Endovascular repair for ruptured abdominal aortic aneurysm confers an early survival benefit over open repair

George A. Antoniou, MD, PhD,a,b George S. Georgiadis, MD, PhD,b Stavros A. Antoniou, MD,c Polyvios Pavlidis, MD,a Dimitrios Maras, MD,a George S. Sfyroeras, MD, PhD, FEBVS,d Efstratios I. Georgakarakos, MD, PhD,b and Miltos K. Lazarides, MD, FEBVS,b Athens, Alexandroupolis, and Crete, Greece

Background: Despite the intuitive advantages of endovascular repair (EVAR) of ruptured abdominal aortic aneurysms (AAAs), uncertainty remains about the optimal management in the absence of convincing high-quality evidence. Our objective was to undertake a comprehensive literature review and perform a meta-analysis of outcome data of treatment modalities for ruptured AAAs.

Methods: Systematic searches were conducted of electronic information sources to identify studies comparing perioperative outcomes of EVAR and open repair for AAA rupture. Summary estimates of odds ratios (ORs) or standardized mean difference and 95% confidence intervals (CIs) were obtained with a random-effects model. Meta-regression models were formed to explore potential heterogeneity as a result of changes in practice over time.

Results: We selected 41 studies for analysis. The entire meta-analysis population comprised 59,941 patients (8201 EVAR patients and 51,740 open repair patients). EVAR was associated with a significantly lower incidence of in-hospital mortality (OR, 0.56; 95% CI, 0.50-0.64; P < .01; meta-analysis of risk-adjusted observational studies and randomized controlled trials: OR, 0.58; 95% CI, 0.46-0.73; P < .01). EVAR patients had a significantly decreased risk of developing respiratory complications (OR, 0.59; 95% CI, 0.49-0.69; P < .01) and acute renal failure (OR, 0.65; 95% CI, 0.55-0.78; P < .01) and a trend toward a reduced incidence of cardiac complications (OR, −0.02; 95% CI, −0.03 to 0.00; P = .05) and mesenteric ischemia (OR, 0.66; 95% CI, 0.44-1.00; P = .05). Patients treated with EVAR had significantly less requirements of intraoperative blood transfusion (standardized mean difference, −0.88; 95% CI, −1.06 to −0.70; P < .01). Random-effects meta-regression revealed no statistical evidence for an association between death and year of publication (P = .19).

Conclusions: Our analysis provides evidence to motivate the adoption of an EVAR-first policy in a nonelective setting and the establishment of standardized protocols for the management ruptured AAAs. (J Vasc Surg 2013;58:1091-105.)

A plethora of cohort studies, randomized trials, and meta-analyses have provided sufficient evidence demonstrating an early survival advantage of elective endovascular treatment for abdominal aortic aneurysms (AAAs) over conventional surgical repair.1,2 On the basis of outcome data, models of service delivery have undergone reconfiguration in several countries to accommodate optimum elective AAA services.3 In recent years, considerable speculation about the relative merits of applying endovascular techniques for the treatment of ruptured AAA has been reflected in the establishment of standardized protocols for the management of this critical condition in the emergency setting by several institutions.

Despite the intuitive advantages of endovascular aneurysm repair (EVAR) related to less physiologic insult to a critically ill patient presenting with ruptured AAA, insufficient quantification of the role of EVAR in the care pathway for these patients exists. Single-center cohort, multicenter cohort, and population-based studies have revealed a trend toward a survival benefit of emergency EVAR for ruptured AAA.4,5 Our objective was to undertake a comprehensive literature review and define the effect of EVAR on the management of AAA rupture by conducting an analysis of the perioperative outcomes of such treatment compared with conventional surgical repair.
METHODS

Eligibility criteria. The methods of analysis and inclusion criteria were prespecified in a protocol. Studies comparing perioperative outcomes of endovascular and open repair of ruptured infrarenal or juxtarenal AAA were considered for analysis. All types of comparative studies, including prospective or retrospective, observational studies, or randomized controlled trials (RCTs) were included. Studies not specifically defining ruptured AAA were arbitrarily presumed to have confirmed the presence of AAA rupture on preoperative computed tomography imaging, by visualization of blood outside the aortic lumen into the retroperitoneal space or the peritoneal cavity (contained or free rupture), or intraoperatively during on-table angiography or laparotomy. Studies reporting patients with acute or symptomatic aneurysm without clearly stating the presence of rupture were excluded.

Types of interventions included conventional endoaneurysmorrhaphy with tube or bifurcated grafts through a transperitoneal or retroperitoneal approach and standard EVAR with bifurcated grafts or an aortouniiliac device, followed by femorofemoral crossover bypass. Studies describing endovascular treatments of complex aneurysms with the chimney technique or with fenestrated or branched grafts were not considered.

The primary outcome measure was defined as the in-hospital or 30-day mortality of any cause. Secondary outcome end points were common perioperative complications (cardiac and respiratory complications, acute renal impairment, mesenteric and lower limb ischemia, and development of abdominal compartment syndrome), requirements for intraoperative blood transfusion, and the hospital length of stay.

Information sources and search strategy. Studies were identified by searching electronic bibliographic databases and scanning reference lists of articles. The search was applied to MEDLINE from the time of the first report of endovascular treatment of ruptured AAA by Yusuf et al.8 in 1994 to the present date. Unfortunately, language constraints were applied because of lack of funding for translation; thus, only English and German language articles were considered.

The following Expanded Medical Subject Headings (MeSH) and keywords were combined with Boolean operators: “aortic rupture” or “aortic aneurysm rupture” or “ruptured aortic aneurysm” and “EVAR” or “endovascular repair” or “open repair.” Relevant articles were retrieved, and the reference lists were manually interrogated as part of a second-level search. A supplementary search of related articles suggested by the PubMed search engine was conducted. The literature search protocol and retrieval of the full text of related articles was conducted in cooperation with a librarian at the University of Athens. The last search was on May 6, 2013.

Methods of data synthesis and analysis. Eligibility assessment and data collection was performed by a single reviewer in consultation with and cross-checked by two other reviewers. A data extraction sheet (based on the Cochrane Consumers and Communication Review Group’s data extraction template) was pilot-tested on the three most recent studies and refined accordingly. Information extracted from each study can be grouped into (1) that related to the study design and characteristics (first author, year of publication, patient recruitment period, type of study, and inclusion/exclusion criteria for patient enrollment); (2) data related to clinical and demographic characteristics of the study populations, including age, sex, presence of hypertension, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), chronic renal insufficiency, and hemodynamic instability; and (3) outcome parameters, as outlined above.

The methodologic quality of the included observational studies was ascertained with the Newcastle-Ottawa scale (NOS),7 and the Jadad scale was applied for the assessment of RCTs. This assessment tool evaluates three main methodologic elements of case-control studies: selection methods (adequate case definition, representativeness of the cases, appropriate selection, and definition of controls), comparability of cases and controls on the basis of the design or analysis, and assessment of exposure (ascertainment of exposure, nonresponse rate). The scale uses a star system, with a maximum of nine stars; studies achieving ≥6 stars were considered to be of higher quality.

Individual study odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from event numbers extracted from each study before data pooling. In calculation of the OR, the total number of patients assigned in each group was used as the denominator. Summary estimates of ORs were obtained with a random effects model. For continuous variables, the standardized mean difference or difference in means and corresponding 95% CI were computed using the random-effects model. The percentage of variability across studies attributable to heterogeneity beyond chance was estimated with the $I^2$ statistic. Potential publication bias was assessed with the Egger test and represented graphically with Begg funnel plots of the natural log of the OR vs its standard error.5

Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual studies one at a time and recalculating the pooled OR estimates for the remaining studies. Separate meta-analyses of risk-adjusted observational studies for in-hospital (or 30-day) mortality and RCTs were undertaken. Acceptable risk-adjustment methods included propensity score analyses and multivariate logistic regression models. We explored potential heterogeneity in estimates with univariate meta-regression to identify trends in the treatment effects over time and by comparing summary results obtained from subsets of studies grouped by study design and quality. A two-sided $P$ value of $<.05$ was regarded as significant for all analyses. Analyses were performed using the Review Manager 5.2 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) and the Comprehensive Meta-Analysis 2.0.
software (Biostat, Englewood, NJ). This meta-analysis was done in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.9

RESULTS

Literature search results and study characteristics.
The search of the electronic bibliographic databases identified 5089 records, of which 44 were reviewed in full text. Studies reporting mixed outcome data of treatments in symptomatic and ruptured AAA, those containing overlapping populations, studies not in English or German, and those reporting inadequate data for analysis were excluded, leaving 32 potentially eligible studies. In one study, inconsistency between values in the abstract and main text was noticed; therefore, we decided not to include it in our analysis. An additional 10 studies were identified during scrutiny of the bibliographies of the included articles, providing 41 studies for meta-analysis.10-50 Fig 1 shows the flow diagram of study selection.

The entire meta-analysis population comprised 59,941 patients, 8201 of whom underwent EVAR and the remaining 51,740 had an open repair of their ruptured AAA. The studies selected for analysis were published between 2002 and 2013, whereas the patient recruitment period extended from 1990 to 2011. Two RCTs were identified, with the remaining reports being single-center or multicenter prospective or retrospective observational studies or population-based reports. The study characteristics and inclusion and exclusion criteria for patient enrollment are presented in Table I. The methodologic quality of the RCTs, represented in the Jadad score, was low. Similarly, a small proportion of the observational studies achieved a NOS score >6 (nine of 29 studies). Main demographic and clinical features of the study populations are outlined in Table II. The perioperative complications were ill-defined and inconsistently reported among the studies (Table III).

Synthesis of results and outcome

In-hospital mortality. All 41 studies reported data of the primary outcome parameter set for the meta-analysis. In-hospital mortality occurred in 30% of patients treated with EVAR and in 42% of the patients who underwent open repair (OR, 0.56; 95% CI, 0.50-0.64; \( P < .01 \)). Significant heterogeneity among the studies was identified (\( I^2 = 36\% \)), and the likelihood of publication bias was low (\( P = .11; \) Fig 2).

Cardiac complications. Twenty studies reported cardiac complications. The incidence of such complications was 14% in the EVAR group and 16% in the open repair group (OR, –0.02; 95% CI, –0.03 to 0.00; \( P = .05 \)). No significant heterogeneity was found among the studies (\( I^2 = 28\% \)), and the possibility of publication bias was low (\( P = .76; \) Fig 3).

Respiratory complications. Data regarding perioperative respiratory complications were reported in 19 studies. Patients undergoing EVAR had a significantly decreased risk of developing a respiratory complication compared with patients treated with open repair (6% vs 11%; OR, 0.59; 95% CI, 0.49-0.69; \( P < .01 \)). No significant heterogeneity among the studies existed (\( I^2 = 22\% \)), and the chance of publication bias was low (\( P = .27; \) Fig 3).

Acute renal failure. Eight studies reported incidences of acute renal impairment during the perioperative period.
### Table I. Study characteristics

<table>
<thead>
<tr>
<th>First author/year</th>
<th>Study period</th>
<th>Type of study</th>
<th>Total patients (No.)</th>
<th>EVAR</th>
<th>Open repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park/2013</td>
<td>2005-2009</td>
<td>Population-based retrospective study</td>
<td>16,557</td>
<td>3796</td>
<td>12,761</td>
</tr>
<tr>
<td>Reimerink/2013</td>
<td>2004-2011</td>
<td>RCT</td>
<td>116</td>
<td>57</td>
<td>59</td>
</tr>
<tr>
<td>Nedeau/2012</td>
<td>2000-2010</td>
<td>Hospital-based retrospective study</td>
<td>74</td>
<td>19</td>
<td>55</td>
</tr>
<tr>
<td>Noorani/2012</td>
<td>2006-2010</td>
<td>Hospital-based retrospective study</td>
<td>102</td>
<td>52</td>
<td>50</td>
</tr>
<tr>
<td>Saqib/2012</td>
<td>2001-2010</td>
<td>Hospital-based retrospective study</td>
<td>148</td>
<td>37</td>
<td>111</td>
</tr>
<tr>
<td>Mayer/2012</td>
<td>1998-2009</td>
<td>Hospital-based retrospective study</td>
<td>361</td>
<td>198</td>
<td>163</td>
</tr>
<tr>
<td>Mandawat/2012</td>
<td>2003-2007</td>
<td>Population-based retrospective study</td>
<td>271</td>
<td>64</td>
<td>207</td>
</tr>
<tr>
<td>Ioannidis/2012</td>
<td>2003-2008</td>
<td>Hospital-based retrospective study</td>
<td>43</td>
<td>20</td>
<td>23</td>
</tr>
<tr>
<td>Sarac/2011</td>
<td>1990-2008</td>
<td>Hospital-based retrospective study</td>
<td>160</td>
<td>32</td>
<td>128</td>
</tr>
<tr>
<td>Holt/2010</td>
<td>2003-2008</td>
<td>Population-based retrospective study</td>
<td>4414</td>
<td>335</td>
<td>4079</td>
</tr>
<tr>
<td>Starnes/2010</td>
<td>2007-2009</td>
<td>Hospital-based prospective observational study</td>
<td>51</td>
<td>27</td>
<td>24</td>
</tr>
<tr>
<td>Bosch/2010</td>
<td>2002-2008</td>
<td>Hospital-based prospective observational study</td>
<td>58</td>
<td>25</td>
<td>33</td>
</tr>
<tr>
<td>Chagpar/2010</td>
<td>2003-2008</td>
<td>Hospital-based retrospective study</td>
<td>167</td>
<td>32</td>
<td>135</td>
</tr>
<tr>
<td>Lyons/2010</td>
<td>2006-2007</td>
<td>Hospital-based retrospective study</td>
<td>57</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Vun/2009</td>
<td>2004-2008</td>
<td>Hospital-based retrospective study</td>
<td>45</td>
<td>7</td>
<td>38</td>
</tr>
<tr>
<td>Verhoeven/2009</td>
<td>2002-2009</td>
<td>Hospital-based retrospective study</td>
<td>159</td>
<td>45</td>
<td>114</td>
</tr>
<tr>
<td>Vogel/2009</td>
<td>2001-2005</td>
<td>Population-based retrospective study</td>
<td>700</td>
<td>82</td>
<td>618</td>
</tr>
<tr>
<td>Visser/2009</td>
<td>2004-2006</td>
<td>Multicenter prospective observational study</td>
<td>201</td>
<td>58</td>
<td>143</td>
</tr>
<tr>
<td>Giles/2009</td>
<td>2005-2007</td>
<td>Population-based retrospective study</td>
<td>567</td>
<td>121</td>
<td>446</td>
</tr>
<tr>
<td>Veith/2009</td>
<td>1994-2008</td>
<td>Hospital-based retrospective study</td>
<td>57</td>
<td>45</td>
<td>12</td>
</tr>
<tr>
<td>Wibmer/2008</td>
<td>2003-2006</td>
<td>Hospital-based retrospective study</td>
<td>47</td>
<td>16</td>
<td>31</td>
</tr>
<tr>
<td>Lee/2008</td>
<td>2002-2006</td>
<td>Hospital-based retrospective study</td>
<td>37</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>Sharif/2007</td>
<td>2001-2006</td>
<td>Hospital-based observational study</td>
<td>126</td>
<td>52</td>
<td>74</td>
</tr>
<tr>
<td>Ockert/2007</td>
<td>2000-2005</td>
<td>Hospital-based retrospective study</td>
<td>58</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Anain/2007</td>
<td>2001-2006</td>
<td>Hospital-based observational study</td>
<td>40</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>Acosta/2007</td>
<td>2000-2004</td>
<td>Hospital-based retrospective study</td>
<td>162</td>
<td>56</td>
<td>106</td>
</tr>
<tr>
<td>Copp/2006</td>
<td>1999-2006</td>
<td>Hospital-based observational study</td>
<td>124</td>
<td>35</td>
<td>91</td>
</tr>
<tr>
<td>Hinchliffe/2006</td>
<td>2002-2004</td>
<td>RCT</td>
<td>52</td>
<td>15</td>
<td>17</td>
</tr>
</tbody>
</table>

| Peppelenbosch/2006 | 2003-2004 | Multicenter prospective observational study | 100 | 49 | 51 |
| Dalainas/2006     | 1998-2005 | Hospital-based observational study | 28 | 20 | 8 |
| Larzon/2005       | 2001-2004 | Hospital-based retrospective study | 41 | 15 | 26 |
| Alsac/2005        | 2001-2004 | Hospital-based observational study | 37 | 17 | 20 |
| Vaddineni/2005   | 1999-2004 | Hospital-based retrospective study | 24 | 9 | 15 |
| Brandt/2005       | 2003-2004 | Hospital-based retrospective study | 24 | 11 | 13 |
| Lee/2004          | 2002-2004 | Hospital-based retrospective study | 17 | 13 | 4 |
| Reichart/2003     | 2000-2002 | Hospital-based retrospective study | 19 | 6 | 13 |
| Resch/2003        | 2001-2002 | Hospital-based observational study | 37 | 14 | 23 |
| Yilmaz/2002       | 1999-2001 | Hospital-based observational study | 46 | 17 | 29 |

**Notes:** AAA, Abdominal aortic aneurysm; CT, computed tomography; EVAR, endovascular aneurysm repair; NOS, Newcastle-Ottawa Scale; NR, not reported; RCT, randomized controlled trial; TAAA, thoracoabdominal aortic aneurysm; US, ultrasound.
Table I. Continued.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>NOS/Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR</td>
<td>CT confirmed ruptured AAA suitable for both EVAR and open repair</td>
<td>Age &lt;60 years</td>
</tr>
<tr>
<td>NR</td>
<td>Juxta-/suprarenal AAA, kidney transplant, horseshoe kidney, allergy to intravenous contrast, connective tissue disease, severe hemodynamic instability prohibiting CT</td>
<td>3</td>
</tr>
<tr>
<td>NR</td>
<td>Aortic neck &lt; 5 mm, diameter larger than the largest available main body graft, severe iliac arterial occlusive disease</td>
<td>7</td>
</tr>
<tr>
<td>Confirmed rupture</td>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>Antecedent AAA repair, symptomatic AAA without rupture, incomplete medical reports</td>
<td>6</td>
</tr>
<tr>
<td>NR</td>
<td>Patients with ruptured AAA transferred for treatment from other hospitals</td>
<td>Ruptured TAAA, ruptured isolated iliac aneurysms</td>
</tr>
<tr>
<td>Ruptured AAA (including rupture after EVAR and rupture with penetrating ulcers)</td>
<td>Thoracic/TAAA aortic dissection</td>
<td>5</td>
</tr>
<tr>
<td>NR</td>
<td>Reoperative AAA, juxtarenal AAA, TAAA, isolated iliac artery aneurysms, symptomatic but not ruptured AAA</td>
<td>7</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
</tr>
<tr>
<td>CT confirmed ruptured AAA suitable for EVAR</td>
<td>NR</td>
<td>Symptomatic but not ruptured AAA</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
<td>Symptomatic but not ruptured AAA</td>
</tr>
<tr>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>Acute nonruptured AAA</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
<td>Congenital connective tissue disease-related ruptured AAA, secondary rupture (after preceding elective repair)</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
<td>Aneurysms involving the origin of the renal/visceral vessels</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
<td>Symptomatic but not ruptured AAA, ruptured TAAA, ruptured traumatic aneurysms</td>
</tr>
<tr>
<td>US or CT or angiographically or intraoperatively confirmed ruptured AAA</td>
<td>Symptomatic but not ruptured AAA</td>
<td>6</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
<td>Nonruptured inflammatory or symptomatic AAA</td>
</tr>
<tr>
<td>CT or intraoperatively or autopsy confirmed ruptured AAA</td>
<td>NR</td>
<td>Symptomatic but not ruptured AAA</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>NR</td>
<td>Patients with ruptured AAA considered suitable for open repair, patients stable enough to undergo CT</td>
<td>Endovascular team/device unavailable, age &lt;50 years, inability to give consent, unconscious patient, allergy to contrast, stainless steel, polyester; severe comorbidity, previous EVAR, women of child-bearing potential, pregnant/lactating women</td>
</tr>
<tr>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>Life expectancy &lt;1 year, not consenting to participate</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>Symptomatic but not ruptured AAA, mycotic AAA or infected aortic pseudo-aneurysms, post-traumatic aneurysms, TAAA</td>
</tr>
<tr>
<td>NR</td>
<td>CT or intraoperatively confirmed ruptured AAA</td>
<td>NR</td>
</tr>
<tr>
<td>CT or intraoperatively confirmed ruptured infrarenal AAA</td>
<td>NR</td>
<td>Isolated iliac artery aneurysms</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>No pre-operative CT</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
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<tr>
<td>NR</td>
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</tr>
</tbody>
</table>
Patients treated with EVAR had a significantly lower risk of developing renal failure than patients undergoing open AAA repair (16% vs 26%; OR, 0.65; 95% CI, 0.55–0.78; \( P < .01 \)). Significant heterogeneity among the studies was identified \( (I^2 = 43\%) \), and the possibility of publication bias was low \( (P = .76; \text{Fig 3}) \).

Acute lower limb ischemia. Eight studies reported rates of acute limb ischemia, with an incidence of 3%...
Table III. Definitions of perioperative complications

<table>
<thead>
<tr>
<th>First author/year</th>
<th>Cardiac complications</th>
<th>Respiratory complications</th>
<th>Acute renal failure</th>
<th>Acute limb ischemia</th>
<th>Mesenteric ischemia</th>
<th>Abdominal compartment syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park/2013</td>
<td>MI</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Reimerink/2013</td>
<td>ND</td>
<td>NR</td>
<td>Temporary or permanent dialysis or permanent renal insufficiency</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Nedeau/2012</td>
<td>Cardiovascular complications</td>
<td>Respiratory/ infectious complications</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Noorani/2012</td>
<td>NR</td>
<td>NR</td>
<td>Requires dialysis</td>
<td>ND</td>
<td>ND</td>
<td>NR</td>
</tr>
<tr>
<td>Saqib/2012</td>
<td>MI</td>
<td>Respiratory failure requiring &gt;7 days of ventilatory support</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>NR</td>
</tr>
<tr>
<td>Mayer/2012</td>
<td>MI</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>NR</td>
</tr>
<tr>
<td>Mandawat/2012</td>
<td>NR</td>
<td>NR</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>NR</td>
</tr>
<tr>
<td>Ioannidis/2012</td>
<td>MI</td>
<td>Pneumonia</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Requiring bowel resection</td>
</tr>
<tr>
<td>Sarac/2011</td>
<td>MI</td>
<td>Postoperative intubation period &gt;48 hours, need for reintubation, positive sputum culture, radiographically confirmed pneumonia</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Holt/2010</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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</tr>
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<td>Starnes/2010</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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</table>

(Continued on next page)
in the EVAR group and 4% in the open repair group (OR, 0.63; 95% CI, 0.37-1.07; \( P = .09 \)). Significant heterogeneity among the studies was found (I\(^2\) = 60%), and the likelihood of publication bias was low (\( P = .76 \); Fig 3).

**Mesenteric ischemia.** Rates of mesenteric ischemia were reported in 15 studies. A trend was found toward a lower incidence of mesenteric ischemia developing among patients treated with EVAR than in those undergoing open repair (4% vs 6%; OR, 0.66; 95% CI, 0.44-1.00; \( P = .05 \)). Significant heterogeneity among the studies was found (I\(^2\) = 69%), and the possibility of publication bias was low (\( P = .91 \); Fig 3).

**Abdominal compartment syndrome.** Data regarding abdominal compartment syndrome was reported in 12 studies. The incidence of abdominal compartment syndrome was 9% in the EVAR group and 8% in the open repair group (OR, 1.06; 95% CI, 0.56-2.03; \( P = .85 \)). Significant heterogeneity among the studies existed (I\(^2\) = 34%), and the chance of publication bias was low (\( P = .12 \); Fig 3).

**Secondary interventions.** Fourteen studies reported data related to secondary interventions within the perioperative period. The incidence of such interventions was 16% in the EVAR group and 21% in the open repair group.

---

### Table III. Continued.

<table>
<thead>
<tr>
<th>First author/ year</th>
<th>Cardiac complications</th>
<th>Respiratory complications</th>
<th>Acute renal failure</th>
<th>Acute limb ischemia</th>
<th>Mesenteric ischemia</th>
<th>Abdominal compartment syndrome</th>
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MI, Myocardial infarction; ND, not defined; NR, not reported.

---

**Fig 2.** Forest plot shows comparison of in-hospital mortality among the studies in the meta-analysis. CI, Confidence interval; EVAR, endovascular aneurysm repair; M-H, Mantel-Haenszel.

---

**Table III.** Continued.
Fig 3. Forest plot of comparison of (a) cardiac complications, (b) respiratory complications, (c) acute renal failure, (d) lower limb ischemia, (e) mesenteric ischemia, (f) abdominal compartment syndrome, (g) secondary interventions, (h) intraoperative blood transfusion, and (i) hospital length of stay among the studies in the meta-analysis. CI, Confidence interval; EVAR, endovascular aneurysm repair; M-H, Mantel-Haenszel; IV, inverse variance; SD, standard deviation.
### Fig 3. Continued

#### Panel d

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>EVAR Events</th>
<th>Open repair Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Year</th>
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</thead>
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<td>1</td>
<td>20</td>
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<td>2005</td>
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<tr>
<td>Hinchcliffe</td>
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<td>Park</td>
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<td>3796</td>
<td>1205</td>
<td>12761</td>
<td>39.9%</td>
<td>2013</td>
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</table>

Total (95% CI) | 6293 | 39128 | 100.0% | 0.63 [0.37, 1.07] |

Total events | 218 | 1612 |

Heterogeneity: Tau^2 = 0.18; Chi^2 = 17.30, df = 7 (P = 0.02); I^2 = 60%

Test for overall effect: Z = 1.72 (P = 0.09)

#### Panel e

<table>
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<tr>
<th>Study or Subgroup</th>
<th>EVAR Events</th>
<th>Open repair Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
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Total (95% CI) | 6823 | 45116 | 100.0% | 0.66 [0.44, 1.00] |

Total events | 272 | 2804 |

Heterogeneity: Tau^2 = 0.20; Chi^2 = 41.91, df = 13 (P < 0.0001); I^2 = 69%

Test for overall effect: Z = 1.97 (P = 0.05)

#### Panel f

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>EVAR Events</th>
<th>Open repair Events</th>
<th>Total</th>
<th>Weight</th>
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Total (95% CI) | 529 | 831 | 100.0% | 1.06 [0.56, 2.03] |

Total events | 48 | 69 |

Heterogeneity: Tau^2 = 0.34; Chi^2 = 15.05, df = 10 (P = 0.13); I^2 = 34%

Test for overall effect: Z = 0.18 (P = 0.85)
(OR, 0.83; 95% CI, 0.60-1.14; \( P = .25 \)). There was no heterogeneity among the studies (\( I^2 = 0 \% \)), and the likelihood of publication bias was low (\( P = .59; \text{Fig 3} \)).

**Intraoperative blood transfusion.** Data regarding the amount of intraoperative blood transfusion suitable for meta-analysis were reported by five studies. Patients treated with EVAR had significantly less requirements of intraoperative blood transfusion than patients undergoing open AAA repair (standardized mean difference, 0.88; 95% CI, -1.06 to 1.50; \( P < .01 \)). There was no heterogeneity among the studies (\( I^2 = 0 \% \)), and the possibility of publication bias was low (\( P = .63; \text{Fig 3} \)).

**Hospital length of stay.** Only four studies reported appropriate data on the hospital length of stay to enter the meta-analysis models. Although these studies found a trend toward a shorter hospital stay in the EVAR group, our analysis found no significant difference between the groups (mean difference, -3.28; 95% CI, -8.18 to 1.61; \( P = .19 \)). Significant heterogeneity among the studies existed (\( I^2 = 65 \% \)), and the likelihood of publication bias was high (\( P = .02; \text{Fig 3} \)).

**Sensitivity and meta-regression analyses**

The combined outcome estimate of mortality was not substantially affected when the primary analysis was repeated with altered data sets after excluding each single study at a time. Furthermore, the effect of EVAR on inhospital mortality was not different in hospital-based
compared with population-based studies (mixed-effects analysis, \(P = .19\) for interaction). Random-effects meta-regression revealed little or no statistical evidence for an association between the log OR for mortality and year of publication (\(P = .19\); Fig 4).

Eleven observational studies provided adjusted ORs for in-hospital mortality. Adjustment was performed for several confounding variables, which varied among the studies. The log OR and the standard error were calculated from the adjusted OR and 95% CI and entered in a separate random-effects meta-analysis model (Fig 5). The ORs of the two RCTs were put in the model as well. Analysis revealed that EVAR was associated with a significantly lower mortality than open repair (OR, 0.58; 95% CI, 0.46-0.73; \(P < .01\) for effect, \(P = .04\) for heterogeneity; \(I^2 = 46\%\)).

DISCUSSION

Concurrent progress in experience and technology in critical care and anesthetic settings during the last decades has not been accompanied by similar improvements in mortality rates of conventional treatment for ruptured AAA.\(^5\) Widespread adoption of endovascular approaches for the elective treatment of AAAs is consistent with solid evidence demonstrating early survival advantages over surgical repair and reflects a paradigm shift in management practice of aortic aneurysmal disease.\(^1\) However, the optimal treatment of ruptured AAA remains controversial in the absence of convincing high-level evidence from randomized trials. The perceived benefits of EVAR for ruptured AAA are supported by several observational studies that reveal a trend toward improved outcomes with this approach compared with open repair and are depicted in the increasing establishment of EVAR protocols by several institutions worldwide. Our objective was to collect the world experience in the endovascular treatment of AAA rupture and consolidate existing evidence by conducting a meta-analysis of outcome data.

In the current meta-analysis comprising data of \(\sim 60,000\) patients, comparisons of early mortality between EVAR and open treatment groups revealed a substantial
The survival benefit of EVAR compared with open repair for ruptured AAA. These results are mainly based on observational reports, which are inevitably afflicted by publication and patient selection bias, with only two RCTs being identified. Furthermore, the methodologic quality of the studies varied, and clinical parameters, such as hemodynamic instability at presentation, are inconsistently reported. The heterogeneity among the studies regarding in-hospital mortality may also be explained by centers with different volumes providing data for analysis and by the variable application of specific management protocols of patients presenting with ruptured AAA. Therefore, because of the heterogeneous study characteristics at the patient and study design level, the pooled estimate of in-hospital mortality should be cautiously interpreted. However, the consistency of this outcome advantage in favor of EVAR among almost all of the studies included in the analysis demonstrates the robustness of our findings.

In the setting of nonrandomized comparisons, various confounding variables, such as comorbid conditions and the presence of hemodynamic instability, may have an effect on the pooled outcome estimate. Several authors have argued that stable patients, whose hemodynamic and physiologic condition permits performance of computed tomography to ascertain the anatomic suitability for EVAR, are preferentially treated with an endovascular approach compared with cardiovascually compromised patients presenting in severe shock, who are taken to the operating theater straightaway for surgical aortic cross-clamping without any preoperative imaging investigation.

In an attempt to circumvent such limitations, separate meta-analysis models were formed to include RCTs and studies providing risk adjustments for several factors that might potentially have an effect on the overall outcome. Our finding was validated by such analyses, providing further evidence for the use of EVAR as a first-line treatment for this critical clinical condition. Unfortunately, the studies selected for analysis did not discriminate patients presenting with hemodynamic instability; therefore, subgroup analyses could not be conducted. However, most studies that provided risk-adjusted outcome data performed adjustments for hemodynamic instability, and the survival benefit of EVAR over open repair persisted even after adjustment for this confounding factor.

Furthermore, sensitivity analyses and subgroup meta-regression comparing outcome measures in hospital-based and population-based reports consistently demonstrated survival superiority of EVAR over open surgical repair of AAA rupture. Even though selective reporting of studies with positive results can seriously bias conclusions, we found no statistical evidence to prove publication bias in almost all of the outcome variables examined.

We further investigated the comparative effectiveness of treatments by exploring differences in main morbidity parameters accompanying ruptured AAA repair. Patients undergoing EVAR were less likely to develop respiratory complications, acute renal impairment, and mesenteric ischemia, reflecting differences in the physiologic effects of a major abdominal operation compared with a minimally invasive endovascular aortic procedure. Furthermore, our analysis did not substantiate previous concerns of increased risk of abdominal compartment syndrome in patients receiving EVAR in the presence of a large retroperitoneal or intraperitoneal hematoma. Other factors, such as visceral edema and fluid shifts resulting from aortic cross-clamping, increased requirements for blood transfusion, and acute inflammatory response might contribute to the development of the syndrome, which requires a secondary intervention.

In all but one synthesis (hospital length of stay), the likelihood of publication bias was low. Analytic tools (Begg funnel plot and Egger test) were used to quantify the potential presence of publication bias; nevertheless, forms of reporting bias cannot be exclusively excluded, and the results of our analysis should be cautiously interpreted.

CONCLUSIONS

Our analysis provides robust outcome data to enhance and motivate the widespread adoption of an EVAR-first policy in a nonelective setting. Ruptured AAAs might be best managed within institutions with a large aortic workload. Centers with instituted protocols are likely to have superior outcomes with endovascular management of ruptured AAA; therefore, implementing such protocols at high-volume centers is recommended. Implementation of specific management protocols should be illustrated in a multidisciplinary approach involving specialized endovascular, radiologic, vascular critical care, and anesthetic teams. Establishment of institutional protocols involves systemic changes in the health care delivery infrastructure, with around-the-clock availability of endovascular devices and auxiliaries along with skilled specialists and nursing teams. The ability to establish institutional protocols also includes the requirement for adequate on-the-shelf stock, usually consigned to the hospital. Although a move toward an endovascular-first approach may be beneficial, widespread adoption may not be feasible presently in larger countries with rural communities. Procedural costs for EVAR are higher, and many smaller hospitals may not have the ability to maintain an on-the-shelf stock of these costly devices to reasonably adopt the EVAR-first approach.

Improvements in outcomes as a result of constantly evolving stent graft designs and endovascular techniques, in tandem with increased endovascular experience, might be expected in the future. The converse should also be noted, namely, the eventual erosion of open surgical technique as trainees are involved in fewer and fewer open AAA cases.

Meta-regression analysis investigating potential effects of the publication date of each study on perioperative mortality in the treatment groups did not explain heterogeneity as a result of changes in practice over time. More conclusive results from large RCTs are expected.
Insufficient data regarding the medium-term and long-term outcomes of EVAR for ruptured AAA are available. The selected studies did not provide patient group stratification according to the proportion of patients that was transferred to another facility before open or endovascular management. Such data may help determine whether the proximity of a tertiary care facility would significantly affect the primary end point and should be a potential field for further research. For example, the availability of stent grafts is more likely in a center with a high volume of endoluminal aortic surgery. The hemodynamic stability of the patient, surgeon preference and experience, and anatomic suitability for EVAR might also significantly affect which method of repair was chosen in the studies included in the analysis. Areas for future research constitute the identification of poor prognostic factors related to EVAR performed in the acute setting and the establishment of risk-prediction models to direct preferential treatment management of this critical clinical condition.

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AUTHOR CONTRIBUTIONS

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Analysis and interpretation: GA, GG, SA, PP, DM, GS, EG, ML
Data collection: GA, GG, SA
Writing the article: GA
Critical revision of the article: GA, GG, SA, PP, DM, GS, EG, ML
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