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Mode of Anaesthesia in Emergency Surgery:

A Scoping Review

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Category

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Previous dissemination

None

Abstract

Background Emergency surgery encompasses >50% of the surgical workload, however research efforts are disproportionally low. The mode of anaesthesia used during emergency surgery may affect outcomes but the extent of research and the impact of the different modes of anaesthesia used are unclear.

Methods Medline and Embase were searched using scoping review methodology with a rapid systematic search strategy, identifying any study comparing locoregional (local, nerve block, subarachnoid, epidural) anaesthesia with general anaesthesia. Identifying all studies describing outcomes of emergency surgery with differing modes of anaesthesia. Excluded were studies published before 2003, studies enrolling patients <18 years and studies using sedation only.

Results 42 studies were identified describing 11 surgical procedures. Most publications were retrospective cohort studies (n=32). A very broad range of clinical and patient reported outcomes were described with wide variation in the outcomes reported in different studies.

Conclusion Reporting of mode of anaesthesia is inconsistent across different procedures, is often absent, and conclusions regarding the impact of the mode of anaesthesia on outcomes cannot be made. There is a need for directed research efforts **to improve the reporting standards of anaesthesia** interventions, to

understand the role of different modes of anaesthesia in specific emergency surgical procedures and to standardise outcome reporting using core outcome sets.

Introduction

Emergency surgery constitutes more than half of UK surgeons' workload and is associated with high morbidity and mortality.¹—³ However, despite the burden of emergency surgery the majority of research is performed in the elective setting.⁴ A research priority exercise conducted by the Royal College of Anaesthetists and James Lind Alliance, has ranked research to improve outcomes for patients undergoing emergency surgery as a key priority.⁵

Surgery is a complex intervention, that requires a number of co-interventions including the mode of anaesthesia.⁶ Recent publications have suggested that there may be potential benefits for patients undergoing emergency endovascular stroke thrombectomy and endovascular repair of ruptured abdominal aortic aneurysms by using locoregional rather than general anaesthetic techniques. These benefits potentially include superior functional outcome, reduced respiratory complications and reduced overall mortality.^{7–10}

The aim of this systematic scoping review was to map the existing evidence from studies that compare locoregional with general anaesthesia techniques in patients undergoing emergency surgery and identify key deficits in current knowledge.

Methods

This scoping review was conducted using the methodological framework described by Arksey & O'Malley and reported according to The Preferred Reporting Items for Systematic Review and Meta-analysis Protocols Extension for Scoping Reviews (PRISMA-ScR) checklist (appendix 1).¹¹,¹² The protocol has been accepted for publication.¹³

Briefly, scoping reviews are designed to rapidly summarise the extent of research activity, including knowledge gaps, and determine the value in a full systematic review. They include a broad search strategy and are presented as a descriptive account of the available research.¹¹ This methodology was chosen to provide an overview across a wide range of surgical interventions, with a number of different modes of anaesthesia, reporting a wide variety of outcomes. The data was likely to be heterogenous, so a conclusion of superiority between locoregional and general anaesthesia would have been invalid, therefore a descriptive approach is the most appropriate.

Information Sources

EMBASE and MEDLINE were the primary information sources. In addition, reference lists from all included papers following the initial search were hand searched and data from any additional eligible papers identified were also extracted.

Search strategy & eligibility criteria

A search was conducted to identify published studies comparing use of anaesthesia in emergency surgery of any specialty in adults (>18 years) between 2003-current. This timeframe was chosen to limit the results to current practice. Emergency operations were defined as unplanned admissions where it was not possible to discharge the patient home prior to surgical intervention. This definition was only used when emergency or elective surgery was not specifically mentioned in the inclusion/exclusion criteria and it was unclear when descriptors of operation described in the paper were reviewed.

Any study comparing general anaesthesia with locoregional anaesthesia (including conscious sedation) was included, post-hoc and subgroup analyses were not excluded. Included types of locoregional anaesthesia were local, subarachnoid, epidural and regional nerve block. Studies including two types of locoregional anaesthesia in a single group were included as long as each patient was only receiving one mode of anaesthesia. Studies reporting conscious sedation as an adjunct were included. Papers were excluded if they; were in a language other than English, studied patients <18 years, were in elective surgery, or reported multi-modal anaesthesia in the same patient (e.g. combination of regional nerve block and general anaesthetic). As mode of anaesthesia in emergency cesarean sections have been extensively studied, these were excluded to allow this paper to focus on the remaining scope of practice.¹⁴ A detailed summary of the search strategy is shown in appendix 2.

Selection of sources of evidence

Screening of abstracts was conducted by a single reviewer, a second reviewer screened subsequent full texts according to the pre-agreed inclusion criteria.

Data collection

Data was extracted by LE and verified by RLM. The data collection form was piloted in the first four included and modifications agreed between authors prior to the remainder of the data collection.

Data Items

Data from the following variables was sought; date of publication, country of study, study design, number of patients included, patient gender as male to female ratio, mean patient age in years and range, name of operation and American Society of Anesthesiologists (ASA) grade if available.

Data were also collected describing mortality, length of stay, intensive care unit (ICU) admission, post-operative pain, acute coronary syndrome (ACS), stroke, thromboembolic events, delirium, surgical site infection (SSI), lower respiratory tract infection (LRTI), acute kidney injury (AKI) and total morbidity, where reported. These outcomes were selected as no current core outcome set (COS) exists for studies describing modes of anaesthesia and represents the most commonly reported outcomes in surgical and anaesthetic trials.¹⁵ A long list of all outcomes reported in the included studies is shown in Table 3.

Synthesis of Results

A descriptive narrative of the data is presented without data analysis following scoping review methodology.¹¹ This is to provide an insight into the and how the groups could be compared. It is not intended to determine the impact of local/regional or general anaesthesia on outcomes. It aims to consider what changes would need to be made (if any) to current research practice in anaesthesia to make meaningful comparison of outcomes possible.

Results

Selection of Sources of Evidence

The initial search strategy identified 2419 studies, of which 75 were potentially relevant after initial screening and 42 included after full text review (Figure 1)

Demographics

The 42 studies described outcomes in 436,310 patients. Of which 70.9% were male (Table 1) and 47.1% of patients were ASA grade 3 or higher. The most common procedure studied was hip fracture (n=22), followed by endovascular stroke therapy (n=7) and ankle fracture fixation (n=3) (Table 2).

Of the 42 studies included , 10 were randomised controlled trials in endovascular stroke therapy (n=3), upper limb trauma (n=1), ankle fracture fixation (n =1), facial fracture fixation (n=1), hip fracture fixation (n = 3), and laparoscopic appendicectomy (n=1) (Table 2).

The vast majority of studies were performed in the United States of America (USA) (n=15), followed by United Kingdom (UK) (n=5) and Canada (n=3) with the remainder from mainly developed countries (Figure 2).

A variety of locoregional anaesthetic techniques were used across the included studies, the most common being epidural/spinal studied in the same group (n=15). For those patients receiving a general anaesthetic the induction and maintenance protocols were often not described (n=27, 64%), a large number of outcomes were reported in the studies relating to a wide range of procedures. The most commonly reported outcome was mortality (Table 3).

Mortality

A total of 27 studies, enrolling 349,317 patients, reported mortality as an outcome. Of these 19 studies found no evidence of a difference in mortality between locoregional and general anaesthetic. Eight studies, including 141,518 patients, reported a statistically significant difference in mortality. Six of these studies showed a decrease in mortality, whilst two reports indicated an increase in mortality with locoregional anaesthesia (Table 4). Time points at which mortality was reported included inhospital, 30 day, 90 day and 1 year.

Overall Morbidity.

There was a large variety in the definition of morbidity and a total of seven studies enrolling 41,573 patients reported overall morbidity. Five studies recruiting 24,269 patients suggested a significant decrease in overall morbidity with locoregional compared to general anaesthetic, (Appendix 3), whilst the remaining two studies reported no difference.

Length of Stay and ICU Admission

Twelve studies reported statistics describing length of stay and recruited 99,481 patients. Five of these reported a statistically significant difference in duration of stay favouring locoregional anaesthesia; (Appendix 4) and seven reported no statistically significant difference.

Three studies, including 104,088 patients, reported ICU admission, all of which reported statistically significant decrease in admission for locoregional compared to general anaesthesia (Appendix 5).

Post-operative Pain

Eight studies reported post-operative pain, seven of which reported a significant difference between groups (Appendix 6). Most studies used the visual analogue scale (VAS) to measure pain, whilst the amount of analgesia used was reported less frequently (opioid consumption in mg/number of rescue doses). Whilst a single study measuring pain using the AOFAS (American orthopaedic foot and ankle society) reported a non-significant difference in reported pain favouring locoregional anaesthetic.

Other Outcomes

Only one of six studies (104,088 patients) reported a significant difference in postoperative stroke. Two of three studies reported a significant difference in venous thromboembolism. Two of eight reported a significant difference in lower respiratory tract infection. Two of six studies reported a significant difference in surgical site infection, one of these analysed subgroups of locoregional anaesthetic separately finding a significant difference with both compared to general anaesthetic (Appendix 7). Of the nine studies reporting cardiac complications, five studies reporting AKI and one study reporting delirium, none reported a significant difference between groups.

Discussion

This review has demonstrated that mode of anaesthesia has been studied most extensively in patients undergoing surgery for hip fractures and less frequently across a range of other emergency surgeries, including stroke thrombectomy and endovascular surgery for ruptured abdominal aortic aneurysms. The majority of this research was in the developed world and most were retrospective cohort studies with only 10 of 42 studies comprising RCTs. This review identified inconsistent reporting of mode of anaesthesia as an intervention and little concordance in reporting of postoperative outcomes.

Whilst a large number of emergency surgical specialties were examined, only one or two relevant papers were found in each of the surgical specialties (hip fractures being the exception). Of the 10 studies found that were RCTs, these were spread across 6 procedures; all of which report a wide variety of outcomes (Table 2) and could therefore not be systematically compared. This shows that there is significant scope for larger prospective studies to investigate mode of anaesthesia in emergency surgical procedures. The majority of studies were published from countries with developed healthcare systems. It is therefore less likely to represent the significant burden that emergency surgery poses in developing countries, where there is arguably more pressure on resources and need to improve post-operative outcomes¹⁶

This study reports a wide range of post-operative outcomes in emergency procedures. Recently there has been a drive for core outcome sets, aiming to standardise outcomes so that reliable conclusions can be drawn from data.¹⁷ Core outcome sets already exist for hip fractures, and are in development for amputation.¹⁸,¹⁹ The development of core outcome sets for other surgical procedures will permit comparison and more meaningful systematic analysis of future research. Indeed, the core outcome measures in anaesthesia and peripoerative medicine (stEP-COMPAC) programme is undertaking an extensive package of work to standardise postoperative outcomes. It has developed 12 key working groups (for example. patient comfort, cognition and stroke, cardiovascular) to identify core outcome measures and many of the areas are also applicable to emergency surgery.¹⁵ Future research relating to mode of anaesthesia in emergency surgery will benefit from these core outcome measures to ensure improved standardisation of outcomes to allow more relevant and applicable conclusions with greater clinical transference.

Of the 42 studies included in our review, there were only 11 descriptions of general anaesthesia, and 15 of comparative locoregional anaesthesia. Crucially, there was

considerable heterogeneity in the detail of these descriptions. Most commonly reported were the anaesthetic agents used in either technique described, but dosing of these agents was inconsistently reported with only 8 studies reporting exact doses administered. The need to improve the reporting of anaesthesia in clinical research has already been identified.²⁰ Anaesthesia is a complex intervention and the impact of not fully reporting all components can result in unreliable and misleading conclusions. Non-randomised studies that conclude non-GA to be superior to GA often have no clear description of the anaesthesia delivered.⁷ By contrast, in meta-analysis of RCTs where extensive descriptions of the type of anaesthesia delivered is reported, including agents and doses used, ventilation parameters and physiological parameters, GA is reported to be superior.^{8,21} Unless all constituent components are reported and accounted for, the discrepancy of reporting of anaesthesia risks conclusions being made with serious confounding. This is in keeping with the Medical Research Council's (MRC) framework, which recognises the difficulty of reporting and evaluating complex interventions, such as anaesthesia.²² One of the recognised barriers to this is the reliance on anaesthesia reporting from national databases and registries, which lack scope to account for all components of anaesthesia.

The question of whether mode of anaesthesia impacts outcomes after emergency surgery is appealing, but definite comparisons or conclusions about superiority fall outside the scope of this study. The challenges of using locoregional anaesthesia in an emergency population include the availability of skilled anesthetists out of hours, time of anaesthetic induction in a time pressured procedure and awareness of patient. Although local anaesthetic can be administered without an anaesthetist present, in the emergency setting they are often required in case conversion to GA is required. These combined factors can cause the surgical team (including the patient) to opt for a general anaesthetic as default. Locoregional anaesthetic is associated with antiinflammatory effects, that may lead to reduced pain, ²³,²⁴ which can lead to earlier mobilization, allowing improved exercise capacity and health related quality of life in an elective population²⁵. Given the link between exercise and cardiovascular mortality, it is likely that this will extend to reducing major events such as stokes, myocardial infarction, death.²⁶ A non-significant trend towards this was shown in the GALA study of urgent carotid endarterectomy at 1 year follow up.²⁷ This may be even more important in emergency surgery; where patients are more unwell and there has been no period to allow for 'prehab.'

The study has several potential limitations. Due to the systematic approach of conducting a scoping review through literature searching and screening, a study was not included if there was no mention in either the title or abstract of comparative anaesthesia use. Therefore, studies where post-hoc analysis of anaesthesia type in emergency surgery has been performed may not have been identified in our search (although one was identified).²⁸ Searching for mode of anaesthesia is further impeded by the lack of 'key words' to identify them, meaning any study comparing them is less easily identified than if these existed.²⁹ Papers were included that reported locoregional anaesthesia with sedation. Sedation could mask any difference between locoregional and general anaesthetic, as the distinction between deep sedation and general anaesthetic is difficult to define in practice.²⁰ In this review, only 2 of the 13 studies which referenced sedation, described measurable assessments and defined

depth of conscious sedation. Large databases (e.g. National Hip Fracture Database and National Vascular Registry) do not allow for the collection of data about coadministered anaesthesia such as sedation.^{10,30} This means that papers reporting results based on these could not report co-administered sedation, although in practice clinicians are aware that it is occasionally used. As these papers were included, so were papers that openly reported use of co-administered sedation. These decisions recognise the additional level of complexity and real-world practice where sedation is often used alongside local or regional anaesthetic techniques.

This work provides a comprehensive systematic overview of studies that compared locoregional and general anaesthesia in emergency surgery. It has shown the need for a directed research effort in specific emergency surgical procedures and more demographic equality. This scoping review identified the inconsistent description of anaesthetic protocols and lack of a core outcome reporting as key areas to address in future studies into the effect of mode of anaesthesia in emergency surgery.

Author Contributions

RLM, LE, JR, RM, RJH were responsible for study design and conception. RLM and LE performed data extraction and analysis. SR developed the search strategy. All authors participated in drafting the final article and gave final approval of the version to be submitted.

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RLM & LE are joint first authors, RM and RJH are joint last authors.

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References

- 1 The Royal College of surgeons of England. Standards for unscheduled surgical care 2011;(February).
- Visser A, Geboers B, Gouma DJ, Goslings JC, Ubbink DT. Predictors of surgical complications: A systematic review. *Surgery* 2015;**158**(1):58–65. Doi: 10.1016/j.surg.2015.01.012.
- 3 Mullen MG, Michaels AD, Mehaffey JH, Guidry CA, Turrentine FE, Hedrick TL, et al. Risk associated with complications and mortality after urgent surgery vs elective and emergency eurgery: implications for defining "quality" and reporting outcomes for urgent surgery. *JAMA Surg* 2017;**152**(8):768–74. Doi: 10.1001/jamasurg.2017.0918.
- Morley RL, Edmondson MJ, Rowlands C, Blazeby JM, Hinchliffe RJ. Registration and publication of emergency and elective randomised controlled trials in surgery: a cohort study from trial registries. *BMJ Open* 2018;**8**(7):e021700.
 Doi: 10.1136/BMJOPEN-2018-021700.
- 5 Boney O, Bell M, Bell N, Conquest A, Cumbers M, Drake S, et al. Identifying research priorities in anaesthesia and perioperative care: final report of the joint National Institute of Academic Anaesthesia/James Lind Alliance Research

Priority Setting Partnership. *BMJ Open* 2015;**5**(12):e010006. Doi: 10.1136/BMJOPEN-2015-010006.

- Blencowe NS, Brown JM, Cook JA, Metcalfe C, Morton DG, Nicholl J, et al.
 Interventions in randomised controlled trials in surgery: issues to consider
 during trial design. *Trials* 2015;**16**:392. Doi: 10.1186/s13063-015-0918-4.
- Brinjikji W, Pasternak J, Murad MH, Cloft HJ, Welch TL, Kallmes DF, et al.
 Anesthesia-Related Outcomes for Endovascular Stroke Revascularization.
 Stroke 2017;48(10):2784–91. Doi: 10.1161/strokeaha.117.017786.
- 8 Campbell BCV, van Zwam WH, Goyal M, Menon BK, Dippel DWJ, Demchuk AM, et al. Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data. *Lancet Neurol* 2018;**17**(1):47–53. Doi: 10.1016/S1474-4422(17)30407-6.
- 9 IMPROVE trial investigators, Powell JT, Hinchliffe RJ, Thompson MM, Sweeting MJ, Ashleigh R, et al. Observations from the IMPROVE trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg* 2014;**101**(3):216–24. Doi: 10.1002/bjs.9410.
- 10 Mouton R, Rogers CA, Harris RA, Hinchliffe RJ. Local anaesthesia for endovascular repair of ruptured abdominal aortic aneurysm. *Br J Surg* 2019;**106**(1):74–81. Doi: 10.1002/bjs.10973.
- Arksey H, O'Malley L. Scoping studies: Towards a methodological framework. *Int J Soc Res Methodol Theory Pract* 2005;8(1):19–32. Doi:
 10.1080/1364557032000119616.
- 12 Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA

Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018;**169**(7):467. Doi: 10.7326/M18-0850.

- 13 Morley RL, Elliott L, Mouton R, Hinchliffe RJ. (In Press) Choice of Anaesthetic in Emergency Operations: A Protocol for a Scoping Review. *BMJ Open* 2019.
- Chibueze C., Nabhan A., Sato M, Usama N, Mori Y, Elfaramawy A, et al. Spinal anaesthesia drugs for caesarean section. *Cochrane Database Syst Rev* 2016;(4). Doi: 10.1002/14651858.CD012134 LK.
- Myles PPS, Grocott MMPW, Boney O, Moonesinghe SR, Myles PPS, Grocott
 MMPW, et al. Standardizing end points in perioperative trials: towards a core
 and extended outcome set. *Br J Anaesth* 2016;**116**(5):586–9. Doi:
 10.1093/bja/aew066.
- 16 Chana P, Joy M, Casey N, Chang D, Burns EM, Arora S, et al. Cohort analysis of outcomes in 69 490 emergency general surgical admissions across an international benchmarking collaborative. *BMJ Open* 2017;**7**(3):e014484. Doi: 10.1136/bmjopen-2016-014484.
- Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al.
 The COMET Handbook: version 1.0. *Trials* 2017;**18**(S3):280. Doi:
 10.1186/s13063-017-1978-4.
- 18 Ambler GK, Bosanquet DC, Brookes-Howell L, Thomas-Jones E, Waldron C-A, Edwards AGK, et al. Development of a core outcome set for studies involving patients undergoing major lower limb amputation for peripheral arterial disease: study protocol for a systematic review and identification of a core outcome set using a Delphi survey. *Trials* 2017;**18**(1):628. Doi:

10.1186/s13063-017-2358-9.

- O'Donnell CM, Black N, McCourt KC, McBrien ME, Clarke M, Patterson CC, et al. Development of a core outcome set for studies evaluating the effects of anaesthesia on perioperative morbidity and mortality following hip fracture surgery. *Br J Anaesth* 2019;**122**(1):120–30. Doi: 10.1016/j.bja.2018.08.017.
- 20 Armstrong RA, Mouton R. Definitions of anaesthetic technique and the implications for clinical research. *Anaesthesia* 2018;**73**(8):935–40. Doi: 10.1111/anae.14200.
- 21 Gravel G, Boulouis G, Benhassen W, Rodriguez-Regent C, Trystram D, Edjlali-Goujon M, et al. Anaesthetic management during intracranial mechanical thrombectomy: systematic review and meta-analysis of current data. *J Neurol Neurosurg & amp; Amp; Psychiatry* 2019;**90**(1):68 LP – 74. Doi: 10.1136/jnnp-2018-318549.
- Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, et al.
 Developing and evaluating complex interventions: the new Medical Research
 Council guidance. *BMJ* 2008;**337**:a1655–a1655. Doi: 10.1136/bmj.a1655.
- Martin F, Martinez V, Mazoit JX, Bouhassira D, Cherif K, Gentili ME, et al.
 Antiinflammatory effect of peripheral nerve blocks after knee surgery.
 Anesthesiology 2008;109(3):484–90. Doi: 10.1097/ALN.0b013e318182c2a1.
- Beilin B, Bessler H, Mayburd E, Smirnov G, Dekel A, Yardeni I, et al. Effects of preemptive analgesia on pain and cytokine production in the postoperative period. *Anesthesiology* 2003;**98**(1):151–5. Doi: 10.1097/00000542-200301000-00024.
- 25 Carli F, Mayo N, Klubien K, Schricker T, Trudel J, Belliveau P. Epidural analgesia enhances functional exercise capacity and health-related quality of life after

colonic surgery. *Anesthesiology* 2002;**97**(3):540–9. Doi: 10.1097/00000542-200209000-00005.

- Lear SA, Hu W, Rangarajan S, Gasevic D, Leong D, Iqbal R, et al. The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. *Lancet (London, England)* 2017;**390**(10113):2643–54. Doi: 10.1016/S0140-6736(17)31634-3.
- GALA Trial Collaborative Group, Lewis SC, Warlow CP, Bodenham AR, Colam B,
 Rothwell PM, et al. General anaesthesia versus local anaesthesia for carotid
 surgery (GALA): a multicentre, randomised controlled trial. *Lancet (London, England)* 2008;**372**(9656):2132–42. Doi: 10.1016/S0140-6736(08)61699-2.
- 28 IMPROVE Trial Investigators I trial, Powell JT, Sweeting MJ, Thompson MM, Ashleigh R, Bell R, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ* 2014;**348**:f7661. Doi: 10.1136/BMJ.F7661.
- Boet S, Etherington N, Nicola D, Beck A, Bragg S, Carrigan ID, et al. Anesthesia interventions that alter perioperative mortality: a scoping review. *Syst Rev* 2018;7(1):218. Doi: 10.1186/s13643-018-0863-x.
- 30 White SM, Moppett IK, Griffiths R, Johansen A, Wakeman R, Boulton C, et al. Secondary analysis of outcomes after 11,085 hip fracture operations from the prospective UK Anaesthesia Sprint Audit of Practice (ASAP-2). *Anaesthesia* 2016;**71**(5):506–14. Doi: 10.1111/anae.13415.