

Laparoscopic liver resection for patients with intrahepatic cholangiocarcinoma using data from the Japanese National Database: A nationwide observational study

Takashi Kokudo^{1,*}, Yasuhide Yamada², Takehiro Sugiyama^{3,4,5}, Yuichiro Mihara¹, Mai Nakamura¹, Rei Goto⁶, Norihiro Kokudo¹

¹ National Center for Global Health and Medicine, Japan Institute for Health Security, Tokyo, Japan;

² Department of Research Management, Japan Institute for Health Security, Tokyo, Japan;

³ Institute for Global Health Policy Research, Bureau of Global Health Cooperation, Japan Institute for Health Security, Tokyo, Japan;

⁴ Diabetes and Metabolism Information Center, National Center for Global Health and Medicine, Japan Institute for Health Security, Tokyo, Japan;

⁵ Department of Health Services Research, Institute of Medicine, University of Tsukuba, Ibaraki, Japan;

⁶ Graduate School of Business Administration, Keio University, Yokohama, Japan.

Abstract: Since 2011, the Ministry of Health, Labour and Welfare (MHLW) has made the data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) available for research purposes. Recent trends in treatments and prognosis for intrahepatic cholangiocarcinoma (ICC) were analyzed using data from this comprehensive database. This repeated cross-sectional study employed NDB open data to determine the number of patients with ICC and those treated for ICC from fiscal years (FY) 2016 to 2020. The International Classification of Diseases version 10 (ICD-10) code of C22.1 (ICC) was used to define ICC patients. The number of patients diagnosed with ICC and treated in Japan did not change during the study period (FY2016: 1,119; FY2017: 1,136; FY2018: 1,213; FY2019: 1,185; FY2020: 1,194). The number of patients who underwent open liver resection (OLR) did not change either (FY2016: 748; FY2017: 771; FY2018: 807; FY2019: 760; FY2020: 753). On the other hand, patients who underwent laparoscopic liver resection (LLR) increased during the study period (FY2016: 84; FY2017: 118; FY2018: 143; FY2019: 171; FY2020: 195). This was primarily due to the increase in the number of patients who received laparoscopic liver resection larger than subsegmentectomy (FY2016, 57; FY2017, 81; FY2018, 98; FY2019, 101; FY2020, 133). The median postoperative survival was 5.25 years in the OLR group and was not reached in the LLR group. The national database analysis revealed that while the number of patients diagnosed with and treated for ICC has remained stable, the adoption of minimally invasive surgery has increased, possibly because of advancements in treatment techniques, resulting in good survival outcomes.

Keywords: intrahepatic cholangiocarcinoma, laparoscopic liver resection, Japanese national database

1. Introduction

The incidence of intrahepatic cholangiocarcinoma (ICC) is increasing globally, and treatment advances are remarkable for patients with ICC (1). Because most ICC patients are diagnosed at advanced stages, the prognosis remains unfavorable (2). The Liver Cancer Study Group of Japan is one of several nationwide registries in Japan (3). Nevertheless, the data submitted to this registry is exclusively sourced from approximately 500 Japanese specialized institutes. The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) open data is another promising data source for analyzing the

number of ICC patients and treatments. Since 2011, the Ministry of Health, Labour, and Welfare (MHLW) has provided comprehensive electronic claims data for insured treatments in this database (4). This database offers a precise understanding of ICC treatments performed in Japan.

Laparoscopic surgery, particularly in colorectal surgery, has gained widespread acceptance based on the positive outcomes demonstrated in randomized controlled trials (5). In the context of liver surgery, numerous studies have reported favorable results following laparoscopic liver resection (LLR) for patients with hepatocellular carcinoma (6-8). However, little is known about the impact of LLR in ICC patients.

Therefore, this study aimed to examine this NDB open data to identify population-based national trends in the number of patients with ICC, their treatments, and their prognosis.

2. Materials and Methods

2.1. Data source

The NDB open data, a comprehensive database that aggregates electronic insurance claims data for all medical services and products covered by Japan's national health insurance system, was utilized in this study (9). Researchers may submit an application to the MHLW to obtain access to the NDB open data, which is subject to their research requirements. The data supplied by MHLW is anonymized. The NDB open data contains comprehensive information on patient demographics, health status, diagnoses, medical and dental procedures, and prescription data, as well as insurance claims and health exam records from all hospitals and clinics in Japan.

For this study, we requested and obtained data on International Classification of Diseases, 10th Revision (ICD-10) codes for liver cancer, spanning the period from April 2015 to September 2021. The MHLW provided our research team with access to 323 million medical records, 130 million Diagnostic Procedure Combination records, and 384,000 prescription records.

2.2. Statement of ethics

The study protocol was reviewed and approved by the Ethics Committee of the National Center for Global Health and Medicine (approval number: NCGM-S-004253-03). The data supporting the findings of this study are available upon request from the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB Open Data) (<https://www.mhlw.go.jp/ndb/opendatasite/>).

The NDB Open Data consists of anonymised data that is publicly available on the website and accessible to third parties, without any personal patient information. Therefore, informed consents were not required for this study.

2.3. Patients selection

At the NDB open data, diagnostic data are categorized employing ICD-10 codes. Patients diagnosed under ICD-10 code C22.1 (ICC) were defined as having ICC. Patients lacking treatment-related data were excluded from the analysis.

2.4. Treatments and outcomes

Interventions for ICC were defined as treatments

administered within 180 days of diagnosis. Liver resection cases were classified as either open liver resection (OLR, procedure code K695) or laparoscopic liver resection (LLR, procedure code K695-2). The extent of liver resection was further categorized into subsegmentectomy or more extensive resection, and partial resection, as documented in the insurance claims. Transarterial embolization (TAE, procedure code K615) and transarterial chemoembolization (TACE, procedure code G003-3) were considered together. Patients treated with sorafenib (medication code 620006778), lenvatinib (622416001 and 622416101), regorafenib (622225801), cabozantinib (622796901 and 622797001), ramucirumab (622417901 and 622418001), bevacizumab (620004872 and 620004873), and atezolizumab (622594601 and 629900601) were categorized as receiving molecular targeted therapies. The information concerning cancer stage, liver function, or margin status was not available due to the nature of the database.

Time to death, defined as the duration from treatment initiation to death, was evaluated for patients who underwent surgery between 2016 and 2020. Time to death was determined from information relating to death that was captured from the "outcome at the time of discharge" field and/or "destination after discharge" field in the Diagnosis and Procedure Combination discharge summary data. The discharge date was used as the date of death for statistical calculations. The patient's insurance information was followed up until September 2021. Patients for whom the date of death could not be confirmed were censored at their latest recorded visit date during the study period (10).

2.5. Statistical analysis

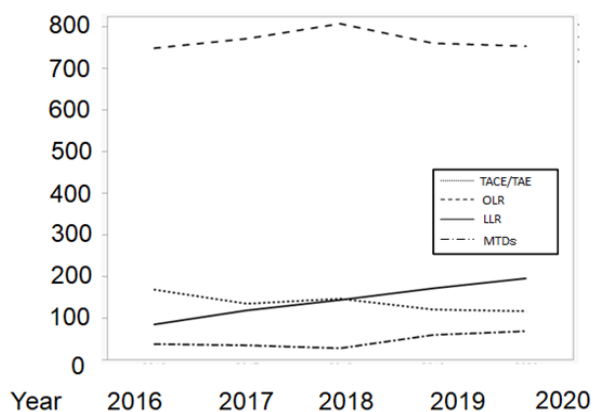
The number and percentage of treated patients were analyzed. Patient counts were ascertained for each fiscal year (FY), commencing in April, between FY2016 and FY2020. Statistical analyses were performed using the R software (version 4.4.2).

3. Results

Table 1 and Figure 1 illustrate the trends of treatment for ICC. During the study period, the number of patients diagnosed with ICC and treated remained comparable (FY2016: 1,119; FY2017: 1,136; FY2018: 1,213; FY2019: 1,185; FY2020: 1,194). Consequently, the number of patients who received OLR remained steady (FY2016: 748; FY2017: 771; FY2018: 807; FY2019: 760; FY2020: 753). Conversely, patients who underwent LLR increased significantly (FY2016, 84; FY2017, 118; FY2018, 143; FY2019, 171; and FY2020, 195). Additionally, we investigated the extent of liver resection for patients who underwent LLR. The number of patients who underwent laparoscopic partial resection increased marginally (FY2016: 27; FY2017:

Table 1. Trends in treatments for intrahepatic cholangiocarcinoma

Treatment	2016 <i>n</i> = 1,119 (%)	2017 <i>n</i> = 1,136 (%)	2018 <i>n</i> = 1,213 (%)	2019 <i>n</i> = 1,185 (%)	2020 <i>n</i> = 1,194 (%)
Open liver resection	748 (66.8)	771 (67.9)	807 (66.5)	760 (64.1)	753 (63.1)
Laparoscopic liver resection	84 (7.5)	118 (10.4)	143 (11.8)	171 (14.4)	195 (16.3)
Transarterial chemoembolization/ transarterial embolization	168 (15.0)	134 (11.8)	146 (12.0)	120 (10.1)	116 (9.7)
Molecular targeted drugs	37 (3.3)	34 (3.0)	27 (2.2)	59 (5.0)	68 (5.7)

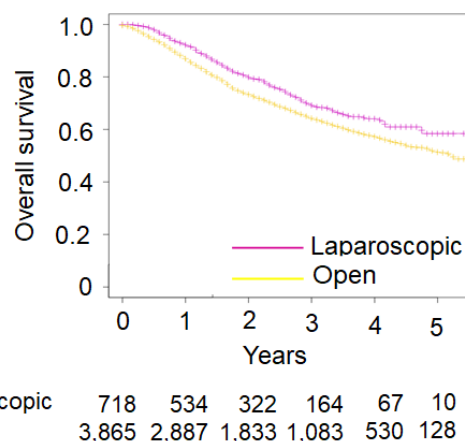
Number of patients**Figure 1. Trends in treatments for intrahepatic cholangiocarcinoma in the national administrative database.** Abbreviations: TACE/TAE, transarterial chemoembolization/transarterial embolization; OLR, open liver resection; LLR, laparoscopic liver resection; MTDs, molecularly targeted drugs.

37; FY2018: 45; FY2019: 70; FY2020: 62). However, there was a substantial increase in the number of patients who underwent laparoscopic procedures that included at least a subsegmentectomy (FY2016: 57; FY2017: 81; FY2018: 98; FY2019: 101; and FY2020: 133). The median postoperative survival was 5.25 years in the OLR group and was not reached in the LLR group. The five-year survival rate was 58.4% in the LLR group and 51.2% in the OLR group (Figure 2).

4. Discussion

The study findings revealed that the number of patients diagnosed with and treated for ICC remained consistent over time. In contrast, the number of those undergoing LLR increased, with good long-term survival outcomes, likely due to advancements in surgical techniques.

Although previous reports from the Liver Cancer Study Group of Japan have documented the number of treated ICC patients, the most recent data pertain only to 2014 to 2015 (3). Consequently, it is imperative to examine the most recent developments in the treatment of ICC. Additionally, previous nationwide surveys have focused exclusively on specialized centers for ICC treatment. Hence, reviewing this extensive and

**Figure 2. Kaplan-Meier estimates of survival by liver resection type using national administrative data.** Numbers below the X-axis indicate the number of patients at risk.

valuable database (NDB open data) is imperative for understanding the current epidemiology of and treatments for ICC.

Technical advancements in LLR have led to its increasing use in treatment of hepatic tumors. This is due to the advantage of reduced intraoperative blood loss, particularly in patients requiring minor liver resections (6). This is consistent with our research, which indicates a substantial increase in the number of patients who are undergoing LLR. Additionally, laparoscopic subsegmentectomy has become increasingly common in recent years (11), contributing substantially to the increase in LLR procedures.

In this study, median postoperative survival was not reached in patients undergoing LLR with a five-year survival rate of 58.4%. This finding may be explained by preferential use of LLR for a higher number of patients with early-stage ICC. Indeed, the frequency of subsegmentectomy or larger was more infrequent in patients who underwent LLR (65.8% vs. 90.0%). Although stage data were not available in this database, the unreached median survival was considered sufficient to justify this treatment strategy for patients with ICC whenever possible. The reported median survival after hepatectomy for ICC using the Surveillance,

Epidemiology, and End Results (SEER) database was 34 months (12). Therefore, survival analysis using NDB, the Japanese national database, revealed that patients receiving LLR had good survival, supporting the recommendation of LLR for patients with ICC whenever suitable. Although a previous study demonstrated an increased risk of lymph node metastasis with LLR in patients with ICC (13), there is growing evidence supporting the feasibility of LLR in these patients (14,15). There is also a recent report exploring the oncological benefit of LLR in patients with ICC, attributed to the lower biological impact of surgery and shorter interval between surgery and initiation of adjuvant treatments (16). Although this database did not include data on lymph node dissection and adjuvant therapies, and laparoscopic lymph node dissection is technically challenging, the survival benefit of LLR might be partly due to differences in nodal staging or adjuvant treatment.

One limitation of our study is that the data were analyzed retrospectively. Furthermore, there was a lack of precise prognostic data and comprehensive patient characteristics. Therefore, prolonged survival in patients receiving LLR might be due to the frequent proportion of early-stage ICC patients. Additionally, the death rate captured in this study only included patients who were admitted before death; therefore, some patients who died before admission were not analyzed which might have led to overestimation of survival and should be considered as proxy measures. However, it is notable that the study revealed a substantial increase in use of minimally invasive surgery, or LLR, in recent years, with good survival outcomes.

In conclusion, while the number of patients diagnosed with and treated for ICC has remained stable, adoption of minimally invasive surgery has increased, possibly because of advancements in treatment techniques, resulting in good survival outcomes.

Funding: This work was supported by a grant from the National Center for Global Health and Medicine, Tokyo, Japan.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Yoo C, Hyung J, Chan SL. Recent advances in systemic therapy for advanced intrahepatic cholangiocarcinoma. *Liver Cancer*. 2023; 13:119-135.
2. Banales JM, Marín JGG, Lamarca A, *et al*. Cholangiocarcinoma 2020: The next horizon in mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2020; 17:557-588.
3. Iijima H, Kudo M, Kubo S, Kurosaki M, Sakamoto M, Shiina S, Tateishi R, Osamu N, Fukumoto T, Matsuyama Y, Murakami T, Takahashi A, Miyata H, Kokudo N. Report of the 23rd nationwide follow-up survey of primary liver cancer in Japan (2014-2015). *Hepatol Res*. 2023; 53:895-959.
4. Suto M, Iba A, Sugiyama T, Kodama T, Takegami M, Taguchi R, Niino M, Koizumi R, Kashiwagi K, Imai K, Ihana-Sugiyama N, Ichinose Y, Takehara K, Iso H. Literature review of studies using the national database of the Health Insurance Claims of Japan (NDB): Limitations and strategies in using the NDB for research. *JMA J*. 2024; 7:10-20.
5. Bonjer HJ, Deijen CL, Abis GA, Cuesta MA, van der Pas MH, de Lange-de Klerk ES, Lacy AM, Bemelman WA, Andersson J, Angenete E, Rosenberg J, Fuerst A, Haglund E; COLOR II Study Group. A randomized trial of laparoscopic versus open surgery for rectal cancer. *N Engl J Med*. 2015; 372:1324-1332.
6. Kokudo T, Takemura N, Inagaki F, Yoshizaki Y, Mihara F, Edamoto Y, Yamada K, Kokudo N. Laparoscopic minor liver resection for hepatocellular carcinoma. *Jpn J Clin Oncol*. 2023; 53:1087-1090.
7. Belli G, Limongelli P, Fantini C, D'Agostino A, Cioffi L, Belli A, Russo G. Laparoscopic and open treatment of hepatocellular carcinoma in patients with cirrhosis. *Br J Surg*. 2009; 96:1041-1048.
8. Han HS, Shehta A, Ahn S, Yoon YS, Cho JY, Choi Y. Laparoscopic versus open liver resection for hepatocellular carcinoma: Case-matched study with propensity score matching. *J Hepatol*. 2015; 63:643-650.
9. Fukuda H, Sato D, Moriwaki K, Ishida H. Differences in healthcare expenditure estimates according to statistical approach: A nationwide claims database study on patients with hepatocellular carcinoma. *PLoS One*. 2020; 15:e0237316.
10. Ueno H, Shimizu K, Fukui A, Nii M, Koto R, Unno M. Evaluation of the treatment duration of Japanese patients with pancreatic cancer in a real-world setting using a large hospital claims database: The SUISEI Study. *Pancreas*. 2024; 53:e492-e500.
11. Xu Y, Chen M, Meng X, Lu P, Wang X, Zhang W, Luo Y, Duan W, Lu S, Wang H. Laparoscopic anatomical liver resection guided by real-time indocyanine green fluorescence imaging: Experience and lessons learned from the initial series in a single center. *Surg Endosc*. 2020; 34:4683-4691.
12. Jiang SS, Wang ZY, Tan LJ, Zhou LX, Wang XY, Han XM, Li SG, Luo JM, Yao HB. Prediction of the prognosis of intrahepatic cholangiocarcinoma patients after hepatectomy *via* propensity score matching: A competitive risk model analysis. *Transl Cancer Res*. 2025; 14:1884-1901.
13. Takayama H, Kobayashi S, Gotoh K, Sasaki K, Iwagami Y, Yamada D, Tomimaru Y, Akita H, Asaoka T, Noda T, Wada H, Takahashi H, Tanemura M, Doki Y, Eguchi H. Laparoscopic liver resection for small, solitary, peripheral-type intrahepatic cholangiocarcinoma, based on preoperative prediction of lymph node metastasis. *J Laparoendosc Adv Surg Tech A*. 2025; 35:640-651.
14. Sheng Y, Zheng J, Tao L, Shen Z, Liang X. Risk factor analysis of conversion in laparoscopic liver resection for intrahepatic cholangiocarcinoma. *Surg Endosc*. 2024; 38:1191-1199.
15. Du C, Cao W, Liu J, Liu J, Jin L, Feng X, Zhang C, Wei F. Utility of a novel scoring system for the difficulty of pure laparoscopic hepatectomy for intrahepatic cholangiocarcinoma. *Sci Rep*. 2024; 14:31546.
16. Ratti F, Maina C, Clocchiatti L, Marino R, Pedica F, Casadei Gardini A, De Cobelli F, Aldrighetti LAM.

Minimally invasive approach provides oncological benefit in patients with high risk of very early recurrence (VER) after surgery for intrahepatic cholangiocarcinoma (iCCA). *Ann Surg Oncol.* 2024; 31:2557-2567.

Received March 10, 2026; Revised April 24, 2026; Accepted May 7, 2026.

Released online in J-STAGE as advance publication May 13, 2026.

**Address correspondence to:*

Takashi Kokudo, National Center for Global Health and Medicine, Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.

E-mail: kokudo-ky@umin.ac.jp