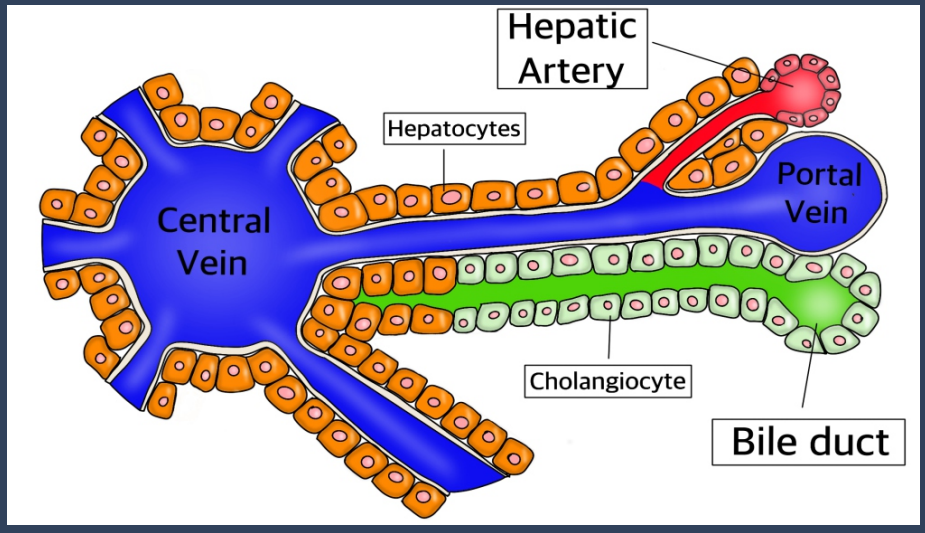
The Official Journal of the Inonu Liver Transplantation Institute

Journal of Inonu Liver Transplantation Institute



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Aim and Scope: The Journal of Inonu Liver Transplantation Institute is a peer-reviewed open-access e-only publication in the field of liver transplantation publishing research articles on clinical, experimental liver transplantation, combined liver and other organ transplantation, and liver diseases. The journal welcomes original research articles, reviews, meta-analyses, case reports, and letters.
Average Duration of the First Review Round: 2 months
Type of Publications: Research Article, Review Article, Meta-Analyses, Case Report, Letter to the Editor
Language of Publication: English
Frequency: 3 issues per year
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JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

Aim and Scope

Aim

The Journal of Inonu Liver Transplantation Institute is a peer-reviewed open-access e-only publication in the field of liver transplantation publishing research articles on clinical, experimental liver transplantation, combined liver and other organ transplantation, and liver diseases. The journal welcomes original research articles, reviews, meta-analyses, case reports, and letters.

Overview

Journal of Inonu Liver Transplant Institute has been founded and established by Inonu Liver Transplant Institute in order to form a source of high-quality research in diseases and therapy of the liver and biliary tract. Both clinicians and basic science researchers are the target population of our journal.

Scope

Hepatobiliary disorders are a complex spectrum of diseases, usually requiring a multi-disciplinary approach that involves interventional radiologists, hepatologists, oncologists, hepatobiliary-transplant surgeons and translational researchers. The Journal of Inonu Liver Transplant Institute (JILTI) is internationally peer reviewed and provides a source for articles on prevention, diagnosis and cutting-edge therapy of hepatobiliary diseases and cancers which also includes liver transplantation, complex hepatobiliary surgical procedures, medical and immune therapies. In accordance with our aims, basic and translational research as applied to these diseases have utmost importance for our journal.

Keywords: Hepatobiliary diseases and cancers, liver surgery, liver transplantation, advanced therapy of hepatobiliary diseases, basic and translational research on hepatobiliary diseases.

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Ethical Responsibilities and Policies

Fee - Charges

The Journal of Inonu Liver Transplantation Institute (The Journal) assesses NO submission fee, publication fee (article processing charges - APC), or page charges.

Publication Ethics

The Journal applies standards throughout the publication process to further our goal of sharing high-quality, objective, reliable, and useful information. We implement these processes to ensure appropriate support for our authors and their institutions, as well as our readers. It is crucial that all of the stakeholders in the process (authors, readers and researchers, publishers, reviewers, and editors) comply with ethical principles.
The Journal is an open access publication and follows the guidelines and policies published by the Committee on Publication Ethics (COPE) (https://publicationethics.org). We expect all participants to observe the ethical responsibilities presented below.

Author's Responsibilities

- Studies submitted for publication must be original works of the author. References to other studies must be cited and/or quoted completely and accurately;
- Only those who provide a substantial intellectual contribution to the content of the work may be cited as an author. Other contributors may be recognized with acknowledgements at the conclusion of the article;
- Competing interests or relationships that may constitute a conflict of interest must be declared and explained in all studies submitted for publication;
- Authors must be able to provide documentation showing that they have the right to use the data analyzed, the necessary permissions related to the research, and any appropriate consent;
- Raw data used in the article must be available and may be requested from the author(s) within the framework of the evaluation process;
- In the event the author(s) notice an error at any point in the publication process or after publication, they have the obligation to inform the journal editor or publisher and cooperate in appropriate corrective action;
- Authors may not submit their article for publication to more than one journal simultaneously. Each application must be initiated following the completion of any previous effort. The Journal will not accept previously published articles;
- Changes in authorship designation (such as adding authors, changing the printed order of the authors, removing an author) once the evaluation process has begun will not be accepted in order to protect all parties involved.

Editor's Role and Responsibilities

General Duties

The editor is responsible for everything published in the journal. In the context of this responsibility, editors have the following duties and obligations:

- Endeavor to meet the needs of readers and authors;
- Maintain continuous development to improve the quality of the journal;
- Consistently work to ensure quality;
- Support freedom of thought;
- Ensure academic integrity;
- Prevent business needs from compromising intellectual and ethical standards;
- Demonstrate clarity and transparency with any necessary corrections or explanations.

Reader Relationship

The editor is to make publication decisions based on expectations of suitable and desirable material. Studies accepted for publication must be original contributions that benefit the reader, researcher, practitioner, and the literature. In addition, editors are obliged to take into account feedback from readers, researchers, and practitioners, and to provide an informative response. Readers will also be informed of any funding provided to support published research.

Author Relationship

- The decision to accept an article is to be based on the importance, original value, validity, and clarity of expression of the work, and the goals and objectives of the journal;
- Studies accepted for evaluation and publication will not be withdrawn unless serious problems are identified;
- The editor will not disregard positive reviewer comments unless there is a serious problem with the study;
- New editors will not change publishing decisions made by previous editor(s) unless there is a serious problem;
- A description of the submission and evaluation process is publicly available;
- Authors are provided with descriptive and informative feedback.

Reviewer Relationship

Reviewers are to be selected according to the subject of the study;
Information and guidance for the evaluation phase is provided;
Any conflicts of interest between authors and reviewers will be disclosed and managed appropriately;
Reviewer identity is to be kept confidential to preserve a blind review process;
Reviewers are to evaluate the study using unbiased, scientific, and constructive comments. Unkind or unscientific commentary will not be permitted;
Reviewers will be evaluated using criteria such as timely response and quality of observations;
The pool of reviewers is to be assessed and supplemented regularly to ensure a broad scope of expertise.

Editorial Board Relationship

The editor works with the members of the editorial board to ensure that they are familiar with journal policies and developments in regular meetings and announcements, and will provide training for new members and assistance to board members during their tenure in their role as a supporter of the journal.

- Editorial board members must be qualified and able to contribute to the journal;
- Members of the editorial board must evaluate studies impartially and independently;
- Editorial board members with the appropriate expertise will be given the opportunity to evaluate suitable articles;
- The editor will maintain regular contact with the editorial board and hold regular meetings regarding the development of editorial policies and other aspects of journal management.

Relations with the Owner of the Journal and the Publisher

The relationship between the editors and the publisher/journal owner is based on the principle of editorial independence and stipulated by contract.

Editorial and Blind Review Processes

The editor will apply the publicly defined publication policies created and enforced to ensure a timely and impartial evaluation process for all submissions.

Quality Assurance

The editor is responsible for confirming that the The Journal publishing policies and standards are upheld for all articles.

Protection of Personal Data

The editor is obliged to ensure the protection of personal data related to subjects or images included in published work. Explicit documented consent of the individuals referenced in the research is required before the study will be accepted. The editors is also responsible for protecting the individual data of authors, reviewers, and readers.

Ethics Committee, Human and Animal Rights

The editor is required to ensure that human and animal rights were protected in the studies submitted for publication.

Measures Against Potential Misconduct

The editor must take action against any allegations of possible misconduct. In addition to conducting a rigorous and objective investigation of complaints, the editor is expected to share the findings and conclusions.

Maintaining Academic Publication Integrity

The editor is expected to ensure that any errors, inconsistencies, or misleading statements are corrected quickly and appropriately acknowledged.

Protection of Intellectual Property Rights

The editor is obliged to protect intellectual property and to defend the rights of the journal and author(s). In addition, the editor is to take the necessary measures to prevent any violation of the intellectual property rights of others in journal publications.

Creativity and Openness

- Constructive criticism is to be encouraged;
- Authors will be given the opportunity to reply to criticism;
- Negative results will not be a reason for submission denial.

Complaints

Editors are to respond to all complaints in a timely and comprehensive manner.

Political and Commercial Concerns

Political or commercial factors will not affect editorial decisions.

Conflicts of Interest

The editor is required to ensure that any conflicts of interest between authors, reviewers, or other editors are disclosed and managed appropriately to provide an independent and impartial process.

Reviewer's Ethical Responsibilities

Peer review of research embodies the scientific method, subjecting the work to the rigorous scrutiny of knowledgeable colleagues. The rigor of the review process directly affects the quality of the literature; it provides confidence in an objective and independent evaluation of the published work. The Journal uses a double-blind review process. All comments and the evaluation are transmitted through the journal management system. Reviewers should:

- Only agree to evaluate studies related to their specialty;
- Return reviews within the designated timeframe;
- Evaluate with impartiality. Nationality, gender, religious beliefs, political beliefs, commercial concerns, or other considerations must not influence the evaluation;
- Refuse to review any work with a potential conflict of interest and inform the journal editor;
- Maintain confidentiality of all information. Only the final published version may be used for any purpose;
- Use thoughtful and constructive language. Hostile or derogatory comments are not acceptable;
- Report any potentially unethical behavior or content to kare@karepb.com via e-mail.

JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

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Information for the Authors

THE JOURNAL

The Journal of Inonu Liver Transplantation Institute (The Journal) is an international, scientific, open access periodical published in accordance with independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Inonu Liver Transplantation Institute, and it is published in April, August and December, three times a year. The publication language of the journal is English.

The Journal aims to contribute to international literature by publishing high-quality manuscripts in the field of diseases and therapy of the liver and biliary tract. The journal's target audience includes academics and expert physicians working in transplantation surgery specialists.

REVIEW PROCESS

Manuscripts submitted to the Journal will undergo a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in their field in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation process of manuscripts submitted by editors or by the editorial board members of the journal. The editor-in-chief is the final authority in the decision-making process for all submissions.

Reviews are typically completed within one month of submission to the journal. Authors will be sent constructive reviewer comments intended to be useful. In general, the instructions, objections, and requests made by the reviewers should be followed. The revised manuscript should clearly and precisely indicate every step taken in accordance with the reviewers' notes. A list of responses and the corrections made to each comment should be provided.

AUTHORSHIP

Each individual listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship be based on the following 4 criteria:

Substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; AND

Drafting the work or revising it critically for important intellectual content; AND

Final approval of the version to be published; AND

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for their own work, authors should have confidence in the integrity of the contributions of their co-authors and each author should be able to identify which co-authors are responsible for other parts of the work.

All of those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged on the title page of the manuscript.

The Journal requires that corresponding authors submit a signed and scanned version of the authorship contribution form (available for download through www.jilti.org) during the initial submission process in order to appropriately indicate and observe authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without further review. As part of the submission of the manuscript, the corresponding author should also send a short statement declaring that they accept all responsibility for authorship during the submission and review stages of the manuscript.

ORCID ID

The Open Researcher and Contributor ID (ORCID) number of each author must be submitted when creating an account for correspondence. To obtain an ORCID number, please visit https://orcid.org/

PLAGIARISM DETECTION

All submissions are screened using similarity detection software at least two times: on submission and after completing revisions. In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, or data falsification/fabrication, the editorial board will follow and act in accordance with COPE guidelines. Plagiarism, including self-plagiarism, that is detected at any stage will result in rejection of the manuscript.

PUBLICATION FEE - CHARGES

This journal assesses no submission fees, publication fees, or page charges.

MANUSCRIPT PREPARATION

Manuscripts should be prepared in accordance with the ICMJE-Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in December 2015 - http://www.icmje.org/icmje-recommendations.pdf). Authors are required to prepare manuscripts in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomized research studies, the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for observational original research studies, the Standards for Reporting Diagnostic Accuracy (STARD) guidelines, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines for experimental animal studies, and the Transparent Reporting of Evaluations with Non-randomised Designs (TREND) guidelines for non-randomized behavioral and public health evaluations.

Manuscripts may only be submitted through the journal's online manuscript submission and evaluation system, http://jag.journalagent.com/jilti/ Manuscripts submitted via any other medium will not be evaluated.

Manuscripts will first be submitted to a technical evaluation process in which the editorial staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the author with requests for technical correction.

The quality and clarity of the language used in a manuscript is very important. The editors may request that authors have the manuscript professionally edited if the language of the submission does not conform to the journal standards. The Journal uses American English. Please submit text of a quality ready for publication. Information about language editing and copyediting services pre- and post-submission may contact Kare Publishing at kare@karepb.com. Please refer to specific formatting requirements noted in the submission checklist and elsewhere in this document.

MANUSCRIPT TYPES

Original Article: This is the most valued type of article, since it provides new information based on original research. The main text of an original article should be structured with Introduction, Methods, Results, Discussion, and Conclusion subheadings. Original articles are limited to 3500 words and 30 references.

Editorial comment: Editorial comments provide a brief critical commentary offered by reviewers with experience and standing in the topic of a research article previously published in the journal. The authors are selected and invited by the journal to provide the benefit of their expertise. The submission should not include an abstract, keywords, tables, figures, and images. The word count is limited to 1200 and 15 references may be included.

Review article: Two kinds of review are accepted for publication in the Journal: narrative review and systematic review. Reviews of relevant topics not recently discussed in this format that will be helpful to readers are welcomed.

Case report: There is limited space for case reports and therefore the journal selects reports of rare cases or conditions that reflect challenges in diagnosis and treatment, those offering new therapies or revealing knowledge not in the literature, or present something otherwise particularly interesting and educative. The abstract with structured of background, case and conclusion, is limited to 150 words and the report must include the subheadings of introduction, case report, and discussion, which includes a conclusion. A case report is limited to 1300 words and 15 references.

Image: Original, high-quality clinical or laboratory images will be considered for publication. If a photo of an identifiable patient is used, a consent form for its use must be completed and signed by the patient and enclosed with the submission. All printed information that might identify the patient or the authors' institution (including, but not limited to the hospital or patient name, date, or place) should be removed from images. The submission should have no more than 3 authors, the case description is limited to a maximum of 200 words, the discussion section may contain no more than 200 words, and only 3 references and 3 figures are permitted.

Letter to the editor: This type of manuscript discusses important observations, overlooked aspects, or details lacking in a previously published article. Noteworthy articles on subjects within the scope of the journal, particularly educative cases, may also be submitted in the form of a "Letter to the editor." No abstract, keywords, tables, figures, images, or other media should be included. The article that is the subject of commentary must be properly cited within the manuscript. The text should be unstructured and is limited to 500 words. No more than 5 references will be accepted.

Table 1. Limitations for each manuscript type.

Type of manuscript	Wordlimit	Abstract word limit	Referencelimit	Table limit	Figure limit
Original Article	3500	350 (Structured)	40	6	6
Review Article	5000	350	50	6	10
Meta analysis	5000	350	50	6	10
Caser Report	1500	200	20	No tables	5
Letter to the Editor	1000	No abstract	10	No tables	1

Title page: A separate title page should be submitted with all submissions and this page should include:

The full title of the manuscript as well as a short title (running head) of no more than 50 characters

Name, affiliation, ORCID ID number, and highest academic degree of the author(s)

Funding and other material support

Name, address, phone number(s), fax number, and email address of the corresponding author

Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria

Manuscripts that have been presented orally or as a poster should include the name, date and place of the event

Abstract: An English-language abstract is required with all submissions except editorial comments, images, and letters to the editor. Systematic reviews and original articles should contain a structured abstract of maximum 250 words with the subheadings of objective, methods, results, and conclusion.

Keywords: Each submission must be accompanied by a minimum of three and a maximum of six keywords for subject indexing included at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html).

Tables: Tables should be uploaded as separate files and not embedded in the main text. They should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the table with footnotes, even if they are defined within the main text. Tables should be created using the "insert table" command of the word processing software and they should be designed for easy reading. Data presented in tables should not be a repetition of the data presented within the main text but should support the main text.

Figures and figure legends: Figures, graphics, and photographs should be submitted as separate files in TIFF or JPEG format through the article submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be

merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legend. Like the rest of the submission, the figures should be blind. Any information within the images that may identify an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100x100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition. Units should be prepared in accordance with the International System of Units (SI). When a drug, device, hardware, or software program, or other product is mentioned within the main text, the name of the product, the manufacturer/copyright holder of the product (not simply the vendor), and city and the country of the company (including the state, if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric Co., Boston, MA, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

References: The editorial team may request that the authors cite related recently published articles (preferably within the last 10 years) in their manuscripts, with the exception of historical papers.

If an ahead-of-print publication is cited, the digital object identifier (DOI) number should be provided. Authors are responsible for the accuracy of references. Journal titles should be abbreviated in accordance with the journal abbreviations in the Index Medicus /MEDLINE/ PubMed. When there are six or fewer authors, all authors should be listed. If there are seven or more authors, the first six should be listed followed by "et al." In the main text of the manuscript, references should be cited using Arabic numerals in parentheses. The reference styles for different types of publications are presented in the following examples.

Journal article: van Erk MD, Dam-Vervloet AJ, de Boer FA, Boomsma MF, van Straaten H, Bosschaart N. How skin anatomy influences transcutaneous bilirubin determinations: an in vitro evaluation. Pediatr Res 2019;86:471-7.

Epub ahead-of-print article: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead-of-print].

Manuscript published in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlEID/cid.htm.

Book section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.

Books with a single author: Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or technical report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

REVISIONS

When submitting a revised version of a paper (include a clean copy and a highlighted copy), the author must submit a detailed response to the reviewers that replies to each issue raised by the reviewers and indicates where changes can be found (each reviewer's comment, followed by the author's reply and line number where changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be withdrawn. If the submitting author(s) believe that additional time is required, they should request this extension within the initial 30-day period.

Accepted manuscripts are copy edited for grammar, punctuation, format, and clarity. Once the publication process of a manuscript is completed, it is published online on the journal's webpage as an ahead-of-print publication before it is included in the scheduled issue. A PDF proof of the manuscript is sent to the corresponding author and their publication approval is requested within 2 days of receipt of the proof.

PUBLICATION PROCESS

Accepted manuscripts will be made available and citable online as rapidly as possible. The stages of publication are as follows;

Uncorrected publication: A PDF of the final, accepted (but unedited and uncorrected) paper will be published online on the journal web page under the "Accepted Articles" section. A DOI will be assigned to the article at this stage.

Ahead-of-print publication: After copy editing, typesetting, and review of the resulting proof, the final corrected version will be added online in the "Ahead-of-Print" section.

Final publication: The final corrected version will appear in an issue of the journal and added to the journal website. To ensure rapid publication, we ask authors to provide your publication approval during the proofreading process as quickly as possible, and return corrections within 48 hours of receiving the proof.

SUBMISSION CHECKLIST

Please use this list and the following explanations to prepare your manuscript and perform a final check before submission to ensure a timely review.

Formatting of text

- Text should be written in 12-point Times New Roman font
- Main headings and subheadings should be in 12-point and bold font
- Type a single space at the end of each sentence
- Do not use bold face for emphasis within the text
- Numbers one to ten are written out in words unless they are used as a unit of measurement, except in figures and tables
- Use a single hard return to separate paragraphs. Do not use tabs or indents to start a paragraph
- Do not use software options for hyphenation, headers, or footers
- Use page numbering
- Use line numbers
- Use US English

Ensure that the following items are present:

- **Cover letter**
- **Title page including:**
  - Article type
  - Article title
  - Running title
  - All author names and affiliations
  - One author has been designated as the corresponding author with contact details
    - Full postal address, phone number(s), and email address
- Acknowledge
- Manuscripts that have been presented orally or as a poster must include the name of the event, the date, and the location
- State financial or other support for the study
- Word count
  - Abstract word count
  - Text word count
- **Main text of the manuscript must include:**
  - Article title
  - Abstract
  - Keywords
  - Text with required subheadings
  - References (ensure written according to journal rules)
  - Figures and tables
- Numbered according to text citation
- Descriptive legends/titles and abbreviations
- Ensure all figure and table citations in the text match the files provided
- **Figures:** to be submitted separately.
- **Tables:** to be submitted separately
- **Ensure that the following forms have been properly completed and submitted:**
- ICMJE Potential Conflict of Interest Disclosure Form (completed by all contributing authors), AND
- Copyright Transfer Form, AND
- Author Contributions Form

These forms are available for download at www.jilti.org

- **Further review**
  - Check the statistical analysis
  - Use the US English spell check and grammar check software functions
  - Check that all references cited in the text are correctly listed in the reference list
  - Permission has been obtained for use of copyrighted material from other sources (including the Internet)
  - All abbreviations have been identified
  - All figures and tables are correctly labeled
  - Journal policies detailed in this guide have been followed.

JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

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JOURNAL OF INONU LIVER
TRANSPLANTATION INSTITUTE

From the Editor

In the Beginning of Our Journey

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Hepatobiliary disorders are a complex spectrum of diseases, usually requiring a multi-disciplinary approach that involves interventional radiologists, hepatologists, oncologists, hepatobiliary-transplant surgeons and translational researchers. The Journal of Inonu Liver Transplant Institute (JILTI) is internationally peer reviewed and provides a source for articles on the etiology, epidemiology, prevention, diagnosis, staging, sub-typing and cutting-edge therapies for hepatobiliary diseases and cancers which also includes liver transplantation, ablation and complex hepatobiliary surgical procedures, loco-regional chemotherapy and radiotherapy, external beam radiation techniques, systemic medical chemotherapies and molecularly targeted therapies and immune modulating therapies.

Approximately 800,000 new cases of hepatocellular carcinoma are expected annually with 70% deaths. The causes are mainly known, yet vaccination-based prevention of hepatitis B infection as a cause of HCC has been replaced by increasing obesity-associated HCC cases. Despite the great variety of available treatment types, only the minority of patients who present with early-stage disease benefit from the surgical therapies that extend survival most. Thus, prevention of the known causes and early detection of the tumor are the areas of activity with the largest expected survival benefit. Furthermore, the large recent efforts in increasing early diagnosis through screening with novel molecular and other biomarkers, including liquid biopsy, of patients with predisposing diseases (cirrhosis of any cause, metabolic syndrome, chronic virus hepatitis) is expected to improve early diagnosis as well as help in specific patient tumor stage sub-classifications to identify patients who might benefit from specific therapies (therapy selection and prognosis). We thus have the paradox of the minority of cases presenting at an early stage of their disease trajectory, when the best treatments can prolong their survival, while a huge body of work continues on the development and application of newer and expensive therapies to the majority of patients who present much later in their liver cancer natural history, when most current therapy is much less effective in enhancing patient lifespan.

In accordance with our aims, basic and translational research as applied to these diseases have great importance for our journal and relevant articles are welcome for submission and review, as are Original articles, reports on Clinical Trials, Reviews, Editorials, Highlights of the world literature, Case Series, Case Reports and Letters to the Editor.

JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

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Review

Surgical Experiences from Europe's Largest Liver Transplant Institute during the February 6, 2023 Cataclysmic Turkish Earthquake

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Abstract

From disasters, we have to deduce some lessons to implement in centers where major surgeries are performed.
The Inonu University Liver Transplant Institute is located in the province of Malatya in southeast Turkey. On February 6, 2023, Malatya suffered two devastating earthquakes, one with a magnitude of 7.8 and another 10 h later, with a magnitude of 7.6, and subsequently thousands of aftershocks, some greater than magnitude 6. The city center looked like a complete rubble with ruined buildings and main roads. From this disaster, we deduced some lessons such as emergency action plans and psychological support programs should be done, people in senior management must be at work and should not leave the hospital, and etc.
This was a significant disaster. As the largest transplant center in Europe, the Inonu University Liver Transplantation Institute has attempted to survive. We now need to move quickly to regain the quality of our previous services.
Keywords: Devastating disaster, Earthquake, Liver transplantation program, Learned lessons, Malatya, Türkiye

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Malatya Inonu University Liver Transplant Institute has performed 3600 liver transplants since its founding in 2002, 90% of which are Living Donor Liver Transplants (LDLT). The institute is Europe's largest volume liver transplant center (ELTR data), which performed 280 liver transplants in 2022.[1,2] The "Malatya criteria"[3, 4], later "expanded Malatya criteria"[5] on hepatocellular cancer and liver transplant were defined by the institute. The institute has 116 patient beds, 36 ICU beds, 12 OR, interventional - diagnostic radiology and ERCP units, and outpatient departments that only liver patients attend, with the master's and doctoral programs. We are one of the few centers to have performed 5 simultaneous LDLTs and then 4-way liver paired exchange.[6]

The institution is located in the province of Malatya, in the southeast of Turkey. Malatya is also the apricot capital of the world with 70% production. On February 6, 2023, Malatya suffered two devastating earthquakes, one with a

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magnitude 7.8 and another 10 hours later, with a magnitude 7.6, and subsequently thousands of aftershocks, some greater than magnitude 6. People felt the first earthquake at 04:17 in the morning. The nurses on duty at the ICU hugged each other in the middle of the unit and began to cry. The doctor on duty checked the ventilators, reassuring the nurses and staff. Despite this, all the nurses and staff remained in the institute, but the ward patients were taken out of the hospital by their relatives. It was snowing outside and the temperature was -12 degrees Celsius. People spent the night either warming up by lighting a fire outside or in their cars. A 38-year-old man died of CO poisoning inside his car. When the sun began to shine, no one had entered their house in the city with a population of 750,000. As the next day dawned, it became clear that there were serious building collapses in the city and the extent of the damage caused by the earthquake began to emerge. The buildings more than 30 000 were uninhabitable or too damaged with 10,000 reduced to rubble, as was the city center and many roads. Many historical monuments were destroyed in this city, which holds more than seventy percent of all apricot production in the world (Figs. 1 and 2).

The hospital staff believed the hospital to be safe (built to be resistant to magnitude 9 earthquakes), so they flocked back to Turgut Ozal Medical Center and the Liver Transplantation Institute with their families. Life began to go on in the hospital since then. All patients and staff entered the hospital, trying to adapt to normal daily work. Unfortunately, at 13:30, the second earthquake with a magnitude of 7.6 occurred. The hospital was feared to be in danger of collapse. All the staff and patients in the hospital immediately removed themselves. Patients from outside the city, if they did not have serious problems, left the city with their relatives in their cars. Only the intubated ICU patients and their nurses and staff stayed in the hospital. All staff and patients gathered on the helipad. A shuttle bus brought in front of the ground floor was heated for pediatric transplant patients and the children were treated there.

Everyone started living outside or in their car at night. The next day, most doctors, nurses, and staff moved their families out of Malatya. Medical staff who were physically well but could not tolerate the event psychologically were not

Figure 1. (a, b) City center before the earthquake. **(a)** Grand Mosque, **(b)** Grand Bazaar.

Figure 2. (a, b) City center after the earthquake. **(a)** Grand Mosque, **(b)** Grand Bazaar.

forced to stay in the hospital or city. No water, bread, fuel, or solid food was available. Only soups can be served in the hospital. On the evening of February 6, pasta was cooked and distributed as bread was unavailable. Only breakfast supplies were distributed on February 8.

We tried to shield the patients from the extent of the disaster. However, many relatives were left under the rubble and died. During patient visits, many patients forgot their problems and cried for their relatives. We comforted them. During this time, the director of the Liver Transplantation Institute (SY), the head of the Department of General Surgery (BI), and the director of the Turgut Ozal Medical Center (AB), who are transplant surgeons, and the Rector of the University (AK), who is an otolaryngologist, did not leave the hospital for 26 days. This attitude created confidence in employees. All of us shared food or clothing donations from outside the province with us in a fair manner. Serious aftershocks still continue on the 26th day of the earthquake. Tent and container city were created, and ecological village studies began. However, no one could enter their homes for fear of house collapse and more injuries.

On the 8th day of the earthquake, we considered writing our scientific articles in process and turned this forced free time to advantage. However, each aftershock had a negative effect on their mental activity. On the 12th day of the earthquake, we had a comprehensive meeting with our Liver Transplant Team and decided to continue with our normal surgical function. Thus, we decided to bring the center back into life. Patients awaiting transplants have been repeatedly reviewed, and LDLT was started on day 14 of the earthquake. As of today, we have made 6 LDLTs.

From this disaster, we deduced some lessons:

- Emergency action plans should be established against such major disasters, and frequent rehearsals should be conducted.
- Psychological support programs should be applied to doctors, nurses, and staff to be more resilient in such disaster situations.
- Hospital buildings should be inspected primarily by competent institutions in terms of earthquake resistance, and necessary measures should be taken according to the results.
- Psychological support is particularly important for the patients. In the absence of a psychologist, the surgeon and nurse should provide psychological support.
- All challenges (limited food, clothing, and hygiene supplies) must be shared with the team. Staff should believe that managers never have privileges with everything shared.
- Leisure time should be used in part for research and writing. Colleagues should be instilled with this motivation, not just due to unexpected free time but also for their psychological well-being.
- People in senior management, such as directors, chairmen, and rectors, must be at work and should not leave the hospital.
- The team should spend most of the time getting together to support each other and keep thoughts away from the disaster for mental well-being and to help people's spirits.

This was a significant disaster. The institute has attempted to survive. We now need to move quickly to regain the quality of our previous services.

Disclosures

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Original Research

Risk Prediction of Liver Cancer based on the Proposed Artificial Intelligence Approach

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Abstract

Objectives: Liver cancer is a primary worldwide public health concern, and it is critical to understand the disease's physiology and create therapies. The aim of this study is to classify open access liver cancer data and identify important risk factors with the Random Forest method.

Methods: The open-access liver cancer dataset was used to construct a predive model in the study. Random Forest was used to classify the disease. Balanced accuracy, accuracy, sensitivity, specificity, positive/negative predictive values were evaluated for model performance. In addition, risk factors were assessed with the logistic regression model.

Results: The accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score metrics obtained with the Random Forest model were 98.9%, 97.9%, 95.8%, 100%, 100%, and 98.3%, and 95.7% respectively. Also, the importance of the variables obtained, the most important risk factors for liver cancer were total proteins, albumin and globulin ratio, albumin, age, total bilirubin, aspartate aminotransferase, direct bilirubin, alamine aminotransferase, alkaline phosphatase, respectively. According to the logistic regression model results, age, direct bilirubin, and albumin variables were statistically significant.

Conclusion: According to the study results, with the machine learning model Random forest used, patients with and without liver cancer were classified with high accuracy, and the importance of the variables related to cancer status was determined. Factors with high variable importance can be considered potential risk factors associated with cancer status and can play an essential role in disease diagnosis.

Keywords: Classification, Liver cancer, Machine learning, Random Forest

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Primary liver cancer is the sixth most common illness and the third leading reason of death from cancer with 906.000 new cases and 830.000 deaths in the last years. The incidence of liver cancer is ranked fifth on a global scale, but it has the second highest mortality rate for males. In most regions, men have two to three times higher rates of both incidence and mortality than women, and liver cancer ranks fifth in terms of global incidence. Cirrhosis is the underlying condition that leads to the majority (90%) of all cases of liver cancer. Infection with hepatitis B virus is the most common risk factor for developing liver cancer in our country. Cirrhosis brought on by alcohol, hepatitis C, and obesity is the three main causes of fatty liver disease. On the other hand, due to the fact that viral infections are un-

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der control and obesity rates are gradually rising, it is anticipated that liver cancers caused by cirrhosis that is brought on by a fatty liver will take the lead in the coming years.[1]

Data mining is a set of methods used to reveal hidden patterns in databases. Data mining is the process of using computer programs to discover relationships and rules that will allow us to forecast the future from enormous amounts of data. The primary goal of data mining, according to the definition, is to keep much of data in the data warehouse and extract meaningful information from it.[2] Machine learning, which is one of these techniques, is a sub-field of data mining that aims to make predictions about new data when exposed to new data by performing data-based learning. Machine learning includes the design and development processes of algorithms aimed at realizing data-driven learning. From the input and output sets given by machine learning, the outputs of the previously unlearned inputs can be predicted.[3]

In 2001, Breiman proposed the Random Forest (RF) method, which is one of the machine learning methods, by developing the bagging method, which envisages combining the decisions of many variables trees, each of which is trained with several training sets, instead of producing a single decision tree. This method uses bootstrapping technique to create different sub-training sets and random feature selection in the development of trees. The difference from the bagging method is that instead of using all the variables in the data set during the tree development phase, as in the bagging method, it branches each node by using the best among the randomly chosen factors at each node. The trees are built according to randomly selected variables.[4]

The aim of this study is to classify patients with and without liver cancer using the RF method. In addition, it is to determine the risk factors related with liver cancer and to find the variable importance of cancer-related factors.

Methods

Dataset

The public dataset "ILPD (Indian Liver Patient Dataset) Data Set" was obtained from "https://www.kaggle.com/jeevannagaraj/indian-liver-patient-dataset" to classify the presence or absence of liver cancer via the RF method in the study. Explanations of the variables in the data set and their properties are given in Table 1.

Random Forest

RF is a classification/regression method proposed by Leo Breiman and Adele Cutler and includes the voting method. It consists of many decision trees coming together, and the individual trees are voted to determine the winning class. The decision trees in the forest are independent of one another and are built using the bootstrap technique from samples drawn from the data set.[4] The RF method is a forest classifier composed of several decision trees, and it can be used to establish classification or regression trees.[5] In the RF method, determining branching criteria and selecting a suitable pruning method are critical issues. The random forest classifier's branching criteria are determined using the Gini index method. The Gini index assesses the degree of weakness of class characteristics.[6] As in other classification methods, the RF method has parameters that the practitioner must determine. These parameters are the number of instances to be used at each node and the number of trees to be created, which are required in establishing the tree structure. In other words, during a classification process, the decision forest is created from K trees determined by the user.[7]

Table 1. Explanations of the variables in the dataset and their properties

Variable	Variable Description	Variable Type	Variable Role
Age	Patient's age	Quantitative	Predictor
Gender	Woman man	Qualitative	Predictor
tot_bilirubin	Total Bilirubin	Quantitative	Predictor
direct_bilirubin	Direct Bilirubin	Quantitative	Predictor
tot_proteins	Total Proteins	Quantitative	Predictor
albumin	Albumin	Quantitative	Predictor
ag_ratio	Albumin and Globulin Ratio	Quantitative	Predictor
sgpt	Alamine Aminotransferase	Quantitative	Predictor
sgot	Aspartate Aminotransferase	Quantitative	Predictor
alkphos	Alkaline Phosphatase	Quantitative	Predictor
is_patient	Sick/Not sick (the presence or absence of liver cancer)	Qualitative	Target

Data Analysis

To see if the variables had a normal distribution, the Kolmogorov-Smirnov test was used. The median (minimum-maximum) was used to summarize quantitative data, and the numbers were used to summarize qualitative variables (percentages). The Mann-Whitney U test was utilized to see if significant difference in the target exits. The logistic regression model was utilized by using a stepwise variable selection approach for target variable estimation. The model's fit was checked with Likelihood Ratio Test. P-value <0.05 was regarded significant. IBM SPSS Statistics 26.0 program was employed in the analysis.

Modeling

RF, one of the machine learning methods, was used in the modeling. Analyzes were carried out using the 10000 repeated bootstrap method. Balanced accuracy, accuracy, sensitivity, specificity, positive/negative predictive values, and F1-score were used as performance evaluation criteria.

Results

In the data set used in the study, there are 416 (71.4) liver cancer patients and 167 (28.6) without liver cancer patients, a total of 583 patients. Of the patients, 142 (24.4) were female, and 441 (75.6) were male.

Descriptive statistics for the target variable examined in this study are presented in Table 2. There is a significant difference between the diagnosis groups regarding other variables apart from the sgpt variable.

The results of the logistic regression model are given in Table 3. Odds ratios, their 95% confidence intervals (CI), and significance levels were also reported for convenience.

The results of the performance metrics obtained according to the results of the Random Forest model are given in Table 4. The model's fit was checked with Likelihood Ratio Tests (Chi-Square=110.048, df=3, p-value<0.001).

Accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score from the Random Forest model were 98.9%, 97.9%, 95.8%, 100%, 100%, and 98.3%, and 95.7% respectively.

In Figure 1, the values of performance criteria obtained from the RF model are plotted for visualization.

Variable importances obtained as a result of RF modeling are given in Table 5.

Figure 2 shows the importance levels of genes that are important for the Random Forest model.

Table 2. Descriptive statistics for target variables

Variables	is_patient		p*
	Patient (416) Median (Maks-Max)	Non Patient (167) Median (Maks-Max)	
Age	46 (7-90)	40 (4-85)	0.002
tot_bilirubin	1.40 (0.40-75)	0.80 (0.50-7.30)	<0.001
direct_bilirubin	0.50 (0.10-19.70)	0.20 (0.10-3.60)	<0.001
tot_proteins	229 (63-2110)	186 (90-1580)	<0.001
albumin	41 (12-2000)	27 (10-181)	<0.001
ag_ratio	53 (11-4929)	29 (10-285)	<0.001
sgpt	6.55 (2.70-9.60)	6.60 (3.70-9.20)	0.437
sgot	3.00 (0.90-5.50)	3.40 (1.40-5)	<0.001
alkphos	0.90 (0.30-2.80)	1.00 (0.37-1.90)	<0.001

*: Mann Whitney U test.

Table 3. Results of Logistic regression analysis

Variables in the Equation	Odds Ratio	95% CI for Odds Ratio		p
		Lower	Upper	
Intercept				0.001
Age	1.019	1.007	1.031	0.002
Direct Bilirubin	1.941	1.362	2.770	<0.001
Albumin	1.015	1.007	1.022	<0.001

Table 4. Values for the metrics of the classification performance of the Random Forest model

Metric	Value (%)
Accuracy	98.9
Balanced Accuracy	97.9
Sensitivity	95.8
Specificity	100
Positive predictive value	100
Negative predictive value	98.3
F1 score	95.7

Discussion

Liver cancer is a significant cause of cancer death, and its incidence is increasing. Liver cancers have a poor prognosis, and the etiology of the disease includes metabolic syndrome, obesity, chronic hepatitis B and C infection, cirrhosis, non-alcoholic steatohepatitis (NASH), and aflatoxin B1 or other mycotoxins and alcohol consumption. Because of the poor prognosis for liver cancer, scientists and doctors are looking for new treatment options to help patients live longer.[8, 9]

This study aims to classify liver cancer and reveal the risk factors associated with liver cancer using the open-access liver cancer dataset. For this purpose, variable importance values were calculated due to modeling by using the Random Forest method, one of the machine learning methods. In addition, the factors associated with cancer were determined by the logistic regression model. The accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score metrics obtained with the Random Forest model were 98.9%, 97.9%, 95.8%, 100%, 100%, and 98.3%, and 95.7% respectively. According to these results, the disease was classified correctly. According to the importance of the variables obtained, the most important risk factors for liver cancer were total proteins, albumin and globulin ratio, albumin, age, total bilirubin, aspartate aminotransferase, direct bilirubin, alamine aminotransferase, alkaline phosphatase, respectively. According to the logistic regression model results, age, direct bilirubin, and albumin variables were statistically significant and included in the model ($p<0.05$). An increase of one unit in the age variable increases the status of liver cancer by 1.02 (OR) fold. An increase of one unit in the direct bilirubin increases the condition of having liver cancer by 1.94 (OR) fold. A 1 (one) unit increase in the albumin variable increases the status of liver cancer by 1.02 (OR) fold. Multiple logistic regression analysis suggested three significant factors (i.e., age, direct bilirubin, albumin) associated with the presence or absence of liver cancer. When the outcomes of the LR model were assessed, the most significant predictor was direct bilirubin (OR=1.96), followed by age (OR=1.019) and albumin (OR=1.015) factors.

A study has presented the NBTree algorithm, a combination of the Decision Tree and Naive Bayes algorithms. The accuracy of the NB Tree method was 67.01%, but the accuracy of the Decision Tree and Nave Bayes algorithms were 66.14% and 56.14%, respectively.[10] Another study used Decision Tree, K-Nearest neighbor, and Logistic Regression models on the same dataset. In conclusion, the accuracy of

Table 5. Variable importances obtained as a result of RF

Variables	Variable importance (%)
tot_proteins	100
ag_ratio	97.44
albumin	93.08
age	81.52
tot_bilirubin	76.21
sgot	70.67
direct_bilirubin	65.32
sgpt	65.08
alkphos	58.76
gender	0

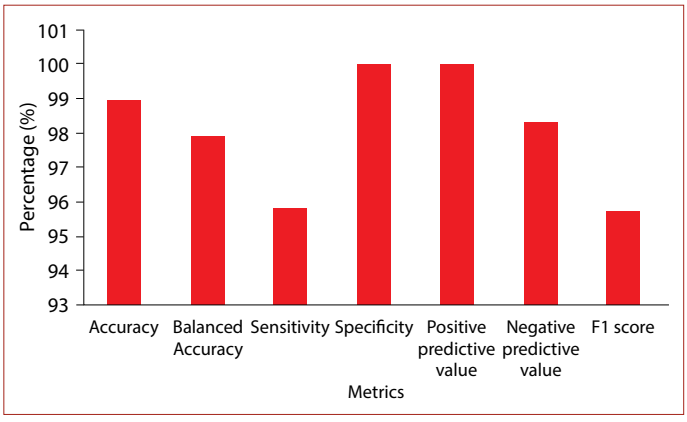

Figure 1. Graph of values for performance criteria obtained from Random Forest models.

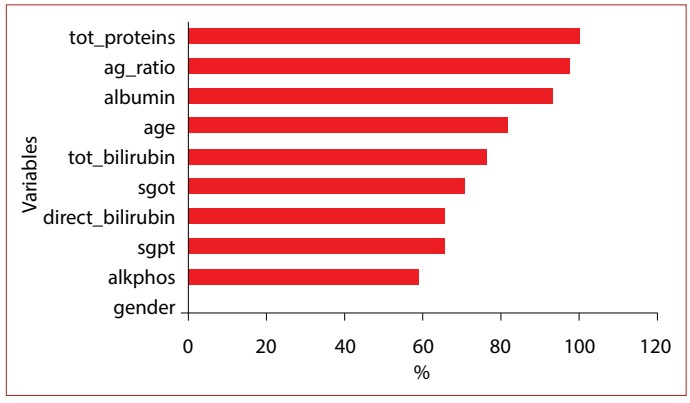

Figure 2. The graphic of variable importance values for the Random Forest model.

the Decision tree with the highest performance was 69.40.[11] In another study, Bayesian Network, Support Vector Machine, J48, Multi-Layer Perceptron, and Random Forest were performed on the same data. Thence, the Random Forest Algorithm produced the best performance with 71.87% accuracy.[12] In another study, they applied a support vector machine and Naive Bayes classification algorithms to the same data set. It was found that SVM outperformed Naive Bayes with 79.66% accuracy.[13] In a study using the same data set, logistic regression, support vector machines, random forest, AdaBoost, and bagging methods were employed for the classification task. The results obtained from the models used in the mentioned study were 73.5, 70.94, 66.66, 74.35, and 72.64, respectively.[14] In another study, the same data set was classified with Boosted C5.0 and CHAID, and the accuracies were obtained as 93.75% and 65%, respectively.[15] In a study that used the Indian Liver Patient Dataset, different classification algorithms such as Logistic Regression, K-NN and SVM were used for classification. The performances of these algorithms were evaluated for assessment metrics, and LR had the highest sensitivity.[16]

According to the study results, the proposed model (i.e., Random forest) can discriminate the patients with and without liver cancer with high performance. Factors with high variable importance can be considered possible risk factors associated with cancer status and can play an influential role in diagnosing the disease.

Disclosures

Ethics Committee Approval: Open-sourced data were used in the current study.

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Original Research

The Faculty of Theology Students' Attitudes, Knowledge Levels and Behaviours on Organ Donation and Xenotransplantation

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Abstract

Objectives: It is known that people's religious beliefs affect the interest in organ donation positively or negatively. This study aimed to evaluate the education level, thinking and behavior styles of the students of the Faculty of Theology, who will be the religious services workers of the future, on organ transplantation, organ donation and xenotransplantation (XTx).

Methods: Data were obtained by conducting a survey from quantitative research methods in order to reveal their knowledge, attitudes and thoughts on organ donation and XTx on 282 Theology Faculty students between 2020 June 2021 December.

Results: A total of 278 students answered the questions and about half of them stated that they would consider organ donation. About 1/3 of the participants who thought negatively about organ donation, but probably 3/4 of them, did so for religious reasons. Less than 9% of the participants had an information on XTx. In general, questions about XTx revealed that students had extremely inadequate knowledge about it. According to the participants, the society was uninterested and ignorant about XTx. Only 9% of the students stated that they would prefer XTx if they had to.

Conclusion: It would be very useful in their hands to inform the public about the acceptance of therapies using animal or transgenic components. However, it is not clear whether the general public accepts therapy with animal organs. Measures to increase the knowledge level of theology faculty students, who will guide the society in the future on organ donation/transplantation and XTx, should be taken in advance.

Keywords: Organ donation, transplantation, theology students, xenotransplantation

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Despite relatively stable deceased and increasing living organ donation rates, the number of patients on the waiting lists is increasing due to the increase in transplant indications. Xenotransplantation (XTx) research, including the genetic engineering, has increased in recent years as it can provide an unlimited supply of organs to solve the problem.[1]

The most important feature that distinguishes organ transplantation from other branches of medical science is that this subject includes philosophical, social and religious dimensions. Since organ transplantation includes death, donation and ethical rules, religion and philosophy are obligatory. It is known that people's religious beliefs affect the interest in organ donation positively or negatively. It is

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known that religious officials are people who play a key role in guiding future generations about organ donation.[2] This study aimed to evaluate the education level, thinking and behavior styles of the students of the Faculty of Theology, who will be the religious services workers of the future, on organ transplantation, organ donation and interspecies organ transplantation also known XTx.

Methods

This descriptive and cross-sectional questionnaire-based study was carried out at Inonu University Liver Transplantation Institute, where organ transplantation, especially liver transplantation, performs intensively. The research was supported by conducting a questionnaire with 282 students of theology faculties of 15 different universities. Within the scope of the study, umber of students were reached by using the convenience sampling method and analyzes were carried out on the obtained data. Within the scope of the study, the survey method, which is one of the quantitative research methods, was used. The survey was anonymous and self-administered. The process was coordinated by two transplant coordinators between February 2020 and December 2021.

The questionnaires were sent to the Faculty of Theology students as online questionnaires and they were answered by giving face-to-face questionnaires. The questionnaire included behavioral questions such as the adequacy and source of information about organ donation and transplantation, the reasons for positive or negative opinions about organ donation, information about XTx, source information about whether XTx is appropriate in terms of Islamic religion.

Statistical Analysis

Evaluation of the obtained data was done with SPSS-16 (Statistical Package for Social Sciences) data analysis program.

Results

The research group consists of 282 students studying at the Faculty of Theology of 15 different universities. A total of 278 students consisted of 141 (50.7%) female and 137 (49.3%) male students answered the questions.

When the participants were asked whether they found their knowledge about organ donation and transplantation sufficient, 278 people answered, and only 37 (13.3%) gave the answer as sufficient, while 145 (52.2%) stated that they were partially sufficient. Roughly, 2/3 of the students of the faculty of theology stated that they had some knowledge on this subject (Table 1).

Among the information sources of the research group, radio/television/social media comes first with 31.14%, while my relative/friend who has an organ transplant is given the answer with 2.19%, the rate of those who say they do not have information is in the second place with 18.73%. Twenty-eight of the people participating in the study have a relative or friend who has had an organ transplant. Even out of 28 people, only 9 people were able to obtain information from a relative or friend who had an organ transplant. This rate is less than 1/3 and it is concluded that even the relatives of organ transplant patients are not adequately informed about organ transplantation and donation (Table 2).

Table 1. Do you find your knowledge about organ donation and transplantation sufficient?

Do you find your knowledge about organ donation and transplantation sufficient?	**n**	**%**
Sufficient	37	13.3
Partially sufficient	145	52.2
Insufficient	96	34.5
Total	278	100.0

Table 2. Information resources of the research group

From which sources did you get information about organ donation and transplantation? (you can choose one or more options)	**n**	**%**
I have no knowledge	77	18.73
Radio/Television/Social media	128	31.14
Newspaper/Magazine/Poster/Brochure	35	8.52
Seminar/Conference	49	11.92
School curriculum	51	12.41
Verse/Hadith/Religious publications	62	15.09
My relative/friend who hashad an organ transplantation	9	2.19

A majority of the participants (95.7%) believe in the importance of organ donation, while 4.3% do not believe in the importance of organ transplantation (Table 3). About half of the participants stated that they have made or are considering organ donation (Table 4). While almost all of the people participating in the study believed in the importance of organ donation, the fact that only half of them stated that they have or will donate organs can be interpreted as a disproportionate result.

At the beginning of the reasons that push the participants who want to donate their organs to this behavior, the desire to give life to others after death is in the first place with 43.75%, and the thought of humanitarian duty is in the second place with 23.75%.

About 67.6% of the participants state that they have reservations yet. While 30.9% stated that they did not know how/where to start, 1.5% stated that they had difficulty in reaching donation channels. About 40.49% of the participants never thought about this issue, 19.62% said that they want my organs to stay in place after death, 16.07% said that they think it is unfavorable in our religion. These rates show that ¾ of the students of theology faculty who do not donate organs think so for religious reasons. Only 8.8% of the participants knew about the studies on XTx (inter-species organ transplantation), while 91.2% had no knowledge about this subject (Table 5). Only 9.5% of the participants reviewed the source stating whether XTx is religiously appropriate (Table 6). While the reference source on XTx was written/visual media and social media in the first place with 37.2%, individuals/opinion leaders came in the second place with 24.15%, only 18.84% gave the answer of education/training that I received from schools. Some of the 41 people who gave the other answer wrote verses and hadiths as explanations and did not specify the source. After a briefing, "would you consider XTx when a relative needs an organ transplant?" only 24.1% of the research group said yes to the question (Table 7). Nearly half of those who were negative or undecided stated that they had such a thought for religious reasons. The research group "Do you receive questions about XTx from your community/environment?" 88.3% answered no to the question (Table 8). "If you need it, which type of organ transplant would you prefer?" 50.2% of them stated that they would prefer living donors, 40.8% from cadavers, and 9.1% from XTx (Table 9).

Discussion

Religions are a major factor in motivating people and guiding them about organ donation decisions. Islam is known to support organ donation and transplantation in ethical and scientific forms. However, in Muslim-majority coun-

Table 3. Do you believe in the importance of organ donation?

Do you believe in the importance of organ donation?	n	%
Yes	265	95.7
No	12	4.3
Total	277	100.0

Table 4. Have you ever donated/do you intend to donate organs?

Have you ever donated/do you intend to donate organs?	n	%
Yes I donated	3	1.1
I think, but I did not donate	142	51.8
No I think	129	47.1
Total	274	100.0

Table 5. Do you know about XTx (interspecies organ transplantation)?

Do you know about XTx (interspecies organ transplantation)?	n	%
Yes	24	8.8
No	248	91.2
Total	272	100.0

Table 6. Have you reviewed a resource that states whether XTx is religiously appropriate?

Have you reviewed a resource that states whether XTx is religiously appropriate?	n	%
Yes	25	9.5
No	238	90.5
Total	263	100.0

Table 7. Would you consider XTx when a relative needs an organ transplantation?

Would you consider XTx when a relative needs an organ transplantation?	n	%
Yes	66	24.1
No	44	16.1
I don't know enough about this	164	59.9
Total	274	100.0

Table 8. Do you receive questions about XTx from the society or your relatives?

Do you receive questions about XTx from the society or your relatives?	n	%
Yes	24	8.5
No	249	88.3
Total	273	96.8

Table 9. If you need an organ transplantation, which type of transplant would you prefer?

If you need an organ transplantation, which type of transplantation would you prefer?	n	%
Living donor liver transplantation	133	50.1
Deceased donor liver transplantation	108	40.8
XTx	24	9.1
Total	265	100.0

tries, a most people do not donate their organs. Religious perspectives on organ donation are one of the important barriers to transplantation. It has been stated that this is not due to the principles of Islam, but rather to ignorance.[3, 4] In this study, we chose theology faculty students as the study group and investigated their thoughts on XTx as well as organ donation. Our aim was to to analyze the acceptance of XTx, a therapy that is still experimental, on young people who will shape the society religiously in the future.

In this study, we can say that although the faculty of theology's students gave positive opinions about organ donation and transplantation, they would only donate their organs in a rate of 50% maximumly. About 1/3 of the participants who thought negatively about organ donation, but probably 3/4 of them, did so for religious reasons. Less than 9% of the participants had an information on XTx. In general, questions about XTx revealed that students had extremely inadequate knowledge about it. Surprisingly, most of the participants disclosed their source of information on XTx. This disproportionate result may be an indication that the participants have an indecisive attitude. According to the participants, the society was uninterested and ignorant about XTx. Only 9% of the students stated that they would prefer XTx if they had to. It would be very useful in their hands to inform the public about the acceptance of therapies using animal or transgenic components. However, it is not clear whether the general public accepts therapy with animal organs. Previous studies have reported the variable acceptance rates of XTx, ranging from 40% to 75%.[5] This study was especially important in our geographic area, which has among the clergy who can be very influential on the society in organ donation and transplantation.

A study from our institute showed that only 60.5% of the Islamic religious officials deemed organ donation as appropriate to Islamic beliefs, which was significantly affected by their level of education.[2] In terms of having adequate knowledge of organ donation, 72.7% of those with a master's or doctorate degree and only 19.7% of those with a high school degree said they have enough information. The level of education significantly affected the willingness of religious officials to donate their organs. About 27.2% of those with a master's or doctorate degree and only 3.9% of those with a high school degree are willing to donate their organs.

Likewise, a study from our institute involving Theology and Nursing students showed that theology students tended to have the question about XTx and only positive attitude towards XTx from halal animals. Interestingly, Theology students' view of XTx towards their senior year became more negative.[6]

As a result, at the end of this study, measures to increase the knowledge level of theology faculty students, who will guide the society in the future on organ donation/transplantation and XTx, should be taken in advance. Related to this, the importance of organ donation/transplantation and XTx should be included in the curriculum of theology faculties, joint workshops with theology faculties should be organized to draw the attention of students to this field, and theology faculty students should be encouraged to write thesis on organ transplantation, organ donation and XTx.

Disclosures

Ethics Committee Approval: This article was produced from a social science thesis project. Therefore, it has been reported by the institute that ethics committee approval is not required.

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Case Report

Biliary Drainage Impairment After Liver Transplantation As a Result of Adhesive Small-Bowel Obstruction

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Abstract

With the improvements of surgical techniques, favorable results in orthotopic liver transplantation surgeries have increased in recent years. Biliary complications are common after liver transplantation. We aimed to discuss a case that developed adhesive small bowel obstruction -related jaundice after liver transplantation and underwent adhesiolysis by surgery in the light of the literature.

The patient, who underwent right lobe liver transplantation with a living donor 7 years ago due to chronic liver damage by hepatitis B, was examined with sudden onset of abdominal pain and jaundice. It was determined that the current situation was connected to the postoperative adhesion and that the adhesion disrupted the biliary drainage and then surgical intervention was performed. It should always be kept in mind that the increase of serum bilirubin levels in patients with liver transplantation may also be caused by any mechanical obstruction in the roux leg of Roux-en Y hepaticojejunostomy.

Keywords: Liver transplantation, post-transplant complications, postoperative adhesion biliary complication

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Liver transplantation continues to be the standard treatment for patients with end-stage liver disease. With the improvements of surgical techniques, favorable results in orthotopic liver transplantation surgeries have increased in recent years. As with all intraabdominal procedures, there is a risk of intraabdominal adhesion in liver transplant patients. Small bowel obstructions are a common morbidity associated with abdominal surgery.[1] Also, biliary complications are a common cause of morbidity following liver transplantation, and approximately 15-20% of all allograft recipients develop a biliary complication within 2 years.[2] Treatment modalities include both operative and nonoperative management.[3] Conservative, nonoperative treatment typically consists of bowel rest, intravenous fluid rehydration, and nasogastric intubation.[3] While most small bowel obstructions resolve without surgical intervention, about 25% require immediate surgical intervention.[3] In biliary complications, 69.3% of liver transplant recipients undergo reconstruction with a biliary-enteric anastomosis, while the management of an anastomotic stenosis is typically based on percutaneous or surgical revision.[2]

In this case, we aimed to present a living donor liver transplant patient with increased serum bilirubin levels due to impaired biliary flow.

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Case Report

A 52-year-old patient, who had an orthotopic liver transplantation with living donor 7 years ago due to chronic liver damage by hepatitis B, presented with jaundice for 2 days and sudden onset of abdominal pain. The donor was the 30-year-old son of the patient and had the same blood type. The graft weight of the donated right lobe was 520 g. There were no symptoms of ileus such as nausea, vomiting, distension, and gas-stool discharge. Laboratory tests at patient admission AST: 278.3 u / L, ALT: 239.7 u / L, ALP: 121 u / L GGT: 400u / L T.Bil: 3.95 mg / dL, D.Bil: 3, 49 mg / dL. White blood cell count was within normal range. Dilatation was observed in intrahepatic bile ducts at Usg. Oral feeding was stopped and intravenous fluids were given for hydration. The next day, control T.Bil: 9.05 mg / dL, D.Bil: 8.29 mg / dL. Meanwhile, insertion of a percutaneous biliary drainage catheter was planned. MR (Magnetic resonans) and CT (Computed tomography) showed dilatation in the proximal jejunal segments, dilation filled with fluid content, and valvula conniventest (Fig. 1). Since other small intestine segments were normal, the patient was considered for adhesion at this level and underwent emergency surgery.

In laparotomy, it was observed that the patient had a roux-en Y choledokojejunostomy and an obstruction in the roux leg due to small bowel adhesion (Fig. 2). It was observed that a band disrupted the intestinal passage and circulation. It was observed that intestinal segments close to adhesion were dilated and ischemic. It was determined that this adhesion prevented the flow of bile. Warm isotonic solution was applied to the intestinal sections after adhesiolysis. The operation was terminated when it was observed that he had intestinal peristalsis and the color and circulation in the intestine returned to normal. The patient recovered completely and was discharged five days after the operation.

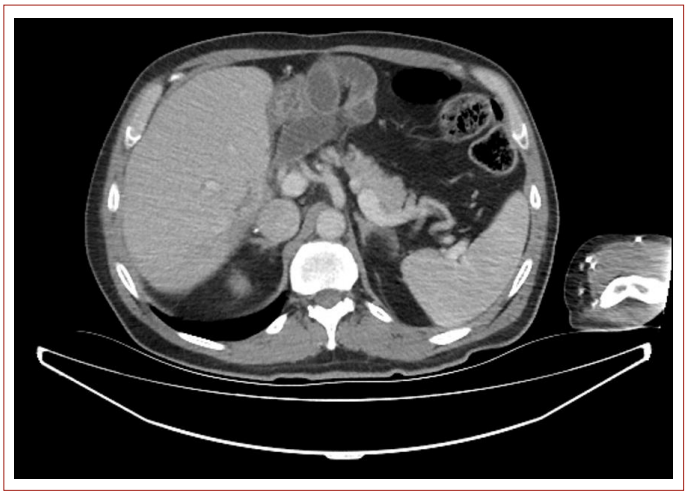

Figure 1. Adhesion appearance on Computed tomography.

Discussion

Complaints such as fever, diarrhea, abdominal pain, and jaundice are common in liver transplant patients and may lead to admission to the emergency room and subsequent hospitalization. However, the underlying cause may be related to a complex condition or to the side effect of immunosuppressive therapy.[3] Biliary complications are another common cause of morbidity following liver transplantation.[2] The two most common biliary complications after living donor liver transplantation are biliary leakage and biliary anastomotic stricture. Early treatment with endoscopic and interventional radiological approaches can provide satisfactory results in biliary complications. If treatment fails with these approaches, the next option would be surgical revision, which is rarely performed.[2]

In our case, firstly we thought that the increase in serum bilirubin levels was caused by a stricture in the biliary anastomosis. Therefore, we planned to use a percutaneous biliary drainage catheter. However, in the radiological examinations of the patient, it was understood that the cause of the deterioration of the biliary drainage was not due to the anastomotic stenosis, but to the adhesion in the roux leg. The patient was taken to an emergency operation and adhesiolysis was performed.

Although a long time has passed since the transplant in patients with liver transplantation, care should be taken in terms of complications that may require surgical procedure, it should always be kept in mind and surgery should always be considered as an option. However, we think that such patients should be followed up in experienced centers due to the difficulty of surgical application and the possibility of prolonging the duration of surgery depending on the developing complication.

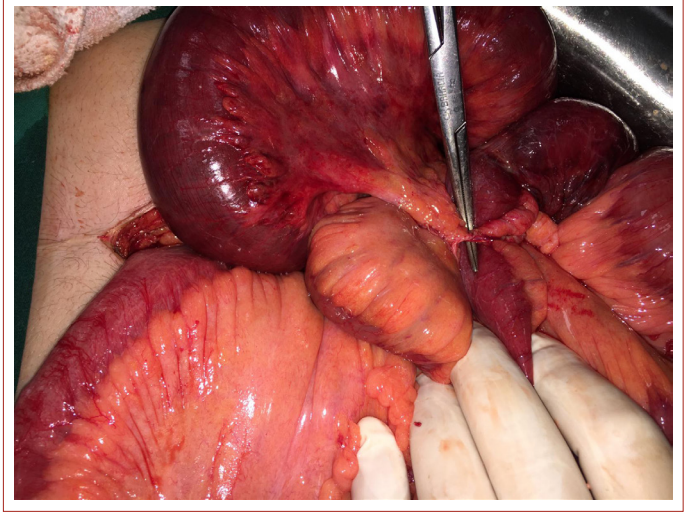

Figure 2. Intraoperative view of adhesion.

In addition to anastomotic stenosis, which is one of the most common complications in patients undergoing liver transplantation, it should always be kept in mind that any mechanical obstruction (post operative adhesion- external compression-gallstones) in the roux leg of Roux-en Y hepaticojejunostomy may also increase serum bilirubin values. Because such reasons require rapid diagnosis and rapid surgical intervention.

Disclosures

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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Case Report

Living Donor Liver Transplantation for Erytropoietic Protoporphyria Liver Disease

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Abstract

Porphyrias are an inherited group of diseases caused by the deficiency of enzymes in the heme synthesis pathway. Erytropoietic protoporphyria is associated with a deficiency of ferrochelatase activity.

Liver transplantation is the most effective treatment in cases of liver failure due to EPP. In this study, a case who underwent LDLT goes liver failure due to EPP is presented.

A 15-year-old boy who had had recurrent photosensitive skin reactions due to erythropoietic protoporphyria since the age of 1 year. The patient had elevated liver enzymes, coagulopathy, advanced jaundice, low ferrochelatase activity, and high erythrocyte protoporphyrin activity. Liver biopsy confirmed extensive protoporphyrin deposition with cirrhosis, and so living donor liver transplantation was performed. The clinical and laboratory course of the patient in the early post-transplant period was quite normal. But, on the 12th posttransplant day, there was duodenal perforation, possibly due to burns caused by reduced headlights or surgeons' headlights during the operation. The patient, who had a very complicated course, died on the 43rd day after LT.

LT is lifesaving if acute or chronic liver disease has developed in EPP. Special precautions are required to protect these patients from porphyric crises and phototoxic reaction. Bone marrow transplantation can be performed after LT to eliminate the cause.

Keywords: Liver, protoporphyria, transplant

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Porphyria is a term that represents a metabolic disease consisting eight sub-groups.Each one is characterized with an enzyme deficiency determined by a gene mutation in the heme synthesis pathway (Fig. 1). Two of these deficiencies may result in an associated liver disease. Porphyria cutanea tarda, associated liver disease, consisting haemochromatosis with alcoholic liver disease, results in porphyria, presenting with blistering, hirsutes and photosensitivity of the skin. However, liver disease of erythropoietic protoporphyria (EPP) is a result of progressive deposition and accumulation of insoluble protoporphyrin IX in hepatocytes and bile ducts. Ferrochelatase, which is an enzyme of mitochondria, catalyses the insertion of ferrous iron into protoporphyrin (PP) to form heme, and when defective or deficient, accumulation of PP ensues (Fig. 1). This enzyme is abundant in cells that produce heme including erythroid precursors in the bone marrow and hepatocytes.[1,2]

Patients with progressive EPP liver disease may present with attacks of clinical exacerbations, that acutely worsen liver function, increase erythrocyte PP levels and frequently manifested by severe abdominal and back pain. Patients

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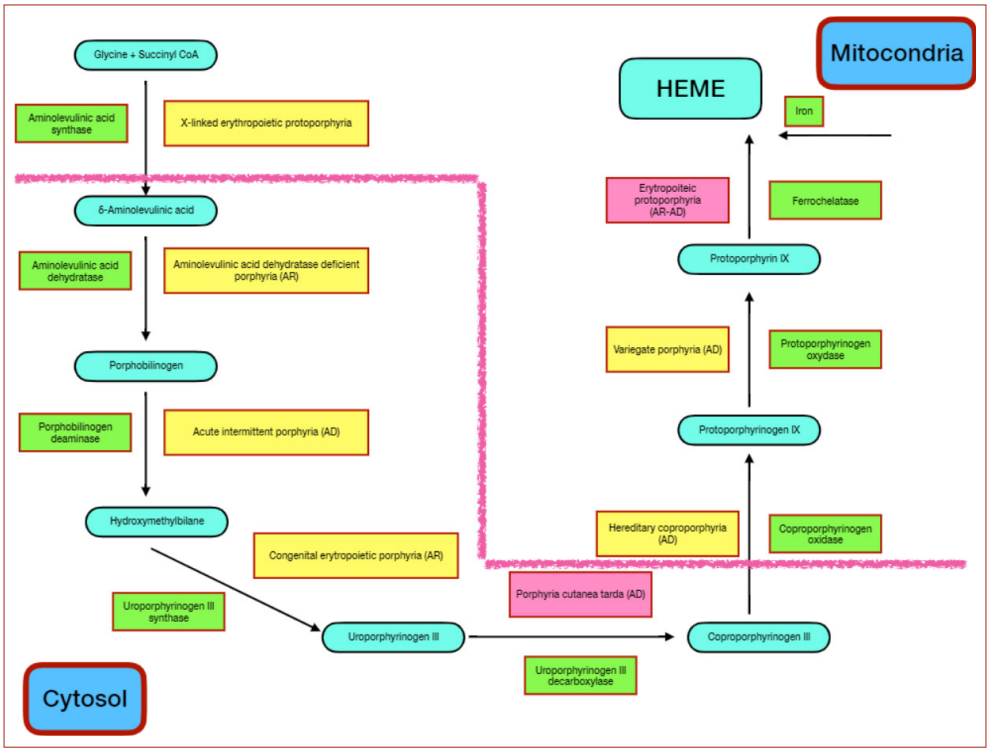

Figure 1. The heme biosynthetic pathway showing the enzyme deficiency and associated porphyria metabolism disorders.

with poor prognosis due to cirrhosis and liver failure significantly benefit from liver transplantation (LT). Unfortunately, LT does not have an impact on the overbundant production of PP by the bone marrow. In this study, a case with liver failure due to EPP in whom we had a living donor liver transplant (LDLT) was presented.

Case Report

A 15-year-old boy patient, who was followed up in another center with the diagnosis of EPP, has hypersensitivity to light since the age of 1 year. Painful rashes appeared on the light-exposed areas, especially on the face and arms. In laboratory tests of the patient, ferrochelatase activity was low and erythrocyte protoporphyrin activity was high. The patient had elevated liver enzymes and jaundice for seven years. He had coagulopathy and advanced jaundice for the last 2 months. When his family history was questioned, it was learned that his brothers aged 19 and 21 died due to the same disease and liver failure. On physical examination, skin and sclera icteric and hepatosplenomegaly were found. There was palpable swelling on the right side of the neck. Doppler sonography revealed a thrombus in the right jugular vein, which was thought to be due to hemin infusion. Liver biopsy performed at the referring center revealed protoporphyrin accumulation and cirrhosis findings. Total bilirubin was 16 mg/dl, INR was 2.3, creatinine was 0.38 mg/dL, and the MELD-Na+ score was 21. Intermittently, hemin infusion and plasmapheresis treatment were started. A living donor liver transplantation was performed for the patient after plasmapheresis. As an operative finding, the black color of the liver due to protoporphyrin accumulation was remarkable (Fig. 2). Headlights and ceilinglights lamps were turned off or dimished to keep the patient from dinjury due to severe light (Fig. 3). Four hundred-forty ml of left lobe (segment 2, 3, 4) from a living donor was transplanted to the patient (Fig. 4). Graft to recipient weight ratio was 1%. There were no complications in the intraoperative period. In the posttransplant period, he was kept from medicines and light exposure that could exacerbate porphyria disease. The macroscopic examination of the explant revealed an enlarged, cirrhotic, and typical black-colored liver with dimensions of 25x16x9 cm (Fig. 5a). The cut surface of the specimen was also black and nodular. Histopathological examination showed a micronodular cirrhotic liver with extensive deposites of dark red-brown porphyrin pigment (Fig. 5b). The porphyrin pigment was present in hepatocytes, Kupffer cells, portal macrophages, bile canaliculi and ductules (Fig. 5c). The deposites were finely granular or lamellar in appearence. These pigment depositions were not positive for iron or copper on special stains. Birefringent pigment crystals were visualized under polarized light. The sections from the lymph nodes

Figure 2. Intraoperative view of the cirrhotic liver with Erytropoietic protoporfiria.

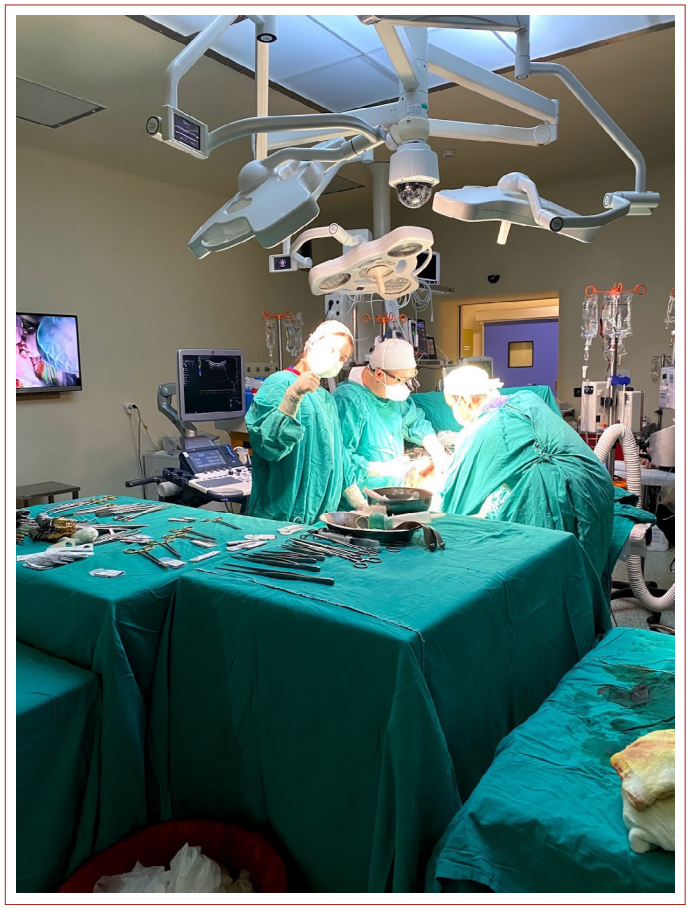

Figure 3. Headlights and ceilinglights lamps were turned off or reduced to protect the patient from damage due to intense light in OR.

both around the liver hilum and the gallbladder neck showed clusters of histiocytes containing cytoplasmic red-brown granular pigment depositions, consistent with sinus histiocytosis with pigmentation (Fig. 5d).

The clinical and laboratory course of the patient in the early post-transplant period was quite normal. On the 12th post-transplant day, there was duodenal perforation, possibly due to burns caused by reduced headlights or surgeons' headlights during the operation, subtotal gastrectomy, duodenal stump was closed to resect the perforated duodenum, and gastrojejunostomy was performed. Percutaneous tracheostomy due to prolonged intubation was performed on posttransplant day 16, hepaticojejunostomy was performed on day 21 due to biliary leak and local peritonitis, and tube duodenostomy was performed on day 33 due to duodenal stump leakage. During this period, the patient had occasional burns on the skin of the anterior abdominal wall. ECMO was performed with pulmonary failure on the 41st posttransplant day and unfortunately the patient died on the 43rd day. The patient required a total of 26 U erythrocyte suspension in the post-transplant period.

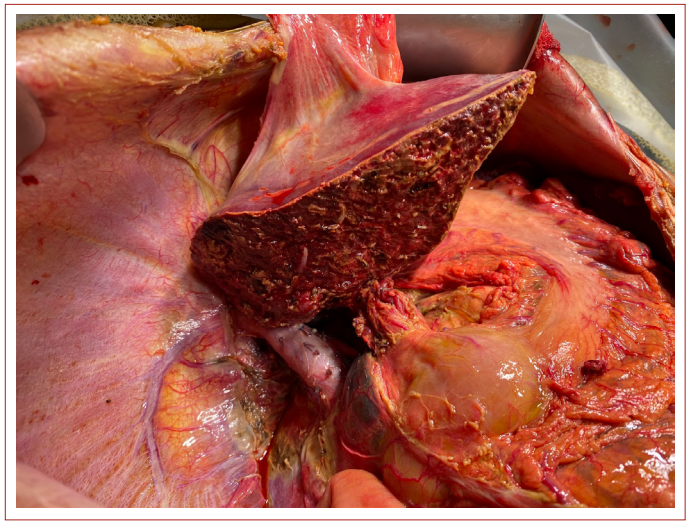

Figure 4. The view of transplanted left lobe liver graft.

Discussion

Heme synthesis is mostly present in liver and bone marrow tissues. EPP is originated from ferrochelatase deficiency, which is the last enzyme of this synthesis pathwa. Some of the EPP patients progress into liver cirrhosis, indicating

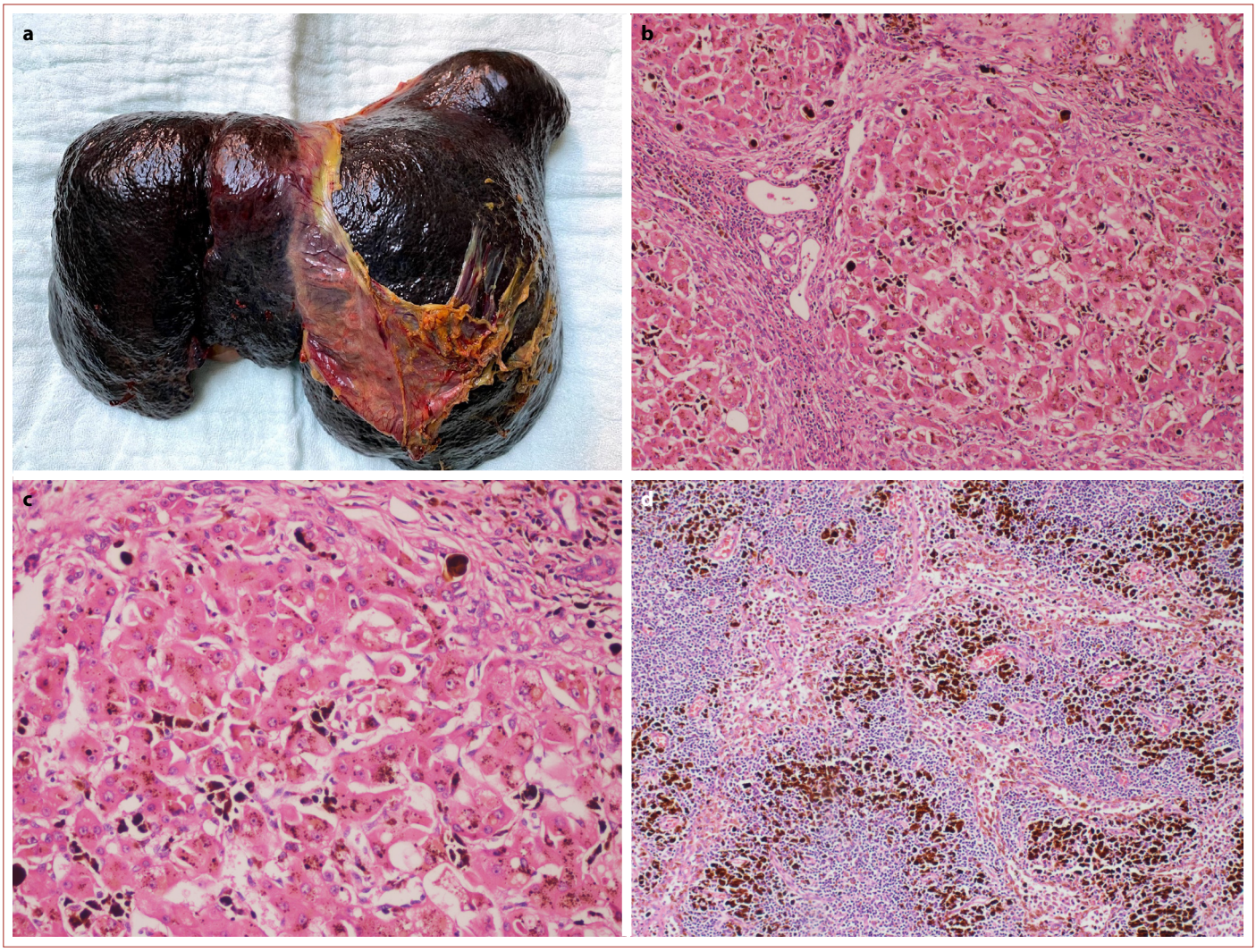

Figure 5. (a) The macroscopic examination of the explant revealed an enlarged, cirrhotic, and typical black-colored liver. **(b)** Micronodular cirrhosis pattern with brown pigmentation in liver paranchyme (H&E,100x). **(c)** Pigmentation in hepatocytes, macrophages and bile canaliculi with associated degenerative changes in hepatocytes (H&E,200x). **(d)** A large number of sinus histiocytes with porphirin deposits (H&E,100x).

LT.[3,4] However, liver transplantation can not be a definitive solutionwhen gene problems in EPP orginate from erythroid cells. The main production site of PP in EPP is erythroid cells. The plasma concentritation of PP will increase as the PP in the red spheres protrude out of cells. PP in plasma is pick up hepatocytes and secrated to the bile ducts. PP in the bile ducts have a cytotoxic effect. This will eventually cause a liver failure.[1,5,6]

EPP attacks are manifested by intolerable abdominal pain, acute liver failure, and increased serum PP levels. The spleen becomes enlarged and hemolysis may ensue. Progressive photosensitivity due to a further reduction in biliary free-PP excretion warns for the upcoming fulminant disease which is rarely reversible and, usually mortal in cases which LT is not offered as a treatment option. EPP may rarely manifest with acute liver failure.[7-9] The presented patient had a more chronic course and had a high MELD-Na score.

If PP crisis is suspected in a patient, it will be necessary to initially look for urinary porphobilinogen. Then, enzyme levels in the HEME synthesis pathway are examined in both urine and plasma. Genetic examination and liver biopsy are the most important diagnostic tools. In our patient, ferrochelatase activity was low and erythrocyte protoporphyrin activity was high. Liver biopsy performed at the referring center revealed PP accumulation and cirrhosis findings.

EPP patients are prone to intra-abdominal organ burns caused by both ceiling and headlight in LT. Specific anti-light filters have been developed to avoid this problem. Damage to the skin and abdominal organs by phototoxic reaction may occur with operating room light. Third-degree skin burns and intraabdominal organ injuries have been published.[10] In the presented case, the ceiling lights were turned off and the head-lights were reduced during LT. Despite this, duodenal perforation was observed in the

patient after LT, and this complication played a leading role in the patient's mortality. Regarding this complication, we can conclude how important the use of a special filter is on PP-induced tissue injuries. Perhaps our attempt to reduce the ceiling and OR head-lights has not been successful. For surgeries of prolonged duration, light filters that limit transmission of wavelengths 340-470 nm.[11] But there have not any special light filter in Turkey for these type of patients.

Respiratory muscle paralysis may occur due to neurological dysfunction after LT. As a matter of fact, ECMO was applied in our patient due to prolonged intubation, loss of proximal motor muscle strength and eventually lung parenchymal failure.

The different forms of treatment for EPP both before and after LT have been directed at specific pathogenetic mechanisms as follows:[1,12] To increase the excretion of PP into bile by the oral administration of the bile salts chenodeoxycholic acid or ursodeoxycholic acid, to reduce PP production by suppressing erythropoiesis using iron, red cell transfusions or infusion of hemin, all of which are intended to reduce the drive for heme synthesis, to reduce the pool of circulating plasma PP by plasmapheresis and haemodialysis, to reduce PP levels by interrupting the enterohepatic circulation with administration of cholestyramine, to reverse oxidative stress in EPP by vitamin E therapy.

In conclusion, LT is lifesaving if acute or chronic liver disease has developed in EPP. Special precautions are required to protect these patients from porphyric crises and phototoxic reaction. Bone marrow transplantation can be confirmed after LT to eliminate the cause.

Disclosures

Informed consent: Written, informed consent was obtained from the patient's family for the publication of thís case report and the accompanying images.

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Letter to the Editor

Comment on The Transition to Microsurgical Technique for Hepatic Artery Reconstruction in Pediatric Liver Transplantation

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To the Editor,

We read the article recently published by Nickel and colleagues, titled "The transition to microsurgical technique for hepatic artery reconstruction in pediatric liver transplantation" published in Plastic and Reconstructive Surgery with great interest.[1] Authors concluded that microsurgical anastomosis using operating microscope (OM) significantly decreased the hepatic artery thrombosis (HAT) and provided higher graft survival when compared with conventional loupe-assisted anastomosis in pediatric liver transplantation (LT).

We would like to share our opinion and critiques about this valuable work:

1. In our opinion retransplantation cases should be included in the studybecause the success of hepatic artery reconstruction (HAR) can be extremely difficult in retransplantation. For this reason this is one of the most important parameters that will show technical success of the hepatic artery anastomosis (HAA) of the center.
2. The authors have contradicted themselves because they have considered the HAT rates within 60 days but did not evaluate the HAT cases due to other causes after that. Majority of HAT cases occur after the first 5 days are unrelated to the technical issues in HAR.[2] Postoperative first 5 days is the optimal interval in any research aiming HAT and the technical aspects of HAR.
3. HAR in partial left lobe liver grafts has some unique technical challenges. Initially, the bulk of left lobe liver grafts can hinder the graft hepatic arteries. This results in technical problems in HAR in infants who have a very small abdominal cavity. In such an environment docking an OM to perform HAR is extremely challenging. Furthermore, the sequence of vascular and biliary reconstructions in left lobe liver grafts is also very important. For this reason, we choose to perform Har before portal vein anastomosis. Following the portal vein anastomosis, the graft is perfused and once the patient is hemodynamically stable, hepatic arterial inflow is provided. In our opinion, using OM in this environment is technically very difficult.
4. The study groups that are compared in the present study is not uniform. In the conventional cohort, the

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authors used 3.5/4.5 times magnified surgical loupes and the 7/0 Polypropylene sutures were used for anastomosis. On the other hand, in the OM group 9/0 Polypropylene sutures were used. The conventional cohort the conditions are unfavorable and therefore the results were inferior to the OM group. Nevertheless, although the authors reported the HAT rates in conventional and OM cohorts as 8.3% and 2%, respectively, these did not reach statistical significance. We suggest using 8.5 times magnified surgical loupes for HAR which has excellent results in our institute.[2]

5. In conventional cohort, the authors reported 15 cases with HAT but they did not include 8 cases with primary non-function who also had HAT. The primary non-function could have been due to the HAT in these 8 patients. If these 8 patients are added, there will be 23 patients (12.8% HAT rate) in the conventional cohort which would be an unacceptably high rate.
6. The authors have stated that "HAR with OM occurs in 39.3 minutes more time". We believe this duration is questionable because docking of OM, performing anastomosis, and undocking of the OM usually takes longer than the extra time that is stated. One important point that needs to be emphasized is the fact that arteries of the left lobe liver grafts are shorter and the anastomosis is technically more challenging under OM. Therefore, our initaial experiences also show that undocking of OM from the operation site prolongs the LDLT procedure by by at least an hour. The prolonged operative time causes a prolonged ICU-stay of the patients; which is what the authors have observed in their study.
7. The autgors have observed higher retransplantation rates in the conventional cohort. We believe this is due to higher rate of Hat (12.8%) observed in this group.
8. In our opinion, it is not correct to assume that shorter cold ischemia times leading to decreased HAT rates in living donor liver transplantation (LDLT). If the HAT rates are high in deceased donor liver transplantation (DDLT), it can be attributed to the technical aspects of HAR such as inappropriate sutures (6/0 Polypropylene) and equipment such as 2.5 and 3.5 times magnified surgical loupes.
9. Using OM for HAR requires microsurgeons to be involved in the operation. They are usually not a part of the transplant team. They are consulted at a alter stage of the procedure. They are not fully experienced with the anatomy of epatic artery. Naturally, they are not aware of the importance of the situation because they are not present from the beginning of the procedure. We do not want to imply that anything about their technical expertise, but liver transplantation is a long procedure that requires a dedicated team. The microsurgeons may not be readily available for prolonged procedures requiring the microsurgeons to come later in the afternoon.
10. Lastly, we would like to stress the importance of microsurgical techniques foer the success of HAR. Therefore, adherence to these methods either using OM or high magnification surgical loupes has paramount importance. The use of high magnification loupes have obtained world-wide acceptance and use of operative microscope has declined.[3]

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Letter to the Editor

Comment on Impact of Middle Hepatic Artery Reconstruction after Living Donor Liver Transplantation using the Left Lobe

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To the Editor;

We read the study published by Harada and colleagues with great interest.[1] The authors suggested that reconstruction of both the middle hepatic artery (MHA) and the left hepatic artery (LHA) in left lobe living donor liver transplantation (LL-LDLT) is a safe strategy that prevents biliary stricture (BS) if the graft has both LHA and MHA stumps. This has been emphasized in other studies as well.[2,3] We would like to emphasize several points regarding the results of this study.

The authors have stated that "hepatic arterial reconstruction (HAR) plays a more important role in duct-to-duct anastomosis than in hepaticojejunostomy after liver transplantation (LT) because the arterial blood supply to the anastomosis site and graft bile duct in duct-to-duct anastomosis originates only from the reconstructed HA…" in 'paragraph 3 of the introduction section. In our opinion this is an insufficient statement.[1] The arterialization of duct-to-duct anastomosis depends on both patent graft hepatic artery and also patient recipient arterial supply to the extrahepatic biliary tree. In Figure 1 of the mentioned article, it is clearly seen that RHA and MHA of the recipient was ligated in group B and BS was common. This is not a surprise because the recipient biliary system received an arterial supply from the capillaries from pancreaticoduodenal artery of the gastroduodenal arterial trunk which is not adequate. We are a center of excellence in living donor liver transplantation (LDLT) and we perform 300 cases annually. Currently, we are preparing a study evaluating the preservation of the biliary supply during HAR and we have found that biliary complications are significantly reduced when the vascular supply of the biliary tract is preserved (unpublished data).

In Group B, left lobe liver grafts had dual arterial supply and the authors have anastomosed the dominant artery. Once the pulsatile backflow was observed from the accessory artery and it was ligated. In addition, segment IV arterial flow in the hepatic parenchyma was determined by Doppler ultrasonography. We would like to as the authors whether the intraparenchymal arterial network was thrombosed in the late period following LDLT? Why didn't the authors attribute the intraparenchymal biliary abscess to

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biliary ischemia in segment IV. It is clear that segment Iva is perfused through MHA in many cases.[4] Histopathological analysis of the circumferential biliary duct biopsy following HAR could give an idea regarding the arterial supply of the biliary ducts. Furthermore, the effects of MHA ligation can be evaluated by obtaining biopsies in the late period from segment IV parenchyma.

HAR in left lobe liver transplants is technically challenging. The bulk of the left lobe liver grafts hinder the recipient hepatic arteries during HAR. Often it is necessary to make HAR before portal vein anastomosis and graft perfusion because it is technically easier. HAR using operative microscope is usually technically difficult. In another study of the same group performing double anastomoses increased the operative times by an average of 80 minutes compared to single anastomoses.[2] We prefer to anastomose the left hepatic artery to common hepatic artery of the recipient and we ligate the accessory artery once we observe the pulsatile backflow. Recipient bile ducts receive the arterial supply from the gastroduodenal artery, proper hepatic artery and the right hepatic artery. If the previous studies of the authors are analyzed, it is obvious that gastroduodenal axis supplies the extrahepatic biliary tree of the recipient but not the graft.[2,3] We have seen that authors have used gastroduodenal artery and left gastric artery (without common hepatic artery connection) for HAR of left lobe liver grafts. We believe that this reconstruction cannot supply the liver adequately.

The studies show that early biliary leaks play an important role in consequent biliary stricture. Biliary ischemia initially manifests itself as biliary leak but in this study the biliary leak rates of all three groups are simila.[1] We believe that this is due to a lack of consensus in definition of biliary leaks and strictures. On the other hand, biliary stricture observed in this study may be caused by other reasons involving technical aspects.

Disclosures

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Letter to the Editor

Comment on the First Two Liver Transplantations in Syria

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To Editors;

We read the recent article titled " The First Two Liver Transplantations in Syria " published by Rayya with great interest. [1] The article about the first two liver transplants from our neighboring country has attracted our attention.[1] Inonu University Liver Transplant Institute is the center with the highest volume in Turkey and Europe (as an ELTR member). Up to 3100 liver transplants have been performed in our institute so far, and 80% of transplants are LDLT because the organ donation rate in Turkey is about 7%, which is quite insufficient. We would like to emphasize a few points regarding the contents of this article :

- In lines 4 and 5, the authors state that the first liver transplant was performed on a girl with hepatocellular carcinoma. However, the girl had hepatoblastoma and her name was Julia Rodrigez.[2]
- The authors transplanted a left lateral lobe liver graft which consists of 2nd and 3rd segments of the liver. The authors have stated that they have perfused a large volume (such as 200 cc) of preservation fluid from the bile ducts of such a small liver graft. Furthermore, they state that they have perfused 200-300 cc preservation fluid from the "thin hepatic artery" during the backtable preparation of the liver graft. We believe this is not appropriate for multiple reasons. Mainly, this is a partial liver graft and perfusion of high volume of fluids, especially, from the arterial system causes damage to the endothelial layer. Perfusion of 20cc of preservation fluid from the biliary system is enough to prevent the autolysis. Our suggestion is perfusion of cold Ringer's Lactate (RL) solution from the portal vein until obtaining clear drainage from the hepatic veins. This step should be followed by perfusing Histidine-tryptophan-ketoglutarate (HTK) solution (500 to 1000 cc). In our opinion the vascular anastomosis between the graft hepatic vein and the recipient hepatic vein orifices should be performed with 5/0 PDS in this age group. We emphasize that using 3/0 Polypropylene is not appropriate.
- Furthermore, the authors stated that they have performed the arterial anastomosis between the recipient common hepatic artery (CHA) and left hepatic artery on the liver graft with 6/0 polypropylene. In our opinion this is not a suitable method. Our suggestion is to use 8/0 Polypropylene for performing end-to-end arterial anastomosis to the left hepatic arterial stump of the recipient. Otherwise, hepatic arterial anastomotic complications will be frequently encountered.[3]
- Also we would like to emphasize our reservations for the bilioenteric anastomosis of the authors. Our suggestion is to use monofilament absorbable suture such as PDS

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instead of multifilament sutures such as polyglactin.

- The authors have performed orthotopic auxiliary liver transplantation as the first case of the transplant center. In our opinion this is not a proper choice as the first case because as it is known very well complication related with portal vein inflow is frequently encountered in auxiliary liver transplantation.[4]
- In the second case, the authors have used the statement "the very thin expression of the graft hepatic artery". In our opinion, this is an indication that this center is not yet ready for such a complex operationThe authors have stated stated that "we performed an auxiliary liver transplant in order not to lose the patient" which shows that they were not confident that the first liver transplant patient will be successful. Liver transplantation is a complex procedure that requires experience and confidence.
- We believe that Damascus University needs to increase their experience and complete the learning curve. Furthermore, they need to be supervised by a more experience center. We believe our institute could provide the necessary support to this center in order to increase the success rate of the procedures and safety of the patients because we are the most experienced center that is geographically closest to this center.

Disclosures

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Authorship Contributions: Concept – S.A., S.Y.; Design – S.A., S.Y.; Supervision – S.Y.; Literature search – S.A., S.Y.; Writing – S.A., S.Y.; Critical review – S.Y.

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