### MEDLINE 1966-August Week 4 2005

<table>
<thead>
<tr>
<th>#</th>
<th>Search History</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>exp Hypertension, Renal/</td>
<td>15140</td>
</tr>
<tr>
<td>2</td>
<td>exp Renal Artery Obstruction/</td>
<td>7388</td>
</tr>
<tr>
<td>3</td>
<td>renal arter$ stenosis.tw.</td>
<td>3264</td>
</tr>
<tr>
<td>4</td>
<td>renal arter$ dis$.tw.</td>
<td>390</td>
</tr>
<tr>
<td>5</td>
<td>renovascular dis$.tw.</td>
<td>613</td>
</tr>
<tr>
<td>6</td>
<td>reno vascular dis$.tw.</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>renal vascular dis$.tw.</td>
<td>156</td>
</tr>
<tr>
<td>8</td>
<td>(arvd or &quot;atherosclerotic renovascular dis$&quot;).tw.</td>
<td>302</td>
</tr>
<tr>
<td>9</td>
<td>renal steno$.tw.</td>
<td>49</td>
</tr>
<tr>
<td>10</td>
<td>steno$ kidney.tw.</td>
<td>137</td>
</tr>
<tr>
<td>11</td>
<td>renovascular steno$.tw.</td>
<td>27</td>
</tr>
<tr>
<td>12</td>
<td>or/1-11</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>limit 12 to humans</td>
<td>20249</td>
</tr>
<tr>
<td>14</td>
<td>limit 13 to english language</td>
<td>10148</td>
</tr>
<tr>
<td></td>
<td>limit 14 to (addresses or bibliography or biography or case reports or congresses or consensus development conference or consensus development conference, nih or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education handout or periodical index or &quot;review of reported cases&quot;)</td>
<td>2736</td>
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<tr>
<td>16</td>
<td>14 not 15</td>
<td>7412</td>
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<tr>
<td>17</td>
<td>limit 16 to &quot;all adult (19 plus years)&quot;</td>
<td>4222</td>
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<td>18</td>
<td>16 not 17</td>
<td>3190</td>
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<td>19</td>
<td>limit 18 to &quot;all child (0 to 18 years)&quot;</td>
<td>488</td>
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<tr>
<td>20</td>
<td>16 not 19</td>
<td>6924</td>
</tr>
<tr>
<td>21</td>
<td>limit 20 to (guideline or practice guideline or &quot;review&quot; or review, academic or &quot;review literature&quot; or review, multicase or review, tutorial)</td>
<td>1316</td>
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<tr>
<td>22</td>
<td>limit 20 to meta analysis</td>
<td>8</td>
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<tr>
<td>23</td>
<td>20 not (21 or 22)</td>
<td>5601</td>
</tr>
<tr>
<td>24</td>
<td>follow-up studies/</td>
<td>303611</td>
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<tr>
<td>25</td>
<td>(follow-up or followup).tw.</td>
<td>332435</td>
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<tr>
<td>26</td>
<td>exp Case-Control Studies/</td>
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<td>(case adj20 control).tw.</td>
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<td>28</td>
<td>exp Longitudinal Studies/</td>
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<td>longitudinal.tw.</td>
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<td>30</td>
<td>exp Cohort Studies/</td>
<td>536922</td>
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<td>31</td>
<td>cohort.tw.</td>
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<td>32</td>
<td>(random$ or rct).tw.</td>
<td>315873</td>
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<tr>
<td>33</td>
<td>exp Randomized Controlled Trials/</td>
<td>38577</td>
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## Appendix A. Search Strategy (continued)

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<th>#</th>
<th>Search History</th>
<th>Results</th>
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<tr>
<td>34</td>
<td>exp random allocation/</td>
<td>53586</td>
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<tr>
<td>35</td>
<td>exp Double-Blind Method/</td>
<td>82631</td>
</tr>
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<td>36</td>
<td>exp Single-Blind Method/</td>
<td>9171</td>
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<td>37</td>
<td>randomized controlled trial.pt.</td>
<td>204593</td>
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<td>38</td>
<td>clinical trial.pt.</td>
<td>412355</td>
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<tr>
<td>39</td>
<td>controlled clinical trials/</td>
<td>2929</td>
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<tr>
<td>40</td>
<td>(clin$ adj trial$).tw.</td>
<td>88180</td>
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<tr>
<td>41</td>
<td>((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.</td>
<td>79196</td>
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<tr>
<td>42</td>
<td>exp PLACEBOS/</td>
<td>23902</td>
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<td>43</td>
<td>placebo$.tw.</td>
<td>90025</td>
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<tr>
<td>44</td>
<td>exp Research Design/</td>
<td>194218</td>
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<tr>
<td>45</td>
<td>exp Evaluation Studies/</td>
<td>529271</td>
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<tr>
<td>46</td>
<td>exp Prospective Studies/</td>
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<td>47</td>
<td>exp Comparative Study/</td>
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<td>48</td>
<td>or/24-47</td>
<td>2748065</td>
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<tr>
<td>49</td>
<td>23 and 48</td>
<td>2167</td>
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## Sample Data Extraction Form

<table>
<thead>
<tr>
<th>Author (first)</th>
<th>Year</th>
<th>Identifier</th>
<th>Interventions</th>
<th>Modifier topics</th>
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</thead>
<tbody>
<tr>
<td>Medline UI:</td>
<td></td>
<td></td>
<td>Angioplasty vs Medical</td>
<td>Pre-intervention predictors of outcome (Q2)</td>
</tr>
<tr>
<td>Ref ID:</td>
<td></td>
<td></td>
<td>Angioplasty only</td>
<td>Treatment variable predictors of outcome (Q3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medical treatment only</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Natural history only</td>
<td></td>
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</table>

### Study Design

<table>
<thead>
<tr>
<th>Intervention Dates:</th>
<th>Follow-up dates</th>
</tr>
</thead>
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<tr>
<td>Randomized controlled trial</td>
<td>Follow-up times</td>
</tr>
<tr>
<td>Non-randomized comparative trial</td>
<td></td>
</tr>
<tr>
<td>Prospective cohort (pre-post, single arm)</td>
<td></td>
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<tr>
<td>Retrospective cohort</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Per patient analysis?</th>
<th>Both?</th>
<th>Setting / Country:</th>
<th>Mean Follow-up</th>
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<tbody>
<tr>
<td>Per Kidney analysis?</td>
<td></td>
<td>Funding:</td>
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### Inclusion criteria

<table>
<thead>
<tr>
<th>Definition of RAS:</th>
<th>Exclusion criteria</th>
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<table>
<thead>
<tr>
<th>Other:</th>
<th>Comments:</th>
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| Were eligibility criteria the same for all arms? (Describe differences) | |

| Comments: | |

### Description of ANGIOPLASTY Intervention

<table>
<thead>
<tr>
<th>Stent type:</th>
<th>BP Goal:</th>
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<tr>
<td>Distal protection device:</td>
<td>Drug</td>
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<tr>
<td>Other adjunct technique:</td>
<td>Dose</td>
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<tr>
<td>Peri-procedural Rx:</td>
<td></td>
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<tr>
<td>Other information:</td>
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| Comments: | |

### Outcomes

<table>
<thead>
<tr>
<th>Incl?</th>
<th>Definitions</th>
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<tbody>
<tr>
<td>Survival / Mortality</td>
<td></td>
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<tr>
<td>Acute / Flash pulmonary edema</td>
<td></td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td></td>
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<tr>
<td>Other CVD outcomes:</td>
<td></td>
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<tr>
<td>Kidney function/structure:</td>
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</table>

B-1
### Blood pressure control:

<table>
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<tr>
<th>Adverse events</th>
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### Comments:

<table>
<thead>
<tr>
<th>Comments:</th>
</tr>
</thead>
</table>

### Cofactors / Predictors

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<tr>
<th>Incl?</th>
<th>Definitions</th>
<th>Threshold</th>
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<tr>
<td>Imaging test:</td>
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<td>Laboratory test:</td>
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<td>Clinical exam test:</td>
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<td>Demographics:</td>
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<td>Concurrent diseases:</td>
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<tr>
<td>Anatomic characteristic:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stenosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral stenoses / solitary kidney stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peri-procedural Rx:</td>
<td></td>
<td></td>
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<tr>
<td>Type of stent:</td>
<td></td>
<td></td>
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<tr>
<td>Distal protection device:</td>
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<td>ARAS etiology:</td>
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<tr>
<td>Predominant clinical presentation:</td>
<td></td>
<td></td>
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<td>Blood pressure:</td>
<td></td>
<td></td>
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<tr>
<td>Other:</td>
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</table>

### Quality Assessment for RCTs

<table>
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<tr>
<th>Allocation concealment?</th>
<th>Other:</th>
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<tbody>
<tr>
<td>Blinding:</td>
<td></td>
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<tr>
<td>Intention-to-treat?</td>
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</table>

### Quality Assessment for non-randomized and cohort studies:

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<th>Comments:</th>
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</table>

### Characteristics of Enrolled Patients at Baseline

<table>
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<tr>
<th>Race:</th>
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<tbody>
<tr>
<td>Mean Age:</td>
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<td>% Male:</td>
</tr>
<tr>
<td>Mean BP</td>
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<tr>
<td>% Stenosis:</td>
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<tr>
<td>% Bilateral stenosis:</td>
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<tr>
<td>Mean GFR/CrCl/SCr:</td>
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<td>CVD:</td>
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<td>Other kidney:</td>
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<table>
<thead>
<tr>
<th>Duration of HTN:</th>
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</thead>
<tbody>
<tr>
<td>Other kidney:</td>
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</tbody>
</table>

B-2
Appendix B. Sample Data Extraction Form (continued)

Medical management at baseline:

Other:

Comments:

Sub-Groups Enrolled & Analyzed

<table>
<thead>
<tr>
<th>N enrolled with RAS (total):</th>
<th>with ARAS:</th>
<th>ARAS analyzed separately (if mixed population)?</th>
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</thead>
<tbody>
<tr>
<td>N analyzed with RAS (total):</td>
<td>with ARAS:</td>
<td></td>
</tr>
<tr>
<td>N analyzed who had angioplasty (total):</td>
<td>plasty+stent:</td>
<td>Stent analyzed separately (if mixed interventions)?</td>
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</table>

Other mixtures of populations:

Comments:

Disposition of Patients (Arteries if nd on patients)

**ANGIOPLASTY**

<table>
<thead>
<tr>
<th>N enrolled:</th>
<th>N had Plasty:</th>
<th>N successful Plasty</th>
</tr>
</thead>
</table>

Other details re: patients:

<table>
<thead>
<tr>
<th>N complete follow-up:</th>
<th>Dropout %:</th>
<th>Dropout reasons:</th>
</tr>
</thead>
</table>

Mean duration follow-up: Duration range:

**MEDICAL TREATMENT**

<table>
<thead>
<tr>
<th>N enrolled:</th>
<th>N received Rx:</th>
</tr>
</thead>
</table>

Other details re: patients:

<table>
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<tr>
<th>N complete follow-up:</th>
<th>Dropout %:</th>
<th>Dropout reasons:</th>
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Mean duration follow-up: Duration range:

Comments:

(Copy a Separate table for each outcome-duration combination)

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<th>Outcome:</th>
<th>Time of follow-up:</th>
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<tr>
<td></td>
<td>ANGIOPLASTY</td>
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<tr>
<td></td>
<td>N Value (or n)</td>
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<tr>
<td>Baseline value</td>
<td></td>
</tr>
<tr>
<td>Final value</td>
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<tr>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>P Difference</td>
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</table>

B-3
Appendix B. Sample Data Extraction Form (continued)

<table>
<thead>
<tr>
<th>Net Difference</th>
<th>P Net difference</th>
<th>(RR/OR/HR)</th>
<th>P (RR/OR/HR)</th>
<th>Comments:</th>
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</thead>
</table>

FOR ANALYSES OF PREDICTORS OF OUTCOMES:

IF GROUPS DIVIDED BY PREDICTORS (eg, Low GFR v High GFR) INCLUDE DETAILED RESULTS BELOW:
- **Univariate:**
- **Multivariate:**

IF GROUPS DIVIDED BY OUTCOMES (eg, Dead v Alive) INCLUDE LIST OF SIGNIFICANT ASSOCIATIONS ONLY BELOW:
- **Univariate:**
- **Multivariate:**

Adverse Events

Comments:

<table>
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<tr>
<th>Quality: (A/B/C)</th>
<th>Comments:</th>
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<tr>
<td>Applicability:</td>
<td>Comments:</td>
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<td>(Low/Medium/High)</td>
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Other comments:
Appendix C. Excluded Studies

Excluded Studies


Pre-1993 (Surgery study)


N<100 (Surgery study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Prospective treatment vs retrospective control (Question 3)


N<30 (PTRA study)

Arlart IP. Digital subtraction angiography (DSA) in renal and renovascular hypertension: diagnostic value and application in follow-up studies after PTA. Uremia Invest 9(2):217-29. 1985

Pre-1993 (Surgery study)


N<100 (Surgery study)


Pre-1993 (Surgery study)


Post-failed PTRA


N<30 (PTRA study)


N<100 (Surgery study)

Prior publication of accepted study

Retrospective (PTRA study)

Retrospective (PTRA study)

Pre-1993 (Surgery study)

N<100 (Surgery study)
Bell GM, Reid J, Buist TA. Percutaneous transluminal angioplasty improves blood pressure and renal function in renovascular hypertension. Qjm 63(241):393-403. 1987

Retrospective (PTRA study)

N<100 (Surgery study)

>20% had previous plasty

Retrospective (PTRA) / N<100 (Surgery)

N<30 (PTRA study)

No intervention

Review

N<30 (PTRA study)

**Retrospective (PTRA study)**


**Post-failed PTRA**


**Exclusion population**


**N<30 (PTRA study)**


**Retrospective (PTRA study)**


**Pre-1993 (Surgery study)**


**N<100 (Surgery study)**


**Retrospective (PTRA study)**


**Pre-1993 (Surgery study)**


**No outcome of interest**


**Retrospective (PTRA) / N<100 (Surgery)**


**Pre-1993 (Surgery study)**
Appendix C. Excluded Studies (continued)


N<100 (Surgery study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Retrospective (PTRA study)


N<100 (Surgery study)

>50% had aortic reconstruction


No outcome of interest


N<30 (PTRA study)
Appendix C. Excluded Studies (continued)


Retrospective (PTRA study)


Pre-1993 (Surgery study)


N<100 (Surgery study)


Pre-1993 (Surgery study)


Retrospective (PTRA) / N<100 (Surgery)


N<100 (Surgery study)


Pre-1993 (Surgery study)


Retrospective (PTRA) / N<100 (Surgery)


N<30 (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)


N<30 (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)

**N<30 (PTRA study)**


**Pre-1993 (Surgery study)**


**Retrospective (PTRA study)**


**N<100 (Surgery study)**


**Retrospective (PTRA study)**


**Retrospective (PTRA study)**


**Pre-1993 (Surgery study)**


**N<100 (Surgery study)**


**N<30 (PTRA study)**


**N<30 (PTRA study)**


**Pre-1993 (Surgery study)**


**N<30 (PTRA study)**
Appendix C. Excluded Studies (continued)


N<100 (Surgery study)


Pre-1993 (Surgery study)

Geyskes GG, Puylaert CB, Oei HY, Mees EJ. Follow up study of 70 patients with renal artery stenosis treated by percutaneous transluminal dilatation. BMJ 287(6388):333-6. 1983

Retrospective (PTRA study)


N<100 (Surgery study)


Retrospective (PTRA study)


N<100 (Surgery study)


<50% with ARAS


N<10 (Medical study)


N<30 (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)


N<30 (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)


N<30 (PTRA study)


Retrospective (PTRA study)
Appendix C. Excluded Studies (continued)

N<100 (Surgery study)

N<100 (Surgery study)

Retrospective (PTRA study)

N<30 (PTRA study)

N<100 (Surgery study)

Pre-1993 (Surgery study)

N<100 (Surgery study)

N<100 (Surgery study)

N<100 (Surgery study)

Pre-1993 (Surgery study)

N<100 (Surgery study)

N<100 (Surgery study)

N<30 (PTRA study; accepted for medical cohort)
Appendix C. Excluded Studies (continued)


Retrospective (PTRA) / N<100 (Surgery)


N<100 (Surgery study)


N<30 (PTRA study)


N<30 (PTRA study)


N<30 (PTRA study)


N<30 (PTRA study)


Post-failed PTRA


N<30 (PTRA study)


<6 mo (nd AE)


<6 mo (nd AE)


Retrospective (PTRA study)


Retrospective (PTRA study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)

**N<30 (PTRA study)**


**Pre-1993 (Surgery study)**


**Retrospective (PTRA study)**


**Retrospective (PTRA study)**


**N<30 (PTRA study)**


**Retrospective (PTRA study)**


**N<30 (PTRA study)**


**Retrospective (PTRA study)**


**N<30 (PTRA study)**


**Pre-1993 (Surgery study)**


**N<100 (Surgery study)**


**Pre-1993 (Surgery study)**


**N<100 (Surgery study)**
Appendix C. Excluded Studies (continued)

Retrospective (PTRA study)

N<30 (PTRA study)

Retrospective (PTRA study)

Pre-1993 (Surgery study)

Retrospective (PTRA study)

Retrospective (PTRA study)

N<30 (PTRA study)

N<100 (Surgery study)

Retrospective (PTRA study)

N<100 (Surgery study)

Pre-1993 (Surgery study)

Retrospective (PTRA study)

Retrospective (PTRA study)

C-11
Appendix C. Excluded Studies (continued)


N<30 (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)


N<30 (PTRA study)


Exclusion population


Pre-1993 (Surgery study)


N<100 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Retrospective (PTRA study)


N<30 (PTRA study)


No outcome of interest


Retrospective (PTRA study)


Retrospective (PTRA study)
Appendix C. Excluded Studies (continued)


**Single dose**


**Retrospective (PTRA) / N<100 (Surgery)**


**N<30 (PTRA study)**


**N<30 (PTRA study)**


**Retrospective (PTRA study)**


**N<100 (Surgery study)**


**Retrospective (PTRA study)**


**Retrospective (PTRA study)**


**Retrospective (PTRA study)**


**Pre-1993 (Surgery study)**


**Retrospective (PTRA study)**


**Exclusion population**


**Single dose**
Appendix C. Excluded Studies (continued)

N<100 (Surgery study)

N<100 (Surgery study)

Retrospective (PTRA study)

N<100 (Surgery study)

No intervention

Retrospective (PTRA study)

Case Report

N<100 (Surgery study)

Retrospective (PTRA study)

N<30 (PTRA study)

N<30 (PTRA study)

N<100 (Surgery study)

N<30 (PTRA study)

Retrospective (PTRA study)
Appendix C. Excluded Studies (continued)

No outcome of interest

No intervention

Retrospective (PTRA study)

Retrospective (PTRA study)

Pre-1993 (Surgery study)

Retrospective (PTRA study)

Retrospective (PTRA study)

Complete occlusion

N<30 (PTRA study)


Exclusion population

No intervention

No intervention

Appendix C. Excluded Studies (continued)

**Retrospective (PTRA study)**

**N<100 (Surgery study)**

**Retrospective (PTRA study)**

**N<30 (PTRA study)**

**Retrospective (PTRA study)**

**Retrospective (PTRA study)**

**Retrospective (PTRA study)**

**N<100 (Surgery study)**

**N<30 (PTRA study)**

**Retrospective (PTRA study)**

**Single dose**

**Retrospective (PTRA study)**

**N<100 (Surgery study)**
Appendix C. Excluded Studies (continued)


Review


Retrospective (PTRA) / N<100 (Surgery)


Retrospective (PTRA study)


N<10 (Medical study)


Retrospective (PTRA study)


N<30 (PTRA study)


N<100 (Surgery study)


Exclusion population


Single dose


N<100 (Surgery study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)
Appendix C. Excluded Studies (continued)

**Retrospective (PTRA study)**

**N<30 (PTRA study)**

**Retrospective (PTRA study)**

**N<30 (PTRA study)**

**No outcome of interest**

**Exclusion population**

**Exclusion population**

**N<30 (PTRA study)**

**Pre-1993 (Surgery study)**

**Pre-1993 (Surgery study)**

**N<100 (Surgery study)**

**Retrospective (PTRA) / N<100 (Surgery)**

**Retrospective (PTRA study)**

**N<30 (PTRA study)**
Appendix C. Excluded Studies (continued)

N<30 (PTRA study)

Retrospective (PTRA study)

N<100 (Surgery study)

Retrospective (PTRA study)

Retrospective (PTRA study)

N<30 (PTRA study)

Pre-1993 (Surgery study)

Retrospective (PTRA) / N<100 (Surgery)

Retrospective (PTRA study)

Pre-1993 (Surgery study)

N<100 (Surgery study)

<6 mo (nd AE)
Appendix C. Excluded Studies (continued)


N<30 (PTRA study)


N<30 (PTRA study)


N<30 (PTRA study)


N<100 (Surgery study)


N<30 (PTRA study)


Retrospective (PTRA) / N<100 (Surgery)


Retrospective (PTRA study)


Retrospective (PTRA study)


N<30 (PTRA study)


Pre-1993 (Surgery study)


N<100 (Surgery study)


Retrospective (PTRA study)


N<100 (Surgery study)

Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


Pre-1993 (Surgery study)


N<100 (Surgery study)


N<100 (Surgery study)


N<100 (Surgery study)


N<30 (PTRA study)


No intervention
Appendix C. Excluded Studies (continued)

N<100 (Surgery study)

Retrospective (PTRA study)

N<100 (Surgery study)

N<30 (PTRA study)

Retrospective (PTRA) / N<100 (Surgery)

Pre-1993 (Surgery study)

Pre-1993 (Surgery study)

Pre-1993 (Surgery study)

N<30 (PTRA study)
Appendix C. Excluded Studies (continued)


N<100 (Surgery study)


Retrospective (PTRA) / N<100 (Surgery)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (PTRA study)


Retrospective (Medical) / N<100 (Surgery)


Retrospective (PTRA study)


Retrospective (PTRA study)


No outcome of interest


Pre-1993 (Surgery study)


Retrospective (PTRA study)
Appendix D. Peer Reviewers

Peer Reviewers

We gratefully acknowledge the following individuals who reviewed the initial draft of this Report and provided us with constructive feedback. Acknowledgments are made with the explicit statement that this does not constitute endorsement of the report by the peer reviewers.

- **Richard Paul Cambria, MD**  
  Professor of Surgery  
  Chief, Division of Vascular and Endovascular Surgery  
  Harvard Medical School  
  Boston, Massachusetts

- **John H. Rundback, MD**  
  Associate Professor of Clinical Radiology  
  College of Physicians and Surgeons of Columbia University  
  New York, New York

- **Richard Chapell, PhD**  
  Outcomes Research  
  Merck & Co., Inc.

- **Robert Safian, MD, FSCAI**  
  Peripheral Vascular Disease Committee  
  Society for Cardiovascular Angiography and Intervention  
  Bethesda, Maryland

- **Scott Gilbert, MD**  
  Assistant Professor of Medicine  
  Tufts University School of Medicine  
  Director, Kidney and Blood Pressure Center  
  Tufts-New England Medical Center  
  Boston, Massachusetts

- **Stephen C. Textor, M.D.**  
  Division of Nephrology  
  Department of Medicine  
  Mayo Clinic  
  Rochester, Minnesota

- **Linda Humphrey, MD, MPH**  
  Scientific Resource Center  
  Oregon Health and Science University  
  Portland, Oregon

- **Katherine R. Tuttle, MD**  
  Director of Research  
  The Heart Institute of Spokane  
  Spokane, Washington

- **Timothy Murphy, MD**  
  Professor, Diagnostic Imaging  
  Brown University School of Medicine  
  Medical Director, Vascular Disease Research Center  
  Rhode Island Hospital  
  Providence, Rhode Island

- **I. David Weiner, MD**  
  Professor of Medicine and Physiology  
  Division of Nephrology, Hypertension and Transplantation  
  University of Florida College of Medicine  
  Chief, Nephrology and Hypertension Section  
  Gainesville, Florida
### Appendix D. Peer Reviewers (continued)

<table>
<thead>
<tr>
<th>Kenneth Rosenfield, MD, FSCAI</th>
<th>R. Eugene Zierler, MD</th>
</tr>
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<td>Chair, Peripheral Vascular Disease Committee</td>
<td>Professor of Surgery</td>
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<tr>
<td>Claudia Ruiz-Zacharek, MD</td>
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<td>Susan J. Duval, PhD</td>
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<td>Division of Nephrology</td>
<td>Assistant Professor of Epidemiology</td>
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<td>Food and Drug Administration</td>
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Drs. Cambria, Gilbert, Rundback, Textor and Tuttle were also members of the EPC’s Technical Expert Panel.

Dr. Cambria served as the EPC technical expert consultant. As such his comments were provided on an ongoing basis.
### Detailed Mortality Figure

**Figure.** Cumulative percent mortality from 6 months to 10 years of followup.

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<th>MAP</th>
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<th>Years</th>
<th>Cumulative Mortality (%) 6 mo - 10 yr of Follow-up</th>
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Years of Followup

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* Excluded patients who died within first 6 months
† Markedly different eligibility criteria for angioplasty and medicine treatment cohorts. See summary table.

N, number of subjects; %Sten, mean percent renal artery stenosis or minimum threshold (indicated by “>”); %Bilat, percent subjects with bilateral renal artery stenosis; MAP, mean arterial pressure; GFR, mean glomerular filtration rate or creatinine clearance in mL/min (or serum creatinine in mg/dL if in brackets); Years, years of intervention (years indicated by “<” mean indicate that year not reported; intervention assumed to have occurred at some time at least one year prior to publication date); Qual, study quality (A, good; B, fair; C, poor); Appl, study applicability (L, low; M, moderate; H, high).

Percentages in brackets indicate that exact time of followup not reported; mean or median time of followup used.

Letters A-D indicate that these studies reported mortality rates for both medical treatment and an invasive intervention. The values of these studies are in larger type to increase ease of comparison.
Appendix F. Detailed Summary Table

## Detailed Summary Table

**Table. Summary of medical, angioplasty and surgical treatments**

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
</thead>
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<td><strong>Angioplasty (or Surgery) vs. Medical Treatment</strong></td>
<td>4 RCTs (1 a mix of medical treatment and delayed angioplasty)</td>
<td>3 RCTs</td>
<td>1 RCT (versus medical treatment)</td>
</tr>
<tr>
<td><strong>Population studied</strong></td>
<td>Medical treatment studies included patients with hypertension, mean blood pressure 172-180/103-106. One study included patients with &gt;50% stenosis, half of whom had bilateral disease. One included a population where 25% had bilateral disease, though the definition of RAS was unclear. The third study did not describe degree of stenosis or bilateral disease. In two studies the mean serum creatinine was 1.3 mg/dL. Patients had mean ages approximately in the mid-50s; however, all studies included patients in their 20s or younger. In all three studies either some patients did not have ARAS or this was not reported. All 3 studies were from the 1980s or earlier.</td>
<td>Patients with ARAS with HTN as the most frequent indication. Also included patients with CKD, CHF About 1/3 of studies included patients populations with &gt;50% stenosis, about 1/4 included only &gt;70% stenosis. Other thresholds were also used. Mostly populations with both uni- and bilateral disease, range of bilateral disease generally 25-50% of patients; some populations of unilateral or bilateral disease only. Comparative studies mostly had about 50% with ostial disease, when reported; cohort studies mostly with about 75% or more with ostial disease. Mean age generally about 65. Mean blood pressure generally in the range of 160-180/90-100. Mean serum creatinine generally in the range of 1.5-2.4 mg/dL, or mean GFR about 55 mL/min.</td>
<td>Patients with ARAS with HTN, CKD, or both HTN and CKD Populations had ≥60% to ≥80% stenosis Populations had unilateral and bilateral diseases; the range of bilateral disease was 40-60% Mean age was in the 60s Mean blood pressure was in the approximate range of 175-200/85-105 Mean serum creatinine was in the approximate range of 1.5-2.5 mg/dL The interventions occurred from 1980-1999</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>6 nonrandomized comparative studies of medical treatment, 4 prospective, 2 retrospective; 3 prospective cohort studies with medical treatments for blood pressure control 8 cohort studies (6 prospective, 1 retrospective, and 1 mixed) of natural history or nonspecified medical treatments</td>
<td>6 nonrandomized comparative studies, 4 prospective, 2 retrospective; 2 included surgical revascularization 20 prospective cohort studies with stent placement 4 prospective cohort studies that used various approaches</td>
<td>2 retrospective comparisons with percutaneous angioplasty 2 retrospective cohorts</td>
</tr>
</tbody>
</table>

---

#### Data Source

- **4 RCTs (1 a mix of medical treatment and delayed angioplasty)**
- **6 nonrandomized comparative studies of medical treatment, 4 prospective, 2 retrospective**
- **3 prospective cohort studies with medical treatments for blood pressure control**
- **8 cohort studies (6 prospective, 1 retrospective, and 1 mixed) of natural history or nonspecified medical treatments**

#### Population studied

- See other columns
- Medical treatment studies included patients with hypertension, mean blood pressure 172-180/103-106. One study included patients with >50% stenosis, half of whom had bilateral disease. One included a population where 25% had bilateral disease, though the definition of RAS was unclear. The third study did not describe degree of stenosis or bilateral disease. In two studies the mean serum creatinine was 1.3 mg/dL. Patients had mean ages approximately in the mid-50s; however, all studies included patients in their 20s or younger. In all three studies either some patients did not have ARAS or this was not reported. All 3 studies were from the 1980s or earlier.
- Patients with ARAS with HTN as the most frequent indication. Also included patients with CKD, CHF About 1/3 of studies included patients populations with >50% stenosis, about 1/4 included only >70% stenosis. Other thresholds were also used. Mostly populations with both uni- and bilateral disease, range of bilateral disease generally 25-50% of patients; some populations of unilateral or bilateral disease only. Comparative studies mostly had about 50% with ostial disease, when reported; cohort studies mostly with about 75% or more with ostial disease. Mean age generally about 65. Mean blood pressure generally in the range of 160-180/90-100. Mean serum creatinine generally in the range of 1.5-2.4 mg/dL, or mean GFR about 55 mL/min.
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Appendix F. Detailed Summary Table (continued)

Table. Summary of medical, angioplasty and surgical treatments

<table>
<thead>
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<th>Population studied, continued</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
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<td>In the 8 natural history studies, populations studied were patients with RAS who received no revascularization interventions and presumably were under standard care by their physician.</td>
<td>Comparative studies almost all did not use stents and included populations from the 1980s and 1990s. 80% of cohort studies used stents and all included populations from the mid 1990s and later.</td>
<td></td>
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<tr>
<td>The mean serum creatinine levels ranged from 1.2 to 3.2 mg/dL at baseline, implying at least stage 2 chronic kidney disease.</td>
<td>• Mean blood pressure ranged from 143-179/77-102, although several studies did not report blood pressure.</td>
<td></td>
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<tr>
<td>The mean stenosis ranged from greater than 20% to greater than 75%.</td>
<td>• The mean age was around 70 years in most studies, though 1 study followed younger patients, between 34-55 years.</td>
<td></td>
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<tr>
<td>The percentage of bilateral stenosis ranged from 17% to 100%.</td>
<td>• Patients were followed from the 1970s through the late 1990s; although several studies did not report time periods.</td>
<td></td>
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<tr>
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</table>

Limitations

- Only 2 RCTs compared angioplasty to medical treatment. Neither used stents. Both were of short duration (1 6-month, 1 with main analyses at 12 months, but patients followed from 3-54 months).
- Other comparative studies were nonrandomized, retrospective, and/or evaluated interventions of secondary interest.
- Data on medical treatments or natural history were from cohort studies without controls.
- Populations studied were highly heterogeneous, limiting comparability across studies.
- 3 studies on medical treatments reported only outcomes of blood pressure control and limited data on mortality and kidney function.
- Treatments were not specified in 8 natural history studies.
- Limited data on cardiovascular outcomes.
- Majority of data on angioplasty from before-after intervention studies (cohorts) without controls.
- Generally short duration of followup, often only single average time estimates of outcomes, despite range of followup time within studies.
- Very limited data on cardiovascular outcomes.
- Analyses of baseline variables as predictors of outcomes frequently inadequate.
## Table. Summary of medical, angioplasty and surgical treatments

<table>
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<th>Medical / Natural history</th>
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<th>Surgical</th>
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<td><strong>Mortality</strong></td>
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<tr>
<td>In the 3 comparative studies with similar patients receiving each intervention, mortality was similar with angioplasty or angioplasty / surgery and with medical treatment.</td>
<td>3 natural history studies found that between 1/3 and 2/3 of patients died within 4-5 years.</td>
<td>Wide range of mortality estimates across studies, from 1-20% at 6 months, and 0.5-23% at 1 year, and 2-53% at about 2 years. Cardiovascular related death was the most frequent reported cause.</td>
<td>5 -year mortality ranged from 12-41% in studies that used surgical revascularization or both surgery and angioplasty.</td>
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<tr>
<td><strong>Kidney outcomes</strong></td>
<td>No difference in kidney function (change in serum creatinine or GFR, worsening kidney function, need for dialysis) after revascularization compared to medical treatment in all but one study. One prospective nonrandomized study found a significant difference between a small decrease in serum creatinine (-0.5 mg/dL) after revascularization and a modest increase (+1.0) on medical treatment.</td>
<td>Kidney function outcomes were reported in seven studies (1 medical treatment and 6 natural history studies). In general patients' kidney function deteriorated over time, although to different degrees in the different studies.</td>
<td>Among cohort studies the improved kidney function ranged from 8-51% with the majority of studies reporting statistically non significant improvements in serum creatinine. Kidney function improvement varied among those with lower baseline kidney function.</td>
</tr>
</tbody>
</table>
## Appendix F. Detailed Summary Table (continued)

### Table. Summary of medical, angioplasty and surgical treatments

<table>
<thead>
<tr>
<th>Blood pressure outcomes</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Comparative studies heterogeneous regarding relative effect of interventions on blood pressure.</td>
<td>• All three studies of medical treatments for blood pressure control showed that, on average, the various treatment regimens examined were effective for lowering blood pressures in RAS patients to normal ranges.</td>
<td>• The cure rates for BP outcome ranged from 4-18%, and the improved rates ranged from 35-79%. The studies also noted decreased use of anti-HTN medications compared to baseline.</td>
<td>• 60 - 70% of patients reported improvements in HTN (2 studies)</td>
</tr>
<tr>
<td>• One RCT of angioplasty vs. medicine found a significant net improvement with angioplasty among patients with bilateral, but not unilateral, disease. The second RCT found a net decrease in both systolic and diastolic blood pressure with angioplasty, but only the change in diastolic pressure was statistically significant. This study also found that after angioplasty, patients required fewer anti-HTN drugs; which was not found in the first RCT.</td>
<td>• Outcomes of blood pressure control were reported in two natural history studies. The results were not comparable due to substantial differences in the RAS populations examined.</td>
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<tr>
<td>• Most other comparative studies found no difference in blood pressure outcomes, regardless of intervention; however 2 found that blood pressure decreased more in patients on medical treatment than after angioplasty, although this effect was not significant.</td>
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</tbody>
</table>

| CVD outcomes | | | |
| 1 RCT of angioplasty vs. medical treatment and 1 RCT of surgery vs. medical treatment both found no differences in CVD outcomes, regardless of treatment. | • CHF events 13% and strokes 13% over 3-54 months (1 study) | • CHF events 9%, strokes 4%, and MI 4% over 3-54 months (1 study) | • Cardiovascular events accounted for most of the late deaths (1 study) |
| | • CVD stop point (including hypertension, death, and also dialysis) 67% at about 6 years (1 study) | • CVD stop point (including hypertension, death, and also dialysis) 68% at about 6 years (1 study) | • Nonfatal cardiovascular events occurred in 28% of patients at an average of almost 5 years (1 study) |
| | • One natural history study reported eight fatal cardiovascular events in 20 patients with severe stenosis (≥ 75%) during 3 to 36 months followup. | • CHF 20%, MI 11%, and stroke 7% at a mean of 21 months (1 study) | | |
| | | • MI 5% at 15 months (1 study) | | |
| | | NYHA class changed by –1.4 at 21 months, which was a significant improvement from baseline (1 study) | | |

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## Appendix F. Detailed Summary Table (continued)

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Comparative studies did not address the relative adverse events or complications between interventions (except that 30-day mortality was similar in one study, 3% vs. 5%).</td>
<td>• No study reported the 30-day mortality.</td>
<td>• The 30-day mortality ranged from 0-3%.</td>
<td>• 30-day mortality ranged from 4-9%.</td>
</tr>
<tr>
<td></td>
<td>• A wide variety of adverse effects were reported for the use of enalapril, timolol, hydralazine, and captopril</td>
<td>• A transient deterioration in kidney function following procedure was reported ranged from 1-24% that included contrast-induced nephropathy. Severe decline in kidney function was also noted.</td>
<td>• Procedural complication rate was significantly higher in combined renal artery and aortic reconstruction compared with renal artery reconstruction alone (2 studies)</td>
</tr>
<tr>
<td></td>
<td>• None of the 8 natural history studies reported adverse events</td>
<td>• Renal artery or parenchymal injury during procedure ranged from 1-10%.</td>
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<tr>
<td></td>
<td></td>
<td>• Periprocedural acute myocardial infarction ranged from 1-7%.</td>
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<tr>
<td></td>
<td></td>
<td>• Other complications included: major hemorrhage; renal artery occlusion or spasm; false aneurysms; severe bleeding; and localized hematoma</td>
<td></td>
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<tr>
<td>Factors that influence outcomes</td>
<td>• The study comparing immediate to delayed or no angioplasty found that of two diagnostic tests, recent hypertension, bilateral stenosis, and severe stenosis (&gt;70%), only bilateral disease was found to be associated with better creatinine clearance at 12 months in those patients who had immediate angioplasty, in contrast to those with unilateral disease, where creatinine clearance was statistically similar in the two groups.</td>
<td>• Among cohort studies of medical treatment, no analyses evaluated baseline variables as predictors.</td>
<td>• Worse baseline kidney function was associated with increased mortality, poor clinical outcomes, and relatively worse blood pressure after revascularization.</td>
</tr>
<tr>
<td></td>
<td>• 4 natural history studies analyzed various predictors of mortality and/or outcomes of kidney function. Percent stenosis and baseline kidney function were f predictors of death (or dialysis) in separate studies. Another study found that nonspiral blood flow in the renal arteries predicted kidney function deterioration. Other variables related to cardiovascular disease were also found to predict death. 1 study found that bilateral versus unilateral disease did not predict progressive kidney disease.</td>
<td>• History of, or markers of, cardiovascular disease was associated with increased mortality, poor clinical outcomes, and relatively worse kidney function after revascularization.</td>
<td>• Preprocedure hemodialysis led to poorer functional kidney recovery but initiation of dialysis prior to surgery was predictive of long-term kidney function improvement in another (2 studies)</td>
</tr>
<tr>
<td></td>
<td>• 1 natural history study found that patients with bilateral disease had higher CVD mortality.</td>
<td></td>
<td>• Preoperative CKD, DM, prior stroke, and severe aortic occlusive disease showed significant and independent associations with death or dialysis during the follow up (1 study)</td>
</tr>
</tbody>
</table>

| F-5 |
Appendix F. Detailed Summary Table (continued)

<table>
<thead>
<tr>
<th>Factors with no effect</th>
<th>Angioplasty (or Surgery) vs. Medical Treatment</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The study comparing immediate to delayed or no angioplasty found that no variable predicted relative effectiveness of intervention strategy when diastolic blood pressure was the outcome.</td>
<td>• Age and beta blocker or diuretic use at baseline were not significant predictors of mortality or other clinical outcomes. • Baseline captopril test, renogram, arterial norepinephrine, and ACE genotype were generally not associated with outcomes. • The association between baseline predictors and outcomes was uncertain for several factors including baseline kidney function as a predictor of followup kidney function, baseline cardiovascular disease as a predictor or blood pressure effect, percent stenosis before angioplasty, bilateral vs. unilateral RAS, and sex.</td>
<td>• The randomized trial of surgical versus medical treatment, found that demographic factors did not help to predict which patients would fare better with either intervention.</td>
<td>• N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

| Periprocedural factors | • N/A | • N/A | • Among the studies that used angioplasty with and without stent, there were no differences in blood pressure and kidney outcomes between the procedures. • No study reported analyses of whether other periprocedural interventions, such as different drugs or different approaches, affected either complications or long-term outcomes. | • N/A |

| Overall Summary | • The 2 applicable RCTs found no difference in kidney cardiovascular, or mortality outcomes between angioplasty without stent placement and medical treatment. The studies suggest a better reduction in blood pressure control after angioplasty, particularly in patients with bilateral disease. | • Data on medical treatments or natural history were from cohort studies without controls. • Populations studied were highly heterogeneous • 3 natural history studies found that between 1/3 and 2/3 of patients died within 4-5 years. • Among 6 studies with medical treatments, wide range of mortality estimates across studies. | • Data mostly from prospective cohorts without a control group that indicate BP outcomes as the significantly improved outcome especially among those with higher baseline kidney function • Mortality was mostly CVD-related; was predicted by lower baseline kidney function, CHF, and influenced by bilateral disease with or without baseline CKD | • Data from retrospective cohort analyses. Some data were poorly reported. • Major outcomes like long-term mortality, improvements in HTN, and proportion of patients who became dialysis-dependent were similar across studies. |
Appendix F. Detailed Summary Table (continued)

<table>
<thead>
<tr>
<th>Overall Summary, continued</th>
<th>Angioplasty (or Surgery) vs. Medical Treatment</th>
<th>Medical / Natural history</th>
<th>Angioplasty</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The other comparative studies mostly agree with these conclusions, although the studies are heterogeneous in regards to blood pressure outcomes.</td>
<td>• In general patients’ kidney function deteriorated over time, although to different degrees in the different studies. • All 3 studies of medical treatments for blood pressure control showed that, on average, the various treatment regimens examined were effective for lowering blood pressures in RAS patients to normal ranges.</td>
<td>• There was no difference in blood pressure and kidney outcomes between procedures with and without stent. Studies did not analyze the predictive value of periprocedural interventions.</td>
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</tr>
<tr>
<td>• The comparative studies do not adequately address comparative adverse events or the predictive value of baseline variables to determine whether any of these factors would favor one intervention over the other.</td>
<td>• Indirect comparisons between cohort studies of revascularization and of medical treatment confirm the lack of difference in mortality rates between treatments, in resultant kidney function, with the caveat that improvement was reported only in cohort studies of revascularization.</td>
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<tr>
<td>• Indirect comparisons between cohort studies of revascularization and of medical treatment confirm the lack of difference in mortality rates between treatments, in resultant kidney function, with the caveat that improvement was reported only in cohort studies of revascularization.</td>
<td>• Across cohort studies, the difference in blood pressure outcomes with either revascularization or medical treatment was uncertain, except that improvement was reported only in cohort studies of revascularization.</td>
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<tr>
<td>• No conclusions could be reached about differences in cardiovascular outcomes or adverse events based on the cohort studies.</td>
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</tbody>
</table>

ARAS, atherosclerotic renal artery stenosis; CHF, congestive heart failure; CKD, chronic kidney disease (renal insufficiency); CVD, cardiovascular disease; DM, diabetes mellitus; GFR, glomerular filtration rate; HTN, hypertension; MI, myocardial infarction; N/A, not applicable; NYHA class, New York Heart Association functional class.