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Type of Anesthesia for Endovascular Abdominal Aortic Aneurysm Repair

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Abstract

Objective: Endovascular aneurysm repair (EVAR) is increasingly used in the management of patients with abdominal aortic aneurysms (AAA), including in the emergency setting for ruptured AAA. The lower mortality amongst patients undergoing emergency EVAR under local anesthesia (LA) observed in the IMPROVE trial has sparked renewed interest in the anesthesia choice for EVAR. This systematic review evaluates the effect of mode of anesthesia on outcomes after EVAR.

Design: The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The primary outcome was in-hospital/30-day mortality and both emergency and elective EVAR were included. The relative risk of death was estimated for each individual study without adjustment for potential confounding factors.

Setting: Hospitals.

Participants: A total of 39,744 patients from 22 non-randomized studies were included in the analysis.

Interventions: None

Measurements and Main Results: Sixteen studies in 23,202 patients compared LA to GA and reported in-hospital/30-day mortality. The unadjusted risk of death after emergency EVAR with LA was lower than with GA. Trends in elective surgery were less clear.

Conclusions: There is some evidence across both emergency and elective settings to suggest that mode of anesthesia may be associated with improved outcomes. In particular, LA appears to have a positive effect on outcome after emergency EVAR. Due to the lack of randomized trial data, a significant risk of confounding remains. The optimal mode of anesthesia for EVAR should be further investigated and the reasons why particular anesthesia techniques are chosen for particular patients identified.

Key words

Anesthesia type, endovascular abdominal aortic aneurysm repair

Introduction

The 30-day mortality rate from emergency surgery for ruptured AAA (rAAA) remains very high with variation among different healthcare systems and countries. The mortality rate for elective surgery, at 1.4-5%, is high compared to other elective surgery[1-3].

Patients who require AAA surgery are often elderly with co-morbidities that contribute significantly to their peri-operative risk[4-5]. Since endovascular aneurysm repair (EVAR) was first reported in the early 1990s[6] it has become increasingly popular for this high-risk group, as it avoids the major physiological insult of a laparotomy[7-9]. The EVAR I trial showed that elective EVAR was associated with lower 30-day mortality, shorter hospital and intensive care stay, less blood loss and less requirement for blood products compared with open repair[7]. However, the incidence of adverse postoperative cardiac events in the longer term was similar[10]. A recent individual-patient-data meta-analysis of three randomized controlled trials comparing EVAR to open repair for rAAA reported that patients were discharged sooner after EVAR, but 90-day survival was similar for both groups[11]. Despite this, earlier discharge from critical care, shorter hospital stay and a higher proportion discharged directly home in the EVAR group means that the EVAR approach is likely to gain further support for use in emergency AAA repair, especially in specialist centres[2].

It was evident from early experience that it is possible to perform EVAR surgery under different types of anesthesia, including general (GA), regional (RA) and local anesthesia (LA)[12,13]. Non-randomized studies conducted 10 years ago, as well as a systematic review, suggested possible patient benefit when local and/or regional techniques are used for EVAR[14-17]. Recently, a post-hoc analysis of the Immediate Management of Patients with Rupture: Open Versus Endovascular Repair (IMPROVE) trial showed that patients who had emergency EVAR surgery for rAAA under LA had a significantly reduced odds of death in the 30-days following surgery compared to those who had GA[18]. The aim of this review is to evaluate the current evidence for the effect of mode of anesthesia on outcome from EVAR.

Methods

The literature was systematically searched as recommended in the Cochrane Collaboration Handbook and reported according to the Preferred Reporting Items for Systematic Review (PRISMA) guidelines[19]. A systematic search of the MEDLINE, Excerpta Medica Database (EMBASE), Web of Science, and Cochrane Library (2011 Issue 4) databases was performed for all types of published article up to March 2018. The electronic search was supplemented by a hand search of material not published by commercial publishers or in peer-reviewed journals, including the Conference Proceedings Citation Index on the Web of Science. The reference lists of articles obtained were also searched to identify further relevant citations. Additionally, the Current Controlled Trials Register (http:// www.controlled-trials.com) and the Cochrane Database of Controlled Trials were searched.

The search terms local anesthesia, regional anesthesia, epidural, spinal, endovascular, surgery, and the medical subject headings (MeSH), Spinal, Anesthesia, Epidural, Anesthesia, Local, Endovascular Procedures, Aortic Aneurysm, and Abdominal were used in combination with the following Boolean operators: (endovascular OR endovascular procedures[MeSH]) AND surgery AND (aortic aneurysm [MeSH]) AND (local anesthesia OR regional anesthesia OR epidural OR spinal OR anesthesia, spinal[MeSH] OR anesthesia, epidural[MeSH] OR anesthesia, local[MeSH]) (+ humans). Inclusion criteria comprised studies in patients undergoing EVAR that reported some comparative data by at least two methods of anesthesia (e.g. GA, RA or LA). Duplicate papers were excluded and all the remaining abstracts were independently scrutinized for suitability by two of the authors (RA and YS). Discrepancies in study selection were resolved by discussion with the review authors. Anesthetic techniques used for EVAR included: (i) GA (intravenous induction and maintenance with either volatile agents or total intravenous anesthesia (TIVA) with propofol); (ii) RA (spinal or epidural, a combination of both or paravertebral blockade + sedation with propofol/midazolam) and (iii) LA (skin infiltration with local anesthetic agent e.g.

lidocaine/levobupivacaine ± sedation with propofol/midazolam). Systematic reviews and case reports were excluded.

The primary outcome measure was 30-day/in-hospital mortality, but the search was not restricted by outcome. Both emergency and elective EVAR surgery were included. Data on patient characteristics (age, sex, body mass index, hyperlipidemia, diabetes, hypertension, American Society of Anesthesiologists (ASA) physical status classification, and the presence of cardiac, cerebrovascular, renal and respiratory disease) were also extracted.

Assessment of risk of bias:

The Scottish Intercollegiate Guidelines Network (SIGN) checklists were used to assess quality and to assign an indicative SIGN evidence level to each study[20,21]. Data were extracted independently by two authors (RA and YS).

Statistical analysis was performed using R Studio (version 1.1.442, RStudio, Inc).

Results

Studies retrieved

Our searches identified a total of 984 articles or abstracts. Of these, 922 were excluded after two authors independently screened the abstracts, leaving 62 full-text articles, which were assessed for eligibility. Forty of the 62 articles were excluded: because they were non-comparative, did not segregate results according to anesthesia type or were review articles. Twenty-two studies met the inclusion criteria (Figure 1). A summary of the 22 selected studies, which date from 1996 to 2018, is shown in Table 1 [14,16,18, 22-33,39,40,43-47]. Twelve of these studies were not included in previous reviews [16,18,22,23,33,39,40,43-47].

Assessment of risk of bias

All were observational studies or secondary analysis of trial data and were classified as SIGN level 2- (non-randomized), indicating that they carry a significant risk of selection bias or confounding. Study sizes ranged from 25 in the smallest study to 13,026 in the largest cohort.

Elective/emergency split

Most studies (14/22) included only patients who had elective EVAR surgery. Three studies included a mix of elective and emergency surgery, although most patients were in the elective group[23,31,46]. Four articles focused exclusively on emergency EVAR: the secondary analysis of the IMPROVE trial[18] (186 patients) and three retrospective database analyses[39,40,47] (total 3183 patients). One did not specify the elective/emergency split[14].

Baseline demographic and clinical characteristics

Eighteen studies reported the age of patients included. The mean age (SD) of patients was 74.6 (8.1) years (LA group), 73.4 (8.1) years (RA group) and 73.1 (8.4) years (GA group). Most patients in all groups were male (>83%). Other baseline clinical characteristics, including diabetes, smoking, hypertension, hyperlipidemia, ASA physical status classification 4/5, body mass index and the presence of cardiac, respiratory, cerebrovascular and renal disease are summarized in Table 2 (see Appendix 1 for full details).

Details of the general anesthesia technique used were described in only 7 out of 22 studies. Regional techniques were inconsistently reported and combined for analysis, and included spinal, epidural, combined spinal epidural, paravertebral and peripheral nerve blockade. The local anesthesia techniques described various doses of lidocaine and bupivacaine with monitored anesthesia care and intravenous sedation (Appendix 2).

Qualitative synthesis

Each of the 22 studies reported one or more clinical outcome in relation to different anesthetic techniques. Thirty-day/in-hospital mortality, duration of surgery and length of hospital stay were the most commonly reported outcome measures. Analgesia requirement was the primary outcome reported in one study[31] and four others reported on analgesia requirements. None included patient-reported outcome measures such as health-related quality of life or functional capacity. There was significant variation in the outcomes reported across the studies (Appendix 3). Furthermore, outcomes were not consistently defined. For example, post-operative acute kidney injury (AKI) was reported in ten studies, but each used a different definition for AKI.

Quantitative analysis

Thirty-day/in-hospital mortality by mode of anesthesia was reported in 20 studies (Table 3). Figure 2 shows the unadjusted relative risk (RR) of death between modes of anesthesia (LA vs GA, panel A; RA vs GA, panel B; LA vs RA, panel C). Studies are grouped by case-mix and results are summarized for each individual study. Pooled estimates were not included due to the serious risk of bias introduced by the potential confounders in the included studies, particularly confounding by indication[48]. Additionally, a confidence interval around an observational estimate is notional as it is not possible to properly account for the uncertainty due to the non-randomized nature of the comparison in a meta-analysis[49].

Local vs General Anesthesia (Figure 2A)

In the emergency setting a benefit was shown favoring LA over GA. The estimated RR of death ranged from 0.40 to 0.68. In the elective setting the estimated RR ranged from 0.08 to 1.53 across nine studies. Most RR estimates were less than 1 (favoring LA), however the numbers of deaths were few and the confidence intervals were wide, all encompassing 1. Three studies contained either a mixture of emergency and elective cases or did not specify. The RR estimates here ranged from 0.32 to 1.21 but again 95% confidence intervals were wide and all included 1.

Regional vs General Anesthesia (Figure 2B)

Ten studies compared RA to GA in the elective setting with the estimated RR of death ranging from 0.17 to 2.68. All studies with a non-zero event rate had a RR estimated less than 1 (favoring RA), however again the numbers of deaths were few and the confidence intervals were wide, all encompassing 1. One study reported only emergency cases; one reported a mixture of elective and emergency; and one did not specify. The 95% confidence interval for the estimated RR for mortality in all of these three studies crossed 1.

Local vs Regional Anesthesia (Figure 2C)

Seven studies compared LA to RA in the elective setting and all the confidence intervals for estimated RR of death were wide and all encompassed 1. One study reported only emergency cases; one reported a mixture of elective and emergency; and one did not specify. The 95% confidence interval for the estimated RR for mortality in all of these crossed 1.

Discussion

We have provided an up to date summary of all the available evidence on the effect of different modes of anesthesia on outcomes after both emergency and elective EVAR. Emergency EVAR has been less extensively studied but there is some evidence to suggest LA may be associated with reduced early mortality compared with GA. However, with no randomized trial data specifically comparing mode of anesthesia, significant risk of confounding remains.

Anesthesia for emergency EVAR

Four studies including 3,324 patients focused exclusively on rAAA: a secondary analysis of the IMPROVE trial and three retrospective database analyses (two from USA and one from the UK) [18, 39, 40, 47]. All reported data on LA versus GA for rAAA; only Mouton et al. also included data on RA versus GA, and LA versus RA. The estimated RR of death in these studies showed a benefit of LA over GA after adjustment for some potential confounders. The use of LA for emergency EVAR is relatively new and previous observational studies have mostly focused on elective EVAR procedures[14-17].

In the IMPROVE trial, 69 (38%) of the 186 patients who underwent emergency EVAR surgery for rAAA were operated under LA only. Subgroup analysis revealed a four-fold reduction in 30-day mortality with LA compared to GA (odds ratio 0.27, 95% CI 0.10 to 0.70 after adjustment for major potential confounders)[18]. However, the magnitude of the effect (i.e. almost 75% reduction in risk) is likely to be the result of unmeasured confounders. Theories about the potential causes of poorer outcomes with GA include relaxation of tissues and subsequent release of tamponade and the significant hemodynamic effects of GA, including a loss in vascular tone, all of which may be exacerbated in rAAA patients who are experiencing shock[38]. The retrospective analyses of data from the National Surgical Quality Improvement Program (NSQIP)[39] and the Vascular Quality Initiative (VQI)[40] showed significantly decreased risk-adjusted 30-day mortality for patients who had emergency EVAR under LA compared to GA. Similarly, a study of UK data from the National Vascular Registry (NVR) reported a reduced in-hospital mortality for patients who had LA versus GA (18.5% vs 28.0%)[47]. However, LA remains an uncommon technique for emergency EVAR in the USA (9.4% in NSQIP and 12.2% in VQI) [39,40]; the NVR analysis covered 2014 – 2016 and found a 40.1% rate of LA for emergency EVAR, with 78% of hospitals offering LA for this procedure[47]. In the anesthetic management of rAAA, the choice of anesthesia often depends on experience and personal preference [38]. The reasons for personal or local preferences from either the surgical or anesthetic team are unknown and as such there is potential for significant allocation bias under these conditions.

Anesthesia for elective EVAR

The majority of studies included in this review focused exclusively on elective EVAR with reported comparisons of LA versus GA; RA versus GA; and LA versus RA. The studies comparing RA and GA (8,189 patients) suggested a lower mortality rate with RA, but a similar trend was not found for the studies comparing RA and LA (2,787 patients) or LA and GA (7,496 patients).

Most studies either focused on elective repair or included a mix of elective and emergency patients. The 30-day mortality after elective EVAR is 1-2% even if it is predominantly performed under GA[36, 37]. This relatively low mortality and good short-term outcome of elective EVAR is unlikely to be improved by a change in anesthetic technique alone.

An analysis of over 5,000 patients from the EUROSTAR database showed that high-risk patients in particular gain outcome benefits from less invasive anesthetic techniques[14,15]. It is known that complex aneurysm morphology plays a bigger role in the outcome from EVAR surgery than patient co-morbidities[34,35]. Unfortunately there is very little information regarding aneurysm morphology in any of the studies that compared mode of anesthesia for EVAR surgery.

The future mode of anesthesia for emergency EVAR

Mortality after emergency EVAR for rAAA is still very high at 25-31% [2,18]. Furthermore, the burden of morbidity is significant in survivors. Therefore, even a small reduction in peri-operative mortality would have a dramatic effect. As the popularity of the EVAR technique for rAAA increases, the significant mortality and morbidity in this patient group needs to be addressed. It is in the emergency EVAR group where use of LA technique is particularly appealing. The benefit observed with LA in all studies looking specifically at emergency AAA repair warrants further investigation [18, 39, 40, 47].

Future studies of mode of anesthesia for emergency EVAR should focus on more patient-centered outcomes such as long-term morbidity and mortality and re-intervention rate rather than 30-day/in-hospital mortality. The GALA trial, which evaluated the effect of LA in carotid artery surgery, was criticized for using a primary endpoint of 30-day mortality rather than an outcome that is more relevant and important to patients [41, 42]. Our hope is that ongoing efforts to standardize the reporting of endpoints in clinical trials will improve this in the future[50]. Before considering a pragmatic multicenter randomized controlled trial to evaluate the effect of mode of anesthesia in emergency EVAR, several issues need to be addressed. These include: establishing the degree of equipoise amongst anesthetic and surgical teams regarding mode of anesthesia; identifying the reasons why particular anesthesia techniques are chosen for particular patients to inform the eligibility criteria for a trial; and defining anesthetic protocols.

Limitations

There are several potential sources of confounding which we were not able to account for in our analyses. Firstly, it was not possible to adjust our risk estimates based on patient or procedural factors, as we had only published aggregate data for the studies. Secondly, the definitions of anesthetic technique are not standardized. The medical literature as it currently stands does not report sufficient detail on the definitions of anesthetic techniques employed, nor by whom they are administered[51]. Further complexity arises when sedation is used alongside LA or RA. Even within GA there are conditions in which volatile and TIVA are shown to have different effects on outcome[52]. Additionally, included studies do not consistently report conversion from one anesthesia type to another (e.g. LA to GA) nor whether any sedation was delivered by the proceduralist or an anesthesiologist. This may introduce bias and is a potential weakness that it was not possible to address due to the limitations of the studies included in this analysis. Finally, all data are observational, with a SIGN grading of 2-, and the decision on whether an individual patient receives LA, RA or GA is determined by a myriad of factors. These include patient preference and demographics; clinician preference including familiarity and operating conditions such as immobility; vascular anatomy and complexity of aneurysms; and institutional practices. Furthermore this decision-making and choice of technique will differ again between elective and emergency presentations. As such, overall results and risk estimates should be treated with caution as the potential for significant allocation bias and confounding remains.

Conclusions

There is some evidence across both emergency and elective settings to suggest that mode of anesthesia may be associated with improved outcomes. In particular, LA appears to have a positive effect on outcome after emergency EVAR. Due to a lack of randomized trial data, significant risk of confounding remains. The optimal mode of anesthesia for EVAR should be further investigated and the reasons why particular anesthesia techniques are chosen for particular patients identified.

Supplementary documents

Appendix 1: Patient characteristics

Appendix 2: Mode of anesthesia

Appendix 3: Variety of outcomes reported

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Figure Legends

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram for study selection

Figure 2: Unadjusted relative risk (RR) of 30-day mortality by mode of anesthesia

2A: Local anesthesia (LA) versus General anesthesia (GA)

2B: Regional anesthesia (RA) versus General anesthesia (GA)

2C: Local anesthesia (LA) versus Regional anesthesia (RA)

Risk ratio (RR) of death with 95% confidence interval (95%-CI). Events = number of deaths. Total = total number of patients in group. Unadjusted estimates of RR are presented for each individual study. For individual studies, the center of the square represents the estimated RR and the size of the square represents the study weighting in the overall fixed effect model. The line extending to the right and left of the square represents the 95% CI.