

ORIGINAL ARTICLE

## 침술과 C형간염 바이러스 전파 위험성: 체계적 문헌 고찰 및 메타분석

현명환<sup>1,2</sup>, 김지훈<sup>3</sup>, 장정원<sup>4</sup>, 송정은<sup>5</sup>, 송도선<sup>6</sup>, 이해원<sup>7</sup>, 조영운<sup>8</sup>, 김기애<sup>9</sup>, 윤아일린<sup>10</sup>, 신동현<sup>11</sup>, 김순선<sup>12</sup>, 임선영<sup>13</sup>, 양현<sup>14</sup>, 안지현<sup>15</sup>

차의과학대학교 일산차병원 암통합진료센터<sup>1</sup>, 차의과학대학교 일산차병원 혈액중양내과<sup>2</sup>, 고려대학교 의과대학 고려대학교구로병원 소화기내과<sup>3</sup>, 가톨릭대학교 의과대학 서울성모병원 소화기내과<sup>4</sup>, 대구가톨릭대학교 의과대학 대구가톨릭대학교병원 소화기내과<sup>5</sup>, 가톨릭대학교 의과대학 성빈센트병원 소화기내과<sup>6</sup>, 연세대학교 의과대학 세브란스병원 소화기내과<sup>7</sup>, 중앙대학교 의과대학 중앙대학교병원 소화기내과<sup>8</sup>, 경희대학교 의과대학 경희대학교병원 소화기내과<sup>9</sup>, 한양대학교 의과대학 한양대학교병원 소화기내과<sup>10</sup>, 성균관대학교 의과대학 삼성서울병원 소화기내과<sup>11</sup>, 아주대학교 의과대학 아주대학교병원 소화기내과<sup>12</sup>, 고려대학교 의과대학 고려대학교안암병원 소화기내과<sup>13</sup>, 가톨릭대학교 의과대학 은평성모병원 소화기내과<sup>14</sup>, 한양대학교 의과대학 한양대학교구리병원 소화기내과<sup>15</sup>

### Risk of Hepatitis C Virus Transmission through Acupuncture: A Systematic Review and Meta-Analysis

Myung Han Hyun<sup>1,2</sup>, Ji Hoon Kim<sup>3</sup>, Jeong Won Jang<sup>4</sup>, Jeong Eun Song<sup>5</sup>, Do Seon Song<sup>6</sup>, Hye Won Lee<sup>7</sup>, Young Youn Cho<sup>8</sup>, Gi-Ae Kim<sup>9</sup>, Eileen L. Yoon<sup>10</sup>, Dong Hyun Sinn<sup>11</sup>, Soon Sun Kim<sup>12</sup>, Sun Young Yim<sup>13</sup>, Hyun Yang<sup>14</sup> and Jihyun An<sup>15</sup>

Integrative Cancer Center, CHA Ilsan Medical Center, Goyang<sup>1</sup>; Department of Oncology and Hematology, CHA Ilsan Medical Center, CHA University, Goyang<sup>2</sup>; Department of Internal Medicine, Korea University College of Medicine, Korea University Guro Hospital, Seoul<sup>3</sup>; Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul<sup>4</sup>; Department of Internal Medicine, Daegu Catholic University Medical Center, Daegu Catholic University School of Medicine, Daegu<sup>5</sup>; Department of Internal Medicine, The Catholic University of Korea, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon<sup>6</sup>; Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul<sup>7</sup>; Department of Internal Medicine, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul<sup>8</sup>; Department of Internal Medicine, Kyung Hee University Hospital, Kyung Hee University College of Medicine, Seoul<sup>9</sup>; Department of Internal Medicine, Hanyang University Seoul Hospital, Hanyang University School of Medicine, Seoul<sup>10</sup>; Department of Gastroenterology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul<sup>11</sup>; Department of Gastroenterology, Ajou University Hospital, Ajou University School of Medicine, Suwon<sup>12</sup>; Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul<sup>13</sup>; Division of Gastroenterology and Hepatology, Department of Internal Medicine, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul<sup>14</sup>; Department of Gastroenterology and Hepatology, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri<sup>15</sup>, Korea

**Background/Aims:** Chronic hepatitis C is a major risk factor for liver cirrhosis, hepatocellular carcinoma, and hepatic failure. Although traditional practices, including acupuncture, tend to increase the risk of HCV infection, the association remains controversial. Therefore, the current meta-analytical study was undertaken to evaluate the risks of acupuncture and hepatitis C transmission.

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교신저자: 안지현, 11923, 구리시 경춘로 153, 한양대학교 의과대학 한양대학교구리병원 소화기내과

Correspondence to: Jihyun An, Department of Gastroenterology and Hepatology, Hanyang University Guri Hospital, Hanyang University College of Medicine, 153 Gyeongchun-ro, Guri 11923, Korea. Tel: +82-31-560-2234, Fax: +82-31-560-2539, E-mail: starlit1@naver.com, ORCID: <https://orcid.org/0000-0002-0110-0965>

교신저자: 양현, 03312, 서울시 은평구 통일로 1021, 가톨릭대학교 의과대학 은평성모병원 소화기내과

Correspondence to: Hyun Yang, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 1021 Tongil-ro, Eunpyeong-gu, Seoul 03312, Korea. Tel: +82-2-2030-2530, Fax: +82-2-2030-2521, E-mail: oneggu@naver.com, ORCID: <https://orcid.org/0000-0001-6588-9806>

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Conflict of interest: None

**Methods:** Two researchers independently screened studies from the databases encompassing the period from inception to May 12, 2022. Baseline demographics, HCV transmission OR, and 95% CIs were extracted, pooled, and analyzed using random-effect models. Subgroup analyses utilizing study design and ethnicity were performed. Heterogeneity and publication bias were analyzed using the Higgins  $I^2$  test and funnel plots, respectively.

**Results:** In all, 28 studies with 194,826 participants (178,583 controls [91.7%] vs. 16,243 acupuncture users [8.3%]) were included in the final analysis. The pooled analysis showed that acupuncture users had a significantly higher HCV transmission rate than controls with heterogeneity (OR, 1.84 [1.46–2.32];  $p < 0.001$ ;  $I^2 = 80\%$ ). In the subgroup analysis, both cross-sectional case-control ( $n = 14$ ; OR, 1.96 [1.47–2.61];  $p < 0.001$ ;  $I^2 = 88\%$ ) and cross-sectional studies ( $n = 12$ ; OR, 1.85 [1.32–2.61];  $p < 0.001$ ;  $I^2 = 0\%$ ) showed significantly higher HCV infection rates in the acupuncture group than in the control group. Both Asian and non-Asian acupuncture users showed a higher HCV transmission risk than the controls (all  $P_s < 0.001$ ). No significant publication bias was observed.

**Conclusions:** Our findings indicate that acupuncture increases the risk of HCV transmission. Due to HCV's contagiousness, unsafe medical and social practices (including acupuncture) should be performed with caution. (*Korean J Gastroenterol* 2023;82:127-136)

**Key Words:** Acupuncture; Hepatitis C virus; Transmission; Meta-analysis

## INTRODUCTION

HCV infection is a global health problem that can elicit liver cirrhosis, hepatocellular carcinoma (HCC), and hepatic failure.<sup>1</sup> The World Health Organization reported that in 2019, approximately 290,000 people died from hepatitis C worldwide, mostly from cirrhosis and HCC.<sup>2</sup> HCV is primarily a blood-borne virus that is transmitted through unsafe therapeutic injections, injection drug use, blood transfusion, accidental needle stick injury, and sexual contact.<sup>3</sup> Despite recent improvements in direct-acting antiviral agents for chronic hepatitis C, the prevention of HCV transmission via unsafe invasive medical practices, including acupuncture, remains inadequate.<sup>4</sup>

Acupuncture was first performed over 2,500 years ago in China and consists of the therapeutic insertion and manipulation of thin needles at more than 2,000 acupuncture points connected by yin and yang pathways.<sup>5</sup> Over the centuries, acupuncture has extended to other continents as a novel treatment strategy for chronic diseases, including musculoskeletal pain and hypertension.<sup>6</sup> In recent decades, medical oriental doctors, physiotherapists, and chiropractors worldwide are applying acupuncture needling approaches to treat musculoskeletal pain and other health problems.<sup>7</sup>

Although acupuncture is more widely applied than before, unsafe acupuncture practices in the community have increased the risk of HCV transmission.<sup>8,9</sup> However, previous meta-analyses showed insufficient data and controversial results.<sup>10-13</sup> Therefore, this study comprehensively analyzes and performs an updated meta-analysis to assess the association between acupuncture and the risk of HCV transmission.

## SUBJECTS AND METHODS

### 1. Search strategy and eligibility criteria

We conducted a systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (Supplementary Table 1). From January 2000 to May 2022, two authors (MHH and YH) independently identified eligible articles from databases such as PUBMED, EMBASE, and the Cochrane Library, using the structured keywords “acupuncture,” “sham,” “piercing,” “tattoo,” “hepatitis C virus,” “HCV,” “chronic hepatitis C,” and “CHC.” For electronic scrutiny, all the study references and relevant review articles were manually searched. Disagreements were resolved through discussion and consensus referrals to a third investigator (JA). All the analyzed studies were published in English. Detailed search terms and strategies are listed in Supplementary Table 2.

The full text of potentially relevant publications of clinical studies was analyzed based on the following inclusion criteria: (1) non-randomized studies that compared the clinical effects of acupuncture and HCV transmission as either primary or secondary outcomes; (2) extractable RR or OR and their corresponding CI, or provided with enough data to compute these parameters; (3) participant age  $> 18$  years; and (4) study sample size  $> 100$ . If the cases included in a study were published in different phases of duplication, the most recent publications or the largest cohort was selected. Studies excluded were non-human studies (animal or cell studies), non-peer-reviewed articles (meeting abstracts, case reports, editorials, clinical trial protocols, correspondence letters, or editorials), and studies that did not meet the inclusion criteria.

## 2. Data extraction and quality assessment

Data extracted included author names, publication year, country, ethnicity, enrollment period, study design, study population, sample size, HCV infection rate, adjusted OR or RR, and 95% CI. Two independent reviewers (MHH and YH) reviewed the selected studies. The study designs were categorized as a cross-sectional case-control study, a cross-sectional cohort study, and a cross-sectional study. Ethnicity was classified as either Asian or non-Asian. The risk of bias was assessed by adapting the quality assessment scale from the modified Newcastle–Ottawa Scale according to three categories: selection (range, 0–5 stars), comparability (range, 0–2 stars), and outcome assessment (range, 0–3 stars).<sup>14</sup> More stars indicate a lower risk of bias. Each item was scored as “yes (star),” “no,” or “unclear,” and an agreement between the three authors (MHH, YH, and JA) was required.

## 3. Statistical analysis

A random-effects model was used to calculate the pooled OR and 95% CI for the association between acupuncture and HCV transmission risk due to the predicted high heterogeneity. The analysis of heterogeneity was assessed using the Higgins  $I^2$  statistic, in which 50% or more was considered significant heterogeneity.<sup>15</sup> Funnel plots and Egger’s test for HCV transmission risk were used to assess publication bias.<sup>16</sup> A subgroup analysis was performed to investigate the source of

heterogeneity according to the study design and ethnicity. Statistical significance was set at  $p < 0.05$ . Statistical analysis was conducted using Review Manager 5.3 (The Cochrane Collaboration).

## RESULTS

### 1. Article selection

Fig. 1 shows the detailed steps of the study selection. Overall, we identified 1,465 potentially relevant studies through database searches and additional records by manual search. After excluding articles subsequent to primary screening, 373 studies were retrieved for full-text review. Of these, 345 articles were excluded as they did not meet the inclusion criteria: 38 conference abstracts only, 245 with other transmission routes, 24 insufficient HCV data, 5 genetic studies, 6 case series, 12 review papers, and 15 no extractable data. Finally, 28 studies with 194,826 participants were included in the systematic review and meta-analysis.<sup>17-44</sup>

### 2. Study characteristics and quality assessment

Among the 194,826 participants included in the 28 studies, 178,583 (91.7%) were control participants and 16,243 (8.3%) had undergone acupuncture. Most studies were cross-sectional case-control studies ( $n=14$  [50.0%]),<sup>17,18,21-24,26,28,29,32,35,38-40</sup> cross-sectional studies ( $n=12$  [42.9%]),<sup>19,20,25,27,31,33-34,36,37,41,43-44</sup> and cross-sectional cohort studies ( $n=2$  [7.1%]).<sup>30,42</sup> Categorizing by ethnicity, 16 (57.1%) studies included Asian populations, whereas 12 studies included non-Asian populations. Most studies analyzed hospital samples ( $n=13$  [46.4%]) and the general population ( $n=9$  [32.2%]). The majority of the studies collected acupuncture data from questionnaires, except for 3 studies procured from medical records.<sup>26,33,44</sup> The baseline demographics of the included studies are presented in Table 1. The quality assessment results (Supplementary Table 3) adopted the Newcastle–Ottawa scale, which showed that most of the included studies scored more than three stars in the selection and outcome assessment sections. However, the comparability section showed diverse results between studies (0–2 stars).

### 3. Association between acupuncture and HCV transmission

In the overall analysis, acupuncture users showed a higher

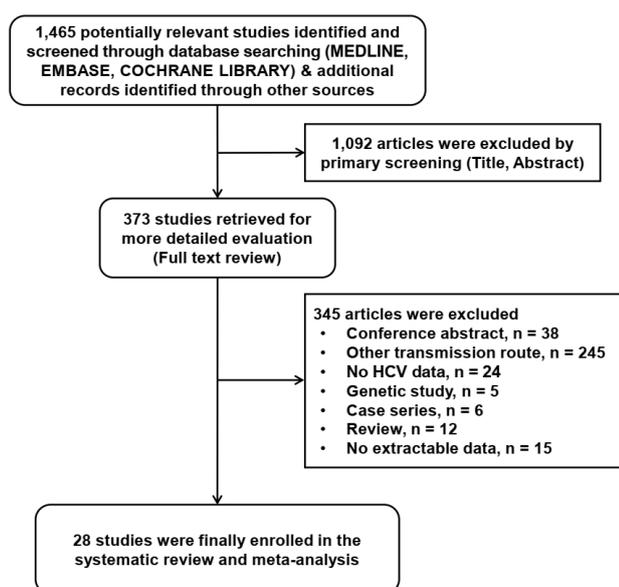


Fig. 1. Study flow chart.

**Table 1.** Characteristics of the Studies Included in the Meta-Analysis

Author name	Year	Enrollment periods	Country	No. of total samples (total)	No. of HCV infections (total)	No. of acupuncture users (acupuncture)	No. of HCV infections (acupuncture)	RR/OR	95% CI	Acupuncture data collection	Study population	Study design
Salama <sup>17</sup>	2020	2011–2012	Egypt	450	150	182	93	3.87	2.56–5.84	Questionnaire	General population	Cross-sectional case-control study
Mohd Suan et al. <sup>18</sup>	2019	2015–2018	Malaysia	510	255	31	12	0.61	0.28–1.28	Questionnaire	Hospital samples	Cross-sectional case-control study
Wasitthankasem et al. <sup>19</sup>	2018	2015–2017	Thailand	3,032	266	55	7	1.53	0.69–3.42	Questionnaire	Hospital samples	Cross-sectional study
Mac Donald-Ottevanger et al. <sup>20</sup>	2016	2012–2013	Suriname	2,092	22	91	1	1.05	0.14–7.88	Questionnaire	Hospital samples	Cross-sectional study
Sohn et al. <sup>21</sup>	2016	2013	Korea	468	234	328	193	3.45	2.26–5.28	Questionnaire	Hospital sample+ Healthy controls	Cross-sectional case-control study
Huang et al. <sup>22</sup>	2015	2011–2012	China	149,175	1,175	10,260	230	3.35	2.89–3.87	Questionnaire	General population	Cross-sectional case-control study
Huang et al. <sup>23</sup>	2015	2009–2011	China	863	174	102	21	1.03	0.62–1.71	Questionnaire	Blood donors	Cross-sectional case-control study
Carney et al. <sup>24</sup>	2013	2004–2006	US	3,871	1,930	704	419	1.61	1.37–1.90	Questionnaire	General population	Cross-sectional case-control study
Kin et al. <sup>25</sup>	2013	2001–2011	US	1,232	33	18	3	7.89	2.17–28.72	Medical records	General population	Cross-sectional study
Seong et al. <sup>26</sup>	2013	2007–2011	Korea	1,669	1,147	1,360	953	1.39	1.07–1.80	Questionnaire	Hospital samples+ Healthy controls	Cross-sectional case-control study
Ahmed et al. <sup>27</sup>	2012	2007–2009	Pakistan	2,000	110	1	0	5.70	0.23–140.72	Questionnaire	General population	Cross-sectional study
Kim et al. <sup>28</sup>	2012	2007–2010	Korea	885	679	711	557	1.54	1.06–2.23	Questionnaire	Hospital samples	Cross-sectional case-control study
He et al. <sup>29</sup>	2011	2007	China	915	305	69	49	5.65	3.29–9.69	Questionnaire	Blood donors	Cross-sectional case-control study
Vickery et al. <sup>30</sup>	2009	1999–2001	Australia	2,000	98	651	33	1.05	0.69–1.62	Questionnaire	Hospital samples (endoscopy)	Cross-sectional cohort study
Nguyen et al. <sup>31</sup>	2007	2002	Vietnam	837	8	249	3	1.42	0.34–6.00	Medical records	General population	Cross-sectional study
Kamochikine et al. <sup>32</sup>	2006	1997–2001	France	1,176	427	323	155	1.97	1.52–2.56	Questionnaire	Hospital samples+General population	Cross-sectional case-control study
Méndez-Sánchez et al. <sup>33</sup>	2006	NE	Mexico	376	3	48	0	0.96	0.05–18.85	Questionnaire	Nurse samples	Cross-sectional study

Table 1. Continued

Author name	Year	Enrollment periods	Country	No. of total samples (total)	No. of HCV infections (total)	No. of acupuncture users (acupuncture)	No. of HCV infections (acupuncture)	RR/OR	95% CI	Acupuncture data collection	Study population	Study design
Dominitz et al. <sup>34</sup>	2005	1998–2000	US	1,241	50	103	5	1.24	0.48–3.19	Questionnaire	Military samples	Cross-sectional study
Hand and Vasquez <sup>35</sup>	2005	2000–2002	US	627	320	9	7	3.41	0.70–16.55	Questionnaire	Hospital samples	Cross-sectional case-control study
Yilcirim et al. <sup>36</sup>	2005	1997–2001	Turkey	302	151	1	1	3.02	0.12–74.72	Questionnaire	Hospital samples	Cross-sectional study
Lee et al. <sup>37</sup>	2004	1999	Taiwan	713	14	19	0	1.20	0.07–20.91	Questionnaire	Adolescents	Cross-sectional study
Brandão and Fuchs <sup>38</sup>	2002	1995–1996	Brazil	534	178	25	10	1.35	0.60–3.08	Questionnaire	Blood donors	Cross-sectional case-control study
Brillman et al. <sup>39</sup>	2002	1996	US	121	18	15	3	1.52	0.38–6.02	Questionnaire	Hospital samples	Cross-sectional case-control study
Kim et al. <sup>40</sup>	2002	1994–1998	Korea	365	139	280	111	1.34	0.82–2.23	Questionnaire	Hospital samples+ Community control	Cross-sectional case-control study
Shin et al. <sup>45</sup>	2002	1999	Korea	700	77	473	63	2.34	1.28–4.27	Questionnaire	General population	Cross-sectional study
Dominguez et al. <sup>42</sup>	2001	1996	Spain	1,258	38	81	3	1.25	0.38–4.17	Questionnaire	General population	Cross-sectional cohort study
Haley and Fischer <sup>43</sup>	2001	1991–1992	US	586	37	33	0	0.21	0.01–3.42	Questionnaire	Hospital samples	Cross-sectional study
Müller et al. <sup>44</sup>	2001	1992	Hungary	585	195	21	9	1.52	0.63–3.68	Medical records	Blood donors	Cross-sectional study

NE, not evaluable.

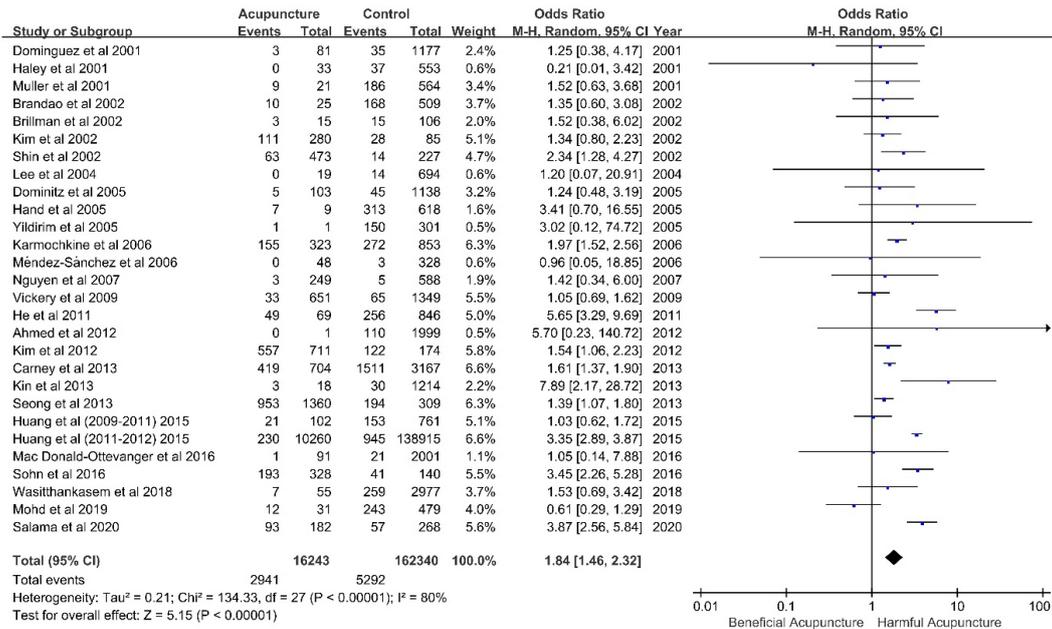


Fig. 2. Pooled analysis of odds ratio for the association between acupuncture and HCV infection. Each dot represents the OR with a 95% CI. The box size represents the weight of the study in the meta-analysis. Weights were obtained using the random-forest model. M-H, Mantel-Haenszel.

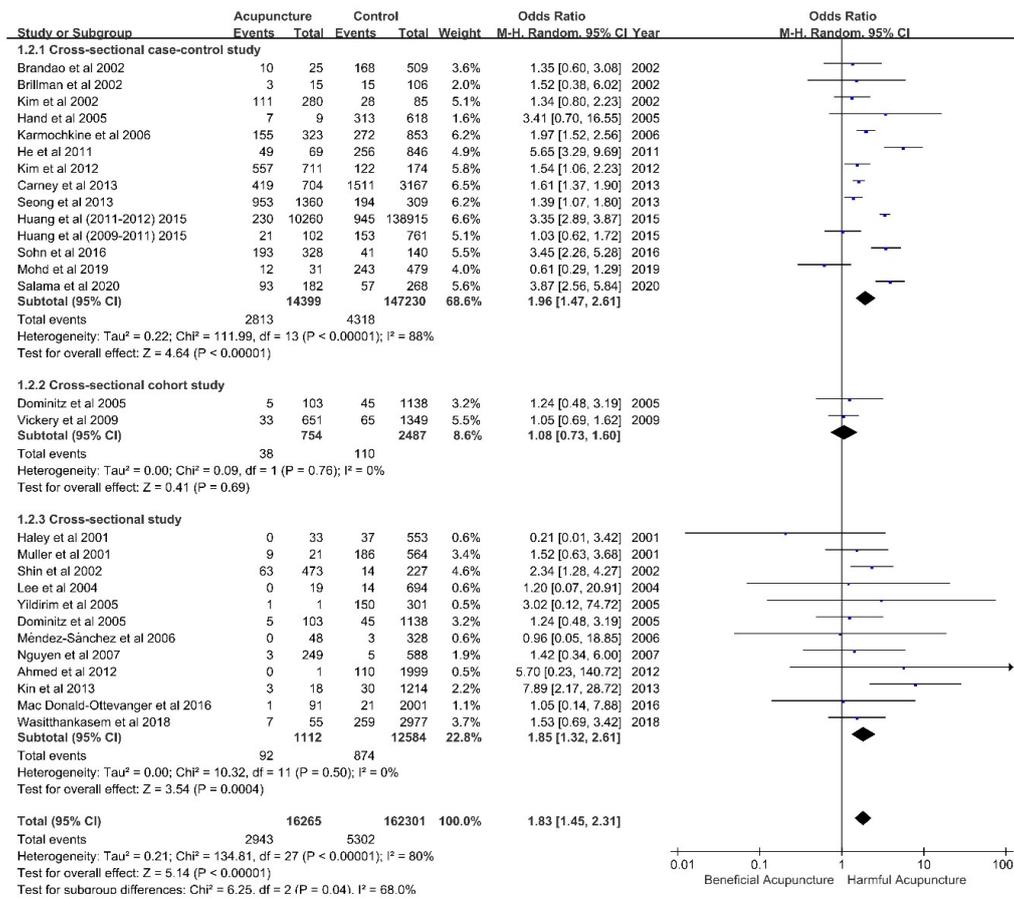
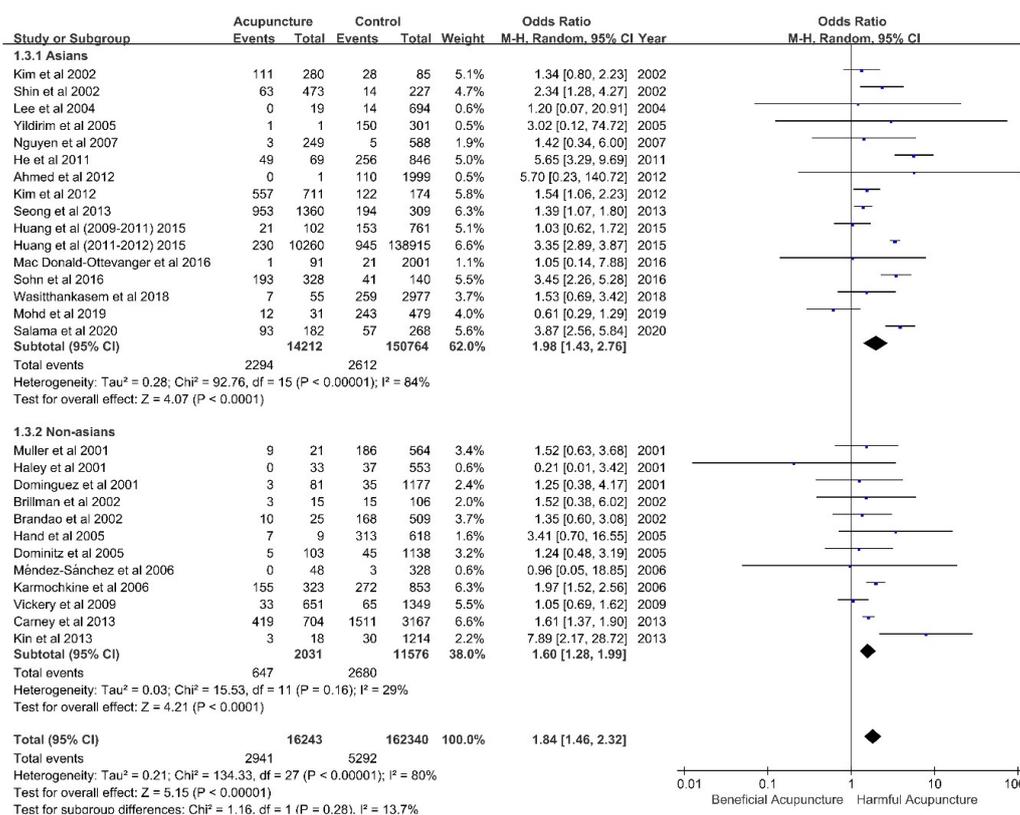
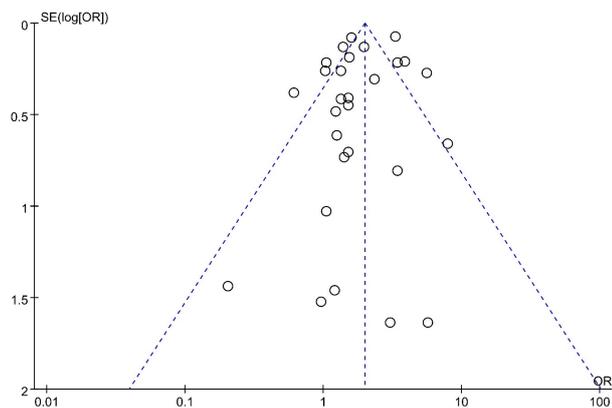


Fig. 3. Pooled analysis of odds ratio for the association between acupuncture and HCV infection according to study design. Each dot represents the OR with a 95% CI. The box size represents the weight of the study in the meta-analysis. Weights were obtained using the random-forest model. M-H, Mantel-Haenszel.



**Fig. 4.** Pooled analysis of odds ratio for the association between acupuncture and HCV infection according to ethnicity. Each dot represents the OR with a 95% CI. The box size represents the weight of the study in the meta-analysis. Weights were obtained using the random-forest model. M-H, Mantel-Haenszel.



**Fig. 5.** Funnel plot for the association between acupuncture and HCV infection. SE, standard error.

HCV transmission rate (17.4% [2,941/16,843]) than control participants (4.6% [8,233/178,583]). The pooled analysis showed statistical significance for the HCV transmission rate in acupuncture users with high-grade heterogeneity (OR, 1.84; 95% CI, 1.46–2.32;  $p < 0.001$ ;  $I^2 = 80%$ ; Fig. 2). Three studies

showed a lower rate of HCV infection in control than in acupuncture subjects.<sup>18,33,43</sup> However, there were no consistent findings between the studies. Among the studies analyzed, four studies reported 0 HCV infection in acupuncture patients due to the small study population.<sup>27,33,37,43</sup>

#### 4. Subgroup analysis and publication bias

Fig. 3 shows the pooled analyses of ORs for the association between acupuncture and HCV transmission, according to the study design. Both cross-sectional case-control studies (OR, 1.96; 95% CI, 1.47–2.61;  $p < 0.001$ ;  $I^2 = 88%$ ) and cross-sectional studies (OR, 1.85; 95% CI, 1.32–2.61;  $p < 0.001$ ;  $I^2 = 0%$ ) showed significantly higher HCV transmission rates in acupuncture users than in controls. However, cross-sectional cohort studies did not show statistical significance between the two groups (OR, 1.08; 95% CI, 0.73–1.60;  $p = 0.760$ ;  $I^2 = 0%$ ). As presented in Fig. 4, both Asian and non-Asian populations showed significantly higher HCV transmission rates in acupuncture users than in controls (Asians: OR, 1.98; 95% CI,

1.43–2.76;  $p < 0.001$ ;  $I^2 = 84\%$ ; non-Asians: OR, 1.60; 95% CI, 1.28–1.99;  $p < 0.001$ ;  $I^2 = 29\%$ ). No significant asymmetry was detected in the funnel plots for the association between acupuncture and HCV infection (Egger's  $p > 0.05$ ; Fig. 5).

## DISCUSSION

This study reports an updated systematic review and meta-analysis of the effects of acupuncture on HCV transmission. By analyzing 28 studies (194,826 participants), we found that acupuncture users showed significantly higher HCV transmission rates than controls (17.4% vs. 4.6%; OR, 1.84; 95% CI, 1.46–2.32,  $p < 0.001$ ). The risk of acupuncture and HCV infection was consistent with the study design (cross-sectional case-control and cross-sectional studies) and ethnicity (Asian and non-Asian populations).

Acupuncture remains popular worldwide and appears to be a relatively safe treatment for the management of lifestyle risk factors, especially for musculoskeletal diseases.<sup>45</sup> The major indications for acupuncture include biological effects on local inflammatory responses, pain control, arthritis, and other joint diseases, as well as a broad range of minor diseases (headaches) that do not respond to conventional treatments.<sup>46,47</sup> However, there is a need for safer acupuncture practices using disposable needles and close monitoring of acupuncturists worldwide.<sup>41</sup> As the prevalence of blood transfusion is less than 1% in the general population, parenteral viral exposure (such as during acupuncture) should be a public health priority to prevent HCV transmission.<sup>48</sup>

A previous meta-analysis regarding percutaneous needle injections, including tattoos, piercings, and acupuncture, showed conflicting results from our study.<sup>10-13</sup> Jafari et al.<sup>10</sup> showed that tattoos were associated with a higher risk of HCV infection (83 studies, 132, 145 participants; pooled OR, 2.24; 95% CI, 2.01–2.50;  $p < 0.001$ ). In this study, non-injection drug users showed the strongest association between tattooing and HCV infection (OR, 5.74; 95% CI, 1.981–6.66).<sup>10</sup> However, Tohme and Holmberg<sup>12</sup> reported no definitive evidence for an increased risk of HCV infection if tattoos and piercings were performed by professional parlors (adjusted OR, 0.8; 95% CI, 0.4–1.7), but a significant risk for tattoos performed in nonprofessional settings (adjusted OR, 3.5; 95% CI, 1.4–8.8). Van Remoortel et al.<sup>13</sup> pooled and analyzed 21 studies and showed that percutaneous needle treatments

(including tattooing, acupuncture, and piercing) increased the HCV infection in blood recipients (tattoo: OR, 5.28; 95% CI, 4.33–6.44;  $p < 0.001$ ; acupuncture: OR, 1.56; 95% CI, 1.17–2.08;  $p = 0.03$ ; piercing: OR, 3.25; 95% CI, 1.68–6.30;  $p = 0.005$ ). The report by Lim et al.<sup>11</sup> analyzed 86 studies investigating tattoos and transfusion-transmitted diseases (HBV, HCV, and HIV) and found that the tattooed group showed a higher risk of HCV infection than the non-tattooed group (OR, 2.89; 95% CI, 2.48–3.37). Although previous meta-analyses have assessed tattooing, piercing, and HCV infection risk, the current study is the first and largest study to focus on acupuncture and HCV infection risk.

This study has several limitations. First, the included studies contained observational data from a cross-sectional design. Second, a substantial degree of heterogeneity may be present; therefore, caution should be taken when interpreting the results. Third, insufficient information on other confounding factors for HCV infection between the acupuncture and control groups may serve as potential limitations. Fourth, since a majority of the studies collected acupuncture data by using questionnaires (25/28; 89.3%) without reporting time intervals between acupuncture and HCV infection, the direct correlation between acupuncture and HCV infection is hard to establish. Lastly, meta-analysis of studies is controversial because uncontrolled confounders may affect pooled estimates. It could be argued that pooling analyses might be inappropriate due to possible heterogeneity which can affect the outcomes of interest.

In conclusion, the evidence from this meta-analysis shows that acupuncture potentially increases the HCV transmission rate. Unsafe medical procedures and social practices, including acupuncture, should be performed with caution. Further large-scale, high-quality studies are warranted in the future.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at the Korean Journal of Gastroenterology website (<https://www.kjg.or.kr/>).

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**Supplementary Table 1.** PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria; participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Methods
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Methods
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Methods
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Methods Table S2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Methods
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Methods
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Methods
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Methods
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Methods
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	Methods
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Methods
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Methods
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Results Figure S1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Results

**Supplementary Table 1.** Continued

Section/topic	#	Checklist item	Reported on page
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Results Table S3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Results
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Results
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Results
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Discussion
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Funding

rom: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009), Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).

**Supplementary Table 2.** Search Strategy

DATABASE	SEARCH KEYWORDS
PUBMED	<p>MEDLINE</p> <ol style="list-style-type: none"><li>1. "acupuncture"[MH] OR "acupuncture therapy"[MH] OR "sham"[ALL] OR "piercing*"[ALL] OR "tattoo*"[ALL] OR "body art"[ALL]</li><li>2. "hepatitis C"[MH] OR "hepatitis C virus"[ALL] OR "HCV"[ALL] OR "hepatitis C, chronic"[MH] OR "chronic hepatitis C"[ALL] OR "CHC"[ALL]</li><li>3. #1 AND #2</li><li>4. "humans"[MH]</li><li>5. #3 AND #4</li></ol> <p>MH = MeSH terms, ALL = All fields Limitation: humans Date of Search: May 12, 2022 Results: 527 articles were found</p>
EMBASE	<p>EMBASE</p> <ol style="list-style-type: none"><li>1. 'acupuncture'/exp OR 'sham' OR 'piercing*' OR 'tattoo'/exp OR 'body art'</li><li>2. 'hepatitis C'/exp OR 'hepatitis C virus'/exp OR 'chronic hepatitis C'/exp OR 'HCV' OR 'CHC'</li><li>3. #1 AND #2</li><li>4. [humans]/lim</li><li>5. #3 AND #4</li></ol> <p>exp = explosion search, lim = limitation Limitation: humans Date of Search: May 12, 2022 Results: 833 articles were found</p>
COCHRANE	<p>CENTRAL database (The Cochrane Library)</p> <ol style="list-style-type: none"><li>1. (acupuncture) explode all trees were searched</li><li>2. (tattoo) explode all trees were searched</li><li>3. (sham) OR (piercing*) OR (body art)</li><li>4. #1 OR #2 OR #3</li><li>5. (hepatitis c) explode all trees were searched</li><li>6. (HCV) OR (CHC)</li><li>7. #5 OR #6</li><li>8. #4 AND #7</li></ol> <p>All field text searched Limitation: none Date of Search: May 12, 2022 Results: 161 articles were found</p> <p>A total of 1,304 articles were screened after the removal of duplicated publications</p>

**Supplementary Table 3.** Quality Assessment Score according to the Adapted Newcastle–Ottawa Scale

Study name	Selection (max 5)				Comparability (max 2)		Outcome assessment (max 3)	
	Sample represent ability (random sampling/whole population)	Adequate sample size (>100)	Non-response rate	Exposure ascertainment	Matching for age/sex	Additional matching	Outcome assessment	Adequate statistical test
Salama <sup>1</sup>	☆	☆		☆			☆☆	☆
Mohd Suan et al. <sup>2</sup>	☆	☆	☆	☆	☆	☆	☆☆	☆
Wasitthanasem et al. <sup>3</sup>	☆	☆	☆	☆			☆☆	☆
Mac Donald-Ottevanger et al. <sup>4</sup>	☆	☆		☆			☆☆	☆
Sohn et al. <sup>5</sup>	☆	☆		☆	☆	☆	☆☆	☆
Huang et al. (2009–2011) <sup>6</sup>	☆	☆	☆	☆			☆☆	☆
Huang et al. (2011–2012) <sup>7</sup>	☆	☆		☆	☆		☆☆	☆
Carney et al. <sup>8</sup>	☆	☆		☆			☆☆	☆
Kin et al. <sup>9</sup>	☆	☆		☆			☆☆	☆
Seong et al. <sup>10</sup>	☆	☆	☆	☆			☆☆	☆
Ahmed et al. <sup>11</sup>	☆	☆	☆	☆			☆☆	☆
Kim et al. <sup>12</sup>	☆	☆		☆			☆☆	☆
He et al. <sup>13</sup>	☆	☆	☆	☆	☆	☆	☆☆	☆
Vickery et al. <sup>14</sup>	☆	☆		☆			☆☆	☆
Nguyen et al. <sup>15</sup>	☆	☆	☆	☆			☆☆	☆
Karmochkine et al. <sup>16</sup>	☆	☆	☆	☆	☆	☆	☆☆	☆
Méndez-Sánchez et al. <sup>17</sup>	☆	☆	☆	☆			☆☆	☆
Dominitz et al. <sup>18</sup>	☆	☆	☆	☆			☆☆	☆
Hand and Vasquez <sup>19</sup>	☆	☆		☆			☆☆	☆
Yildirim et al. <sup>20</sup>	☆	☆	☆	☆			☆☆	☆
Lee et al. <sup>21</sup>	☆	☆	☆	☆			☆☆	☆
Brandão and Fuchs <sup>22</sup>	☆	☆	☆	☆			☆☆	☆
Brillman et al. <sup>23</sup>	☆	☆	☆	☆			☆☆	☆
Kim et al. <sup>24</sup>	☆	☆		☆			☆☆	☆
Shin et al. <sup>25</sup>	☆	☆	☆	☆			☆☆	☆
Domínguez et al. <sup>26</sup>	☆	☆	☆	☆			☆☆	☆
Haley and Fischer <sup>27</sup>	☆	☆	☆	☆			☆☆	☆
Müller et al. <sup>28</sup>	☆	☆	☆	☆			☆☆	☆

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