Hôpitaux Universitaires Genève

Cholangitis definition and treatment after Kasai hepatoportoenterostomy for biliary atresia: TRACK-BA study (TRacking Cholangitis post Kasai in Biliary Atresia)

Study information

Protocol ID 2021-01251

NCT number pending

Date 16th April 2025

Abstract

Background: Acute cholangitis is a serious complication following Kasai hepatoportoenterostomy for biliary atresia, negatively impacting prognosis, and leading to liver transplantation. Of note, biliary atresia is the leading pediatric indication for liver transplantation. Despite the significance of cholangitis following Kasai hepatoportoenterostomy, no standardized diagnostic criteria exist, leading to inconsistent treatment. A 2022 international consensus developed by the Swiss Pediatric Liver Center proposed definitions and treatment guidelines through a Delphi process. This study aims to assess the feasibility of applying these definitions for suspected and confirmed cholangitis in clinical practice.

Methods: This prospective, observational study will be conducted across hospitals managing pediatric biliary atresia patients. Data on suspected cholangitis cases in the first year post Kasai hepatoportoenterostomy will be collected by mini-teams of three healthcare providers over twelve months. Data will be anonymized, and the study will adhere to international ethical standards.

Inclusion Criteria:

- Patients with biliary atresia suspected of cholangitis within one year post Kasai hepatoportoenterostomy.
- Data from specialties including pediatric surgery, pediatric hepatology, and pediatric emergency care.

Exclusion Criteria:

- Recurrent cholangitis or cholangitis after one-year post Kasai hepatoportoenterostomy.

Definitions: Cholangitis will be defined by clinical confirmation, improvement with antimicrobial therapy, and lab value changes.

Primary Aim: To assess the application of consensus definitions for suspected and confirmed cholangitis.

Secondary Aim: To evaluate the proposed duration of treatment for cholangitis and compare it to clinical practice.

Data Collection: Data will be stored using the secure REDCap platform, managed by the University of Geneva. Local investigators are responsible for ethical approvals.

Expected Results: This study will assess the practicality of applying expert panel definitions for cholangitis after Kasai hepatoportoenterostomy and gather feedback from clinicians. A sample size of 40 patients is targeted, with 20 in each group (suspected and confirmed). Findings will help refine diagnostic criteria.

Introduction to the topic, importance of research

Acute cholangitis is one of the most serious complications after Kasai hepatoportoenterostomy for biliary atresia due to its negative impact on prognosis, repeated bouts of cholangitis decreasing patient survival and leading earlier to liver transplantation.

In the absence of standard criteria for diagnosis of acute cholangitis after Kasai hepatoportoenterostomy, practical treatment guidelines have never been established; over and under-treatment might be avoided, and reporting might be standardized.

Definition and treatment of cholangitis after Kasai hepatoportoenterostomy were established through a Delphi method, an extensive literature review, iterative rounds of surveys and expert panel discussions*. The criteria's clinical utility, correlations with the physician's judgement, and impact on treatment outcomes have been analyzed in a retrospective study**.

This feasibility study will collect data about biliary atresia patients clinically diagnosed to have cholangitis during the 1st year after Kasai, so that data for suspected and confirmed cholangitis can be assessed.

*** Cholangitis definition and treatment after Kasai hepatoportoenterostomy for biliary atresia: a Delphi process and international expert panel**
Ana M. Calinescu, Omid Madadi-Sanjani, Cara Mack, Richard Schreiber, Riccardo Superina, Deirdre Kelly, Claus Petersen, Barbara E. Wildhaber
Journal of Clinical Medicine, 2022

**** Retrospective analysis of the standardized BARD criteria for acute cholangitis in biliary atresia patients**
Omid Madadi-Sanjani, Ana M. Calinescu, Nathalie Rock, Valerie A. McLin, Marie Uecker, Joachim F. Kuebler, Claus Petersen, Barbara E. Wildhaber
Journal of Pediatric Gastroenterology and Nutrition Reports, 2024

Aims

To assess the applicability of the definitions for suspected and confirmed cholangitis found after an international consensus of a panel of experts led by the Swiss Pediatric Liver Center within the Geneva University Hospitals.

We aim to prospectively apply the diagnostic criteria to the patients suspected of acute cholangitis after Kasai hepatoportoenterostomy on a clinical basis.

Research plan

- Prospective observational feasibility study.
- All hospitals caring for patients with biliary atresia are eligible to participate.
- Collaborators will collect data on all consecutive eligible cases.
- Data will be completely anonymized and subjects cannot be re-identified.
- A mini-team of three collaborators will collect data over 12 months:
    - Multiple mini-teams may participate at the same hospital.
    - We suggest that at least one mini-team participating within a speciality should include a senior (consultant/ attending) doctor.

Inclusion criteria

- Any biliary atresia patient within 1 year after Kasai suspected to have cholangitis.
- All connected specialities including: pediatric surgery, pediatric hepatology, pediatrics, pediatric emergency care, and pediatric intensive care.
- Outpatient clinic and inpatient included.

Exclusion criteria

- Recurrent cholangitis.
- Cholangitis >1 year after Kasai.

In this study, patients were considered to have had acute cholangitis based on three criteria:

1. clinical confirmation by clinicians.
2. clinical remission due to antimicrobial therapy.
3. laboratory values improvement after antimicrobial therapy.

Primary aim

To assess the applicability of the definitions (Figure 1) for suspected and confirmed cholangitis.

Primary analysis

Prospective application of diagnostic criteria to the patients suspected of acute cholangitis on a clinical basis.

Secondary aim

To validate the duration of treatment for suspected and confirmed cholangitis

Secondary analysis

Assess the actual duration of treatment and compare it with the proposed duration of antibiotic treatment

Data will only be released at regional and/or country-level.

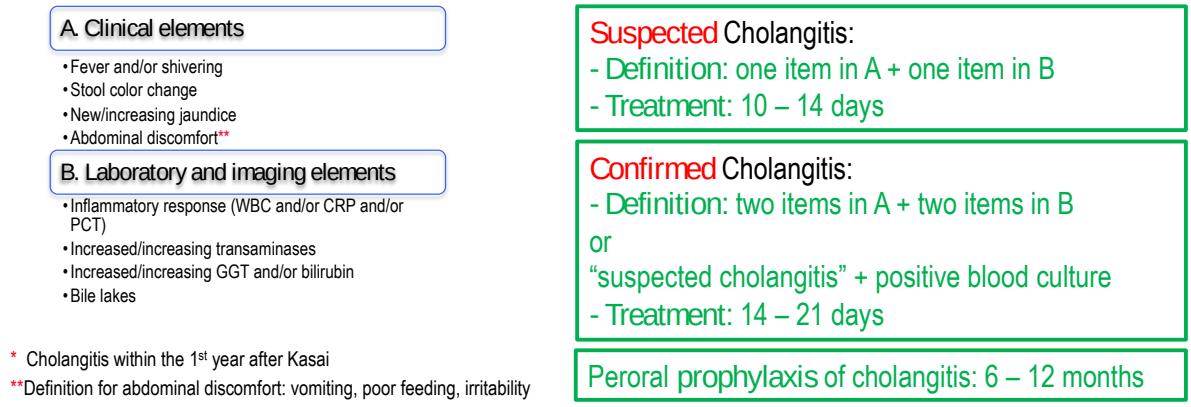

Figure 1: definitions of suspected and confirmed cholangitis, used in this study. Bile lakes were defined as bile containing solitary or multiple cystic intrahepatic lesions following the portal tracts.

Follow-up

This is an observational study; no changes should be made to normal patient pathways, and no additional patient follow-up is required. Patients should have a clinical follow-up as per normal practice at their hospital. Follow-up data should be entered at the end of the study period following the first presentation based on written patient notes, computer records, or telephone/in-person follow-up.

Data collection

Data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application. REDCap allows collaborators to enter and store data in a secure system. A designated collaborator at each participating site will be provided with REDCap project server login details, allowing them to securely submit data on to the REDCap system. The REDCap server is managed by the Geneva University Hospitals, Switzerland. Only anonymized data will be uploaded to the database. No patient identifiable data will be collected. The study will be carried out by national and international guidelines, as well as the basic principles of the protection of the rights and dignity of Human Beings, as set out in the Helsinki Declaration (75th Assembly Fortaleza, Brazil, in October 2024), and according to local applicable legislation.

Local approvals

Principal investigators at each participating site are responsible for obtaining necessary local approvals in line with their hospital's regulations. Collaborators will be required to confirm that local approval is in place at the time of uploading each patient record to the study database. Whatever approval pathway is followed, it should be highlighted that this is an investigator-led, non-commercial, observational (no changes to normal patient care) study which is extremely low risk, as only routinely available non-identifiable data will be collected.

Possible pathways to register this study include:

- Research (e.g. research ethics committee or institutional review board approvals). Your local ethics committee should only take written patient consent if required.
- Existing databases.
- Service evaluation.
- Clinical audit (e.g. approval process in the UK).

Expected results

The results of this study will describe the feasibility of the clinical application of the definition of suspected and confirmed cholangitis and of the management of cholangitis after Kasai hepatoportoenterostomy for biliary atresia. Feedback from the clinician's viewpoint is sought to evaluate the definition when compared to the clinical judgement.

Sample size calculation with a risk estimated for the control group of 60% and 100% for the confirmed cholangitis group (95% power and 0.05 type I error) gives a target sample size of a minimum of 40 patients with 20 patients in each group.

Next steps

After the feasibility evaluation, the next step will be validation through implementation and assessment in actual clinical practice. The sensitivity and specificity of the diagnostic criteria will need to be evaluated on a larger scale.

Timeline