A systematic review and meta-analysis of the management of visceral artery aneurysms

Patricia Barrionuevo, MD,[a] Mahmoud B. Malas, MD, MHS,[b] Besma Nejim, MBChB, MPH,[c] Abdullah Haddad, MD,[d] Allison Morrow, BA,[a] Oscar Ponce, MD,[a] Bashar Hasan, MD,[a] Mohamed Seisa, MD,[a] Rabih Chaer, MD,[e] *and* M. Hassan Murad, MD, MPH,[a] *Rochester, Minn; San Diego, Calif; and Philadelphia and Pittsburgh, Pa*

ABSTRACT

Background: The evidence supporting management decisions of visceral artery aneurysms (VAAs) is sparse. Practice guidelines are needed to help patients and surgeons choose between endovascular and open surgery approaches.

Methods: We searched MEDLINE, EMBASE, Cochrane databases, and Scopus for studies of patients with VAAs. Studies were selected and appraised by pairs of independent reviewers. Meta-analysis was performed when appropriate.

Results: We included 80 observational studies that were mostly noncomparative. Data were available for 2845 aneurysms, comprising 1279 renal artery, 775 splenic artery, 359 hepatic artery, 226 pancreaticoduodenal and gastroduodenal arteries, 95 superior mesenteric artery, 87 celiac artery, 15 jejunal, ileal and colic arteries, and 9 gastric and gastroepiploic arteries. Differences in mortality between open and endovascular approaches were not statistically significant. The endovascular approach was used more often by surgeons. The endovascular approach was associated with shorter hospital stay and lower rates of cardiovascular complications but higher rates of reintervention. Postembolization syndrome rates ranged from 9% (renal) to 38% (splenic). Coil migration ranged from 8% (splenic) to 29% (renal). Otherwise, access site complication were low (<5%). Pseudoaneurysms tended to have higher mortality and reintervention rates.

Conclusions: This systematic review provides event rates for outcomes important to patients with VAAs. Despite the low certainty warranted by the evidence, these rates along, with surgical expertise and anatomic feasibility, can help patients and surgeons in shared-decision making. (J Vasc Surg 2019;70:1694-9.)

Keywords: Aneurysm; Guideline; Meta-analysis; Visceral

Visceral artery aneurysms (VAAs) are rare vascular pathologies with reported incidence rates of 0.01% to 0.2%. Aside from renal artery aneurysms, which some view as a separate entity, hepatic and splenic artery aneurysms are the most common.[1,2] Perhaps one in four VAAs may present with rupture, which can be life threatening.[3-6] Most VAAs (62%) are atherosclerotic, but some are associated with connective tissue diseases and inflammatory and genetic conditions.[7] For example, renal artery aneurysms, which constitute 22% of all visceral artery aneurysms,[8] tend to occur preferentially in patients with connective tissue diseases such as fibromuscular dysplasia, Marfan syndrome, and Ehlers-Danlos syndrome.[9,10] Pseudoaneurysms caused by trauma can also occur in the visceral arteries.

The natural history of VAAs suggests that their growth is slow and that they tend to not rupture when they are small. For example, a review of a 20-year experience at the Mayo Clinic suggests that splenic artery aneurysms are less likely to require treatment unless they are symptomatic, ≥2 cm in diameter, or affect women of childbearing age.[11] This natural history, however, is not well defined and differs based on VAA location.

Treatments of VAAs can follow an open or endovascular approach. Open surgical repair options include ligation, total or partial excision and patching (vein or prosthetic), primary repair, plication, and ex vivo repair. Endovascular techniques, including embolization, coiling, and covered stents, have been widely adapted to treat VAAs because of the minimally invasive nature, anticipated shorter recovery time, and generally lower risk of morbidity and death.

Empirical evidence comparing the outcomes of open and endovascular approaches remains unclear, however. On one hand, Kunzle et al[10] reported that endovascular treatment was associated with a lower incidence of complications, lower median length of stay, and lower rates of discharge to skilled nursing facilities.[10] On the other hand, other studies demonstrated no difference in

From the Evidence-based Practice Center, Mayo Clinic, Rochester[a]; the Division of Vascular and Endovascular Surgery, the University of California, San Diego Health System, San Diego[b]; the Department of Vascular Surgery, Penn State Health, Milton S. Hershey Medical Center,[c] and the Section of Cardiology, Temple University-Lewis Katz School of Medicine,[d] Philadelphia; and the University of Pittsburgh Medical Center, Pittsburgh.[e]

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Correspondence: M. Hassan Murad, MD, Division of Preventive Medicine, Mayo Clinic, 200 1st St SW, Rochester, MN 55905 (e-mail: murad.mohammad@mayo.edu).

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operative mortality[11] or in renal function decline[12] between open and endovascular approaches. Therefore, there is lack of consensus about the comparative effectiveness of either approach in managing VAAs.

The Society for Vascular Surgery has convened a committee of experts to develop clinical practice guidelines on the management of VAAs. To support this guideline, we conducted a systematic review and meta-analysis to summarize the best available evidence of comparing open to endovascular approaches for VAAs.

METHODS

This systematic review follows a protocol established a priori by a committee from the Society for Vascular Surgery. This report is consistent with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[12]

Study eligibility, data sources, and search strategies. We included studies with ≥10 patients that reported outcomes of patients with VAAs treated with open or endovascular approaches. Studies were comparative or noncomparative but had to have longitudinal follow-up and evaluate an outcome of interest, including mortality, need of reintervention, myocardial infarction, stroke, end-organ ischemia, end-organ infarction, deep vein thrombosis, pulmonary embolism, postembolization syndrome (PES), respiratory complications, gastrointestinal complications, coil migration, rupture after endovascular aortic repair, rupture during intervention, or wound complications (eg, surgical site infection).

A comprehensive search of several databases from 1980 to March 27, 2017, was conducted without language restrictions. The databases included MEDLINE Epub Ahead of Print, MEDLINE In-Process & Other Non-Indexed Citations, MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Scopus. The search strategy was designed and conducted by a medical reference librarian with input from the investigators. Controlled vocabulary supplemented with keywords was used to search for studies of open or endovascular repair of VAAs. The actual strategy is available in the Appendix (online only).

Study selection, data extraction, and methodologic quality assessment. Studies were selected and data were extracted by pairs of independent reviewers. Data extracted included patient and setting description, procedure description, risk of bias indicators, and outcome data. Because the studies were nonrandomized, we adapted[13] items from the Newcastle Ottawa tool[14] that assess the three main domains of cohort selection, comparability, and outcome assessment. We focused on patient selection (consecutive sample or not), hemodynamic assessment at baseline and follow-up, independent event adjudication, core laboratory imaging assessment, loss to follow-up, and funding source. A global judgment about risk of bias was made for each study.

Statistical analysis and certainty in evidence. For comparative studies, we calculated the relative risk and 95% confidence intervals (CIs). For noncomparative studies, we calculated the event rate of patients with outcomes for each intervention (endovascular and open). We estimated the related Wilson CIs and transformed the proportion using the Freeman-Tukey double arcsine transformation.[15] For studies that reported the number of aneurysms, we calculated the incidence rate and related Poisson CIs. Because of anticipated heterogeneity, the DerSimonian and Laird random-effects model[16] was used to pool estimates from the included studies. The I^2 statistic was used to estimate heterogeneity. Analysis was done using Stata 15 software (StataCorp LLC, College Station, Tex). Subgroup analyses were planned based on the anatomic location, aneurysm size, rupture status, true vs pseudoaneurysms, and for urgent vs elective procedures.

We used the GRADE (Grading of Recommendations Assessment Development and Evaluation) approach to evaluate certainty in the evidence (also called quality of evidence).[17] In this approach, randomized trials start at a high level of certainty, and observational studies start at a low level of certainty. Certainty can be graded down owing to study limitations, imprecision, indirectness, inconsistency, or publication bias. Certainty can also be increased, for example, for a large effect size.[18]

RESULTS

Available studies. The literature search resulted in 1304 references, from which 80 were included in quantitative synthesis. Only six studies were comparative. Appendix Fig 1 (online only) depicts the process of study selection. Appendix Table 1 (online only) includes the characteristics of the included studies. Data from comparative studies were sparse and imprecise; hence, this report focuses on event rates from noncomparative studies. Appendix Table 2 (online only) includes an evaluation of the methodologic quality of the included studies. Appendix Tables 3 and 4 (online only) report results from noncomparative and comparative studies, respectively. Feasible subgroup analyses are summarized in Appendix Table 5 (online only). Fig 1 shows the distribution of the number of aneurysms by location and treatment approach. Very few studies reported data exclusively for pseudoaneurysms, and they had small sample sizes. Ghoneim et al[19] reported 15 renal pseudoaneurysms, and Kunzle et al[10] reported six hepatic pseudoaneurysms.

Figs 2 and 3 depict the event rates of mortality and reintervention by aneurysm location for endovascular and open approaches, respectively. The outcome of PES

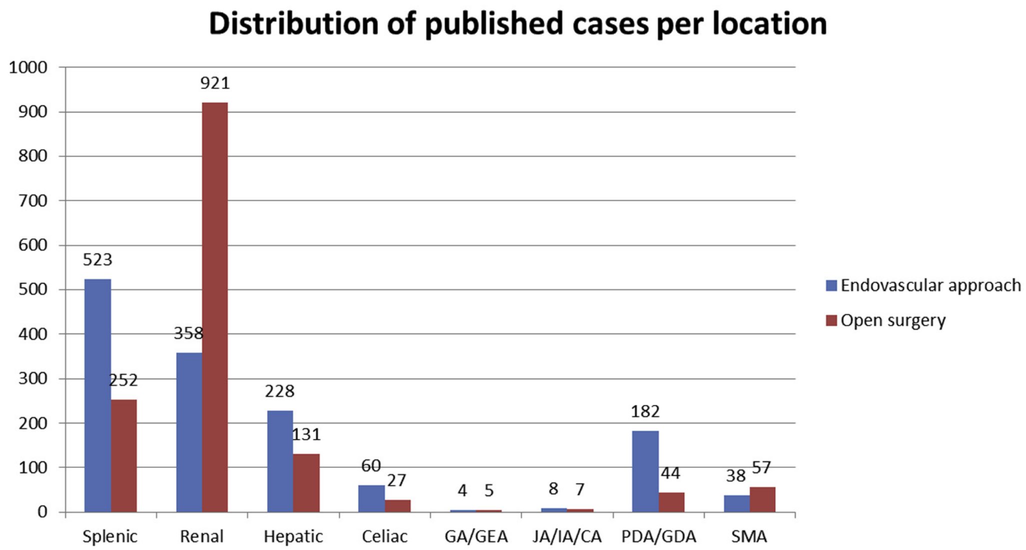

Fig 1. Distribution of published cases of visceral artery aneurysms (VAAs) by aneurysm location. Data from a national sample of renal artery aneurysms were not included to prevent overlap. Patient numbers were included whenever possible, but a few studies only reported the number of aneurysms instead. *CA,* Colic artery; *GA,* gastric artery; *GDA,* gastroduodenal artery; *GEA,* gastroepiploic artery; *IA,* iliac artery; *JA,* jejunal artery; *SMA,* superior mesenteric artery; *PDA,* pancreaticoduodenal artery.

was poorly described in most studies and had various definitions. After procedures of renal artery aneurysms, PES was defined as hyperpyrexia, abdominal pain, nausea, and vomiting,[19] and after splenic artery aneurysms, it was defined as left upper-quadrant pain, with or without a documented splenic infarct,[20] or as fever, abdominal pain, and slow bowel transit after a splenic infarction.[21]

Renal artery aneurysms. The largest series was a nationwide sample of 6234 renal artery aneurysm repairs performed between 1988 and 2011[22] and reported outcomes of 1082 patients who underwent endovascular surgery and 1267 who underwent open surgery. Complication rates in this largest sample were 12.4% for open repair and 10.5% for endovascular repair ($P = .13$). There were more cardiac (2.2% vs 0.6%; $P = .001$) and peripheral vascular complications (0.6% vs 0.0%; $P = .01$) with open repair. Open repair was associated with a longer length of stay (6.0 vs 4.6 days; $P < .001$). In-hospital mortality was significantly higher for endovascular repairs than for all open repairs; however, this difference was not significant after adjustment.[22]

The meta-analysis, excluding the nationwide sample series,[22] included 28 case series of 358 renal artery aneurysms treated with an endovascular approach and 26 case series of 921 renal artery aneurysms treated with open surgery (a total of 1279 aneurysms). Short-term and long-term mortality rates were very low and not significantly different between the two interventions. The need of reintervention and incidence of end-organ infarction and respiratory complications were not significantly different between the two approaches. The incidence of pulmonary embolism and deep venous thrombosis, complications expected with open repair, was low and similar between the two groups. The risk of extended length of stay was also similar between the two groups.

The need for reintervention rate (at the longest study follow-up) was higher for the endovascular approach than for open surgery, although these CIs overlapped (0.16 [95% CI, 0.00-0.42] vs 0.03 (95% CI, 0.00-0.08]).The need for reintervention rate on pseudoaneurysms trended to be higher than the rate for true aneurysms, although these CIs also overlapped (0.07 [95% CI, 0.00-0.32]) vs 0.00 [95% CI, 0.00-0.52]). Rates of PES and coil migration were 0.09 (95% CI, 0.00-0.25) and 0.29 (95% CI, 0.04-0.71), respectively.

Splenic artery aneurysms. We included 33 case series of 523 splenic artery aneurysms treated with an endovascular approach and 22 series of 252 splenic artery aneurysms treated with open surgery. Short-term and long-term mortality rates were very low and not significantly different between the two interventions. Mortality was high for ruptured aneurysms treated with an open approach, with an event rate of 0.29 (95% CI, 0.04-0.71). End-organ infarction and gastrointestinal complications rates were not significantly different between the two approaches. The need for reintervention was lower for open surgery 0.00 (95% CI, 0.00-0.11) than for the endovascular approach 0.07 (95% CI, 0.01-0.17). The risk of access site complications for the endovascular approach was low at 0.02 (95% CI, 0.00-0.09). Rates of PES and coil

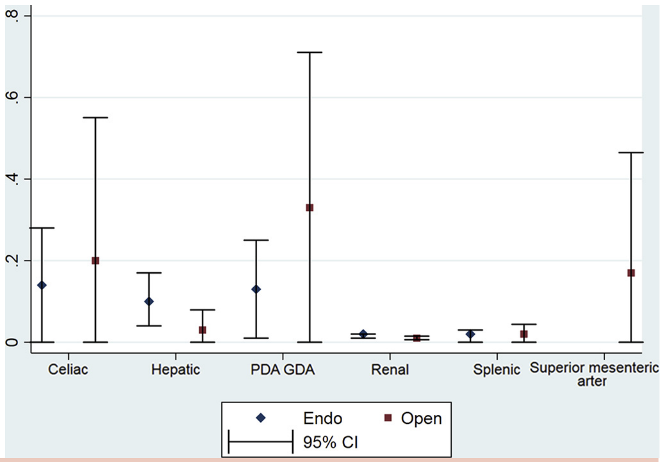

Fig 2. Mortality rates for open and endovascular (*Endo*) approaches according to aneurysm location. *CI,* Confidence interval; *GDA,* gastroduodenal artery; *PDA,* pancreaticoduodenal artery.

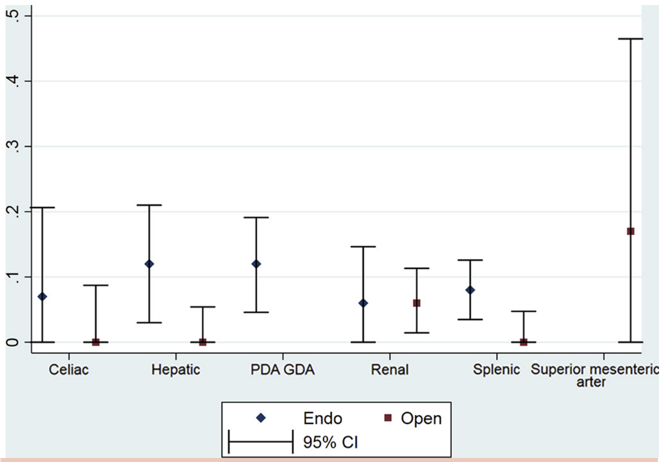

Fig 3. Reintervention rates for open and endovascular (*Endo*) approaches according to aneurysm location. *CI,* Confidence interval; *GDA,* gastroduodenal artery; *PDA,* pancreaticoduodenal artery.

migration were 0.38 (95% CI, 0.04-0.79) and 0.08 (95% CI, 0.00-0.24), respectively. Data were insufficient to identify a difference in mortality based on aneurysm size.

Hepatic artery aneurysms. We included 33 case series of 228 hepatic artery aneurysms treated with an endovascular approach and 22 series of 131 hepatic artery aneurysms treated with open surgery. Short-term and long-term mortality rates were low and not significantly different between the two interventions. The need for reinterventions after the endovascular approach was high for hepatic artery aneurysms at 0.40 (95% CI, 0.05-0.85). Mortality and the need for reintervention for hepatic pseudoaneurysms treated with the endovascular approach were also high at 0.50 (95% CI, 0.12-0.88) and 0.17 (95% CI, 0.00-0.64), respectively, with very sparse data on the open approach (Appendix Tables 3-5, online only).

Other VAA locations. There were 87 published cases of aneurysms in the celiac artery (60 were treated via an endovascular approach and 27 via open surgery), 95 in the superior mesenteric artery (38 were treated via an endovascular approach and 57 via open surgery), 226 in the pancreaticoduodenal and gastroduodenal arteries (182 were treated via an endovascular approach and 44 via open surgery), 15 in the jejunal, ileal, and colic arteries (8 were treated via an endovascular approach and 7 via open surgery), and 9 in the gastric and gastroepiploic arteries (4 were treated via an endovascular approach and 5 via open surgery). Event rates of the outcomes of interest are reported in Appendix Tables 3-5 (online only). Most of these VAAs were treated with an endovascular approach. Comparative inferences were not possible with the available data, and event rates were quite imprecise (ie, had wide CIs).

Certainty in estimates and publication bias. The certainty in the estimates (event rates) was low owing to the observational and noncomparative nature of the evidence. Almost all of these rates, except those for renal artery aneurysms, were imprecise because of the small sample size. Although we were unable to statistically evaluate for publication bias, this type of bias is likely present in a body of evidence that consists of small case series that do not require registration. It is plausible that published results are more favorable than unpublished ones. Many planned subgroup analyses were not feasible (Appendix Table 5, online only).

DISCUSSION

Main findings. We conducted a systematic review and meta-analysis to support the Society for Vascular Surgery guideline on the management of VAAs. This evidence synthesis primarily reports surgical case series with minimal comparative inferences. We therefore report event rates of outcomes of interest, which generally do not show statistically significant differences in mortality between the open and endovascular approach. Whether this imprecision is due to the small sample sizes of studies of a rare entity is unclear. Reintervention rates after endovascular procedures were high, but procedure complications were generally low, without important access site complications.

Implications. This systematic review suggests a possible equipoise in mortality between open surgery and endovascular repair of VAAs. This may be a true finding but can also reflect that VAAs are rare and that the small number of events across studies makes achieving statistically significant differences less likely.

It is important to note that numerous complications are more likely to occur with the open approach and may justify a recommendation for pursuing the endovascular approach as a first choice. These complications include those related to laparotomy, wound infection, hospital length of stay, and respiratory and cardiac complications, all of which are typically lower with endovascular interventions in various anatomic locations. Open reconstructive techniques for the elective repair of most of these aneurysms are reasonable when the endovascular approach is not feasible.

Limitations and strengths. An obvious limitation in this body of evidence is the small sample size of case series of these rare conditions and the noncomparative uncontrolled nature of the available studies. The lack of anatomic variables that determine the feasibility of the endovascular approach is another major limitation of this body of evidence. The outcome of PES had varied definitions across studies. Whether the outcome of coil migration was symptomatic or detrimental to the patient was not well described.

Future research efforts could focus on establishing rigorous registries that document the clinical and anatomic presentations, treatment choices, and outcomes of VAAs. The current systematic review followed a rigorous approach that was strengthened by collaboration with content experts and presents the largest collection of VAA cases. The guideline by the Society for Vascular Surgery will use this evidence along with the surgical expertise of the committee and other considerations, such as patient values, feasibility, and resource availability, to produce recommendations on the management of VAAs.

CONCLUSIONS

This systematic review provides event rates for outcomes important to patients with VAAs. Despite the low certainty warranted by the evidence, these rates along with surgical expertise and anatomic feasibility, can help patients and surgeons in shared decision-making.

AUTHOR CONTRIBUTIONS

Conception and design: PB, MBM, RC, MHM
Analysis and interpretation: PB, RC, MHM
Data collection: PB, BN, AH, AM, OP, BH, MS
Writing the article: MBM, MHM
Critical revision of the article: PB, MBM, BN, AH, AM, OP, BH, MS, RC, MHM
Final approval of the article: PB, MBM, BN, AH, AM, OP, BH, MS, RC, MHM
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PB and MBM contributed equally to this article and share co-first authorship.

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