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Interventional radiology versus operative management for splenic injuries: a study protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Over the past decades, the treatment for blunt splenic injuries has shifted from operative to non-operative management. Interventional radiology such as splenic arterial embolisation generally increases the success rate of non-operative management. However, the type of intervention, such as the first definitive treatment for haemostasis (interventional radiology or surgery) in blunt splenic injuries is unclear. Therefore, we aim to clarify whether interventional radiology improves mortality in patients with blunt splenic trauma compared with operative management by conducting a systematic review and meta-analysis.

Methods and analysis We will search the following electronic bibliographic databases to retrieve relevant articles for the literature review: Medline, Embase and the Cochrane Central Register of Controlled Trials. We will include controlled trials and observational studies published until September 2018. We will screen search results, assess the study population, extract data and assess the risk of bias. Two review authors will extract data independently, and discrepancies will be identified and resolved through a discussion with a third author where necessary. Data from eligible studies will be pooled using a random-effects meta-analysis. Statistical heterogeneity will be assessed by using the Mantel-Haenszel χ^2 test and the I^2 statistic, and any observed heterogeneity will be quantified using the I^2 statistic. We will conduct sensitivity analyses according to several factors relevant for the heterogeneity.

Ethics and dissemination Our study does not require ethical approval as it is based on the findings of previously published articles. This systematic review will provide guidance on selecting a method for haemostasis of splenic injuries and may also identify knowledge gaps that could direct further research in the field. Results will be disseminated through publication in a peer-reviewed journal and presentations at relevant conferences.

PROSPERO registration number CRD42018108304.

Strengths and limitation of this study

- We will conduct a systematic review and meta-analysis of the effects of interventional radiology and operative management on mortality in patients with blunt splenic injuries using appropriate methodologies and quality assessment tools.
- We will also perform subgroup analyses according to the presence of shock, another site of trauma except for the spleen and classification of splenic injuries to compare and evaluate the efficacies of interventional radiology versus operative management.
- The results of this systematic review and meta-analysis will be highly dependent on the quality of the included primary research studies; many observational studies might be included.

INTRODUCTION

Blunt abdominal trauma is regularly encountered in the emergency department,[1] and the spleen is among the most commonly injured intra-abdominal organs.[2 3] The primary goal for blunt abdominal trauma is the diagnosis and prompt management of potentially life-threatening haemorrhage. Therefore, emergent splenectomy remains a lifesaving measure for many patients.

Haemodynamically stable blunt splenic injuries are normally managed non-operatively to avoid the morbidity of unnecessary surgery and the risk of overwhelming postsplenectomy sepsis.[4] The current Eastern Association for the Surgery of Trauma practice management guidelines recommend initial non-operative management (NOM) for all haemodynamically healthy patients.[5] However, in some cases, a higher risk of failure of NOM is predicted, and identification and management of these patients is challenging.[5] In NOM of blunt splenic injuries, interventional radiology such as splenic arterial embolisation (SAE) is used as an adjunct to observation to increase the success rate of NOM.[6] NOM with SAE is more favourable than observational management alone in severe splenic injuries.[7 8] However, the challenge is in identifying the cases of severe splenic injuries in which interventional radiology or operative management is more

appropriate than observational management alone.[9] The management approach may vary from institution to institution depending on the resources, haemodynamic status of the patient, grade of splenic injury and presence of other injuries and medical comorbidities.[5 10 11] The effect of interventional radiology on mortality of blunt splenic injuries compared with surgical management remains unclear.

Therefore, we aim to clarify if, compared with surgery, interventional radiology improves mortality in patients with blunt splenic trauma, by conducting a systematic review and meta-analysis.

METHODS AND ANALYSIS

Protocol registration

This study protocol has been registered in PROSPERO (http://www.crd.york.ac.uk/PROSPERO/).[12] The protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statements,[13 14] and the systematic review and meta-analysis will be reported according to the PRISMA statement (see online supplementary file 1).[15 16]

Database searches

We will search the following major electronic bibliographic databases to retrieve relevant articles for the literature review: Medline (Ovid), Embase (Proquest) and The Cochrane Central Register of Controlled Trials. Search terms will include 'splenic injury', 'spleen rupture', 'interventional radiology', 'endovascular procedures' and 'therapeutic embolisation'. We will consult a librarian for the database search. We will assess the references of relevant articles to determine if additional studies can be found. The detail of the search strategy is available in the online supplementary file 2.

Types of studies

We will include controlled trials (including randomised controlled trials and other controlled trials) and observational studies (including prospective and retrospective cohort studies, case–control studies and before-after studies) that reported data on our primary or secondary outcomes published until September 2018. Studies will be excluded if they did not clearly report the population, treatment or outcomes of interest. Animal studies will be excluded. Grey literature such as conference proceedings and abstracts will be included. If two or more studies were published using the same or overlapping cohorts, the most recent or larger cohort will be included. No language restrictions will be applied. We will handle non-English language publications using appropriate translation services.

Study population

We will include adult patients (ie, those aged ≥16 years) admitted to the hospital with blunt splenic injuries requiring invasive intervention for haemostasis, such as interventional radiology or surgery. We will not restrict our review by country and will include all types of splenic injuries. Patients with penetrating abdominal trauma, patients without invasive intervention, and paediatric patients will be excluded.

Intervention and control

Intervention types of interest will be SAE as the initial definitive treatment for haemostasis, including any embolisation technique (distal embolisation, proximal splenic artery embolisation or a combination) and the material used for embolisation (coils, gelatin sponge, or n-butyl-2-cyanoacrylate). Meanwhile, comparators will be any operative management such as splenorrhaphy, partial splenectomy and splenectomy as the initial definitive treatment for haemostasis including both laparoscopic approach and open abdominal exploration.

Outcomes

The primary outcome will be in-hospital mortality due to all causes. Secondary outcomes will be 30 day mortality, further intervention, complications such as abdominal compartment syndrome and infection, length of intensive care unit stay and length of hospital stay.

Data extraction

Citations will be stored, and duplicates will be removed using EndNote software (Thomson Reuters, Toronto, Ontario, Canada). We will use Rayyan software for the systematic review process.[17] Titles and abstracts of studies retrieved using the search strategy will be screened independently by two review authors (MK and NY) to identify studies that potentially meet the inclusion criteria. The full text of these potentially eligible studies will be retrieved and assessed independently by two review authors (MK and NY). Any disagreement about the eligibility of studies will be resolved through a consult with a third reviewer (KY). The flow chart of the study, which is based on the PRISMA statement,[16] is shown in figure 1.

Data from the included studies will be extracted for assessment of study quality and data synthesis using a standardised prepiloted form. The extracted information will include the following: study setting; study population and participant baseline characteristics; details of the intervention and control conditions; study methodology; outcomes and times of measurement and information for the assessment of risk of bias. Two review authors (MK and NY) will extract data independently, and discrepancies will be resolved through a discussion with the third author (KY). Authors will not be contacted to request the provision of any missing data.

Assessment of risk of bias in individual studies

Independent reviewers (MK and NY) will assess the risk of bias in individual studies as methodological quality of articles, and disagreements will be resolved by a discussion with a third reviewer (KY). We will apply uniform criteria for evaluating the risk of bias associated with individual randomised control trials based on the Cochrane risk of

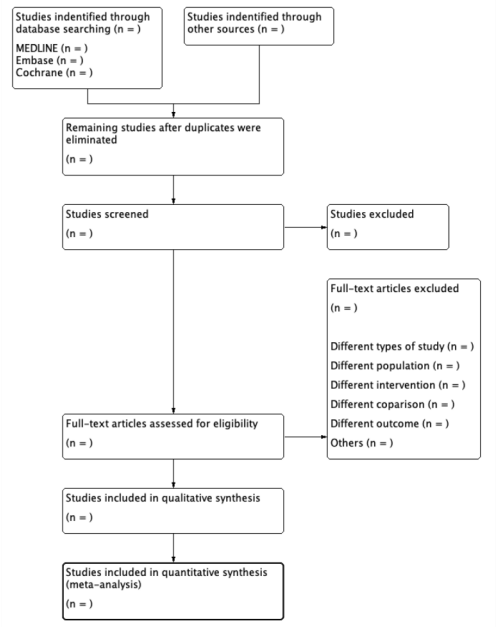

Figure 1 Flowchart of the study selection process.

bias tool.[18] Each study will be assessed for (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of related outcomes assessment, (5) incomplete outcome data, (6) selective reporting and (7) other bias. We will also apply the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS) to assess the risk of bias of observational studies, which is compatible with the Cochrane risk of bias tool.[19] In particular, there is a potential risk of time-dependent bias, including immortal time bias, in eligible studies. We will evaluate how appropriate statistical methods, such as marginal structural models, have been used in each eligible study, to manage time-dependent bias.

Summarising data

We will perform a meta-analysis when data are available in one or more trials according to the 'Cochrane Handbook for Systematic Reviews of Interventions'. For dichotomous variables (eg, mortality, need for further intervention and complication of abdominal compartment syndrome and infection), values for the risk ratio (RR) or the OR will be expressed as a point estimate with 95% CIs. Continuous outcomes, such as length of intensive care unit stay and length of hospital stay, will be expressed as their mean difference with 95% CIs and p value. If quantitative synthesis is not appropriate for a particular outcome, we will provide a qualitative summary.

Data synthesis

We will provide estimates of the findings from the included studies according to a random-effect model. A random-effect model incorporates statistical heterogeneity and provides a more conservative estimate of the pooled effect size than a fixed-effect model. We will not perform multiple imputation for missing data. We will perform data synthesis and analysis of randomised trials and observational studies separately.

All statistical analyses including the risk of bias within studies and across studies will be performed with Review Manager V.5.3. (RevMan; The Cochrane Collaboration 2014, The Nordic Cochrane Centre, Copenhagen, Denmark) and STATA software V.14.0 (Stata Corporation, College Station, Texas, USA). The statistical significance will be set at a p value of <0.05.

Assessment of heterogeneity

Statistical heterogeneity will be assessed via the Mantel-Haenszel χ^2 test and the I^2 statistic as the proportion of total variability explained by heterogeneity. Substantial heterogeneity is predefined as a p value of <0.10 with the Mantel-Haenszel χ^2 test or an I^2 value of >50%.[20] Possible sources for heterogeneity will be investigated via meta-regression analysis. The log RR of death in the interventional radiology group will be plotted against the control mortality rate for each study. A linear meta-regression weighted to reflect the variance of the individual studies will be used to model the data. The presence of clinical heterogeneity will be considered in the decision to conduct a quantitative synthesis of data or to perform sensitivity analyses, as below.

Sensitivity and subgroup analysis

We will examine the robustness of the meta-analyses by conducting sensitivity analyses according to different components of the Cochrane risk of bias tool or RoBANS, as appropriate. If the necessary data are available, subgroup analyses will be done according to the country, sample size, publication year (published in the last 10 years vs published 10 years ago or longer), presence of shock at admission, other site of trauma except for the spleen and American Association for the Surgery of Trauma classification of splenic injuries.[21]

Assessment of reporting bias

To assess publication bias, we will create funnel plots for mortality in which the log RRs will be plotted against their SEs, and we will test the symmetry of the funnel plots using the Begg's rank correlation test and Egger's linear regression test.[22]

Rating the certainty of evidence using the GRADE approach

Two authors (MK and NY) will independently assess the strength of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[23] The quality of evidence will be assessed for each outcome and categorised as high, moderate, low or very low according to the GRADE approach.

Trial sequential analysis

Cumulative meta-analyses have the potential risk of type I errors due to repeated significance test.[24] Therefore, we will apply trial-sequential analysis. Trial-sequential analysis combines information size estimation for meta-analysis with an adjusted threshold for statistical

significance in the cumulative meta-analysis. Information size will be calculated as diversity-adjusted information size, suggested by the relative risk reduction of the intervention in the included trials.[25 26] In principle, strong evidence is likely to be established if the trial sequential monitoring boundary is crossed before reaching the required information size. If this boundary is not crossed, it is highly likely that trials will need to be continued.[27]

Patient and public involvement

This study will not involve any patient or the public.

DISCUSSION

Determining the appropriate type of intervention, that is, surgery versus interventional radiology, for haemostasis in blunt splenic injuries remains a challenge for emergency physicians, trauma surgeons and interventional radiologists. Moreover, the influence of interventional radiology on the mortality of blunt splenic injuries compared with operative management remains unclear. Therefore, we will conduct a systematic review and meta-analysis of the effects of interventional radiology compared with surgery on mortality in patients with blunt splenic injuries.

Several observational studies have demonstrated that NOM is more successful with the adjunctive use of SAE.[28–34] NOM is performed in over 50% of haemodynamically stable patients without increasing mortality even in grade 4 or 5 splenic injuries.[28 35] The success rates for SAE vary depending on institutional policies, embolisation technique, arterial accessibility, interventional radiologist skill and the type of embolisation material.[36 37]

Several systematic reviews and meta-analyses of patients with blunt splenic injuries have been reported.[7–9] Two studies compared NOM with and without SAE.[7] The results showed that SAE is associated with significantly higher splenic salvage rates in grades 4 and 5 splenic injuries.[7 8] SAE significantly reduced the failure of NOM in patients with grades 4 and 5 splenic injuries but had minimal effect in those with grades 1 –3 injuries.[8] Meanwhile, one study compared NOM (including with and without splenic arterial management) and operative management.[9] NOM was associated with decreased mortality in minor splenic injuries.[9] However, integrating the results for severe splenic injuries was difficult because of the substantial heterogeneity and potentially inappropriate comparison groups.[9]

The results of the above studies indicate that NOM with SAE is more favourable than observational management alone in severe splenic injuries.[7 8] However, the challenge is in determining the appropriate intervention for haemostasis in severe splenic injuries (interventional radiology vs operative management), not observational management alone. To the best of our knowledge, no systematic review and meta-analysis has directly compared the effect of interventional radiology including SAE with that of operative management. Our systematic review and meta-analysis will be the first study focused on interventional radiology versus operative management. This systematic review and meta-analysis will provide current evidence for researchers in this field and useful information for treatment of patients with blunt splenic injuries.

ETHICS AND DISSEMINATION

Our findings will be presented at relevant scientific conferences and disseminated through publication in a peer-reviewed journal.

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Collaborators Takaaki Suzuki.

Contributors MK, NY and KY contributed to the conception of the study. The manuscript protocol was drafted by MK and was revised by NY and KY. The search strategy was developed by all of the authors and will be performed by MK. MK and NY will also independently screen the potential studies, extract data from the included studies, assess the risk of bias and complete the data synthesis. KY will arbitrate in cases of disagreement and ensure the absence of errors. All authors approved the publication of this protocol.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Approval from an ethics committee is not required because this systematic review will use publicly available data without directly involving human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement There are no data in this work.

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