Does Previous Transradial Catheterization Preclude Use of the Radial Artery as a Conduit in Coronary Artery Bypass Surgery?

ABSTRACT: The radial artery (RA) is a commonly used conduit for coronary artery bypass grafting, and recent studies have demonstrated that it provides superior long-term patency rates to the saphenous vein in most situations. In addition, the RA is also being used with increasing frequency as the access point for coronary angiography and percutaneous coronary interventions. However, there has been concern for many years that these transradial procedures may have a detrimental impact on the function of RA grafts used in coronary artery bypass grafting, and there is now comprehensive evidence that such interventions cause morphologic and functional damage to the artery in situ. Despite this, there remain remarkably few studies investigating the use of previously cannulated RAs as grafts in coronary artery bypass surgery, and there are no clear guidelines on the use of the RA in coronary artery bypass grafting after its catheterization. This article will review concisely the evidence that transradial procedures cause damage to the RA, and discuss the impact this could have on previously cannulated RAs used as coronary artery bypass grafting conduits. On the basis of the evidence assessed, we make a number of recommendations to both surgeons and cardiologists regarding use of the RA in cardiovascular procedures.

Coronary artery bypass grafting (CABG) is the most frequently performed cardiac surgery operation worldwide, and it remains the gold standard therapy for the majority of patients with multivessel coronary artery and left main coronary artery disease.1 Traditionally, CABG primarily has involved the long saphenous vein alongside the left internal mammary artery2; however, it is becoming increasingly apparent that arterial grafts provide superior outcomes to venous grafts in most situations, and, therefore, the use of total arterial revascularization is expected to increase.3 In particular, it has now been demonstrated convincingly that bilateral internal mammary artery grafting using the left internal mammary artery and the right internal mammary artery provides additional survival benefit over single internal mammary artery grafting.4,5

In addition to the established benefits of bilateral internal mammary artery grafting, there also is increasing evidence to support the use of radial artery (RA) grafts in coronary artery bypass surgery.6 Carpentier and colleagues7 were the first to describe RA grafting for CABG in 1973, although the group subsequently advised against its use in 1975 because of poor short-term outcomes attributable to spasm8 and intimal hyperplasia.9 In 1992, however, Acar and associates10 discovered incidentally that previous RA grafts were patent at 18 years follow-up, and, since the introduction of pharmacologic prophylaxis and improved surgical techniques to minimize spasm,11 numerous studies have demonstrated that RA grafts provide excel-
lent long-term patency rates when targeted to severely stenosed coronary vessels\textsuperscript{12–14} (Figure 1). Throughout recent years, the outcomes of RA grafting has been extensively compared with long saphenous vein grafting; in all studies with a mean follow-up time extending beyond a year postoperation, significant benefits in terms of graft patency have been demonstrated for RA grafts.\textsuperscript{15} Furthermore, a recent meta-analysis by Zhang et al\textsuperscript{16} also has found RA use to be associated with reduced incidence of cardiac death, myocardial infarction, and the need for repeat coronary procedures in comparison with long saphenous vein grafting. The data comparing RA grafting with right internal mammary artery grafting are more limited; however, the current evidence indicates that the arteries are comparable in terms of outcomes, with the RA seeming to be a better choice in patients at increased risk of sternal or pulmonary complications.\textsuperscript{15,17}

In addition to its role in CABG, the RA also is being used with increasing frequency as the access point for coronary angiography and percutaneous coronary interventions in the diagnosis and management of coronary artery disease, respectively.\textsuperscript{18} Although, traditionally, the femoral artery has been the preferred route, recent studies have demonstrated that the transradial (TR) approach holds numerous advantages over the transfemoral approach, including decreased bleeding site complications, reduced cost, and a reduction in mortality.\textsuperscript{19,20} Moreover, patients prefer the TR approach because of its shorter hospital stay, increased comfort, and better physical functioning postprocedure.\textsuperscript{21,22}

There has been concern for many years, however, that these TR procedures may damage the RA and, as a result, many surgeons opt to avoid its use in CABG for a period of time following catheterization.\textsuperscript{23} Despite this, there has been a remarkable lack of investigation into the function of previously cannulated RAs as grafts in coronary artery bypass surgery, and there are no clear guidelines on the use of the RA in CABG following its catheterization. This review will attempt to summarize the data available in this field, and advise on methods to take the issue forward. In addition, recommendations will be made to both surgeons and cardiologists regarding use of the RA in cardiovascular procedures.

**MORPHOLOGIC AND FUNCTIONAL IMPACT OF TR PROCEDURES ON THE RA**

### Structural Damage to the RA Wall

The RA is composed of a thin continuous intima of endothelial cells, a single internal elastic lamina, and a thick medial layer of densely packed smooth muscle cells.\textsuperscript{6} As shown in Table 1, it has now been demonstrated through a variety of techniques that TR procedures cause significant structural damage to the RA wall. Kamiya et al\textsuperscript{24} histologically evaluated the distal section of the RA being used as a graft in coronary artery bypass surgery, and compared those from 16 patients who had undergone preoperative TR catheterization (group 1) with 34 patients who had not (group 2). Intimal hyperplasia was observed in 68% of RAs from group 1 in comparison with just 39% of those from group 2 ($P=0.046$).

A similar study was subsequently performed by Staniloae et al,\textsuperscript{25} as they histologically examined the distal and proximal ends of harvested RA segments and compared 15 previously catheterized RAs (TRA group) with 19 noncatheterized RAs (NCA group). The distal ends of the TRA group showed significantly more intimal hyperplasia (73.3% versus 21.1%; $P=0.03$), adventitial inflammation (33.3% versus 0%; $P=0.01$), and periarterial tissue or fat necrosis (26% versus 0%; $P=0.02$) than the distal ends of the NCA group. No significant histologic differences were found between the proximal ends of the 2 groups.

A recent study by Gaudino et al\textsuperscript{18} has provided further evidence of endothelial damage following TR procedures. This group examined 50 patients who underwent TR coronary angiography (RA-CA) before RA harvesting for CABG, and split the patients into 3 groups depending on the time interval between the RA-CA procedure and the evaluation of their RA ($<24$ hours), ($>24$ hours to $<7$ days), and ($\geq7$ days). Immunohistochemical analysis demonstrated extensive endothelial injury in all examined RAs, with a trend toward a reduction in damage over time.

Structural damage to the RA wall also has been demonstrated by using optical coherence tomography. Yonetsu et al\textsuperscript{26} examined the RAs of 69 patients immedi-

![Figure 1. Angiogram demonstrating the patency of a previously uncannulated radial artery graft at a follow-up time of 20 years.](http://circ.ahajournals.org/)

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ately after TR coronary intervention, and found intimal tears in 67.1% of these arteries and medial dissections in 35.6%. Although these acute injuries were more prevalent in the distal portion of the intervened RA, importantly they were also seen in proximal portions, indicating that TR procedures produce diffuse damage along the RA. Similar results have also been found by Di Vito et al;27; by using optical coherence tomography, this group imaged intimal tears in the RAs of 37% of patients following TR coronary intervention and medial dissections in 9.8% (Figure 2). However, both of these studies were limited by a lack of control RAs.

**Impact on Vasomotor Function**

Flow-mediated dilatation (FMD) and nitroglycerin-mediated dilatation (NMD) are methods frequently used to assess noninvasively endothelial and smooth muscle layer vasomotor function, respectively. The studies performed to date have consistently demonstrated that, at least in the short-term, both of these parameters are significantly impaired in the RA following TR procedures (Table 2).

The persistence of these impairments over time is less clear. Burstein et al28 found that, although the NMD response showed some trend for recovery over time, the FMD response of the RA was almost completely abolished after 9 weeks. A study subsequently performed by Yan et al30 yielded remarkably similar results, with the FMD response being almost completely eliminated at 3 months postprocedure. In support of this persisting deficiency in vasomotor function over time, Buturak and colleagues32 found both FMD and NMD to be significantly reduced from baseline at 6 months post-TR procedure. In contrast, although Dawson et al29 also reported an early impairment in FMD and NMD following RA-CA, these authors found that endothelial and smooth muscle vaso-

| Table 1. Studies Demonstrating Structural Damage to the RA Wall After TR Procedures |
|------------------------------------------|-----------------|----------------|----------------|------------------------------------------|
| Study                                   | Methodology     | N (Ca) | N (Ctl) | Main Findings |
| Kamiya (2003)24                         | Histology       | 16     | 34     | Significantly more intimal hyperplasia in distal ends of Ca RAs than in Ctls |
| Staniloae (2009)25                       | Histology       | 15     | 19     | Significantly more intimal hyperplasia, adventitial inflammation, and periaarterial tissue or fat necrosis in distal ends of Ca RAs than in Ctls |
| Gaudino (2015)18                         | Immunohistochemistry | 50   | …     | Endothelial injury seen in all previously Ca RAs, with a trend for reduction in damage over time |
| Yonetsu (2010)26                         | Optical coherence tomography | 69   | …     | Intimal tears and medial dissections seen in 67.1% and 35.6% of RAs, respectively, after TRI |
| Di Vito (2014)27                         | Optical coherence tomography | 51   | …     | Intimal tears and medial dissections seen 37% and 9.8% of RAs, respectively, after TRI |

Ca indicates cannulated; Ctl, control; N, number; RA, radial artery; TR, transradial; and TRI, transradial coronary intervention.

Figure 2. Representative images of acute injuries (A and B) and spasm (C) following transradial coronary intervention documented by optical coherence tomography. A, Representative image of intimal tear (arrow) characterized by a luminal surface discontinuity involving only the intimal layer. B, Representative image of medial dissection (arrows) shows a discontinuity involving intima and media layers. C, Representative image of spasm characterized by a circumferential and symmetrical reduction of vessel lumen with an increase of media width (smooth muscle cell contraction). Reprinted from Di Vito et al27 with permission of the publisher. Copyright © 2013, Springer Science+Business Media Dordrecht.
motor function almost completely returned to baseline after a recovery period of 3 months. Similarly, Madsen et al.\(^{34}\) reported no significant difference in FMD and NMD between control and cannulated RAs at a time period of 12 months postcannulation.

**Impact on RA Diameter**

Through use of ultrasound imaging, it has also been consistently demonstrated that the diameter of the RA is decreased following TR procedures (Table 3). This is an important parameter to consider, because a reduction in diameter would appear to increase the susceptibility of these arteries to turbulent flow and the competitive flow phenomenon when used as CABG conduits.\(^6\)

Similarly to vasomotor function, however, it is currently unclear whether the diameter progressively declines postcannulation or recovers over time. Nagai et al.\(^{36}\) examined the intervened RAs of 162 patients who underwent TR catheterization before, early (mean of 2 days), and late (mean of 95 days) after the procedure, and demonstrated a continuous reduction in diameter over time, with the RA diameter significantly reduced late after the procedure compared with early. In contrast, both the studies performed by Yan and colleagues\(^{30,37}\) found a trend for recovery of diameter over time. Importantly, however, in all the studies conducted to date, the diameter of the intervened artery never completely returned to baseline, indicating that the reduction in diameter is attributable to persisting structural changes in the RA wall, as opposed to transient arterial spasm.

In addition, complete occlusion of the RA, which would certainly preclude its use as a conduit in CABG, has also been demonstrated following TR interventions. In a recent meta-analysis by Bagur et al.,\(^{38}\) which included a total of 66 studies and 31,345 participants, the incidence of RA occlusion was demonstrated to be 7.7% within 24 hours and 5.5% at >1 week post-TR procedures. The group also found the most efficacious measure in reducing RA occlusion to be high-dose heparin, with the use of a smaller sheath size also reducing RA occlusion incidence.

### USE OF PREVIOUSLY CANNULATED RAS IN CABG

To date, there have been only 2 studies specifically examining the impact of previous TR procedures on the

### Table 3. Studies Investigating the Impact of TR Procedures on RA Vasomotor Function

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Time Post-Ca</th>
<th>FMD (%)</th>
<th>NMD (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burstein (2007)(^{28})</td>
<td>22</td>
<td>Baseline</td>
<td>13.2</td>
<td>18.9</td>
<td>No significant change in FMD or NMD in Ctls</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;24 h</td>
<td>3.6 (P&lt;0.01)*</td>
<td>3.7 (P&lt;0.01)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;9 wk</td>
<td>0.2 (P&lt;0.01)*</td>
<td>8.6 (P&lt;0.05)*</td>
<td></td>
</tr>
<tr>
<td>Dawson (2010)(^{29})</td>
<td>17</td>
<td>Baseline</td>
<td>8</td>
<td>17</td>
<td>No significant change in FMD or NMD in Ctls</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 day</td>
<td>4 (P&lt;0.05)*</td>
<td>7 (P&lt;0.05)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mo</td>
<td>8 (ns)*</td>
<td>13 (ns)*</td>
<td>Only 11 patients completed 3 mo follow-up</td>
</tr>
<tr>
<td>Yan (2014)(^{30})</td>
<td>65</td>
<td>Baseline</td>
<td>11.5</td>
<td>17.6</td>
<td>No significant change in FMD or NMD in Ctls</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 day</td>
<td>4.1 (P&lt;0.05)*</td>
<td>5.4 (P&lt;0.05)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mo</td>
<td>0.7 (P&lt;0.01)*</td>
<td>6.3 (P&lt;0.05)*</td>
<td></td>
</tr>
<tr>
<td>Aykan (2015)(^{31})</td>
<td>136</td>
<td>Baseline</td>
<td>7.5</td>
<td>12.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 mo</td>
<td>5.9 (P&lt;0.001)*</td>
<td>10.5 (P&lt;0.001)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mo</td>
<td>0.7 (P&lt;0.01)*</td>
<td>6.3 (P&lt;0.05)*</td>
<td></td>
</tr>
<tr>
<td>Buturak (2016)(^{32})</td>
<td>56</td>
<td>Baseline</td>
<td>9.45</td>
<td>9.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 mo</td>
<td>5.66 (P=0.0001)*</td>
<td>6.64 (P=0.018)*</td>
<td></td>
</tr>
<tr>
<td>Turan (2016)(^{33})</td>
<td>52</td>
<td>Baseline</td>
<td>15.3</td>
<td>8.6</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 wk</td>
<td>10.3 (P=0.019)*</td>
<td>6.9 (P=0.005)*</td>
<td></td>
</tr>
<tr>
<td>Madsen (2006)(^{34})</td>
<td>30</td>
<td>12 mo</td>
<td>Ca=8.4</td>
<td>Ca=15.5</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ctl=8.0 (ns)†</td>
<td>Ctl=16.7 (ns)†</td>
<td></td>
</tr>
<tr>
<td>Gaudino (2015)(^{35})</td>
<td>45</td>
<td>Up to 30 days</td>
<td>Ca=11.6</td>
<td>Ca=20.2</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ctl=14.2 (P&lt;0.01)†</td>
<td>Ctl=24.7 (ns)†</td>
<td></td>
</tr>
</tbody>
</table>

Ca indicates cannulated; Ctl, control; FMD, flow-mediated dilatation; N, number of intervened RAs; NMD, nitroglycerin-mediated dilatation; ns, not significant; RA, radial artery; and TR, transradial.

*Comparing postprocedure value with baseline.
†Comparing control value with cannulated value.
The Radial Artery in Cardiovascular Procedures

function of RAs used as conduits in coronary artery bypass surgery. In the study by Kamiya et al., the group angiographically assessed the patency of RA grafts at 1 month postoperation, and compared the grafts from arteries that had undergone preoperative catheterization with those which had not. The authors reported that, although the stenosis-free patency rates of nonradial grafts were similar between groups, there was a significant reduction in stenosis-free patency rates of RA grafts in the group with previous RA catheterization (77%, 17/22 patients) in comparison with the control group (98%, 48/49 patients; \(P=0.017\)). The authors also performed a subanalysis on the relationship between occurrence of graft stenosis and TR catheterization, which indicated that the number of previous TR catheterizations was the most likely factor affecting graft patency \(P=0.07\). This has been supported by subsequent studies demonstrating that repeatedly intervened RAs are significantly more damaged than first-time intervention RAs.

The other study investigating the use of previously cannulated RAs in CABG was published by Watson et al. in 2015. Here, the patency of RA grafts was angiographically assessed in 16 patients who had undergone preoperative RA-CA. The authors stated, however, that the records they analyzed inconsistently specified whether the right or left RA had been used for any particular graft, and, hence, there was no way for the authors to know whether the RA graft under investigation had actually been previously cannulated. Given this crucial flaw, the results of this study are of little meaningful value, and will not be discussed here further.

### Table 3. Studies Investigating the Impact of TR Procedures on the RA Diameter

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Time Post-Ca</th>
<th>Diameter (mm)</th>
<th>% reduction from baseline</th>
<th>Significance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagai (1999)</td>
<td>162</td>
<td>Baseline 2.5</td>
<td>2.4</td>
<td>4</td>
<td>(P&lt;0.01^*)</td>
<td>RA diameter at 95 days significantly more reduced than at 2 days (P&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean 95 days 2.3</td>
<td>8</td>
<td>(P&lt;0.01^*)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yan (2010)</td>
<td>355</td>
<td>Baseline 2.37</td>
<td>1.95</td>
<td>17.7</td>
<td>(P&lt;0.01^*)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 day</td>
<td>2.23</td>
<td>5.9</td>
<td>(P&lt;0.05^*)</td>
<td></td>
</tr>
<tr>
<td>Yan (2014)</td>
<td>65</td>
<td>Baseline 2.4</td>
<td>2</td>
<td>(P&lt;0.05^*)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 day</td>
<td>2.0</td>
<td>16.7</td>
<td>(P&lt;0.05^*)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mo</td>
<td>2.2</td>
<td>8.3</td>
<td>(P&lt;0.05^*)</td>
<td></td>
</tr>
<tr>
<td>Aykan (2015)</td>
<td>136</td>
<td>Baseline 2.97</td>
<td>2.82</td>
<td>5.1</td>
<td>(P&lt;0.001^*)</td>
<td></td>
</tr>
<tr>
<td>Buturak (2016)</td>
<td>56</td>
<td>Baseline 2.85</td>
<td>2.74</td>
<td>3.9</td>
<td>(P=0.0001^*)</td>
<td></td>
</tr>
<tr>
<td>Maddsen (2006)</td>
<td>30</td>
<td>12 mo Ca=2.58</td>
<td>2.71</td>
<td>(P&lt;0.05^*)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Ca indicates cannulated; Ctl, control; N, number of intervened RAs; RA, radial artery; and TR, transradial.
*Comparing postprocedure value with baseline.
†Comparing control value with cannulated.

According to the Society of Thoracic Surgery database, the RA was used in 5.5% of all primary CABGs in the United States in 2009. However, with the recent evidence of superior outcomes of RA grafting in comparison with long saphenous vein grafting, this number surely will increase. In addition, the RA is now the preferred route of most cardiologists for coronary angiography and percutaneous coronary intervention, because it is associated with fewer complications than the previously favored transfemoral approach. Nonetheless, there has been concern for many years that these TR procedures may detrimentally affect the ability of RA grafts used as CABG conduits.

As demonstrated above, there is now comprehensive evidence that RA-CA and TR coronary intervention cause severe morphologic and functional damage to the intervened RA, which could undoubtedly impact its function as a graft in coronary artery bypass surgery. The duration of this damage, however, is less clear; although a number of studies have demonstrated recovery of the RA with time, others have shown a progressive deterioration in function. Additional studies investigating the long-term impact of TR procedures on RA function are therefore warranted. Similarly, the extent of the damage along the length of intervened
RA is also not clear from the present evidence. Although Staniloe et al,25 for instance, found no significant histologic differences between the proximal ends of manipulated and control RAs, Yonetsu et al26 reported intimal damage along the length of the RA investigated.

Despite the clear evidence of RA damage after TR procedures, there remain remarkably few studies examining the function of previously catheterized RAs when used as CABG conduits. This is even more surprising given that the Kamiya et al24 study, which demonstrated an alarming reduction in the patency of grafts from previously catheterized RAs, was published as long ago as 2003. Therefore, there is a need for additional retrospective studies to examine the effect of previous cannulation on RA graft outcomes. However, given the existing evidence of damage to the RA after catheterization, in our opinion, there is not clinical equipoise to justify randomized trials comparing previously instrumented RAs with untouched RAs as CABG conduits.

Although additional retrospective studies will be useful, on the basis of the evidence already available, it is clear that both surgeons and cardiologists should give careful consideration to their use of the RA in cardiovascular procedures. Below we make a number of recommendations regarding how we believe the current evidence should affect clinical practice.

1. Whenever possible, surgeons should give preference to uncannulated RAs compared with cannulated RAs, and particular consideration of alternative conduits should be made when a RA has been previously cannulated on multiple occasions.24

2. In situations where conduit options are limited and the surgeon thinks the RA remains the best choice available despite previous catheterization, the surgeon should (a) perform Doppler ultrasound of the artery preoperatively to assess its patency and diameter and (b) avoid use of the distal end of the artery.

3. Cardiologists should weigh the benefits of the TR approach against the risk of damage to the artery when deciding on the optimal access point for percutaneous coronary intervention or coronary angiography, in terms of the future procedures that the patient may require. Although, in most instances, the cardiologist would be warranted fully in choosing the RA for access, in patients with extremely limited alternative conduit options and at high risk of needing subsequent CABG surgery, or those with significant renal impairment who may require formation of an arteriovenous fistula in the near future, the cardiologist may feel that a transfemoral approach is more appropriate.

4. When cardiologists do perform a TR approach, efforts should be made to minimize damage to the RA, such as through choosing the smallest possible catheter along with use of high-dose heparin.38

5. Cardiologists should be vigilant in noting the side on which TR procedures are performed, and ensure that this information is readily available for future retrospective studies and future medical interventions.2 Surgeons should clearly document which RA was used for grafting.

It is important to acknowledge that, in most instances, TR catheterization will not preclude use in future CABGs; the surgeon can use the opposite RA to that catheterized. However, although a large majority of operators use the right RA as the initial side for catheterization, in >10% of cases, the left RA is initially used and, moreover, in cases of initial access failure, many operators switch to using the contralateral RA.41 It is important, therefore, that cardiologists clearly document the side of RA entry, and discuss this with surgeons at multidisciplinary team meetings should the patient subsequently require CABG.

CONCLUSIONS

Overall, additional retrospective studies comparing the patency of grafts from previously cannulated RAs in CABG patients are needed. Furthermore, given the convincing evidence of RA damage following catheterization, and the reduction in graft patency demonstrated by Kamiya et al,24 we think that surgeons should take great caution before using previously cannulated RAs in CABG, and that cardiologists should consider the appropriateness of using the RA for access with regard to the future procedures that may be required by the patient. With the enhanced survival associated with RA use in CABG and the decreased complications of a TR approach for coronary techniques, the potential conflict raised by the impact of TR procedures on RA graft function emphasizes the need for a Heart Team approach to revascularization strategy in complex patients.42

DISCLOSURES

None.

AFFILIATIONS

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FOOTNOTES

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REFERENCES


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