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Guidelines for Perioperative Care for Liver Transplantation: Enhanced Recovery After Surgery (ERAS) Society Recommendations

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CONFLICT OF INTEREST: None.

AUTHORS CONTRIBUTIONS

RB performed the systematic review, planned the e-delphi consensus, wrote and edited the manuscript;

AM performed the systematic review, participated to the consensus, wrote 1 part of the manuscript and edited the manuscript;

SS performed the systematic review, participated to the consensus, wrote 1 part of the manuscript and edited the manuscript;

ES and DP performed the systematic review, participated to the consensus, revised critically and edited the manuscript;

SW and ND participated to the consensus, offered insights, revised critically and edited the manuscript.

All the remaining Authors participated to the consensus, revised critically and edited the manuscript.

OS moreover supervised the strategy and revised critically and edited the manuscript.

ABSTRACT

BACKGROUND:

Enhanced Recovery After Surgery (ERAS) is a multimodal, evidence-based, program of care developed to minimize the response to surgical stress, associated with reduced perioperative morbidity and hospital stay. This study presents the specific ERAS Society recommendations for liver transplantation (LT) based on the best available evidence and on expert consensus

METHODS:

PubMed and ClinicalTrials.gov were searched in April 2019 for published and ongoing RCTs on LT in the last 15 years. Studies were selected by 5 independent reviewers, and were eligible if focusing on each validated ERAS items in the area of adult LT. An e-Delphi method was used with an extended interdisciplinary panel of experts to validate the final recommendations.

RESULTS:

Forty-three articles were included in the systematic review. Consensus was reached among experts after the second round. Patients should be screened for malnutrition and treated whenever possible. Prophylactic nasogastric intubation and prophylactic abdominal drainage may be omitted, and early extubation should be considered. Early oral intake, mobilization and multimodal-balanced analgesia are recommended.

CONCLUSIONS:

The current ERAS recommendations were elaborated based on the best available evidence and endorsed by the e-Delphi method. Nevertheless, prospective studies need to confirm the clinical use of the suggested protocol.

PROSPERO CRD4201913279

BACKGROUND

Enhanced Recovery After Surgery (ERAS) is a multimodal, evidence-based, program of care developed to minimize the response to surgical stress.[1,2]

The concept is based on a multidisciplinary team working around the patient, to ensure the synergic application of 20 program elements throughout each phase of the patient's journey.[2]

The implementation of ERAS recommendations in major surgery domains including colorectal,[3] pancreatic[4] and liver[5] surgery is associated with an improved recovery with a reduction in postoperative complications and hospital length of stay but without an increase in readmission rates .[6–8]

Liver Transplantation (LT) is a life-saving treatment for end-stage liver disease (ESLD),[9] with 1 and 5 years survival of 83%-92% and 71%- 87%, respectively.[10–13] In spite of these positive survival results complications are common and frailty, preoperative comorbidities, surgical challenges and postoperative immunosuppression are responsible of 40%-92% all-confounded morbidity.[10,14–18]

Liver surgery and liver transplantation share many points in common and the same principles of enhanced recovery may apply for liver transplantation. Nevertheless, little evidence exists on the application of an ERAS program in LT, apart from 2 feasibility studies reporting on the effectiveness of such a program on the length of stay after LT.[19,20]

This study aims to develop the specific ERAS Society recommendations for liver transplantation based on the best available evidence and on expert consensus.

METHODS

An international panel of liver transplant surgeons and anaesthesiologists from 12 international centers, including the steering committee (Liège-Belgium, Sao Paulo-Brazil, Montréal-Canada, Torino-Italy, Pisa-Italy, Kyoto-Japan, Groningen-Netherlands, Paris-France, Alicante-Spain, Genève-Switzerland, Portland-US, Edinburgh-UK) were invited to participate.

These guidelines were realized according to the Recommendations from the ERAS® Society for standards for the development of enhanced recovery after surgery[21] and the Appraisal of Guidelines, Research and Evaluation (AGREE) recommendations,[22] with LT surgeons, anaesthesiologists or LT hepatologists as target users.

Items analysed

The ERAS Guidelines for Liver Surgery[5] were used as working basis to develop the present guidelines, including the list of examined items. Hence, given some particular aspects of LT, a preliminary draft including the list of items on which the guideline would focus on was submitted for approval to all the experts. These agreed to remove the Mechanical/Oral bowel preparation item, considered as irrelevant in LT context, and "prehabilitation", "temporary portocaval shunt", "early extubation", "postoperative education" items were added. The final list included 22 items. According to the methodology used for the development of the previous ERAS guidelines on Liver Surgery[5], 22 different search equations were realized, 1 for each keywords group defining a validated ERAS item (preadmission counselling, prehabilitation, fluid and carbohydrate loading, no prolonged fasting, no/selective bowel preparation, antibiotic prophylaxis, thromboprophylaxis, no premedication, short acting anaesthetic agents, temporary portocaval shunt, mid-thoracic epidural anaesthesia, no drains, avoidance of salt and water overload, maintenance of normothermia, no nasogastric tubes, prevention of nausea and vomiting, early extubation, early removal of catheter, early oral nutrition, early mobilisation, nonopioid oral analgesia, stimulation of gut motility, postoperative education, audit of compliance and outcomes).

Literature search and data extraction

The coordinator centre (Pitié Salpêtrière, Paris, France) realized a digital search Medline through PubMed for published studies and ClinicalTrials.gov for ongoing trials, focusing on each validated ERAS items in the area of liver transplantation. Each single validated ERAS

item was defined by a group of specific keywords extracted from official ERAS guidelines and 1 pilot study on ERAS and LT.[2,3,5,19,23,24]

Participants/population

Human adult patients (18 years or older) undergoing LT, with a graft (whole or split) coming from a deceased (after brain or cardiac death) or living donor, no matter the indication for LT. Articles focusing on re-transplantation or combined LT (with kidney, hearth, lung, pancreas or intestine) were not considered because of different patterns of morbidity and mortality. Studies focusing on paediatric LT and experimental studies including animals were not considered for inclusion.

Intervention(s), exposure(s)

No restriction on the type of intervention tested were applied, provided that the target population is composed of patients undergoing LT. According to the ERAS protocol, interventions could be during the preoperative, intraoperative or postoperative period immediately after LT.

Comparator(s)/control

None

Main outcome(s)

Outcomes assessed: all primary outcomes reported in the result section were extracted with the related definition, and severity score when provided. Measures of effect were classed (e.g. clinical outcome, surgical outcome, mortality, morbidity, recovery outcome, patients reported outcomes[25]) as well as the direction of effect (in favour vs against).

Setting

No restriction on study location or settings were applied.

Language

We will consider articles reported in English, French, German, Italian or Portuguese. Studies

in other languages will be included only if the translation can be adequately obtained through Google translate.

Types of study included

Were considered for inclusion prospective or retrospective studies (cohorts or registry), case control or randomized clinical trials (RCT). If relevant, reviews and meta-analyses were evaluated for inclusion. Case reports were excluded, as well as any study including less than 10 patients. Abstracts, letters to the editor or conference posters were not considered for inclusion because of the lack of complete methods and results description.

Manual cross-references among the included studies were searched, for relevant related citations. The searches were done from 15/04/2019 – to 28/04/2019. The results of the literature research were screened by 5 investigators (2 surgeons: RB, DP, 3 anaesthesiologists: AM, SS, ES) on the basis of title and abstract through an on-line support.[26] Doubtful inclusions were resolved through discussion. A standardized data collection form, specifically designed for the purpose of this study, was used by 3 investigators for data extraction from published articles or for ongoing trials at ClinicalTrials.gov. After selection and inclusion for qualitative analysis, each trial was scored for quality (Risk of Bias tool - Cochrane collaboration's tool,[27] Jadad score,[28] and GRADE[29]).

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement[30]: the protocol was registered on the International Prospective Register of Systematic Reviews[31] current May 2019 (PROSPERO CRD42019132798).

Recommendation drafting

Based on the results of the literature search, a working group composed by 3 investigators (RB, AM, SS) prepared, for each item

- *The supporting text*: concise, focused on relevant publications to support the evidence of the recommendations. If necessary, a few additional publications could be cited to support and explain the supporting text but without providing an extensive review of the literature.
- *The recommendation*: was defined as a statement that contained a course of action such as a preventive or treatment activity. Recommendations should contain the verbs can/may (weak), should or shall (strong) depending on the recommendation grade. Recommendations were based not only on quality of evidence but also on the balance between desirable and undesirable effects and on the values and the preferences. The latter implies that, in some cases, strong recommendations may be reached from low-quality data and vice versa.[29]
- *The grade of evidence* based on the Oxford level of evidence[32] (ranging from 1 to 5) and GRADE quality of evidence[29] (‘‘high’’, ‘‘moderate’’, ‘‘low’’ and ‘‘very low’’). Shortly, the GRADE assessment approach provides a structured way to consider key factors that may increase or decrease confidence towards a synthesized body of evidence, and particularly on the quality of evidence in the body of literature supporting the evidence itself. The final analysis may be classified as high, moderate, low and very low depending on the importance of outcomes, risk of bias, heterogeneity, indirectness, imprecision and publication bias.[21]
- *The strength of recommendation* There was not necessarily a 1:1 relation between strength of the recommendation (strong/weak) and the quality of the evidence. The strength of recommendation should also take into account criteria such as consistency of study results, clinical relevance of endpoints (outcomes) and effect sizes, risk-benefit ratio, patient preferences, application to the relevant patient group, application to

healthcare setting, legal and economic considerations. Based on these criteria, upgrading or downgrading of grades of recommendation was allowed.[33]

Consensus process (Delphi)

The strength of recommendation, quality of evidence and conclusions were assessed and agreed by a 3 round e-Delphi process. The Delphi technique is a structured research tool for building consensus within a panel of experts around a specific topic through multiple interactions with questionnaires.[34–36] We sought to compose a heterogeneous panel in order to bring a range of disciplinary viewpoints, mirroring the multidisciplinary management of LT across caregivers and the "core philosophy" of multimodal ERAS management. Experts in LT surgery, anesthesiology and critical care from 12 high-volume LT centers (Liège-Belgium, Sao Paulo-Brazil, Montréal-Canada, Torino-Italy, Pisa-Italy, Kyoto-Japan, Groningen-Netherlands, Paris-France, Alicante-Spain, Genève-Switzerland, Portland-US, Edinburgh-UK) were contacted by e-mail in November 2019 and invited to participate. There is no consensus on the sample size of participants required for a Delphi panel, but a minimum of 10 is considered acceptable.[37] Here we invited 27 experts in this phase.

We used the modified electronic Delphi design, where the 'modified' term refers to the use of systematic literature review and expert discussion to drive the first provisional checklist for the initial questionnaire round rather than open interview on a broad list of items.[38,39] Online Delphi studies are free of charge compared to paper-based Delphi or face-to-face meetings, and are particularly suitable when experts are scattered across countries.[38] We consequently predefined a 3-phase sequence of rounds with iterative feedback.[40] We solicited each expert up to 3 times after each round. Consensus was considered as reached if more than 80% the of experts rated the item within the highest region of the scale (7, 8 or 9 on the 9-point Likert scale).[41] Once consensus was reached for a given item, that item was removed and no longer proposed in the following round. Experts were given 2 weeks to respond to each round,

followed by 2 reminders to complete the questionnaire that were sent out after 7 and 14 days. A 2-week interval between rounds was used to summarize the data and develop the next questionnaire.

We did not plan an external revision of final recommendations, but an updating procedure will be proposed every 5 years.

RESULTS

Among the 2685 references identified by the PubMed search, 43 were included. From the search on Clinicatrials.gov, we identified 62 references and included 6 ongoing trials. The selection process is detailed in Figure 1, and the complete list of trials can be found in Supplementary_material_study_list http://links.lww.com/TP/C225 .

Characteristics of the included trials

Among the included studies, 40 (93%) were from single centers, including a median of 105 (38.5-171.5) patients. The design was prospective in 25 (55.8%) of included studies, with 12 (27.9%) randomized. The experimental intervention was nonpharmacological, pharmacological and combined in 23 (53.5%), 19 (44.2%) and 1 (2.3%) of studies.

The indication of LT was detailed in 32 studies (74.4%), with the use of deceased donor graft, LDLT or both reported in 15 (34.9%), 9 (20.9%) and 3 (7.0%) of cases, respectively. The reported level of evidence according to the GRADE[29] was rated as high in 3 (7%), moderate in 16 (37.2%), low in 16 (37.2%) and very low in 7 (16.3%) of the 43 published references. More details in Table 1.

e-Delphi process results.

Among the 27 experts invited, 21 (81%) replied from 12 international LT centers reporting a median volume of 70 (40-112.5) LT per year: n=7 centres reported low-intermediate volume (<75 LT/year[42–44]), and 5 high-volume (>75-100 LT/year[42–44]).

The round-1 questionnaire was sent in November 2019, and data collection was completed

within 3 months, in February 2020. Figure 2 gives further information on the e-Delphi panel, with an average 15.7±7.86 years of experience. After round 1, consensus was reached for 16/22 criteria, with 2 of them requiring minor rewording. Changes were made to the wording used to describe the criteria, prompted by the panel's suggestions, and after round 2, consensus was reached for all the remaining criteria. The figure 3 shows the trend of consensus rating for each criterion across the last 2 rounds.

Within the Table 2 are summarized the ERAS recommendations for each item and the respective level of evidence, and in the supplementary_material_supporting_text http://links.lww.com/TP/C225 is exposed the rationale for each recommendation.

CONCLUSIONS

This systematic review highlights how current available evidence on enhanced recovery pathways in liver transplantation is scarce, and lacks standardization. The highest level of evidence (level 1 or 2) was available for 13 out of 22 items. While the value of ERAS pathways has now been demonstrated in liver, colorectal and pancreas surgery showing benefit in morbidity, cost and medico-economic outcomes, there is a clear need to perform high-quality studies to confirm the benefit of ERAS pathways in liver transplantation. In conclusion, the proposed ERAS pathway for liver transplantation is based on the best available evidence, which still needs to be further explored.

To allow benchmarking and comparison across trials using the new proposed liver transplantation ERAS recommendations, there is a need for consensual and standardized outcomes in liver transplantation, which are currently lacking.[25] In this line, a standardized and consensual checklist criteria to assess readiness for hospital discharge (or functional recovery) after LT was recently proposed.[45] Moreover, as highlighted by Muller X. et al[46] in a multicentre analysis to define benchmarks in LT, 82% of patients developed at least 1

complication during 1-year follow-up. When the latter is taken into account, probably the weight of morbidity as an outcome in ERAS guidelines validation should be reconsidered. Lastly, as with all existing ERAS pathways, the assessment of adherence to the protocol (compliance) is of utmost importance, and the compliance with the new proposed liver transplantation ERAS protocol should be documented, as part of further trial to allow benchmarking.

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TABLE 1 Characteristics of the selected studies.

TABLE 2 Summary of ERAS recommendations for each item and the respective level of evidence.

FIGURE 1 Flowchart of included studies

FIGURE 2 Characteristics of the expert panelists (experience, specialty, and LT volume).

FIGURE 3 Trend of consensus rating for each criterion across the e-Delphi rounds. The asterisks on the items 4 (antibiotic prophylaxis) and 13 (fluid and blood management) mean that an agreement was reached within the first round, but major rephrasing was proposed by the panel. The consensus rate was maintained above 80% for these 2 items during the second round.

Supplementary_material_study_list http://links.lww.com/TP/C225 . List and characteristics of included studies

Table 1. Characteristics of the selected studies	
	Overall (n=43)
Publication Year	
2000	1 (2.3%)
2002	1 (2.3%)
2007	1 (2.3%)
2009	1 (2.3%)
2010	3 (7.0%)
2011	2 (4.7%)
2013	2 (4.7%)
2014	5 (11.6%)
2015	4 (9.3%)
2016	7 (16.3%)
2017	8 (18.6%)
2018	4 (9.3%)
2019	4 (9.3%)
Location Corresponding Author	
Africa	1 (2.3%)
Asia	8 (18.6%)
Australia	2 (4.7%)
Europe	16 (37.2%)
North America	13 (30.2%)
South America	3 (7.0%)
Study Design	
Cohort	17 (39.5%)
RCT	12 (27.9%)
Case-control	7 (16.3%)
Before-after	6 (14.0%)
Outcome research	1 (2.3%)
If observational	
Prospective	24 (55.8%)
Retrospective	19 (44.2%)
If RCT	
Unblinded	8 (18.6%)
Double blind	4 (9.3%)
Single blind	1 (2.3%)
Single/multicenter	
Single center	40 (93.0%)
Multicenter, National	2 (4.7%)
Multicenter, International	1 (2.3%)
Total number of patients enrolled	
Mean (SD)	227 (496)
Median [25th, 75th]	105 [40, 171]
Level of Evidence, Oxford	
1	12 (27.9%)

2	15 (34.9%)
3	7 (16.3%)
4	9 (20.9%)
Indication of LT (reported)	
Yes	32 (74.4%)
No	11 (25.6%)
Type of graft	
Deceased donor	15 (34.9%)
LDLT	9 (20.9%)
Both	3 (7.0%)
Not detailed	16 (37.2%)
Timing of intervention	
Preoperative (including prehabilitation)	3 (7.0%)
Intraoperative or perioperative	24 (55.8%)
Early postoperative (up to discharge)	11 (25.6%)
Late postoperative or followup	5 (11.6%)
Class of intervention	
Medical treatment (including antibiotherapy)	13 (30.2%)
Anesthesiology	11 (25.6%)
Nutritional support	6 (14.0%)
Physical therapy	5 (11.6%)
Other	4 (9.3%)
Surgical technique	3 (7.0%)
Psychology education	1 (2.3%)
Type of intervention	
Non pharmacologic	23 (53.5%)
Pharmacologic	19 (44.2%)
Combined	1 (2.3%)
Impact on Morbidity	
Decreased	11 (25.6%)
No difference	13 (30.2%)
Unclear	2 (4.7%)
Increased	1 (2.3%)
Impact on Mortality	
No difference	16 (37.2%)
Decreased	1 (2.3%)
Unclear	1 (2.3%)
Impact on Liver Graft Dysfunction	
Decreased	5 (11.6%)
Increased	1 (2.3%)
No difference	17 (39.5%)
Impact on Length of Stay	
Decreased	5 (11.6%)
Increased	1 (2.3%)
No difference	17 (39.5%)
JADAD score	

-2	1 (2.0%)
-1	2 (4.0%)
0	1 (2.0%)
1	3 (6.0%)
2	2 (4.0%)
3	1 (2.0%)
5	2 (4.0%)
6	1 (2.0%)
GRADE Level of Evidence	
High	3 (6.0%)
Moderate	19 (38.0%)
Low	18 (36.0%)
Very Low	10 (20.0%)
Selection bias	
No	6 (14.0%)
Unclear	1 (2.3%)
Yes	5 (11.6%)
Allocation concealment bias	
No	6 (14.0%)
Unclear	4 (9.3%)
Yes	2 (4.7%)
Performance bias	
No	5 (11.6%)
Yes	7 (16.3%)
Detection bias	
No	4 (9.3%)
Yes	8 (18.6%)
Attrition bias	
No	6 (14.0%)
Unclear	3 (7.0%)
Yes	3 (7.0%)

RCT= randomized controlled trial, SD=standard deviation, LT=liver transplantation, LDLT=living donor liver transplantation,

Table 2. ERAS Item	Summary	Evidence Level	Grade of recommendation
1 PREOPERATIVE COUNSELING	Patients on waiting list should receive dedicated, multidisciplinary educational counselling.[47,48]	Low	Strong
2 PREHABILITATION	***Adapted Physical therapy*** There is no evidence yet of the benefit or harm of physical exercise in cirrhotic patients before liver transplantation.[49,50]	Low	Weak
	Preoperative nutritional screening Patients with cirrhosis should be screened for malnutrition, using a validated tool, and addressed to a multidisciplinary team for nutritional intervention.[51,52]	Moderate	Strong
	Preoperative nutrition cirrhotic patients malnourished or in the preoperative period should receive 30-35 Kcal x kg^{-1} x d^{-1} and a protein intake of 1.5 g x kg^{-1} x d^{-1}, through a standard nutrition regimen minimizing periods of starvation, with no need of protein restriction in case of HE.[51]	High	Strong
	Probiotics Some evidence supports the use of probiotics, prior to, or on the day of liver transplantation. The duration of the treatment and the number of strains included are variable across the studies.[53,54]	High	Weak
	Preoperative immunonutrition the available evidence is nonconclusive, and no recommendation can be given for systematic IN before LT.[55]	High	Weak
3 PERIOPERATIVE FASTING AND CARBOHYDRATE LOADING	***Preoperative fasting*** Preoperative fasting does not need to exceed 6 h for solids and 2 h for liquids. Caution should be considered in case of risk factors for delayed gastric emptying (tense ascites, diabetes or autonomic dysfunction).[5,51]	Low	Strong
	Carbohydrate loading Carbohydrate loading may be recommended at patient admission for liver transplantation, at least 2 h before induction of anaesthesia.[5,56] Caution should be considered in case of risk factors for delayed gastric emptying (tense ascites, diabetes or autonomic dysfunction).	Low	Weak
4 ANTIMICROBIAL PROPHYLAXIS	It is recommended to administer antibiotic prophylaxis only during the intraoperative period. Extending the duration of prophylaxis does not provide any advantages. Systematic selective digestive decontamination is not recommended.[57,58]	Moderate	Strong

5 ANTITHROMBOTIC PROPHYLAXIS	***Antithrombotic prophylaxis*** There is no evidence in favour or against thrombotic prophylaxis, but compressive stockings and intermittent pneumatic compression devices during LT may be recommended.	Very Low	Weak
	Anticoagulation prophylaxis There is insufficient evidence to provide any formal recommendation on antiaggregation or anticoagulation. When available, the viscoelastic coagulation monitoring may be used to guide the therapeutic decision.	Very Low	Weak
6 ANESTHETIC PREMEDICATION	Long-acting anxiolytic drugs should be avoided. Dose-adjusted, short-acting anxiolytics may be considered in selected patients.	Very Low	Weak
7 INCISION	The choice of incision is at the surgeon's discretion, depending on the graft and patient's morphology. Mercedes-type incision may probably be avoided due to higher risk of incisional hernia.	Low	Weak
8 TEMPORARY PORTOCAVAL SHUNT	The available evidence suggest that the use of temporary porto-caval surgical shunt may be beneficial in reducing the red blood cell transfusion requirement, length of stay, PNF and mortality rates.[59,60] Its use is however submitted to the surgeon and anaesthesiologist's decision during surgery.	Low	Weak
9 SHORT ACTING ANESTHETIC PROTOCOL	Short acting anesthetics can be considered in LT, and within anesthetic gases, little evidence suggest that sevoflurane may be preferred to desflurane.[61] Cerebral or nociception monitoring anesthetic titration may be critically used. Neuromuscular monitoring should guide the appropriate level of muscle relaxation and reversal.	Low	Strong
10 PERIOPERATIVE ANALGESIA	We recommend using multimodal and balanced analgesia to manage perioperative analgesia after LT. There is not enough published evidence to state in favor or against an opioid-sparing management: PCA-based morphine may be considered, with caution among patients at high risk for delirium. TAP block may be considered, while TEA cannot be recommended after LT.[62,63]	Low	Strong
11 EARLY EXTUBATION	Each patient undergoing LT should be screened for eligibility to early extubation (< 3-8h).[64] The eligibility should rely on published scores and on local policies and organization for postoperative monitoring.[65,66]	Low	Strong

12 ABDOMINAL DRAINAGE	There is insufficient evidence to recommend no routine drain policy in liver transplantation.[67] Whenever a drain is used, it may be advisable to remove as soon as possible. It can be considered to systematically drain the peritoneal cavity of patients affected by refractory ascites.	Low	Weak
13 FLUID MANAGEMENT	A restrictive fluid management strategy may carefully be considered during LT over a more liberal one.[68] Indirect evidence from other major surgery population suggest that a goal-directed fluid therapy may provide better outcomes than standard of care. TEE may be considered to target fluid therapy.	Low	Weak
	Intraoperative blood product management When available, Viscoelastic tests as Thromboelastography (TEG) or Rotational Thromboelastometry (ROTEM) might be used to drive the management of blood products and factor concentrates during LT.[69]	Low	Weak
14 PERIOPERATIVE NORMOTHERMIA	Perioperative normothermia should be maintained during liver transplantation.[70,71]	Low	Strong
15 PROPHYLACTIC NASOGASTRIC PROBE	Indirect evidence suggest that routine postoperative nasogastric probe after liver transplantation is not indicated. Nasogastric tubes placed during surgery should be removed before reversal of anaesthesia.	Low	Strong
16 POSTOPERATIVE NAUSEA AND VOMITING	Indirect evidence suggest the use of a multimodal approach to PONV, with 2 antiemetic drugs as prophylaxis (e.g. 5-HT3 antagonist and steroids).	Low	Strong
17 EARLY ORAL NUTRITION	Normal food oral intake and/or enteral nutrition (nasogastric tube or jejunostomy) should be started 12-24h after liver transplantation, according to patient's tolerance. Parenteral nutrition should be considered as the very last option, when the use of oral route (enteral feeding tubes or jejunostomy) is not possible.[51]	Very Low	Strong
	Nutritional supplements There is no clear evidence of the benefit of nutritional supplements after liver transplantation.[72,73]	Low	Weak
18 EARLY MOBILISATION	Early mobilization after LT should be encouraged with early-goal directed interventions, from the morning after LT until hospital discharge.[75,76] Physical rehabilitation may be continued after discharge.	Moderate	Strong

19 GLYCEMIC CONTROL	We recommend a protocolized approach to blood glucose management in LT patients targeting an upper blood glucose level ≤180 mg/dL from the intraoperative period to the early postoperative period (first 24-48 hours postoperatively in the absence of complications and/or organ failure).[77–80]	Moderate	Strong
20 POSTOPERATIVE ILEUS	There are no acknowledged strategies to prevent postoperative ileus after LT.	Low	Weak
21 POSTOPERATIVE EDUCATION	Systematic educational programs after liver transplantation may increase patient awareness and knowledge on the immunosuppressive therapy and on physical changes after LT. Such multidisciplinary programs could include a clinical pharmacist, and should be continued over a long period after liver transplantation.[80-82]	Low	Strong
22 AUDIT	Systematic audit improves compliance and clinical outcome in healthcare practice.[2,4,5]	Moderate	Strong

LT=liver transplantation, Kcal=kilocalories, IN=immunonutrition, h=hours

Figure 1

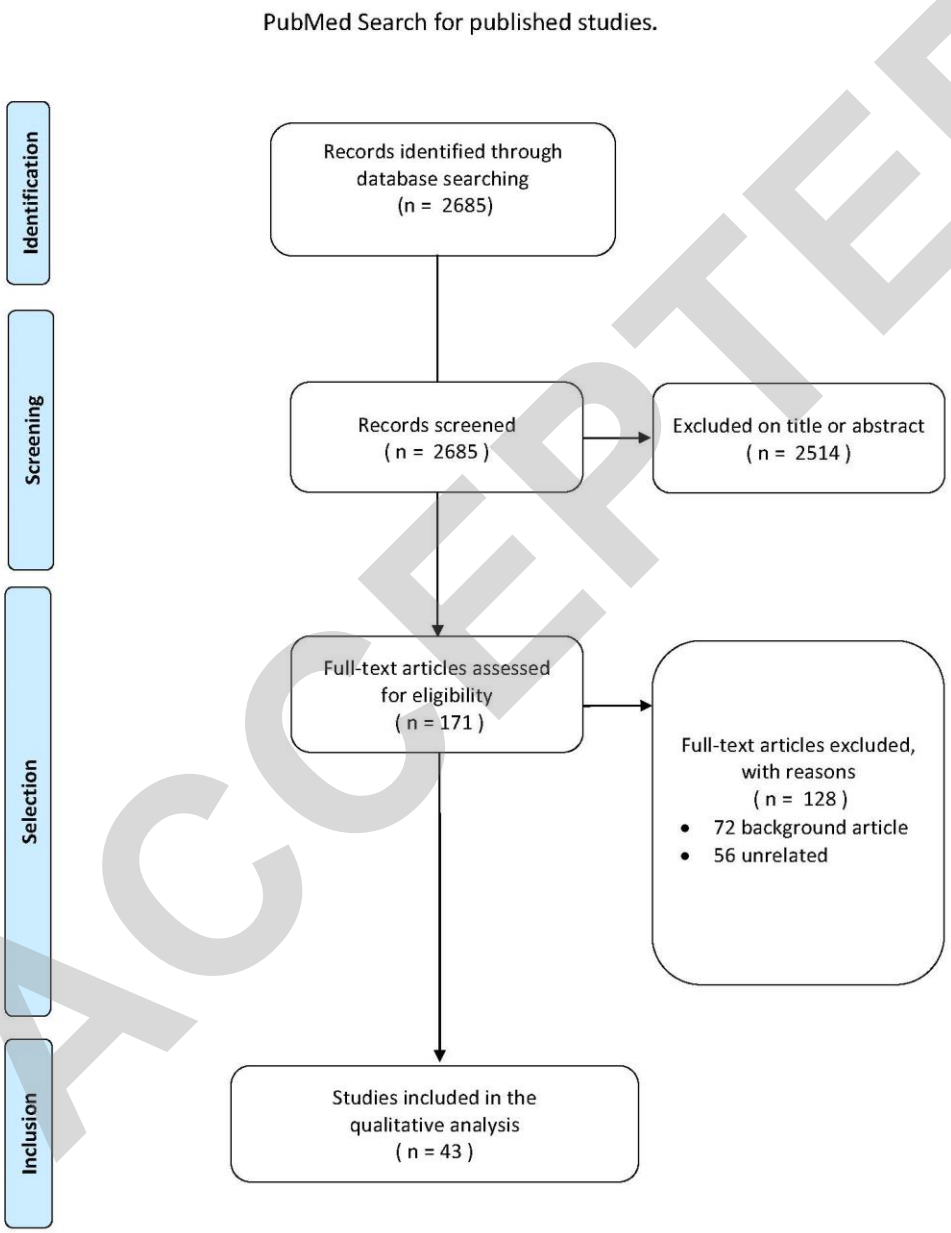

Figure 2

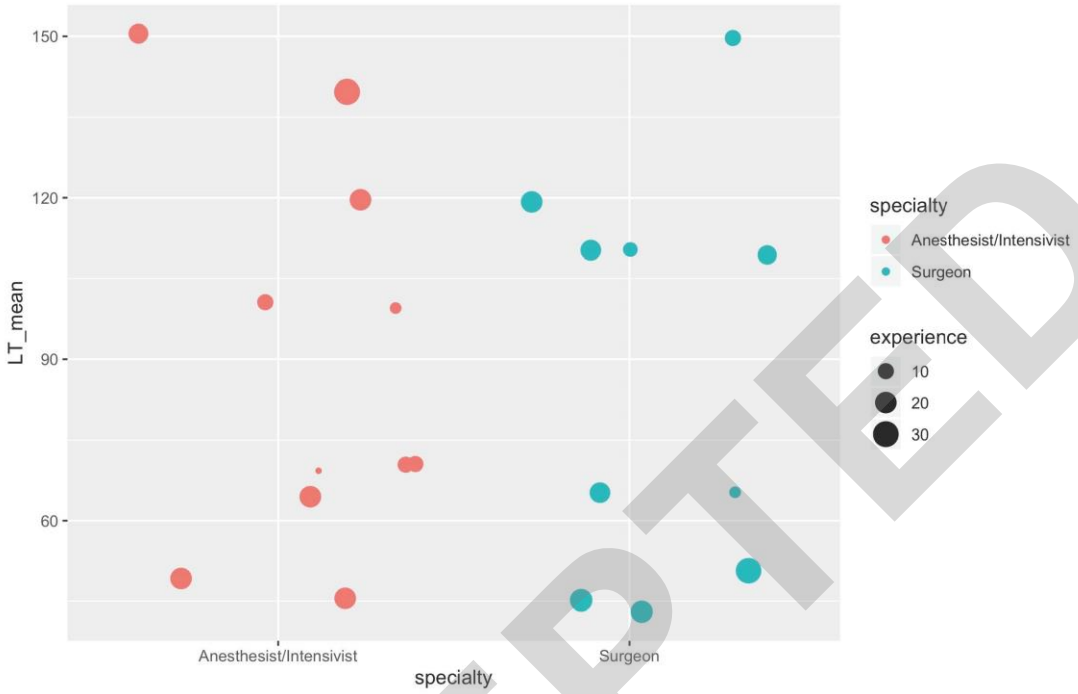

Figure 3