Predictors of decreased short- and long-term survival following open abdominal aortic aneurysm repair

Derek P. Nathan, MD, Clayton J. Brinster, MD, Benjamin M. Jackson, MD, Grace J. Wang, MD, Jeffrey P. Carpenter, MD, Ronald M. Fairman, MD, and Edward Y. Woo, MD
Philadelphia, Pa; and Camden, NJ

Objectives: The purpose of this study was to identify predictors of decreased survival after open abdominal aortic aneurysm (AAA) repair at a single university hospital.

Methods: Patients undergoing open AAA repair from June 2003 to June 2009 were identified. Primary outcomes were 30-day and 5-year survival. Preoperative, intraoperative, and postoperative variables were assessed for their influence on outcomes using univariate and multivariate analysis, as appropriate. One- and 5-year survival were determined by Kaplan-Meier analysis.

Results: Four hundred eight patients (289 men; 70.8%) with a mean age of 72.4 ± 8.3 years underwent open AAA repair. Sixty-seven patients (16.4%) underwent nonelective repair. The clamp site was infrarenal in 137 patients (33.6%), suprarenal in 97 patients (23.8%), and supraceliac in 174 patients (42.6%). Thirty-day survival was 95.6%. One- and 5-year survival were 90.0% ± 1.5% and 65.1% ± 3.0%, respectively. Seventy-nine patients (19.4%) had decreased renal function postoperatively compared to preoperatively, 71 patients (17.4%) sustained cardiac complications, and 45 patients (11.0%) sustained pulmonary complications. Patients with chronic obstructive pulmonary disease (91.9% vs 97.2%; P = .004) and chronic renal insufficiency (92.0% vs 98.3%; P = .009) had decreased 30-day survival. Patients with chronic obstructive pulmonary disease (55.8% ± 5.8% vs 67.3% ± 3.6%; P = .013), chronic renal insufficiency (51.2% ± 5.2% vs 72.8% ± 3.7%; P = .043), and cerebrovascular disease (46.8% ± 7.4% vs 67.4% ± 3.4%; P = .003) had decreased 5-year survival. Patients who had decreased postoperative renal function (41.0% ± 7.4% vs 72.2% ± 3.4%; P = .004), and patients who sustained pulmonary complications (45.6% ± 8.8% vs 66.3% ± 3.3%; P = .042) had worse 5-year survival.

Conclusions: Open AAA repair can be done with low morbidity and mortality in the era of endovascular aneurysm repair. Careful consideration should be given to preoperative optimization and perioperative care in patients with chronic obstructive pulmonary disease, chronic renal insufficiency, and cerebrovascular disease. Postoperative decrease in renal function and pulmonary complication portend decreased 5-year survival; strategies to ameliorate these factors should be sought.

CLINICAL RESEARCH STUDIES

From the Society for Clinical Vascular Surgery

Endovascular aneurysm repair (EVAR) has become the treatment of choice for the majority of patients with aneurysms of the infrarenal aorta. Compared to open abdominal aortic aneurysm (AAA) repair, EVAR has a short-term survival benefit, as well as other perioperative advantages, such as decreased blood transfusion and shorter-length of hospital stay. However, a significant number of patients with infrarenal AAAs continue to undergo open repair. Open surgery remains the definitive treatment for patients with infrarenal AAA of mycotic or connective tissue disease etiology. In addition, anatomic constraints, such as hostile aneurysm neck and difficult vascular access, continue to preclude stent graft repair in a portion of patients with infrarenal AAA. Last, although EVAR may have a short-term survival benefit over open AAA repair, this does not seem to translate into a long-term survival advantage.

Meanwhile, open repair is still the standard of care at most institutions for juxtarenal, pararenal, and extent IV thoracoabdominal aortic aneurysms. In fact, the most common indication for open AAA repair in the current era of stent grafting is involvement of the renal and visceral arteries. While various off-label endovascular techniques, as well as devices approved
outside of the United States, have demonstrated the short-term safety and efficacy of fenestrated or branched endograft therapy for AAAs involving the renal and visceral arteries, long-term data regarding aneurysm sac behavior, and visceral ostia patency remain lacking.

In order to assess the mortality and morbidity of open AAA repair during the current era of EVAR, and in an effort to evaluate predictors of decreased perioperative and long-term survival after open repair, we analyzed a single institution’s experience.

METHODS

A prospectively maintained vascular database was used to retrospectively analyze data on patients (n = 1123) who underwent AAA repair between June 2003 and June 2009 at the Hospital of the University of Pennsylvania. Of these patients, 715 (63.7%) underwent endovascular repair of infrarenal AAA, and 408 (36.3%) underwent open AAA repair. The 408 patients who underwent open AAA repair are the focus of this study. The aneurysms treated included infrarenal, pararenal, suprarenal, and extent IV thoracoabdominal aortic aneurysms (TAAAs). This study was conducted with the approval of the institutional Human Research Ethics Committee.

Primary outcomes were 30-day and 5-year survival. Secondary outcomes included cardiac and pulmonary complications and decreased renal function. Cardiac complication was defined as arrhythmia, or myocardial ischemia or infarction, as determined by electrocardiographic or laboratory evaluation. Pulmonary complications included ventilator-dependent respiratory failure, pneumonia, pleural effusion requiring drainage, or reintubation. Decreased renal function was defined as worse postoperative renal function compared to preoperative renal function, as measured by chronic kidney disease stage. For example, a patient with preoperative stage II chronic kidney disease (estimated glomerular filtration rate [eGFR], 60-90) who postoperatively had stage III kidney disease (eGFR 30-60) was classified as having decreased renal function. Creatinine levels at discharge were used for calculation of postoperative renal function. Estimated eGFR was determined by the Modification of Diet in Renal Disease formula, and chronic renal insufficiency was defined as eGFR less than 60.

The influence of patient-related, disease-related, and treatment-related variables on 30-day mortality and secondary outcomes were assessed using logistic regression for multivariate analysis, and Pearson χ² and t test for univariate analysis. Patient-related independent variables examined were age, gender, race, statin usage, chronic renal insufficiency (CRI), coronary artery disease (CAD), coronary revascularization, cerebrovascular disease (CVD), chronic obstructive pulmonary disease (COPD), and previous open or endovascular AAA repair. Disease-related independent variables examined were aneurysm size, timing of repair (elective, urgent, or emergent), and proximal clamp site (infrarenal, suprarenal, or supraceliac). Treatment-related independent variables examined were clamp time, retroperitoneal vs transperitoneal approach, the performance of a left renal artery bypass, the administration of mannitol, and estimated blood loss (EBL).

Long-term survival was determined with Kaplan-Meier life table methods, and analyzed using log-rank (univariate) and Cox regression (multivariate) analysis. All tests of significance were at the P < .05 level, and all statistical analyses were performed with SPSS software (SPSS, Chicago, Ill).

RESULTS

Preoperative characteristics. Patient characteristics are summarized in Table I. Sixty-seven patients (16.4%) underwent nonelective repair: 24 patients (5.9%) underwent emergent repair due to ruptured aneurysms, and 43 patients (10.5%) underwent urgent repair (within 24 hours of unplanned admission) due to symptomatic aneurysms. The remaining patients (n = 341) underwent elective repair. Of the 145 patients who had undergone coronary revascularization, 46 (32.2%) underwent percutaneous coronary intervention and 97 (67.8%) underwent coronary artery bypass grafting. Fifty-five patients (13.5%) had undergone previous infrarenal AAA repair with EVAR (n = 21) or open surgery (n = 34). Indications for open AAA repair after EVAR included eight patients with proximal type I endoleak (six of whom failed attempts at endovascular salvage), five patients with graft migration and aneurysm expansion, four patients with type II endoleak and aneurysm expansion (all of whom had failed multiple attempts at endovascular salvage), and four patients with aneurysmal degeneration proximal to the stent graft.

The reason for open repair in the patients with previous open AAA repair was aneurysmal degeneration proximal to the previous graft in all cases.

Operative details. The majority of patients (n = 388; 95.1%) were not candidates for endovascular repair based on anatomic criteria (Table II). Nine patients with ruptured infrarenal AAAs underwent open repair due to surgeon preference. In addition, six patients underwent open repair due to mycotic or connective tissue disorder aneurysm etiology, and five patients underwent open AAA repair due to surgeon and patient preference.

Mean aneurysm size was 6.3 ± 1.4 cm. A retroperitoneal approach (n = 303; 74.3%) was used in the majority of
cases, mostly due to the proximal extent of the aneurysm. In total, 137 patients (33.6%) had infrarenal aortic clamps, 97 patients (23.8%) had suprarenal aortic clamps, and 174 patients (42.6%) had supracaeliac aortic clamps. A tube graft was used in 325 patients (79.7%), with the remaining 83 patients (20.3%) requiring a bifurcated graft. A transperitoneal approach was used in 59.0% (49/83) of the bifurcation cases, mostly due to the proximal extent of the aneurysm. In total, 137 patients (33.6%) had infrarenal aortic clamps, 97 patients (23.8%) had suprarenal aortic clamps, and 174 patients (42.6%) had supracaeliac aortic clamps. A tube graft was used in 325 patients (79.7%), with the remaining 83 patients (20.3%) requiring a bifurcated graft. A transperitoneal approach was used in 59.0% (49/83) of the bifurcation cases.

Suprarenal and supracaeliac ischemic times for patients undergoing open AAA repair were 21.1 ± 7.5 and 22.3 ± 9.0 minutes, respectively. Ischemic times were available for 237 (87.5%) of the 271 repairs requiring suprarenal or supracaecal cross-clamping. In 114 patients (27.9%), after construction of a bevelled proximal anastomosis incorporating the ostia of the right renal artery and/or visceral arteries, separate reimplantation of the left renal artery was performed. This left renal artery bypass was performed with a median additional left kidney ischemic time of 10 minutes.

Including ruptured aneurysms, mean EBL was 1.7 ± 1.4 liters, which differed by clamp site (infrarenal 1.0 ± 0.5 L, suprarenal 1.4 ± 1.3 L, and supracaecal 2.4 ± 1.7 L; P < .001). At the discretion of the surgeon, 176 patients (43.1%) received mannitol. Renal cooling was not performed during any of the procedures.

Thirty-day survival. Overall 30-day survival was 95.6% for the entire cohort. In-hospital survival was also 95.6%. Neither overall 30-day survival (infrarenal 96.4%, suprarenal 95.9%, and supracaecal 94.8%; P = .800), nor elective 30-day survival (infrarenal 97.3%, suprarenal 96.6%, and supracaecal 96.4%; P = .911) differed by clamp site. Thirty-day survival did differ by timing of repair (elective 96.8%, urgent 93.0%, and emergent 83.3%; P = .035) by multivariate analysis.

Compared to patients without these risk factors, patients with COPD (91.9% vs 97.2%; P = .004) and CRI (92.0% vs 98.3%; P = .009) had decreased 30-day survival by multivariate analysis. Neither a history of CAD, lack of statin usage, EBL, nor the performance of renal bypass predicted decreased 30-day survival. Post-hoc analysis demonstrated that patients with CAD who had undergone coronary revascularization had an improved 30-day survival compared to patients with CAD who had not undergone coronary revascularization (98.6% vs 91.7%; P = .026).

Long-term survival. Mean follow-up for patients was 38.1 ± 24.8 months. Twelve percent of patients were lost to follow-up. Mean survival was 65.3 ± 1.8 months. One- and 5-year survival were 90.0% ± 1.5% and 65.1% ± 3.0%, respectively (Fig 1). Clamp site (infrarenal 73.9% ± 4.5%, suprarenal 64.5% ± 6.8%, supracaecal 52.9% ± 5.3%; P = .001), and statin usage (71.1% ± 3.7% vs 57.2% ± 5.1%; P = .005) predicted 5-year survival by univariate but not multivariate analysis. Timing of repair (elective 68.3% ± 3.4%, urgent 45.0% ± 9.1%, and emergent 43.2% ± 11.5%; P = .011) predicted 5-year survival by multivariate analysis.

Patients with COPD (55.8% ± 5.8% vs 67.3% ± 3.6%; P = .013), CRI (51.2% ± 5.2% vs 72.8% ± 3.7%; P = .043; Fig 2, A), and CVD (46.8% ± 7.4% vs 67.4% ± 3.4%; P = .003) had worse 5-year survival by multivariate analysis. In addition, patients who had worse renal function postoperatively (41.0% ± 7.4% vs 72.2% ± 3.4%; P = .004; Fig 2, B), and patients who sustained pulmonary complications (45.6% ± 8.8% vs 66.3% ± 5.3%; P = .042) had poorer 5-year survival by multivariate analysis. Neither a history of CAD nor cardiac complication predicted decreased Kaplan-Meier survival.

Major complications. Seventy-nine patients (19.4%) sustained worsened renal function postoperatively; of these, seven patients (1.7%) developed worsening renal function requiring long-term dialysis. Overall, the mean preoperative serum creatinine was 1.30 ± 0.86 mg/dL, and the mean discharge serum creatinine was 1.32 ± 0.94 mg/dL (P = .510). While renal ischemic time did not predict decreased renal function, more proximal clamp site did predict worsened renal function by univariate (P = .001) but not multivariate analysis (P = .589).

Cardiac complications occurred in 71 patients (17.4%). Twenty-nine patients (7.1%) sustained myocardial ischemia or infarction, and 42 patients (10.3%) sustained arrhythmias, most commonly atrial fibrillation. Forty-five patients (11.0%) sustained pulmonary complications. Additional complications included 12 patients (2.9%) requiring return to the operating room for bleeding, eight patients (2.0%) requiring intervention for limb ischemia, four patients (1.0%) requiring laparotomy for intestinal ischemia, and two patients (0.5%) sustaining cerebrovascular accidents. Three patients (0.7%), all of whom had supracaecal cross-clamps, sustained spinal cord ischemia: one patient sustained an intraoperative cardiac arrest and awoke with paraplegia, another patient thrombosed his/her aortic graft postoperatively leading to paraplegia and multisystem organ failure, and the last patient had an extent type IV TAAA repair complicated by paraparesis that resolved.

DISCUSSION

A large contemporary, single-center experience with open AAA repair has been presented. The 30-day and 5-year survival rates in this series compare well with those reported in the literature (Table III).5-6,13-20 The current cohort includes patients who underwent emergent and

### Table II. Primary indication for open repair (as opposed to endovascular repair)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Open AAA (n = 488)</th>
</tr>
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<tbody>
<tr>
<td>Involvement of renal or visceral arteries</td>
<td>271 (66.4%)</td>
</tr>
<tr>
<td>Hostile proximal neck</td>
<td>53 (13.0%)</td>
</tr>
<tr>
<td>Aortobialical aneurysm/insufficent distal landing zone</td>
<td>42 (10.3%)</td>
</tr>
<tr>
<td>Difficult vascular access (aortic occlusion, inadequate size of iliac vessels)</td>
<td>22 (5.4%)</td>
</tr>
<tr>
<td>Ruptured aneurysm</td>
<td>9 (2.2%)</td>
</tr>
<tr>
<td>Preference of patient and surgeon</td>
<td>6 (1.5%)</td>
</tr>
<tr>
<td>Mycotic or connective tissue disorder etiology</td>
<td>5 (1.2%)</td>
</tr>
</tbody>
</table>

AAA, Abdominal aortic aneurysm.
urgent repair for ruptured and symptomatic aneurysms, which predicted decreased 30-day and long-term survival by multivariate analysis. While patients with symptomatic AAAs that undergo urgent repair do not have the physiological derangements of patients with ruptured aneurysms, urgent operation does preclude optimization of cardiovascular and pulmonary risk factors.

It is interesting that more proximal clamp site did not predict decreased 30-day survival, but did predict decreased 5-year survival by univariate analysis. Other studies have found that more proximal clamp placement results in decreased perioperative survival. Cross-clamping above the renal arteries or celiac artery poses technical challenges, including high retroperitoneal access and the performance of renal bypass, which often translate to increased blood loss and operative duration, and greater rates of renal insufficiency, bowel ischemia, and perioperative mortality. Myers et al. demonstrated that clamping above the renal arteries results in decreased creatinine clearance, while more proximal clamping above the superior mesenteric artery induces mesenteric ischemia/reperfusion injury and further deterioration of renal function. Kidney dysfunction has been shown to be an independent risk factor for long-term mortality. The finding that more proximal cross-clamping predicts decreased renal function may explain the association between more proximal clamp site and decreased 5-year survival.

The authors believe that several technical aspects are important in achieving the results herein reported. First, manipulation of visceral and renal vessels is kept to a minimum in order to prevent injury and subsequent thrombosis or bleeding. In this context, visceral and renal vessels are rarely dissected out and occluded distally while the anastomosis is performed. While this may result in increased blood loss due to back-bleeding, we find that most of this can be recovered through the use of cell saver. Second, open AAA repair is always done in a manner to minimize visceral and renal ischemic time. In the case of an AAA involving the renal and visceral arteries, whenever possible, the celiac artery, superior mesenteric artery, and/or right renal artery are incorporated into a beveled proximal anastomosis. If a left renal artery bypass is necessary, it is performed immediately after the proximal anastomosis. Last, preoperative optimization is crucial, as the majority of patients in the current study had at least one of the risk factors of CAD, COPD, and CRI, which have been shown to decrease survival.

Recently, several studies have highlighted the importance of hospital and surgeon volume in outcomes after open AAA repair. Landon et al. investigated the relationship between institutional volume and perioperative mortality, and found a steady increase in survival with increasing volume of open repair. In their study, hospitals that performed over 50 open AAA repairs per year had lower perioperative mortality than lower volume centers. In
another study, McPhee et al.\textsuperscript{34} showed that surgeon volume, not hospital volume, was the primary determinant of in-hospital mortality after open AAA repair. Surgeons who performed more than nine open AAA repairs a year had decreased in-hospital mortality compared to lower volume surgeons.\textsuperscript{34} The results of these studies support the regionalization of AAA repair not only to high-volume hospitals, but also to high-volume surgeons.

Patients who sustained worse renal function postoperatively had poorer 5-year survival, which is confirmed by recent studies.\textsuperscript{30-32} Bihorac et al.\textsuperscript{30} found that kidney injury after major abdominal and cardiothoracic surgery was associated with an independent long-term risk of death, and concluded that kidney injury should no longer be viewed only as an indicator of overall severity of illness, but also as an independent predictor of long-term outcome. Interrogation of the National Surgical Quality Improvement Program database in the Veterans Administration confirmed that postoperative complications, such as decreased renal function, could be more important than preoperative and intraoperative factors in determining long-term survival.\textsuperscript{32} This National Surgical Quality Improvement Program study showed that the negative effect of postoperative complications on long-term survival was not due solely to increased 30-day mortality.\textsuperscript{32} This finding is supported by a qualitative assessment of Fig 2, B, which demonstrates that the Kaplan-Meier survival curves of patients who had stable vs worse postoperative renal function continue to diverge past 30 days. Although it is not certain how postoperative renal dysfunction results in decreased long-term survival, it seems to lead to ongoing progressive kidney damage and the development of chronic kidney disease, which is an

Fig 2. A, Kaplan-Meier survival curve for patients undergoing open abdominal aortic aneurysm repair preoperative
estimated glomerular filtration rate (eGFR) less than or greater than 60. B, Kaplan-Meier survival curve for patients undergoing open abdominal aortic aneurysm repair by stable vs worse postoperative renal function.
Table III. Summary of survival in contemporary studies of open repair of abdominal aortic aneurysms

<table>
<thead>
<tr>
<th>Aneurysm Type</th>
<th>No. of patients</th>
<th>Thirty-day survival</th>
<th>Long-term survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infra renal aortic clamp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current series</td>
<td>137</td>
<td>97.3%</td>
<td>76.1% at 5 years</td>
</tr>
<tr>
<td>DREAM trial</td>
<td>174</td>
<td>95.4%</td>
<td>69.9% at 6 years</td>
</tr>
<tr>
<td>EVAR trial</td>
<td>626</td>
<td>95.7%</td>
<td>54% at 8 years</td>
</tr>
<tr>
<td>Chong et al</td>
<td>849</td>
<td>98.8%</td>
<td>69.1% at 5 years</td>
</tr>
<tr>
<td>Landry et al</td>
<td>103</td>
<td>97.1%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Supraprenal aortic clamp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current series</td>
<td>97</td>
<td>96.6%</td>
<td>69.1% at 5 years</td>
</tr>
<tr>
<td>Chong et al</td>
<td>171</td>
<td>98.2%</td>
<td>67.7% at 5 years</td>
</tr>
<tr>
<td>Landry et al</td>
<td>82</td>
<td>93.9%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Supraceliac aortic clamp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current series</td>
<td>174</td>
<td>94.8%</td>
<td>52.9% at 5 years</td>
</tr>
<tr>
<td>Nathan et al</td>
<td>108</td>
<td>94.4%</td>
<td>50.0% at 5 years</td>
</tr>
<tr>
<td>Coselli et al</td>
<td>329</td>
<td>96.4%</td>
<td>65.3% at 5 years</td>
</tr>
<tr>
<td>Kieffer et al</td>
<td>171</td>
<td>86.6%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Richards et al</td>
<td>53</td>
<td>94.0%</td>
<td>78.0% at 3 years</td>
</tr>
</tbody>
</table>

Note: Thirty-day survival refers to survival within 30 days postoperatively. Long-term survival refers to survival at specified intervals.

Independent risk-factor for increased cardiovascular events and death.30-32

Strategies to prevent or mitigate kidney injury with open AAA repair may, therefore, improve outcomes. Continuous cold perfusion of the kidneys during open AAA repair requiring supraprenal clamping has been shown to reduce postoperative renal complications.35,36 In addition, statin usage has been associated with improved recovery of renal function in patients who developed postoperative kidney injury and with improved long-term survival after vascular surgery.37 Consistent with these results, we found that statin usage predicted improved 5-year survival. Although these strategies may be useful adjuncts, minimizing ischemia to the kidneys by limiting clamp time remains the most important strategy in preventing postoperative decrease in renal function. In addition, the performance of renal artery endarterectomy at the time of aneurysm repair has been shown to improve renal function postoperatively.16

Neither a history of CAD nor cardiac complication predicted decreased survival. Several factors may explain this finding. First, the majority of our patients were on statins preoperatively. In a randomized control trial, Schouten et al22 demonstrated that statin usage before vascular surgery decreased postoperative myocardial ischemia and death from cardiovascular causes. Second, posthoc analysis showed that patients with CAD who had undergone coronary revascularization had improved 30-day survival. While the latter findings do not coincide with the results of several randomized control trials in which coronary revascularization was performed in anticipation of major vascular surgery, it is possible that in this cohort of patients, coronary revascularization protected against postoperative myocardial infarction and death.38-40

Finally, given the morbidity and mortality associated with open repair of AAAs involving the visceral arteries, several studies have reported on the use of endovascular therapy to treat this complicated disease process.7,8 Greenberg et al7 assessed the use of fenestrated endovascular grafts to treat juxtarenal AAAs in 30 patients, and reported eight renal events and two deaths over a follow-up of 2 years. Haulon et al8 reported on 80 patients who underwent elective fenestrated aortic endograft placement for juxtarenal, suprarenal, and extent type IV TAAAs, and reported a 1- and 2-year survival of 92%. While these studies highlight the intermediate safety of elective endovascular repair of AAAs involving the visceral arteries, long-term follow-up of aneurysm sac behavior, visceral artery patency, and aneurysm-related and overall mortality remains lacking.

In summary, this study demonstrates that open AAA repair can be performed with acceptable morbidity and mortality. CRI and COPD predicted decreased 30-day survival, while CRI, COPD, and CVD predicted decreased 5-year survival. Postoperative decrease in renal function and pulmonary complications resulted in decreased 5-year survival. These findings suggest that careful consideration should be given to preoperative optimization and perioperative care in patients with COPD, CRI, and CVD. Last, investigation of strategies to ameliorate postoperative renal dysfunction and pulmonary complications is warranted.

AUTHOR CONTRIBUTIONS

Conception and design: DN, BJ, EW
Analysis and interpretation: JC, GW, RF
Data collection: DN, CB
Writing the article: DN, BJ, CB, EW
Critical revision of the article: GW, JC, RF
Final approval of the article: DN, CB, GW, BJ, JC, RF, EW
Statistical analysis: DN, BJ
Obtained funding: Not applicable
Overall responsibility: EW

REFERENCES


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