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Evidence map of liver surgery: study protocol of a living systematic review

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ABSTRACT

Introduction The amount of scientific data on liver surgery is exploding. There is a critical unmet need to develop tools that will facilitate navigating the literature and offer easy, fast and accurate access to data with a high level of evidence. Evidence maps (EM) combining living systematic reviews (SR) and user-friendly synthesis with graphs and figures were developed for this purpose in other medical fields and showed promising results but remain yet unavailable in liver surgery. The present study protocol aims to generate an EM in liver surgery, gathering randomised clinical trials (RCT) and SR.

Methods and analysis A systematic search will be conducted in the Cochrane Central Register of Controlled Trials, Web of Science, Embase and Medline to identify all RCT and SR concerning liver surgery. RCT and SR will be classified in research topics. Selected endpoints will be extracted and meta-analysed. Results will be freely available for patients, clinicians and researchers via a web-based evidence map platform. EM and meta-analyses (MA) will be updated at regular intervals.

Ethics and dissemination Including publicly available data, this type of study design did not require ethical committee approval. EM displays the required properties to facilitate literature search and to get a rapid overview of the current evidence, an unavailable tool in liver surgery, to date. Generating such an aid may considerably help patients, clinicians and researchers in many aspects: accessing accurate data, helping in decision-making and identifying gaps in the field. On completion of the project, results will be published, freely available via www.evidencemap.surgery and permanently updated.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The thorough search of the literature and selective inclusion of studies will provide a precise mapping of the evidence in liver surgery.
⇒ Only by gathering studies with a high level of evidence (ie, randomised clinical trials and systematic reviews), the evidence map (EM) will substantially facilitate access to evidence-based data in liver surgery.
⇒ EM will also help identify gaps in the field, warranting future research.
⇒ The creation and the maintenance of an up-to-date EM is particularly demanding and requires substantial effort and resources.
⇒ EM only becomes pertinent if it is used by clinicians, researchers and patients: an efficient dissemination strategy will be pivotal.

BACKGROUND

Liver surgery is characterised by several challenges. It is the gold-standard treatment to cure complex cancerous and non-cancerous diseases such as primary liver cancers (ie, hepatocellular carcinoma and cholangiocarcinoma), colorectal liver metastases or alveolar echinococcosis. The rising epidemiological courses of these conditions explain the increasing incidence of patients requiring liver surgery.[1 2] Furthermore, it entails major procedures associated with a substantial risk of adverse outcomes.[3–5] Being mostly performed in academic centres, liver surgery has been the centre of attention of numerous research efforts, which yielded a tremendous volume of data and literature. While being an encouraging perspective per se, it also complexifies navigating within the available literature, even for experts. Tools providing easy, updated and synthetic access to studies of high level of evidence would be of incomparable value and yet represent an unmet need.

An evidence map (EM) is a recent concept combining living systematic reviews (LSR) and graphical mapping of evidence. Unlike conventional systematic reviews (SR) that will ultimately become outdated, LSR are updated at regular and predetermined intervals.[6–8] Evidence mapping is a complementary approach when exploring a scientific topic that provides a synthesis with a user-friendly format such as visual figures or graphs.[9] The combination of these two designs advantageously results in a living and up-to-date map of the evidence in a specific domain. It has been recently established in pancreatic surgery,[10] offering an easy-to-use app available both on computers and smartphones/tablets, showing multiple functions of valuable help (https://www.evidencemap.surgery). Hence,

EM appears to be a promising tool that unfortunately remains unavailable in liver surgery to date.

AIM

The present study aims to generate an LSR-based map of the evidence in liver surgery.

METHODS/DESIGN

Design

Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines will be followed, whereas guidelines on the publication and update of SR and meta-analyses (MA) will be applied whenever possible and necessary[11] (online supplemental appendix 1). The protocol was prospectively registered in PROSPERO (CRD42023489201) and published here with open access for transparency purposes. EVIglance Studio will be used to generate the EM. This platform was previously established and used to create an EM in pancreatic surgery.[12]

Systematic search of the literature

All major databases relevant to surgical literature[13] will be systematically searched: Cochrane Central Register of Controlled Trials, Web of Science, Embase and Medline. The dedicated algorithms for each database are detailed in online supplemental appendix 2. Duplications will be automatically removed through the EVIglance Studio via article digital object identifiers. Preliminary results suggested that this search will yield >65 000 articles for screening with an estimation of ~300 RCT and ~500 SR selected in the first version of the EM.

Study selection

Potentially eligible studies will be independently screened by two co-investigators (SH and HG). Eventual disagreement will be resolved by a co-investigator (IL). Inclusion and exclusion criteria are summarised in table 1 (PICO box). Randomised clinical trials (RCT) and SR with or without MA will be the only eligible study designs. The quality requirement for inclusion of SR is the search of a minimum of two literature databases for SR and a critical appraisal with a validated tool (ie, Cochrane Collaboration tool for assessing risk bias 2.0) to assess the risk of bias of RCT.[14] Quality assessment will not be used as a selection factor to include or exclude studies; it will solely be informative.

Extraction of data

Data will be independently extracted by two co-investigators (SH and HG) and eventual disagreement will be resolved by a third co-investigator (IL). Items related to the interventions () will be extracted to a user interface and saved in a dedicated database, as previously described.

Data synthesis and evidence map creation

The evidence map will be created based on clusters according to the study subject, branching out from a central topic. Available SR and RCT will be shown for each subject. If three or more RCT are carried out on the same subject, the outcomes () will be pooled into the living meta-analyses which will be available from the map.

Table 1 PICO question

Population	
Inclusion	Patients undergoing liver resection for any given diagnosis.
Exclusion	Patients undergoing liver transplantation.
Interventions	
Inclusion	All kinds of interventions interfering with surgical outcomes: surgical techniques and modifications of liver surgery (approach, type of resection, concomitant biliary or vascular reconstruction), preoperative strategies (loco-regional therapy, embolizationembolisation, biliary drainage), pre- and rehabilitation interventions, perioperative management, drug therapy (e, perioperative steroid therapy), use of medical devices, nutritional supplements and combination of liver surgery with other treatments such as radiofrequency ablation (RFA).
Exclusion	Diagnostic procedures, liver transplantation, completely radiological interventions (eg, TACE, SIRT, etc), laparoscopic-assisted RFA.
Control	
Any kind of control compared with the eligible interventions.	
Outcomes	
Survival, recurrence, mortality, morbidity, postoperative biliary leakage, haemorrhage, post-hepatectomy liver failure, length of stay, duration of surgery, blood loss, surgical site infection, pulmonary complications, acute kidney failure, re-operation, readmission, quality of life, inoperability and resection margin status.	

SIRT, selective internal radiation therapy; TACE, transaterial chemoembolization.

Statistical analysis

Data from every selected RCT will be extracted for MA. If ≥3 RCT focus on the same subject, living meta-analyses will be performed. Binary data will be pooled by the Mantel-Haenszel model to calculate OR and associated 95% CI. For continuous data, mean differences and corresponding 95% CI will be generated using an inverse-variance model. The certainty of the evidence will be assessed by the GRADE system[15] for each endpoint. Quantitative data from SR will not be extracted. A state-of-the-art Bayesian network MA will be conducted if an analysis comparing >2 interventions is available within the same research topic. Linear or logistic random effects models will be applied accordingly. Funnel plots will be generated in case of >10 available trials and a risk of publication bias based on the Harbord test.

Ethics and dissemination

Including publicly available data, this type of study design did not require ethical committee approval. The complete map will be freely available at www.evidencemap.surgery as well as on the EVIglance application for Android and iOS. Further dissemination is planned *via* national and international conferences, social media, scientific publications and societies of hepato-pancreatico-biliary (HPB) surgery.

Timeline and updates

The project was launched in May 2023. Article screening started in July 2023 and will be completed by October 2024, while the first version of the map may be available by the end of the first semester of 2025. To keep the map up-to-date and further the LSR in a field with ever-emerging publications, a new literature search will be conducted every 6 months in order to screen for any new studies to be included in the map. Whenever possible, new living meta-analyses will be conducted. Although demanding, this task is feasible; the available EM on pancreatic surgery acts as a proof-of-concept for the feasibility to conduct and maintain the present EM.[10]

Patient and public involvement

Patients and/or the public were not involved in this study.

DISCUSSION

The present study protocol was designed to create a living map recapitulating the available data with a high level of evidence in liver surgery.

The volume of scientific data on liver surgery is not only already enormous, but it is foremost continuously rising. While a positive perspective, the quantity of data must remain under control and not become overwhelming. The only way to accurately navigate within this amount of studies is by developing new tools. Similarly to gold diggers using pans to filter stones and detect gold nuggets, research efforts must strive to design tools capable of easily, rapidly and accurately selecting the most precious data, namely the ones with a high level of evidence. EM were precisely developed to tackle this challenge. To date, they remain rare in surgery, particularly in HPB surgery. The concept was recently applied in pancreatic surgery.[10] Authors conducted a randomised trial that nicely illustrated the contribution of EM in this field. Briefly, students, residents and board-certified consultants were enrolled and randomised into two groups: a group using the EM EVIglance and a control group using PubMed to conduct a literature search and answer a clinically relevant question.[16] Results demonstrated the performance of this tool that offered a faster and more accurate literature search compared with conventional methods. There is no EM specifically dedicated to liver surgery so far. Of note, an EM in hepatobiliary surgery has been reported, but the study was not prospectively registered, also included biliary procedures and appeared less inclusive in terms of literature search compared with the present EM.[17] Perspectives of an EM in liver surgery are numerous. It will not only provide a precise mapping of the field and facilitate literature search, but it will also identify gaps within the available literature[18]: domains that must be further investigated and/or questions with available RCTs for which MA were not conducted yet.

The rapidly growing role of artificial intelligence (AI) in medicine is another lead to overcome the issue of filtering high-evidence data.[19] Although promising preliminary data show that AI may be helpful in performing some tasks of the literature search,[20] numerous limitations remain to be solved before considering the use of AI-derived tools as a standard of the literature search.[21]

In summary, there is an unmet need to generate EM in liver surgery. The present study protocol designs an EM aiming to facilitate navigating within the available data in liver surgery and providing other insightful applications such as identifying gaps in the current literature.

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Contributors SH, HG, FH, PP and IL conceived and designed the study. SH, HG and IL executed the study and contributed to data collection, analysis and interpretation. SH, HG and IL wrote the original draft of the manuscript. All authors revised the article, gave final approval and agreed on the journal to which the article has been submitted. All authors had final responsibility for the decision to submit for publication. IL acted as the guarantor.

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Competing interests FH and PP are founders of the company EVIglance Inc. (www.EVIglance.com) providing software services for researchers to conduct their own evidence maps. SH, HG, EU, GRJ, EM and IL declare no conflict of interest.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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