The long-term outcome of the Kasai operation in patients with biliary atresia: a systematic review

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ABSTRACT

Background: Biliary atresia (BA) is a progressive inflammatory destructive process of the bile ducts occurring in about one of every 20,000 live births. If left untreated, biliary atresia can lead to liver failure. The only effective treatments for BA at the moment are the Kasai operation and liver transplantation. Kasai portoenterostomy increases the survival of children with BA and postpones subsequent liver transplantation. Because long-term survival is rare, there is not much known about the long-term efficacy of the Kasai operation.

Methods: The aim of this review was to study the outcome of patients with BA who survived more than 20 years on their native liver. We performed a systematic search on PubMed using MeSH terms for articles describing the long-term outcomes of patients with biliary atresia. We searched for patients who have lived at least 20 years with their native liver and we registered the number of complications. The endpoints identified in these articles were: death, cholangitis, portal hypertension and gastrointestinal bleeding.

Results: From 53 articles we included 14 articles for analysis. In total 184 patients were above the age of 20 years. Of these 162 patients, 88% (162/184) were still alive with their native liver and 60.5% (98/162) were suffering from liver-related complications.

Conclusions: It is possible for patients with biliary atresia to survive more than 20 years on their native liver after undergoing the Kasai operation during early infancy. However, 60.5% of the long-term survivors alive on their native liver end up suffering from progressive liver-related complications.

KEYWORDS

Biliary atresia/surgery, cholangitis, follow-up, portoenterostomy, survival rate

INTRODUCTION

Biliary atresia (BA) is a progressive inflammatory destructive (obliterative) process of the bile ducts.¹ It is characterised by a perinatal complete obstruction of all or part of the extrahepatic bile ducts and is always associated with abnormalities of the intrahepatic biliary tree.¹ If left untreated, biliary atresia will lead to liver failure. Biliary atresia is a rare condition with a prevalence of about one patient per 20,000 live births; patients are destined for a fatal outcome if they are not treated during the first few months of life. The only effective treatments for BA at present are hepatic portoenterostomy (Kasai operation) and liver transplantation.

The Kasai operation was introduced in 1959,³ and consists of constructing a new bile drainage system, generally by creating an anastomosis of the jejunum by a Roux-en-Y loop to the porta hepatis region to re-establish a connection between the intrahepatic bile ducts and the intestine. If successful, Kasai portoenterostomy increases the survival of children with BA and consequently postpones subsequent liver transplantation. Studies have reported 20-year survival rates in patients with their native liver of 21%,⁴ 25%,⁵ 22%,⁶ 23%² and 44%.⁷ However, most long-term survivors develop complications.⁸ Until the age of 18, BA patients are generally managed by paediatricians or paediatric surgeons. After the age of 18 these patients are referred to and managed by gastroenterologists. It is
therefore important that gastroenterologists become aware of the fact that in long-term survivors who have undergone the Kasai operation, complications such as recurrent cholangitis and portal hypertension may occur.

The aim of this review is to study liver condition and liver-related complications in patients treated with this operation during early infancy after a follow-up of 20 years while retaining their own liver. This review attempts to give an overview of the most important complications suffered by these patients and the prevalence of these complications.

METHODS

Literature search
The PubMed database was searched on 7 January 2012 using the MeSH term combination: (“Biliary Atresia/surgery”[MeSH Terms] AND (“Follow-Up Studies”[MeSH Terms] OR “Survival Analysis”[MeSH Terms] OR “cholangitis”[MeSH Terms] OR “Portoenterostomy, hepatic”[MeSH Terms])). The limits were set to ‘English’ and ‘Aged 19+ years’.

Selection of studies
Articles were excluded based on title and abstract when research on liver transplantation, non-gastrointestinal complications, diagnostic tools used for follow-up and alternative postoperative treatment were described. Articles that described studies with a population younger than 20 years, articles that did not contain information on BA or the added complications and articles that were not available for Erasmus MC were also excluded.

After reading the articles, some were excluded because the minimum follow-up was shorter than 20 years or the age of the population was unclear. One article contained no information on the complications of biliary atresia. After excluding all these articles, the references of the remaining articles were scanned, which yielded additional relevant articles. Some articles that were retrieved described the same population, thereby creating an overlap. To resolve this issue we included the most recent article that described the whole population.

Outcome
Using the articles retrieved from the systematic review we defined a cohort of patients that survived for 20 years after a hepatopporto-enterostomy with their own liver. Within this cohort the number of patients who died or underwent a liver transplant after they had reached 20 years of age and the number of patients who are still alive with their native liver were described. We also retrieved information on complications in patients aged 20 years or older, who are still alive with their native liver after 20 years of age as the secondary outcome. The complications described in this article are: cholangitis, portal hypertension and gastrointestinal bleeding.

Data analysis
We extracted the study characteristics and the primary and secondary outcome measures from each article. The study characteristics included the authors, year, journal of publication, country of study and population above 20 years of age. For each outcome (death, alive with/without liver transplantation, with/without complications, cholangitis, portal hypertension, gastrointestinal bleeding or hepatocellular carcinoma) separately, we counted the number of patients in each article, summed them up and displayed them in a table or graphic.

RESULTS

The literature search and selection of studies
The results of our systematic literature search and our study selection is shown in a flowchart (Figure 1). From the literature search we identified 53 studies, from which

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**Figure 1. Results of systematic literature search and study selection**

- **Search (hits)**
  - PubMed 53

- **Screened on title/abstract**
  - 19 Hits
  - 14 Articles included

- **Screened on full text**
  - 14 Articles included

- **Included studies**
  - 4 Articles included
    - By screening the reference lists of included articles
  - 4 Studies included
    - The results of systematic literature search and study selection

- **Excluded studies**
  - 14 Articles excluded
    - 17 studies about liver transplantation
    - 5 studies about non-gastrointestinal complications
    - 5 studies about diagnostic tools for follow-up
    - 1 article was not retrievable
    - 5 studies with a population <20 years
    - 2 studies not about biliary atresia or the added complications
    - 1 study about alternative postoperative treatment
  - 5 Studies excluded
    - 4 studies with a population or age <20 or were unclear about the age of the population
    - 1 study contained no information about complications

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Bijl et al. Long-term survival after Kasai operation.
34 studies were excluded based on title and abstract. We read the full text of 19 articles from which five articles were excluded. We screened the reference lists of the 14 remaining articles; this resulted in four additional articles. Finally, we excluded four articles because they contained an overlap in population. Thus, 14 articles were included for further analysis.

Characteristics of the articles
Of the 14 articles included, seven described a follow-up study, three articles described a retrospective cohort study and four articles were case reports. Of the 14 studies, eight studies are from Japan. There are ten studies that described very few or only one patient. Four articles described a larger patient group (table 1).

Population
The 14 studies included a total group of 184 patients above 20 years of age. In this group, eight patients died and 14 were alive with liver transplantation after 20 years of age. There were 162 patients living with their native liver (table 2). All patients who died or had undergone liver transplantation had end-stage liver disease or suffered from severe liver-related complications.

Complications
Of the 162 patients who are alive with their native liver, 39.5% (64/162) are alive without complications. The remainder of the patients have developed complications (table 2).

All the patients who developed complications had experienced episodes of cholangitis. Of the 98 patients with cholangitis, 86% (83/98) developed portal hypertension. Of the patients with portal hypertension, 45% (35/78) experienced gastrointestinal bleeding. In one patient a hepatocellular carcinoma was found (table 2).

DISCUSSION
This systematic review shows that there are patients born with biliary atresia who can survive for more than 20 years with their native liver. This review included 184 patients of which 60.5% of the patients eventually developed severe complications such as cholangitis, portal hypertension, gastrointestinal bleeding and hepatocellular carcinoma. One can assume that in the end, most of these patients will need to undergo a liver transplantation.

It was not possible to calculate a survival rate because not all the included articles were follow-up studies, other included articles did not provide information on deceased and transplanted patients before the age of 20. Earlier publications have described 20-year survival rates on a native liver, which varies from 21% to 44%.4-7

The importance of these findings can be extrapolated to clinical practice where until the age of 18 these patients are generally managed by a paediatrician or paediatric
surgeon. After the age of 18 most of these patients are managed by the gastroenterologist. It is especially necessary for the gastroenterologist to realise that in long-term survivors after Kasai operation developing recurrent cholangitis and portal hypertension liver transplantation should be considered early to avoid death to liver-related mortality. This review shows that the majority of these patients have severe liver disease that requires close follow-up. Almost all the articles we included for this review describe only a small population of BA patients. This is why we also took case reports into account. Some case reports described detailed outcomes that were not available in other articles. When analysing the complications, it became difficult to understand which patients suffered from which complications in the articles. To avoid overlap in patients who had more than one complication we assumed the following: cholangitis led to portal hypertension which led to gastrointestinal bleeding. That means that we assumed that patients who had portal hypertension were the same patients who suffered from cholangitis. Most of the articles we analysed were publications from Japan. The Kasai operation was introduced in Japan in 1959 and at first was probably only used in Japan to treat biliary atresia. It only became accepted in America and the Netherlands in around 1970. Before that, Japan was practically the only country using the operation to treat BA. This could be the reason why Japan has more long-term survivors.

We would suggest that more research is needed on the further development of the disease after 20 years of survival on a native liver. It could be a great asset to assess whether patients should be added to the liver transplantation waiting list after clinical manifestation of cholangitis. Altman et al. provided an important insight into survival rates in patients with biliary atresia. However, due to the fact that suffered complications were not described, this article had to be excluded from this review.

Taking everything into account, we can conclude that there is an extensive lifelong follow-up needed in these patients, so complications can be identified and the optimal treatment can be initiated.

REFERENCES