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Original article

Association between prophylactic antibiotic use for transarterial chemoembolization and occurrence of liver abscess: a retrospective cohort study

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ABSTRACT

Objectives: Clinical evidence on prophylactic antibiotics for transarterial chemoembolization (TACE) to prevent liver abscess is limited because liver abscess is a rare event. This study aimed to analyse the association between prophylactic antibiotic use for TACE and the occurrence of liver abscess after TACE.
Methods: Using the nationwide Diagnosis Procedure Combination database in Japan, we retrospectively identified patients who underwent TACE for hepatic cancer between July 2010 and March 2017. The primary outcome was liver abscess requiring procedural intervention within 30 days of TACE. Secondary outcomes included 30-day in-hospital mortality and length of stay. Propensity score matching was performed to adjust for potential confounding factors and compare outcomes between patients with and without prophylactic antibiotics.
Results: Among 167 544 eligible patients, 134 712 received antibiotics and 32 832 did not. In the matched cohort of 29 211 pairs, the proportion of patients with liver abscess requiring procedural intervention was significantly lower in the antibiotics group than in the no-antibiotics group (0.08% vs. 0.22%, p 0.001; relative risk (95% confidence interval), 0.35 (0.22–0.57); absolute risk reduction, 0.0014 (0.0008 –0.0021); and number needed to treat, 696 (476–1223)). There was no significant difference in 30-day in-hospital mortality between the groups. The length of stay was longer in the antibiotics group than in the no-antibiotics group (median, 10 vs. 9 days, $p < 0.001$).
Conclusions: Prophylactic antibiotic use in patients undergoing TACE was associated with a reduced occurrence of liver abscess requiring procedural intervention. **Shingo Yoshihara, Clin Microbiol Infect 2021;27:1514.e5–1514.e10**

Introduction

Liver abscess is a major complication in hepatic cancer treated with transarterial chemoembolization (TACE). Liver abscess occurs in approximately 0.2% to 2% of patients after TACE [1–5] and requires long-term administration of antibiotics. Severe cases require drainage or resection, with some deaths resulting [1–7]. The risk factors for liver abscess after TACE include bilioenteric anastomosis,

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duodenal sarcoma [1], diabetes [8], leukopenia, a previous liver abscess after TACE and grade 2 particulate embolization or oily portogram [9].

Prophylactic antibiotic therapy during TACE may be effective in preventing liver abscess. However, the literature on prophylactic antibiotics for TACE has been confined to small-scale studies. Two randomized controlled trials ($n = 15$ and $n = 37$) showed no liver abscess in either the group with and without antibiotics [10,11]. In an observational study of 499 patients who received ceftriaxone, no patient developed liver abscess [12]. Another observational study of 243 patients without antibiotics demonstrated similar results [13].

Because liver abscess after TACE is a rare event, previous studies on this aspect were underpowered. Thus, the effect of antibiotic prophylaxis on preventing liver abscess after TACE is uncertain. Unnecessary antibiotic use renders an excessive risk of allergy and anaphylaxis and contributes to the development of bacterial resistance to antibiotics [14]. Therefore, the necessity for prophylactic antibiotics in TACE requires further study.

This study aimed to examine the association between prophylactic antibiotic use for TACE and liver abscess occurrence after TACE using a nationwide Japanese database.

Methods

Ethical considerations

This study was approved by the institutional review board of the University of Tokyo. Owing to the retrospective study design and anonymity of data, the requirement for informed consent was waived.

Data source

This study obtained data from the Diagnosis Procedure Combination (DPC) database, a national inpatient database in Japan. Eighty-two academic hospitals (university hospitals and national centres) are obliged to adopt the DPC system, whereas adoption is voluntary for community hospitals. Approximately 1000 hospitals have been providing data to the DPC database, which covers approximately 50% of all acute-care inpatients in Japan [15]. Data included in the DPC database are shown in Supplementary Table S1. Using the International Classification of Diseases, 10th revision (ICD-10), codes for comorbidities, the updated Charlson comorbidity index was calculated [16]. Drugs administered during surgical procedures were identified by indicators of drugs ordered together with procedures.

We also obtained data on the following hospital characteristics from the 2014 Annual Report for Functions of Medical Institutions [17]: hospital type (academic hospital, nonacademic advanced treatment hospital, etc.); and existence of an infectious disease unit.

Patients

We retrospectively identified patients who underwent TACE for hepatic cancer between July 2010 and March 2017. The antibiotics group included those who received antibiotic monotherapy on the day of TACE. The definition of hepatic cancer and the antibiotics provided are presented in Supplementary Table S2. Patients who did not receive antibiotics on the day of TACE comprised the no-antibiotics cohort.

The exclusion criteria were as follows: (a) age <18 years, (b) therapeutic procedures for liver cancer other than TACE (transarterial embolization, radiofrequency ablation, microwave ablation or hepatectomy) during the same hospitalization, (c) two or more TACE during the same hospitalization, (d) antibiotics initiated before the day of TACE, (e) use of multiple antibiotics or antibiotics other than the ones listed above and (f) missing hospital data (type of hospital and infectious disease unit).

Outcomes

The primary outcome was the occurrence of liver abscess requiring procedural intervention (percutaneous transhepatic abscess drainage (PTAD), percutaneous transhepatic abscess puncture or liver abscess incision) within 30 days of TACE. Patients who were discharged within 30 days but underwent PTAD and other procedures within 30 days of TACE during a readmission to the same hospital were also considered to have an occurrence of liver abscess (Fig. 1). However, we excluded patients who were readmitted and had PTAD and other procedures after undergoing a second procedure for hepatic cancer during the readmission because abscess would have been noted on the screening performed before the second procedure for hepatic cancer was performed. Secondary outcomes were in-hospital mortality within 30 days of TACE, length of stay and total cost of hospitalization (€1 = ¥120). The requirement for red blood cell transfusion within 30 days of TACE was used as a falsification endpoint, which was expected not to differ between groups [18,19]. We also compared the proportion of patients with suspected *Clostridioides difficile* infection (CDI) after admission, which was defined by diagnosis record of CDI (ICD-10 code A047) after admission or need for oral vancomycin on the day of or after TACE during hospitalization.

Statistical analysis

To adjust for measured confounding factors, we estimated propensity scores using a logistic regression model with prophylactic antibiotic use as the dependent variable. Independent variables in the model are shown in Supplementary Table S3. Patients with missing data were excluded. A *c* statistic was calculated to evaluate the discriminatory ability of the model. Using the estimated propensity scores, we conducted a nearest-neighbour one-to-one matching without replacement between the antibiotics and no-antibiotics groups. To achieve a balance of patient characteristics between the groups, the cutoff for a difference in propensity score was set at 0.2 multiplied by the standard deviation of the estimated propensity scores. An absolute standardized difference of >10% was considered to indicate imbalance in the baseline covariate [20].

The chi-square test was used to compare the proportions of liver abscess, in-hospital mortality and requirement for red blood cell transfusion between the propensity-matched pairs. The Mann-Whitney *U* test was used to compare the median length of stay and cost of hospitalization. The relative risk, absolute risk reduction, number needed to treat and their 95% confidence intervals (CIs) were calculated. We compared the proportion of patients with liver abscess requiring procedural intervention between those receiving first-generation cephalosporin and those receiving other antibiotics. We also compared the in-hospital mortality in patients who developed liver abscess during hospitalization for TACE to estimate the severity of the abscess.

We conducted five sensitivity analyses. First, we included patients receiving multiple antibiotics using intravenous aminoglycoside or metronidazole on the day of TACE. Second, we limited patients in the antibiotics group to those who had antibiotics ordered together with the TACE procedure. Third, we included patients who received another procedure after TACE. Fourth, we separately analysed outcomes occurring during the hospitalization for TACE and outcomes occurring during readmissions. Finally, we

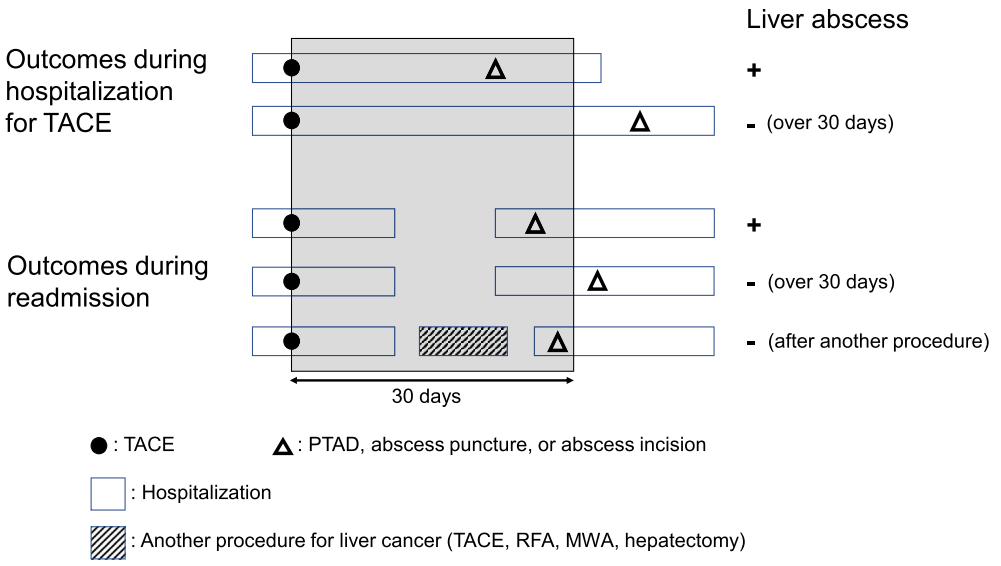

Fig. 1. Timing of outcomes. MWA, microwave ablation; PTAD, percutaneous transhepatic abscess drainage; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

changed the definition of outcomes to PTAD and other procedures performed within 15 days of TACE and conducted the main analysis and fourth sensitivity analysis.

A p value of <0.05 was considered statistically significant. Propensity score matching was conducted using the psmatch2 command in Stata SE 15.0 (StataCorp, College Station, TX, USA). Other analyses were performed by SPSS for Windows 25.0 (IBM, Armonk, NY, USA).

Results

Among 223 107 patients who underwent TACE during the study period, 167 544 from 936 hospitals were included. Of these patients, 134 712 (80.4%) received prophylactic antibiotic monotherapy, whereas 32 832 (19.6%) did not receive antibiotics. Propensity score matching yielded 29 211 pairs from both groups (Fig. 2). The *c* statistic for the model estimating the propensity score was 0.55.

Baseline characteristics before and after propensity score matching are compared in Table 1. After propensity score matching, baseline characteristics were well balanced between groups. Classes of antibiotics used in the antibiotics group are shown in Table 2. First-generation cephalosporin was most frequently used in this group. The proportion of patients who received antibiotics for 3 days or fewer was 64.0% in the matched cohort.

Outcomes in both groups before propensity score matching are compared in Supplementary Table S4. Outcomes after propensity score matching are compared in Table 3. The proportion of patients requiring procedural intervention for liver abscess was significantly lower in the antibiotics group than in the no-antibiotics group (0.08% vs. 0.22%, p < 0.001; relative risk, 0.35 (95% CI, 0.22–0.57); absolute risk reduction, 0.0014 (95% CI, 0.0008–0.0021); number needed to treat, 696 (95% CI, 476–1223)). Among patients in the antibiotics group, the rate of outcomes was similar between those receiving first-generation cephalosporin and those receiving other antibiotics (10/12 127, 0.08% vs. 13/17 084, 0.08%; p 0.848)).

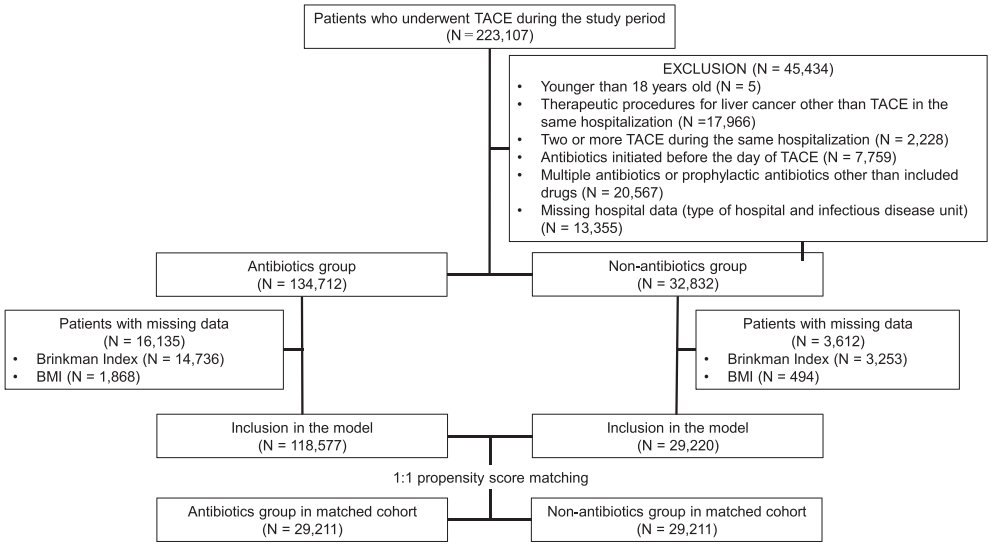

Fig. 2. Patient selection flowchart. BMI, body mass index; TACE, transarterial chemoembolization.

Table 1
Baseline characteristics of all eligible and propensity-matched patients

Characteristic	All eligible patients					Matched cohort				
	Antibiotics		No antibiotics		SD (%)	Antibiotics		No antibiotics		SD (%)
	(*N* = 134 712)		(*N* = 32 832)			(*N* = 29 211)		(*N* = 29 211)		
Male	96 694	(71.8)	23 685	(72.1)	0.66	21 100	(72.2)	20 789	(71.2)	−1.93
Age (years), mean (standard deviation)	72.8	(8.9)	72.7	(8.8)	−1.39	72.3	(9.3)	72.8	(8.8)	5.08
BMI										
<18.5 kg/m^2	8819	(6.5)	2142	(6.5)	−0.07	2158	(7.4)	1937	(6.6)	−2.40
18.5–24.9 kg/m^2	83 948	(62.3)	20 399	(62.1)	−0.31	17 664	(60.5)	18 476	(63.3)	4.66
25–34.9 kg/m^2	39 063	(29.0)	9551	(29.1)	0.17	9162	(31.4)	8589	(29.4)	−3.47
≥35 kg/m^2	1014	(0.8)	246	(0.7)	−0.03	227	(0.8)	209	(0.7)	−0.58
Brinkman index										
0	68 951	(51.2)	16 783	(51.1)	−0.11	15 536	(53.2)	16 563	(56.7)	5.77
1–399	11 962	(8.9)	3094	(9.4)	1.55	3570	(12.2)	3054	(10.5)	−4.50
400–999	26 189	(19.4)	6620	(20.2)	1.48	7000	(24.0)	6546	(22.4)	−3.00
≥1000	12 874	(9.6)	3082	(9.4)	−0.47	3105	(10.6)	3048	(10.4)	−0.52
CCI, mean (standard deviation)	2.1	(1.8)	2.0	(1.8)	−6.07	1.9	(1.8)	2.0	(1.8)	3.87
Chronic heart failure	3320	(2.5)	685	(2.1)	−2.04	608	(2.1)	621	(2.1)	0.25
Cerebral stroke and paralytic disease	4116	(3.1)	913	(2.8)	−1.32	805	(2.8)	804	(2.8)	−0.02
Chronic pulmonary disease	3328	(2.5)	716	(2.2)	−1.55	574	(2.0)	623	(2.1)	0.97
Diabetes	39 927	(29.6)	9165	(27.9)	−3.10	8063	(27.6)	8125	(27.8)	0.39
Chronic kidney disease	3126	(2.3)	761	(2.3)	−0.01	758	(2.6)	671	(2.3)	−1.56
Severe liver disfunction	11 989	(8.9)	2827	(8.6)	−0.83	2876	(9.8)	2553	(8.7)	−3.08
Metastasis	1454	(1.1)	531	(1.6)	3.94	663	(2.3)	466	(1.6)	−3.89
Lip TACE	77 089	(57.2)	18 974	(57.8)	0.93	17 627	(60.3)	17 185	(58.8)	−2.52
History of liver abscess (≤180 days)	120	(0.1)	28	(0.1)	−0.10	28	(0.1)	23	(0.1)	−0.47
Previous procedure for hepatic cancer (≤180 days)	52 053	(38.6)	13 139	(40.0)	2.31	12 060	(41.3)	11 698	(40.0)	−2.06
Type of hospital										
Academic	39 651	(29.4)	8673	(26.4)	−5.46	6353	(21.7)	7152	(24.5)	5.34
Advanced treatment hospital	23 595	(17.5)	7297	(22.2)	9.80	8064	(27.6)	6565	(22.5)	−9.58
Other	71 466	(53.1)	16 862	(51.4)	−2.77	14 794	(50.6)	15 494	(53.0)	3.92
Hospital volume[a]										
<51	40 578	(30.1)	10 717	(32.6)	4.45	9961	(34.1)	9765	(33.4)	−1.16
51–100	35 591	(26.4)	8681	(26.4)	0.04	8343	(28.6)	7781	(26.6)	−3.50
≥101	58 543	(43.5)	13 434	(40.9)	−4.20	10 907	(37.3)	11 665	(39.9)	4.36
Presence of an infectious disease unit	9461	(7.0)	2623	(8.0)	3.02	2401	(8.2)	2053	(7.0)	−3.62
Fiscal year of admission[b]										
2010	12 818	(9.5)	3120	(9.5)	−0.03	2735	(9.4)	2692	(9.2)	−0.41
2011	20 233	(15.0)	5343	(16.3)	2.83	5402	(18.5)	4807	(16.5)	−4.35
2012	21 113	(15.7)	5093	(15.5)	−0.36	4504	(15.4)	4535	(15.5)	0.24
2013	19 395	(14.4)	5111	(15.6)	2.69	4860	(16.6)	4538	(15.5)	−2.44
2014	22 438	(16.7)	5557	(16.9)	0.59	4958	(17.0)	5008	(17.1)	0.37
2015	21 321	(15.8)	4868	(14.8)	−2.26	3995	(13.7)	4392	(15.0)	3.19
2016	17 394	(12.9)	3740	(11.4)	−3.77	2757	(9.4)	3239	(11.1)	4.49

BMI, body mass index; CCI, Charlson comorbidity index; Lip, lipiodol; TACE, transarterial chemoembolization; SD, standardized difference.
[a] Number of TACE procedures performed annually at each hospital.
[b] Japanese fiscal year begins in April and ends in March.

Table 2
Classes of antibiotics provided to patients in the antibiotics group

Class	All eligible patients (*n* = 134 712)		Matched cohort (*n* = 29 211)	
First-generation cephalosporin	58 258	(43.2)	12 127	(41.5)
Second-generation cephalosporin	14 693	(10.9)	2988	(10.2)
Third-generation cephalosporin	9655	(7.2)	2020	(6.9)
Cefoperazone/sulbactam	25 140	(18.7)	5858	(20.1)
Ampicillin/sulbactam	2072	(1.5)	378	(1.3)
Oxacephem	4538	(3.4)	1082	(3.7)
Cephamycin	20 356	(15.1)	4758	(16.3)

For the propensity score–matched patients, there were no significant differences in the in-hospital mortality. Requirement for red blood cell transfusion within 30 days was significantly but slightly higher in the antibiotics group than the no-antibiotics group. The length of stay was longer in the antibiotics group than in the no-antibiotics group (median (interquartile range), 10 (8–14) days vs. 9 (8–12) days; $p < 0.001$). Total cost of hospitalization was higher in the antibiotics group than the no-antibiotics group. The occurrence of suspected CDI in the matched cohort was not significantly different but was higher in the antibiotics group than the no-antibiotics group (24/29 211, 0.08% vs. 13/29 211, 0.04%; p 0.070) (Table 3).

Among 88 patients receiving procedural interventions after matching, 11 (47.8%) of 23 patients in the antibiotics group and 40 (61.5%) of 65 patients in the no-antibiotics group required procedural intervention during hospitalization for TACE. For these patients, the in-hospital mortality was 9.1% (1/11) and 5.0% (2/40), respectively.

Table 3
Comparison of outcomes between groups in the matched cohort

Outcome	Antibiotics (n = 29 211)		No antibiotics (n = 29 211)		Relative risk (95% CI)	Risk reduction (95% CI)	p
Liver abscess requiring procedural intervention	23	(0.08)	65	(0.22)	0.35 (0.22 to 0.57)	0.0014 (0.0008 to 0.0021)	<0.001
In-hospital mortality (≤30 days)	112	(0.38)	111	(0.38)	1.01 (0.78 to 1.31)	−0.00003 (−0.0010 to 0.0010)	0.947
RBC transfusion (≤30 days)	611	(2.1)	542	(1.9)	1.13 (1.01 to 1.26)	−0.0024 (−0.0046 to −0.0001)	0.04
Length of stay (days), median [mean] (interquartile range)	10 [12.2]	(8–14)	9 [11.3]	(8–12)	—	—	<0.001
Total cost of hospitalization (€), median [mean] (interquartile range)	5532 [6091]	(4862–6524)	5242 [5778]	(4614–6172)	—	—	<0.01
Clostridioides difficile infection[a]	24	(0.08)	13	(0.04)	1.85 (0.94 to 3.63)	−0.0004 (−0.0008 to 0.00004)	0.070

Data are shown as n (%) unless otherwise specified. Pearson chi-square test was used for proportions and Mann-Whitney U test for length of stay and total cost of hospitalization. CI, confidence interval; ICD-10, International Classification of Diseases, Tenth Revision; RBC, red blood cell.
[a] Defined by record of CDI (ICD-10 code A047) after admission or need for oral vancomycin on day of or after transcatheter arterial chemoembolization.

In the sensitivity analysis for multiple antibiotics, antibiotics ordered together with TACE and multiple procedures, the proportion of patients requiring procedural intervention was also significantly lower in the antibiotics group (Supplementary Tables S5, S6 and S7). In the analyses of outcomes according to timing and discharge status, liver abscess requiring procedural intervention occurred less frequently in the antibiotics group at ≤15 days of TACE. This trend was consistent in outcomes during the hospitalization for TACE and outcomes during readmissions (Supplementary Table S8).

Discussion

This study investigated the association between prophylactic antibiotic use for TACE and liver abscess requiring procedural intervention after TACE. We used a large nationwide database and conducted propensity score matching to adjust for patient and hospital characteristics. Prophylactic antibiotic use was associated with a significant reduction in procedural intervention for liver abscess but a slight increase in the length of stay and the total cost of hospitalization.

To our knowledge, this is the first study with sufficient sample size to evaluate liver abscess after TACE. Because liver abscess is rare, previous studies on this condition did not have enough statistical power to compare occurrence rates [10,11]. In our study, we used the DPC database, a nationwide database in Japan, and analysed approximately 30 000 patients in each group.

We defined prophylactic antibiotics as those prescribed on the day of TACE. Considering a possibility of including therapeutic antibiotics initiated on the day of TACE, we conducted a sensitivity analysis limiting antibiotics to those ordered together with the TACE procedure. The main outcome of the study was defined by procedures. Although abscesses smaller than 3 to 5 cm can be treated by antibiotics alone [21], previous observational studies showed that 40% to 100% of liver abscesses after TACE required abscess drainage [1,3,5,8]. Considering the possible effect of differences in threshold for performing a treatment procedure for liver abscess, we conducted another sensitivity analysis of liver abscess according to timing and discharge status. There was no significant difference between both groups in the in-hospital mortality among patients with liver abscess. This suggests that the severity of liver abscess was similar in both groups.

Biliary abnormalities and previous biliary interventions are important risk factors for liver abscess after TACE [1,22]. Two guidelines recommended routine prophylactic antibiotics for patients undergoing TACE [23,24], while another guideline recommended using prophylactic antibiotics only in patients with risks such as biliary abnormalities [25]. Although we adjusted for a history of liver abscess within 180 days, we could not observe all biliary abnormalities or previous biliary interventions. Currently, there is no Japanese guideline describing the necessity of antibiotics before TACE. The guidelines for perioperative antimicrobials for other procedures was updated during the study period. In order to reduce the effect of the change in guidelines, we adjusted the fiscal year of admission in the logistic regression model. However, there could be residual confounding.

We used the requirement for blood transfusion as a falsification endpoint. A slightly higher number of patients in the antibiotics group experienced blood transfusion after matching, suggesting that the general status of patients in the antibiotics group was no less severe than that of the no-antibiotics group. Median length of stay was longer and total cost of hospitalization was higher in the antibiotics group than the no-antibiotics group. The increase in cost can be attributed to a 1-day increase in the length of stay. These differences may be due to antibiotic side effects or other unmeasured confounders and may be important from perspective of patients or hospital management. Further detailed study is warranted to investigate factors for length of stay and total cost of hospitalization.

Because liver abscess is rare, the recommendation of prophylactic antibiotics for TACE may depend on the frequency of adverse effects. In our study, the effect size of the antibiotics for preventing liver abscess was relatively small; the number needed to treat was 696 (95% CI, 476–1223). The proportion of suspected CDI was marginally higher in the group with antibiotics (0.08% (24/29 211) vs. 0.04% (13/29 211), p 0.07). Further research on other complications is required to conclude whether the preventive effect of prophylactic antibiotics for TACE outweigh their adverse effects.

This study has several limitations. First, we used surrogate outcomes for liver abscess. Results of the sensitivity analyses of outcomes according to timing and admission status suggest that the characteristics of the liver abscess were similar in the two groups. However, the analysis did not account for liver abscesses that were treated without procedural intervention. If the effect of prophylactic antibiotics is larger for small abscess, our results may be an underestimation of the overall effect. Second, biliary abnormalities, which are a major risk factor of liver abscess after TACE, were not directly measured in our database. Third, the DPC database did not contain data on several risk factors for liver abscess, such as biliary abnormalities, dose and timing of prophylactic

antibiotics and size of embolized area. Fourth, we could not clearly distinguish between therapeutic and prophylactic antibiotics. The antibiotics group could contain some patients with therapeutic antibiotics on the day of TACE. Because these patients were likely to be at higher risk of liver abscesses, the effect of prophylactic antibiotics may be underestimated. Fifth, our database did not contain microbiologic information. Sixth, this study was conducted in Japan, where the minimum inhibitory concentration of cefazolin for the majority of *Escherichia coli* or *Klebsiella pneumoniae* is low. Hence, the results of this study may not be applicable to areas with a high prevalence of resistant bacteria. Finally, outcomes after discharge could not be observed when the liver abscess was treated at a hospital different from the hospital where TACE was performed.

In conclusion, although prophylactic antibiotic use was associated with a slightly longer length of stay and hospitalization cost, it was significantly associated with a reduction in outcomes indicative of liver abscess. Further investigation about benefits and harms is required to justify the routine administration of prophylactic antibiotics for TACE.

Transparency declaration

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2021.01.014.

References

[1] Song SY, Chung JW, Han JK, Lim HG, Koh YH, Park JH, et al. Liver abscess after transcatheter oily chemoembolization for hepatic tumors: incidence, predisposing factors, and clinical outcome. J Vasc Interv Radiol 2001;12:313–20.
[2] Jia Z, Tu J, Cao C, Wang W, Zhou W, Ji J, et al. Liver abscess following transarterial chemoembolization for the treatment of hepatocellular carcinoma: a retrospective analysis of 23 cases. J Cancer Res Ther 2018;14:S628–33.
[3] Tu J, Jia Z, Ying X, Zhang D, Li S, Tian F, et al. The incidence and outcome of major complication following conventional TAE/TACE for hepatocellular carcinoma. Medicine (Baltimore) 2016;95:e5606.
[4] Lv WF, Lu D, He YS, Xiao JK, Zhou CZ, Cheng DL. Liver abscess formation following transarterial chemoembolization: clinical features, risk factors, bacteria spectrum, and percutaneous catheter drainage. Medicine (Baltimore) 2016;95:e3503.
[5] Kim W, Clark TWI, Baum RA, Soulen MC. Risk factors for liver abscess formation after hepatic chemoembolization. J Vasc Interv Radiol 2001;12:965–8.
[6] Hope WW, Vrochides DV, Newcomb WL, Mayo-Smith WW, Iannitti DA. Optimal treatment of hepatic abscess. Am Surg 2008;74:178–82.
[7] Sun Z, Li G, Ai X, Luo B, Wen Y, Zhao Z, et al. Hepatic and biliary damage after transarterial chemoembolization for malignant hepatic tumors: incidence, diagnosis, treatment, outcome and mechanism. Crit Rev Oncol Hematol 2011;79:164–74.
[8] Arslan M, Degirmencioglu S. Liver abscesses after transcatheter arterial embolization. J Int Med Res 2019;47:1124–30.
[9] Woo S, Chung JW, Hur S, Joo SM, Kim HC, Jae HJ, et al. Liver abscess after transarterial chemoembolization in patients with bilioenteric anastomosis: frequency and risk factors. AJR Am J Roentgenol 2013;200:1370–7.
[10] Castells A, Bruix J, Ayuso C, Brú C, Montayà X, Boix L, et al. Transarterial embolization for hepatocellular carcinoma. Antibiotic prophylaxis and clinical meaning of postembolization fever. J Hepatol 1995;22:410–5.
[11] Plentz RR, Lankisch TO, Bastürk M, Müller CC, Kirchhoff T, Gebel M, et al. Prospective analysis of German patients with hepatocellular carcinoma undergoing transcatheter arterial chemoembolization with or without prophylactic antibiotic therapy. J Gastroenterol Hepatol 2005;20:1134–6.
[12] Wang Q, Hodavance M, Ronald J, Suhocki PV, Kim CY. Minimal risk of biliary tract complications, including hepatic abscess, after transarterial embolization for hepatocellular carcinoma using concentrated antibiotics mixed with particles. Cardiovasc Interv Radiol 2018;41:1391–8.
[13] Watchmaker JM, Lipnik AJ, Fritsche MR, Baker JC, Mouli SK, Geevarghese S, et al. Are prophylactic antibiotics necessary prior to transarterial chemoembolization for hepatocellular carcinoma in patients with native biliary anatomy? J Surg Oncol 2018;117:1312–7.
[14] Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096.
[15] Yasunaga H, Matsui H, Horiguchi H, Fushimi K, Matsuda S. Clinical epidemiology and health services research using the diagnosis procedure combination database in Japan. Asian Pac J Dis Manag 2015;7:19–24.
[16] Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011;173:676–82.
[17] Ministry of Health, Labour and Welfare, Japan. Reporting system for functions of medical institutions and formation of community health care visions. In Japanese. Available at: https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000055891.html.
[18] Prasad V, Jena AB. Prespecified falsification end points: can they validate true observational associations? JAMA 2013;309:241–2.
[19] Jena AB, Sun E, Goldman DP. Confounding in the association of proton pump inhibitor use with risk of community-acquired pneumonia. Gen Intern Med 2013;28:223–30.
[20] Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Commun Stat Simul C 2009;38:1228–34.
[21] Lardière-Deguelte S, Ragot E, Amroun K, Piardi T, Dokmak S, Bruno O, et al. Hepatic abscess: diagnosis and management. J Visc Surg 2015;152:231–43.
[22] Basile A, Carrafiello G, Ierardi AM, Tsetis D, Brountzos E. Quality-improvement guidelines for hepatic transarterial chemoembolization. Cardiovasc Interv Radiol 2012;35:765–74.
[23] Chehab MA, Thakor AS, Tulin-Silver S, Connolly BL, Cahill AM, Ward TJ, et al. Adult and pediatric antibiotic prophylaxis during vascular and IR procedures: a society of interventional radiology practice parameter update endorsed by the cardiovascular and interventional radiological society of europe and the Canadian association for interventional radiology. J Vasc Interv Radiol 2018;29:1483–1501.e2.
[24] Ourania K, Hallam Caroline. Trust guideline for the management of: antibiotic prophylaxis in adults undergoing procedures in interventional radiology. Available at: http://www.nnuh.nhs.uk/publication/download/antibiotic-prophylaxis-in-adults-undergoing-procedures-in-interventional-radiology-v-4.
[25] Moon E, Tam M, Kikano R, Karuppasamy K. Prophylactic antibiotic guidelines in modern interventional radiology practice. Semin Interv Radiol 2010;27:327–37.