</td>
<td>49</td>
<td>F</td>
<td>AS-L</td>
<td>31</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>3</td>
<td>59</td>
<td>F</td>
<td>AS-L</td>
<td>24</td>
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<tr>
<td></td>
<td>4</td>
<td>57</td>
<td>M</td>
<td>AS-L</td>
<td>24</td>
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<tr>
<td></td>
<td>5</td>
<td>46</td>
<td>M</td>
<td>AS-L</td>
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<tr>
<td></td>
<td>6*</td>
<td>64</td>
<td>F</td>
<td>AS-R</td>
<td>24</td>
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<tr>
<td></td>
<td>7</td>
<td>39</td>
<td>M</td>
<td>AS-2R + L</td>
<td>24</td>
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<tr>
<td></td>
<td>8</td>
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<td>M</td>
<td>AS-R</td>
<td>9</td>
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Average 51 ± SD ± 8

Fibromuscular dysplasia

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<th>Age (years)</th>
<th>Sex</th>
<th>Type of lesion</th>
<th>Follow-up (months)</th>
<th>Data before dilatation</th>
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<td>Repeat dilat.</td>
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<tr>
<td>9</td>
<td>50</td>
<td>F</td>
<td>FMD-L</td>
<td>39</td>
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<td>10</td>
<td>34</td>
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<td>FMD-L</td>
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<td>11*</td>
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<td>FMD-L</td>
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<td>12</td>
<td>34</td>
<td>M</td>
<td>FMD-R</td>
<td>18</td>
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<tr>
<td>13*</td>
<td>25</td>
<td>M</td>
<td>FMD-L + R</td>
<td>12</td>
<td>0.9</td>
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<tr>
<td>14</td>
<td>36</td>
<td>F</td>
<td>FMD-R</td>
<td>6</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6R,1L</td>
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Average 34† ± SD ± 9

Vasculitis

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<th>Age (years)</th>
<th>Sex</th>
<th>Type of lesion</th>
<th>Follow-up (months)</th>
<th>Data before dilatation</th>
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<td></td>
<td></td>
<td>Initial dilat.</td>
<td>Repeat dilat.</td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>M</td>
<td>Vasc-R + L</td>
<td>27</td>
<td>1.0</td>
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<tr>
<td>16*</td>
<td>41</td>
<td>F</td>
<td>Vasc-R + L</td>
<td>15</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6R,2L</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Patients with repeat dilatations.
†Significantly different from the group with AS (p < 0.01).
‡Significantly different from the group with AS (p < 0.05).
Abbreviations: AS = atherosclerosis; FMD = fibromuscular dysplasia; L = left; R = right; Dilat. = transluminal dilatation; Creat. = serum creatinine; BP = blood pressure.

of the dilatation catheter, either contrast material may be injected to ascertain the correct position of the catheter tip or blood pressure in the poststenotic renal artery may be measured before and after dilatation. To perform the dilatation, the balloon segment of the catheter is placed under fluoroscopic control at the site of the stenosis. The balloon is inflated for approximately 5 seconds under manometric control by hand or with a pressure pump with diluted contrast media. After the first or repeated inflation, blood pressure measurements distal to the stenosis were made through the terminal orifice. In most instances, a sep-
The contralateral femoral artery for simultaneous measurement of aortic pressure during dilatation and for renal angiograms immediately after withdrawal of the dilatation system. In the patient with three stenosed renal arteries and in the one with bilateral stenosis, two sessions were needed for dilatation.

The patients were dismissed from the hospital an average of 4 days after the procedure. During the time of the intervention and for the next few hours, the renalovascular surgeon was available for emergency intervention in case of bleeding or imminent loss of kidney function. Five thousand units of heparin were injected during the procedure; subsequently, oral anticoagulants were given to five patients and salicylates (1.0 g/day) to nine others for 3 months or longer.

### Results

Table 1 is a summary of the clinical results after a mean follow-up time of 21.8 months for patients with atherosclerotic and nonatherosclerotic renal artery stenosis.

#### Renal Artery Changes

Figures 1A and B are angiograms from a patient with renal artery stenosis caused by atherosclerosis. Figures 1C and D show a renal artery stenosis due to FMD (medial type) before and after dilatation. The dilatory effect in each of the 16 stenosed renal arteries in the 13 patients was confirmed angiographically immediately after the procedure. Every patient had an increased poststenotic renal artery pressure after balloon segment deflation under constant aortic pressure conditions (fig. 2).

#### Blood Pressure

Blood pressure dropped within the first few hours after dilatation in every patient. Mean and individual values of blood pressure and the number of antihypertensive substances before and after dilatation are shown in figure 3. At dismissal from the hospital (first month), systolic pressure had decreased from an average of 190 ± 20 to 143 ± 9 mm Hg, and diastolic pressure from 109 ± 12 to 89 ± 8 mm Hg (both p < 0.001). Average blood pressure did not change significantly during the follow-up period. In 12 patients, the number of antihypertensive agents was reduced by transluminal dilatation (p < 0.001). In four patients, blood pressure increased between the third and ninth month of the follow-up. All of them were redilated successfully. Table 1 shows the detailed data and the final classification of the therapeutic result.

At the end of the follow-up, hypertension was considered as cured in only one of eight patients with atherosclerosis, compared with five of six patients with FMD. This difference is statistically significant (p < 0.05). Hypertension in the remaining patients was classified as improved according to the criteria described above except for four cases. Two are patients with atherosclerosis in whom the clinical results are regarded as uncertain, because in both the antihypertensive therapy had to be changed to stabilize blood pressure. Also, two patients with vasculitis had uncertain results; one was being treated with steroids in addition to antihypertensives and the other was redilated recently because of restenoses.

#### Renal Function

Figure 4 shows the renal vein renin ratio before dilatation. It exceeded the normal limit of 1.50a in every one of the 16 cases. Follow-up renin determina-

### Table 1

<table>
<thead>
<tr>
<th>Creat. (mg/dl)</th>
<th>BP (mm Hg)</th>
<th>Treatment (mg)</th>
<th>Clinical results</th>
</tr>
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<tr>
<td>1.1</td>
<td>140/85</td>
<td>Atenolol 100</td>
<td>Improved</td>
</tr>
<tr>
<td>1.3</td>
<td>140/85</td>
<td>Benzthiazide 50</td>
<td>Improved</td>
</tr>
<tr>
<td>3.8</td>
<td>150/90</td>
<td>Furosemide 120</td>
<td>Improved</td>
</tr>
<tr>
<td>1.6</td>
<td>170/90</td>
<td>Furosemide 80</td>
<td>Uncertain</td>
</tr>
<tr>
<td>1.3</td>
<td>140/80</td>
<td>None</td>
<td>Cured</td>
</tr>
<tr>
<td>1.1</td>
<td>160/80</td>
<td>Oxprenolol 160</td>
<td>Improved</td>
</tr>
<tr>
<td>1.1</td>
<td>160/90</td>
<td>Captopril 150</td>
<td>Uncertain</td>
</tr>
<tr>
<td>1.3</td>
<td>145/100</td>
<td>None</td>
<td>Improved</td>
</tr>
<tr>
<td>1.6</td>
<td>146/89</td>
<td>None</td>
<td>Cure rate 1:7</td>
</tr>
<tr>
<td>0.9</td>
<td>135/80</td>
<td>None</td>
<td>Cured</td>
</tr>
<tr>
<td>0.7</td>
<td>130/80</td>
<td>None</td>
<td>Cured</td>
</tr>
<tr>
<td>1.3</td>
<td>150/90</td>
<td>None</td>
<td>Cured</td>
</tr>
<tr>
<td>1.1</td>
<td>125/90</td>
<td>None</td>
<td>Cured</td>
</tr>
<tr>
<td>0.9</td>
<td>140/90</td>
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<td>140/90</td>
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<td>Cured</td>
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<td>1.0</td>
<td>138/89</td>
<td>Benzthiazide 50</td>
<td>Uncertain</td>
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<tr>
<td>0.9</td>
<td>180/90</td>
<td>Oxprenolol 240</td>
<td>Unimproved</td>
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<tr>
<td>0.9</td>
<td>180/110</td>
<td>Chlorothalidone 100</td>
<td>Unimproved</td>
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</table>

tion was done in 13 patients an average of 4.5 months after dilatation. Only the three patients in whom a relapse was suspected on the angiographic and clinical findings had an elevated value. In patients 4 and 8, in whom renin determinations were done 30–60 minutes after dilatation, the values were normalized. The creatinine values before dilatation had not changed significantly on the average 1 or 6 months after dilata-

![Angiogram of a patient with atherosclerotic stenosis before dilatation.](image)

![Smooth vessel walls and regression of poststenotic dilatation 8 months later (arrows).](image)

![Left-sided stenosis in a patient with fibromuscular dysplasia before dilatation.](image)

![Patent left renal artery 9 months after dilatation. Arrow indicates intimal tears.](image)

**Figure 1.** (A) Angiogram of a patient with atherosclerotic stenosis before dilatation. (B) Smooth vessel walls and regression of poststenotic dilatation 8 months later (arrows). (C) Left-sided stenosis in a patient with fibromuscular dysplasia before dilatation. (D) Patent left renal artery 9 months after dilatation. Arrow indicates intimal tears.
tion. No signs of renal infarction were noted on post-
dilatation angiograms or in the urine analysis.

Redilatations and Complications

Four patients needed repeat dilatation (table 1). In
patient 6, who required redilatation, an intimal dissec-
tion was made accidentally during the first dilatation.
Although no immediate adverse reaction ensued, a
severe stenosis at the site of the dissection developed
during the next 9 months associated with progressive
hypertension. Dilatation was repeated, and blood
pressure and renin ratio were reduced. The only com-
pliation that required surgery was a retroperitoneal
hemorrhage from the femoral puncture site in one
patient.

Other redilatations were done in two patients with
FMD (nos. 11 and 13) because of circumscribed new
stenoses in the dilated and in the contralateral arteries.
Increased blood pressure and renal vein renin ratio
were normalized after redilatation in both patients
with FMD. In the fourth patient (no. 16), the recur-
cent hypertension and renin ratio elevation was inter-
preted as due to a progression of his arteritis in the
dilated as well as in the contralateral renal artery. This
case responded to repeated dilatations of the reoc-
cluded and the contralateral artery recently per-
formed.

Discussion

Extended experience with surgery in patients with
renovascular hypertension has been acquired. Al-
though the results in some studies are remarkably
good, nephrectomies and reoperations are not infre-
fquent, and mortality ranges from 1–9%.13–23 It is too
early to compare the results of transluminal dilata-
tion conclusively, but similar prognostic conclusions
emerge for dilatation as for surgery. Patients with
atherosclerosis and those with FMD may profit from
dilatation.

The patients with FMD in our study have a signifi-
cantly better chance of being improved or cured com-
pared with the patients with atherosclerosis, perhaps
because they are younger and do not have generalized
vascular disease (table 1). Such patients appear to
have a more favorable prognosis after either inter-
vention — dilatation or surgery.13–23

The fact that both stenosed arteries and those with
FMD are amenable to transluminal dilatation is not
surprising; peripheral lesions in renal arteries have
been treated for several years by surgical graduated
renal artery dissection in the relapsing patient was managed by repeated dilatation. However, other complications, such as acute thrombosis, perforation and hemorrhage, could necessitate emergency surgical interventions.\textsuperscript{14, 15} Transluminal dilatation merits further study to obtain sufficient follow-up data for comparison with surgical series. Given comparable results, at least in some subgroups, transluminal dilatation appears to be the first step in the therapy program because it is much less invasive and less costly than surgery. In case of failure of transluminal dilatation, surgery should not be precluded as a secondary procedure.\textsuperscript{13}

**Addendum**

Since the submission of this paper, each of the 16 patients has had one more control examination, increasing the mean follow-up time to 28.5 months (range 12–47 months). The clinical results as classified in table 1 are unchanged except in patient 13 with fibromuscular dysplasia, whose outcome has improved.

**References**


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**Figure 4.** Selective renal vein renin ratio in 16 patients before and in 15 patients after transluminal dilatation. In 13 patients examined 2–9 months after dilatation, the average ratio dropped from 2.14 ± 0.45 to 1.24 ± 0.20 (p < 0.001). The three cases with values above the normal range (cross-hatched area) after dilatation were hypertensive. The open circles are renin ratios obtained 30–60 minutes after dilatation in two patients. Internal dilatation.\textsuperscript{19, 34} The outcome in the two patients with vasculitis in our series was uncertain.

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The marked increase of the reduced poststenotic pressure indicates acute hemodynamic improvement of significant arterial obstructions by transluminal dilatation. Reduction of the increased selective renal vein renin ratio at the time of the control angiogram in 13 patients demonstrates that the initial hemodynamic improvement persisted. The three cases with improved, but still elevated, renin ratios after dilatation had recurrent hypertension as well as renal artery obstruction. Thus, renin ratio corresponded very well to the clinical findings. On the other hand, it may be assumed that a normalized renin ratio corresponded to persistent renal artery patency in the patients examined clinically beyond the time of the follow-up angiography and renin determination.

In our study and in other reports,\textsuperscript{7, 14, 15} patients with recurrence responded well to second dilatations. However, transluminal renal artery dilatation should not be done without the back-up of a vascular surgeon because of possible complications. The acute
Pulsus Alternans Determined by Biventricular Simultaneous Systolic Time Intervals

YOSHIYUKI HADA, M.D., CARLA WOLFE, AND ERNEST CRAIGE, M.D.

SUMMARY This investigation was performed to determine the presence of unilateral or bilateral pulsus alternans in the systemic and pulmonary circulations in heart failure and to estimate the prevalence of pulsus alternans in congestive cardiomyopathy. The subjects were 36 adult patients in heart failure due to a variety of cardiopulmonary diseases. We measured left- and right-sided systolic time intervals from simultaneous dual echocardiograms of both semilunar valves. The alternans was left-sided in seven patients, right-sided in one patient and bilateral in six patients. Pulsus alternans was induced by ventricular premature complexes (VPCs), except in one patient with bilateral and persistent alternans. For a VPC to precipitate alternans, the early beat itself must be associated with an abbreviated ejection time.

Echophonocardiographic records of 100 patients with congestive cardiomyopathy were reviewed for evidence of pulsus alternans. We found persistent alternans in 10 patients and VPC-induced alternans in seven patients. We could not measure any difference in severity of disease in patients with pulsus alternans compared with those without.

PULSUS ALTERNANS was first described by Traube more than a century ago. Although hemodynamic studies have been made in humans and efforts to reproduce the condition have been undertaken, its physiologic mechanism is uncertain; nor has its incidence been determined in the deteriorated forms of heart disease in which it is considered to be a useful diagnostic sign. Pulsus alternans is ordinarily recognized from the carotid and peripheral pulse or blood pressure, but hemodynamic studies have revealed its presence in the pulmonary circulation as well.

Echocardiography provides a means of observing intracardiac structures continuously and noninvasively. The presence of pulsus alternans can thus be determined by timing semilunar valve movements. This method can be applied to both right- and left-sided events. Right-sided pulsus alternans may be observed by other noninvasive methods, such as external registration of pulmonary arterial pulsations, but this method is impractical.

The only reliable method available for determining bilateral alternation has been the simultaneous recording of pressures or flow velocity from the systemic and pulmonary circulations. These invasive methods are unsuitable for observations under physiologic conditions or for repeated observations in the same patient. The development in our laboratory of dual echocardiography, permitting the registration of M-mode echograms from two intracardiac structures, has lowered recording both semilunar valves simultaneously. This method is ideal for determining the presence of symmetrical or asymmetrical pulsus alternans.

Pulsus alternans is a characteristic feature of severe ventricular dysfunction, but its incidence is unknown. Using the computerized recording and retrieval system that has been used in our laboratory for 7 years, we can identify and study the records of a large number of patients with congestive cardiomyopathy and determine the prevalence of pulsus alternans.

Materials and Methods

Definition

Pulsus alternans is a beat-to-beat alternation of strong and weak contractions without significant
Lasting improvement of renovascular hypertension by transluminal dilatation of atherosclerotic and nonatherosclerotic renal artery stenoses. A follow-up study.
F Mahler, P Probst, M Haertel, P Weidmann and A Krneta

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