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Cigarette smoking and bladder cancer risk: an evaluation based on a systematic review of epidemiologic evidence in the Japanese population

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Abstract

Objective: Although several epidemiological studies have demonstrated that cigarette smoking is an important risk factor for bladder cancer, no systematic review in the Japanese population has yet been performed. Accurate evaluation of bladder cancer risk in relation to smoking for Japanese populations can provide necessary information for Japanese policy-makers and doctors to enlighten the importance of smoking cessation. We reviewed epidemiologic data to estimate the strength of the association between cigarette smoking and bladder cancer in the Japanese population.

Methods: We identified previous cohort and case-control studies, extracting data from databases in the MEDLINE (PubMed) and *Ichushi*. The magnitude of association and strength of evidence were evaluated in each study, and a meta-analysis was conducted to obtain summary estimates for the overall magnitude of association.

Results: Three cohort and eight case–control studies were identified. Except for one case–control study, all studies showed a strong positive association between cigarette smoking and bladder

cancer. The summary relative risk for ever smokers relative to never smokers was 2.14 (95% confidence interval 1.87–2.44) in a fixed-effect model.

Conclusions: We conclude that cigarette smoking is a convincing risk factor for bladder cancer among Japanese.

Key words: systematic review, epidemiology, cigarette smoking, bladder cancer, Japanese

Introduction

The International Agency for Research on Cancer (IARC) clearly identified a causal relationship of smoking with urinary tract cancer both in men and women (1). Several large cohort studies in Europe and the USA have demonstrated that cigarette smoking is an important risk factor for bladder cancer (2,3), and the difference in incidence between sexes is frequently attributed to different historical smoking pattern (4). In Japan, age-adjusted incidence rate of bladder cancer has increased in recent years to ~12.3 per 100 000 people (5), therefore, it is important to take measures for decreasing the risk of bladder cancers.

The incidence rate of bladder cancer varies worldwide, being higher in Europe and North America and lower in Asia (4,6). Further, recent studies have noted that genetic polymorphism differs by race and modulates the risk of bladder cancer for cigarette smoking (7–9). These findings suggest that the impact of smoking on bladder cancer might vary among geographic areas. The recent meta-analysis conducted by Cumberbatch et al. (10) included only three Japanese articles written in English, and no systematic review among the Japanese population has yet appeared. Accurate evaluation of bladder cancer risk associated with smoking only for Japanese populations can provide necessary information for Japanese policy-makers and doctors to enlighten the importance of quitting smoking.

Here, we reviewed epidemiologic data to estimate the strength of the association between cigarette smoking and bladder cancer among Japanese. This report is one of a series of articles by our research group, which is investigating the association between lifestyles and cancers in Japan (11).

Methods

The details of the evaluation method have been described elsewhere (11). In brief, we identified previous cohort and case–control studies which investigated the association between cigarette smoking and bladder cancer among the Japanese population by extracting studies from the MEDLINE (PubMed) and *Ichushi* (*Japana Centra Revuo Medicina*, the largest databases of medical papers written in Japanese, URL: jamas.or.jp) databases. This search was complemented by searching the reference literature of identified papers. Our search was conducted on 30 June 2015, and included articles written in Japanese and English. The search terms were as follows: bladder cancer, urinary tract cancer, urothelial cancer, smoking, cigarette, Japan and Japanese (the details are shown in Supplementary data, S1). We reviewed titles and abstracts, and excluded studies performed in populations outside of Japan or lacking information on the association between cigarette smoking and risk of bladder cancer. Accepted articles are summarized in the tables, listed separately as cohort and case–control studies. If multiple reports from a single study were identified, the report with the primary endpoint of incidence or with the largest population was included. A flowchart for research and selection of publications is shown in Supplementary data, S-2.

An evaluation was made based on the magnitude of association and the strength of evidence. The former was assessed by classifying each study into one of four categories based on relative risk (RR) and statistical significance (SS, statistical significance; NS, not statistical significance) as follows: (1) strong association (symbol ↓↓↓ or ↑↑↑), RR < 0.5 or RR > 2.0 (SS); (2) moderate association (symbol ↓↓ or ↑↑), either (i) RR < 0.5 or RR > 2.0 (NS), (ii) 0.5≤RR < 0.67(SS) or (iii) 1.5 < RR≤2.0 (SS); (3) weak association (symbol ↓ or ↑), either (i) 0.5 ≤ RR < 0.67(NS), (ii) 1.5 < RR ≤ 2.0 (NS) or (iii) 0.67 ≤ RR ≤ 1.5(SS); (4) no association (symbol −), 0.67 ≤ RR ≤ 1.5(NS). When multiple RRs were shown in a single study, we primarily adopted the RRs in smoking status categorized as never or ever smokers. If this was not evaluated, we adopted the largest RR for other smoking-related variables (e.g. number of cigarettes per day or pack-years). Table 1 shows summarized criteria for the magnitude of association.

After this process, the strength of evidence was evaluated in a similar manner to that used in the WHO/FAO Expert Consultation Report (12), where evidence was categorized as 'convincing', 'probable', 'possible' or 'insufficient' (11). We assumed that biological plausibility corresponded to the judgment of the recent evaluation from the IARC (1). The final judgment is made based on the consensus of research group members. When there was 'convincing' or 'probable' evidence of an association, we conducted a meta-analysis to obtain summary estimates for the overall magnitude of association.

Meta-analysis was conducted using STATA statistical software version 13.1 (StataCorp LP, College Station, Texas, USA). When RR and its 95% confidence interval (CI) were not provided in articles, we estimated them from 2 × 2 tables. Summary RR and 95% CI were calculated using the STATA command 'metan' (13). We assessed heterogeneity between studies using the I^2 statistic and P value associated with the Q-statistic (14), and determined the model (random- or fixed-effect model) to consolidate data for meta-analysis. Publication bias was assessed using a funnel plot and Egger's test (15). Two-sided P values < 0.05 were considered statistically significant.

Results

Our search identified five (16–20) cohort and eight (21–28) case–control studies. We excluded two reports (17,18) because of data overlap with other reports (16,19), leaving three (16,19,20) cohort and

Table 1. Evaluation of the magnitude of association

Magnitude of association	Definition	Statistical significance	Symbol
Strong	RR < 0.5 or RR > 2.0	SS	↑↑↑ or ↓↓↓
Moderate	RR < 0.5 or RR > 2.0	NS	↑↑ or ↓↓
	1.5 < RR ≤ 2.0	SS	
	0.5 ≤ RR < 0.67	SS	
Weak	1.5 < RR ≤ 2.0	NS	↑ or ↓
	0.5 ≤ RR < 0.67	NS	
	0.67 ≤ RR ≤ 1.5	SS	
No association	0.67 ≤ RR ≤ 1.5	NS	-

RR, relative risk; SS, statistically significant; NS, not statistically significant.

Table 2. Cigarette smoking and bladder cancer risk, cohort studies among Japanese populations

Author (reference no.)	Study period	Study population								
		Number of subjects for analysis, sex, age	Source of subjects	Event followed	Number of incident cases or deaths	Category	Relative risk (95% CI)	*P* value for trend	Confounding variables considered	Comments
Hirayama (16)	1965–81 (17 years)	122 261 men 142 857 women ≥40 years old	Population-based Kagoshima Okayama Hyogo Osaka Aichi Miyagi	Death	173 men	Smoking status Non-smoker Daily smoker[a] Number of cigarettes per day Non-smoker 1–9 10–19 ≥20 Age at start of smoking Non-smoker 0–19 ≥20 Years after smoking cessation Non-smoker 1–4 5–9 ≥10	 1.0 1.61 (1.03–2.51) 1.0 1.07 (0.50–2.27) 1.60 (0.99–2.59) 1.96 (1.22–3.14) 1.0 0.94 (0.42–2.10) 1.63 (1.03–2.58) 1.0 1.69 (0.49–5.83) NA 1.83 (0.46–7.23)	Not described	Adjusted for age	Follow-up by death certificate, residential registry, 95% CI converted from 90% CI
					75 women	Smoking status Non-smoker Daily smoker[a] Number of cigarettes per day Non-smoker 1–9 10–19 ≥20 Age at start of smoking Non-smoker 0–19 ≥20 Years after smoking cessation Non-smoker 1–4 5–9 ≥10	 1.0 2.29 (1.33–3.95) 1.0 1.70 (0.70–4.12) 2.28 (0.99–5.28) 1.79 (0.24–13.50) 1.0 5.26 (0.91–30.46) 1.87 (0.95–3.69) 1.0 NA 7.95 (0.65–97.03) NA			
Sakauchi et al. (19)	1988–97 (10 years)	26 464 men 38 720 women 40–79 years old	Population-based 24 Areas in Japan JACC study	Incidence	95 men 28 women	Smoking index Non-smoker <799 ≥800[a]	 1.0 2.16 (1.21–3.86) 2.75 (1.49–5.08)	*P* = 0.002	Adjusted for age and sex	Including 12 renal pelvis and 7 ureter cancers

Continued

Table 2. Continued

Author (reference no.)	Study period	Study population								
		Number of subjects for analysis, sex, age	Source of subjects	Event followed	Number of incident cases or deaths	Category	Relative risk (95% CI)	*P* value for trend	Confounding variables considered	Comments
Kurahashi et al. (20)	1990–2005 (16 years)	49 566 men 54 874 women 40–69 years old	Population-based JPHC study	Incidence	164 men	Smoking status		$P = 0.01$	Adjusted for age and area	
						Never	1.0			
						Former	1.32 (0.80–2.16)			
						Current[a]	1.69 (1.09–2.63)			
						Pack-years in current smokers		$P < 0.01$		
						<20	1.14 (0.53–2.44)			
						20–29	1.39 (0.74–2.61)			
						30–39	1.39 (0.77–2.50)			
						40–49	2.24 (1.26–3.99)			
						≥50	2.61 (1.49–4.56)			
						Years after smoking cessation		Not described		
						Never	1.0			
						<10	1.88 (1.10–3.21)			
						10–19	0.71 (0.31–1.63)			
						≥20	0.98 (0.40–2.40)			
					42 women	Smoking status		Not described		
						Never	1.0			
						Former	-			
						Current[a]	5.45 (2.56–11.61)			
						Pack-years in current smokers		$P < 0.01$		
						<25	6.91 (3.00–15.93)			
						≥25	4.06 (0.96–17.17)			

CI, confidence interval; NA, not available.

[a]Categories from which the magnitude of association was judged.

Table 3. Cigarette smoking and bladder cancer risk, case–control studies among Japanese populations

Author (Reference)	Study period	Study subjects				Category	Relative risk (95% CI)	*P* value for trend	Confounding variables considered	Comments
		Type and source	Definition	Number of cases	Number of controls					
Ohno et al. (21)	1976–78	Population-based (Nagoya Bladder Tumor Registry, 19 hospitals and responsible urologists in Nagoya area)	Cases: those diagnosed with lower urinary tract cancer Controls: those selected from electoral registers in the same area	293 (227 males and 66 females) (20–89 years old)	589 (443 male and 146 female) (20–89 years old)	Smoking status Male		Not described	Matched for age, sex and residence	Including renal pelvis and ureter cancers (details not provided)
						Non-smoker	1.0		Adjusted for age	
						Smoker[a]	1.89 (1.15–3.10)			
						Female				
						Non-smoker	1.0			
						Smoker[a]	3.53 (1.71–7.27)			
Nishio et al. (22)	1975–87	Hospital-based (Kyoto University Hospital)	Cases: patients admitted to the hospital for the treatment of bladder cancer Controls: patients admitted to the hospital for the treatment of benign urological diseases	278 (200 males and 78 females) (31–86 years old)	278 (200 males and 78 females) (31–86 years old)	Smoking status Male		Not described	Matched for age and sex	
						Never	1.0			
						Ex-smoker	1.56 (0.98–2.47)			Ex-smoker: quit smoking > 5 years
						Smoker	1.45 (0.97–2.16)			Smoker: current or quit smoking ≤5 years
						Smoker + Ex-smoker[a]	3.33 (1.94–5.70)			
						Female				
						Never	1.0			
						Ex-smoker	0.66 (0.11–4.03)			
						Smoker[a]	4.36 (1.73–10.96)			
						Smoker + Ex-smoker	3.21 (1.41–7.32)			
						Smoking (Tobacco index)				Tobacco index was defined as number of cigarettes per day multiplied by years smoked
						Male				
						<500	1.0			
						≥500	2.03 (1.36–3.04)			
						Female				
						<300	1.0			
						≥300	4.38 (1.63–11.78)			

Continued

Table 3. Continued

Author (Reference)	Study period	Study subjects				Category	Relative risk (95% CI)	*P* value for trend	Confounding variables considered	Comments
		Type and source	Definition	Number of cases	Number of controls					
Tachiki et al. (23)	1980–89	Hospital-based (five hospitals in Muroran area)	Cases: outpatients diagnosed with bladder cancer, residing in Muroran area Controls: outpatients diagnosed with benign urological diseases, residing in the area	67 (56 males and 11 females) (age: not described)	306 (238 males and 68 females) (age: not described)	Smoking status Male			Not adjusted	OR and 95% CI were estimated from 2×2 table
								$P < 0.01$		
						Never	1.0			
						Ever[a]	4.70 (1.41–15.67)			
						Female		$P = 0.45$		
						Never	1.0			
						Ever[a]	1.75 (0.40–7.58)			
Nakata et al. (24)	1987–92	Population-based (Selected municipality in Gunma Prefecture)	Cases: untreated men diagnosed with bladder cancer, residing in Gunma Prefecture Controls: those randomly selected from municipalities in Gunma Prefecture	303 males (40 years or older, age mean: 70.1)	303 males (40 years or older, age mean: 70.2)	Smoking status		Not described	Matched for age (±1 year)	
						Never	1.0			
						Ever[a]	2.40 (1.42–4.04)			
						Number of cigarettes per day		$P < 0.01$		
						Never	1.0			
						≤10	1.28 (0.68–2.42)			
						11–20	2.87 (1.66–4.96)			
						≥21	2.78 (1.46–5.29)			
						Years of smoking		$P < 0.01$		
						Never	1.0			
						≤29	1.55 (0.80–3.01)			
						30–49	2.33 (1.29–4.21)			
						≥50	2.56 (1.34–4.92)			
						Smoking (Brinkman index)		$P < 0.01$		
						Never	1.0			
						≤499	1.20 (0.63–2.27)			
						500–999	2.89 (1.61–5.19)			
						≥1000	3.09 (1.64–5.83)			
						Age at start of smoking		$P < 0.01$		
						Never	1.0			
						≤19	2.57 (1.36–4.87)			
						20–24	2.84 (1.65–4.90)			
						≥25	1.25 (0.65–2.38)			
						Inhalation style		$P < 0.01$		
						Never	1.0			
						No inhalation	1.12 (0.57–2.18)			Details of inhalation style not provided
						Moderate	2.81 (1.64–4.84)			
						Deep	2.91 (1.51–5.63)			

Murata et al. (25)	1984–93	Hospital-based (Chiba Cancer Association) nested case-control study	Cases: those diagnosed with bladder cancer in the cohort (participants of a gastric mass screening), identified by Chiba Cancer Registry Controls: those with no cancer selected from the same cohort	38 males (age: not described)	76 males (age: not described)	Number of cigarettes per day Non-smoker 1–10[a] 11–20 ≥21	 1.0 2.57 (0.74–8.95) 2.25 (0.91–5.55) 1.29 (0.29–5.66)	Not described	Matched for birth year (±2 year) and first digit of the address cord	95% CI was estimated from 2 × 2 table smoker: quit smoking <2 years Non-smoker: never or quit smoking ≥2 years
Wada et al. (26)	1994–99	Hospital-based (Osaka City University Hospital)	Cases: those admitted to the hospital for the treatment of bladder cancer Controls: those admitted to the hospital for the treatment of benign urological diseases	141 (117 males and 24 females) (45–85 years old) (age mean: 66.4 in male, 64.5 in female)	128 (99 males and 29 females) (46–82 years old) (age mean: 68.0 in male, 61.7 in female)	Smoking status Non-smoker Smoker[a]	 1.0 2.07 (1.23–3.49)	Not described	Not adjusted	 Smoker: ≥10 cigarettes per day for ≥1 year
Wakai et al. (27)	1994–2000	Hospital-based (Aichi Cancer Center Hospital)	Cases: outpatients first diagnosed with bladder cancer Controls: outpatients with no history of cancer	124 (100 males and 24 females) (mean age: 61.9)	620 (500 males and 120 females) (mean age: 61.9)	Smoking (pack-years) 0 1–19 20–39 40–59[a] ≥60	 1.0 1.30 (0.65–2.59) 1.58 (0.82–3.05) 2.90 (1.55–5.42) 2.41 (1.21–4.78)	$P = 0.0009$	Adjusted for age, sex and year of first visit	including 5 renal pelvis and 6 ureter cancers
Nobata et al. (28)	2008–11	Hospital-based (Seirei Yobo Kennshin Center; medical health check-up)	Cases: those who had a history of bladder cancer when receiving medical health check-up Controls: those who had no history of bladder cancer when receiving medical health check-up	52 (42 males and 10 females) (36–77 years old)	30,337 (17 938 males and 12,399 females) (age: not described)	Smoking status Non-smoker Smoker[a]	 1.0 2.04 (1.15–3.61)	$P = 0.0126$	Not adjusted	OR and 95% CI were estimated from 2 × 2 table

[a]Categories from which the magnitude of association was judged.

Table 4. Summary of association between cigarette smoking and bladder cancer risk, cohort studies

Author	Study period	Study subjects					Category	Magnitude of association
		Sex	Number of subjects	Age range (years)	Event	Number of incident cases or deaths		
Hirayama	1965–81	Male	122 261	≥40	Death	173	Smoking status[a]	↑↑
		Female	142 857	≥40	Death	75	Smoking status[a]	↑↑↑
Sakauchi et al.	1988–97	Male	26 464	40–79	Incidence	95	Smoking index[b]	↑↑↑
		Female	38 720	40–79	Incidence	28		
Kurahashi et al.	1990–2005	Male	49 566	40–69	Incidence	164	Smoking status[a]	↑↑
		Female	54 874	40–69	Incidence	42	Smoking status[a]	↑↑↑

↑↑↑, Strong positive association; ↑↑, moderate positive association.
[a]Categorized as never or ever smokers.
[b]Categorized as number of cigarettes per day multiplied by years smoked.

Table 5. Summary of association between cigarette smoking and bladder cancer risk, case–control studies

Author	Study period	Study subjects				Category	Magnitude of association
		Sex	Age range (years)	Number of cases	Number of controls		
Ohno et al.	1976–78	Male	20–89	227	443	Smoking status[a]	↑↑
		Female	20–89	66	146	Smoking status[a]	↑↑↑
Nishio et al.	1975–87	Male	35–84	200	200	Smoking status[a]	↑↑↑
		Female	31–86	78	78	Smoking status[a]	↑↑↑
Tachiki et al.	1980–89	Male	Not described	56	238	Smoking status[a]	↑↑↑
		Female	Not described	11	68	Smoking status[a]	↑
Nakata et al.	1987–92	Male	≥40	303	303	Smoking status[a]	↑↑↑
Murata et al.	1984–93	Male	Not described	38	76	Number of cigarettes per day	↑↑
Wada et al.	1994–99	Male and female	45–85	141 (M: 117, F: 24)	128 (M: 99, F: 29)	Smoking status[a]	↑↑↑
Wakai et al.	1994–2000	Male and female	20–79	124 (M: 100, F: 24)	620 (M: 500, F: 120)	Pack-years	↑↑↑
Nobata et al.	2008–11	Male and female	36–77	52 (M: 42, F: 10)	30337 (M: 17938, F: 12399)	Smoking status[a]	↑↑↑

↑↑↑, Strong positive association; ↑↑, moderate positive association; ↑, weak positive association; M, male; F, female.
[a]Categorized as never or ever smokers.

eight (21–28) case–control studies (Tables 2 and 3). Of these cohort studies, two (16,20) presented the results by sex and one (19) for men and women combined. Among case–control studies, three (21–23) presented the results by sex, three (26–28) for men and women combined and two (24,25) for men only. One cohort (19) and two case–control (21,27) studies included renal pelvis and ureter cancer in cases—we kept these studies because only 12% of total patients had renal pelvis or ureter cancers, and RRs of these studies were similar to those of the other studies.

A summary of the magnitude of association for the cohort and case–control studies is shown in Tables 4 and 5, respectively. All cohort studies and seven of eight case–control studies showed a strong positive association between cigarette smoking and bladder cancer, while the remaining study (25) showed a moderate positive association. A dose–response relationship was indicated in all cohort studies (16,19,20) and in three case–control studies (22,24,27), but not one (25).

Meta-analysis was conducted to evaluate the magnitude of cigarette smoking among the Japanese population (Fig. 1). Because heterogeneity testing with the I^2 statistic and Q-statistic was not significant ($I^2 = 0.0$, $X^2 = 7.23$, $P = 0.704$), a fixed-effect model was selected to calculate summary RR and 95% CI. The summary RRs for ever smokers relative to never smokers in the cohort and case–control studies were 1.93 (95% CI 1.58–2.36) and 2.30 (95% CI 1.94–2.73), respectively, and the summary RR for all studies combined was 2.14 (95% CI 1.87–2.44). Although Egger's test showed no significant publication bias ($P = 0.095$), visual inspection of the funnel plot could not completely rule out the possibility of this bias (Fig. 2).

Discussion

The present study indicates a high risk of bladder cancer for ever smokers and a reasonably consistent dose–response relationship between cigarette smoking and bladder cancer. The findings can make Japanese medical doctors aware of the importance of antismoking education for preventing incidence of bladder cancer.

A recent meta-analysis reported a summary RR for bladder cancer incidence among ever smokers compared with never smokers (10). The summary RR for the total world was 2.46 (95% CI 2.16–2.81), and 2.98 (95% CI 2.67–3.36), 2.36 (95% CI 2.10–2.65) and 2.26 (95% CI 1.79–2.86) for Europe, America and Asia, respectively. Although RR among the Asian population was lower, a significant difference by geographic region was not shown ($P = 0.08$). The summary RR of the present study was 2.14, similar to that of Asia in the meta-analysis, and apparently somewhat lower than in Europe and America.

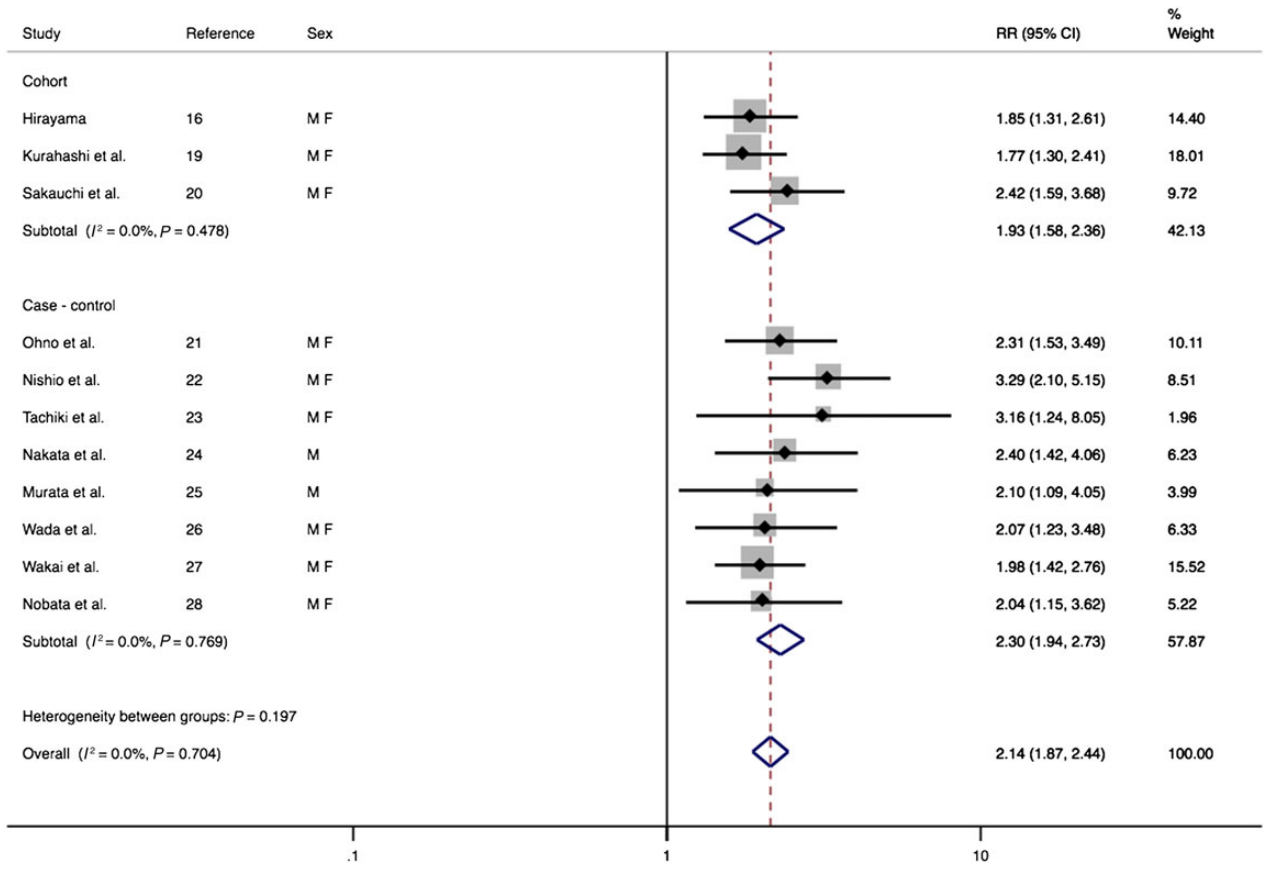

Figure 1. Forest plot of summary relative risk with 95% confidence interval for bladder cancer among ever smokers compared with never smokers.

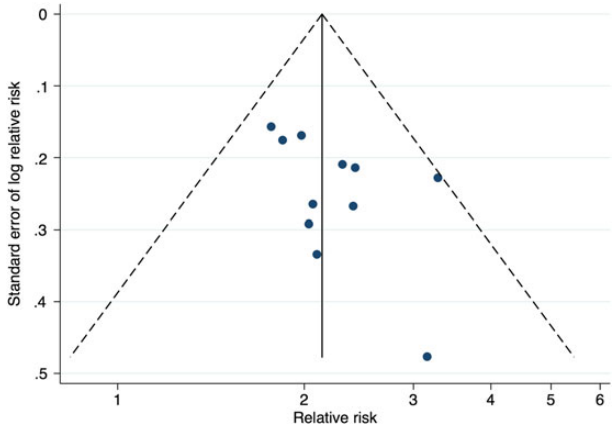

Figure 2. Funnel plot with 95% confidence limits.

The lower RR in Japan might be explained as follows. Smoking exposure for smokers may be lower in Japan than in Europe and America. Studies of the association between cigarette smoking and lung cancer indicated that age at the initiation of smoking was relatively later and the number of cigarettes per day was 10% lower among Japanese than Americans (29). Some data also suggested that the shift from non-filter to filter cigarettes in the 1950s and 1960s occurred more rapidly in Japan than in America (30), and that the use of filter cigarettes was associated with about a half reduced risk compared with non-filter cigarettes (31,32). These differences in smoking style and cigarette type might modify the effect of smoking on bladder cancer. The lower risk in Japanese smokers might also be explained by genetic variations. *N*-acetyltransferase 2 (NAT2) is considered an important enzyme for the detoxification of carcinogens (33). Among previous studies, a meta-analysis suggested that the NAT2 slow acetylator genotype might be a risk factor for bladder cancer (8), and significantly increased the risk of bladder cancer for smokers among Japanese (7,9). Prevalence of the slow acetylator genotype differs, at 56% in Europeans versus 11% in Asians (8). The lower incidence rate of bladder cancer in Japan might be due to the lower prevalence of this genetic polymorphism.

This study has several potential limitations. First, we were unable to estimate the summary RR for current smokers relative to never smokers because all but two studies (20,22) reported bladder cancer risk for ever smokers only. If we estimated RR for current smokers relative to never smokers based on the two studies, we observed consistently increased RR (2.79 (95% CI 2.06–3.80)). Second, one study (16) included in this meta-analysis used death as outcome measure. However, its RR and 95% CI were similar to the other studies using incidence. Third, smokers were classified differently; for example, one study classified short-term smokers (less than 1 year) in the non-smoker group, and another included former smokers with a short duration of smoking cessation in the smoker group. These differences might have attenuated the association between cigarette smoking and bladder cancer. Fourth, each questionnaire categorized smoking exposure differently (e.g. smoking status, number of cigarettes, smoking index). However, heterogeneity among articles was not high, and the magnitude of the effects of these problems might have had only a small influence on our findings.

Another methodological problem was that some studies (19,21,27) included cases with upper urinary tract cancer (i.e. renal pelvis and ureter cancer). When we limited analysis to these three articles only, the summary RR for ever smokers was 2.19 (95% CI 1.75–2.73), similar to that of all articles. This may be because the proportion of patients with upper urinary tract cancer was considerably low, and cigarette smoking confers almost the same risk for upper urinary tract cancer as bladder cancer (34). Resolving these limitations will likely require a pooled analysis of Japanese cohort studies.

Evaluation of evidence on cigarette smoking and bladder cancer risk in Japanese

From these results and on the basis of assumed biological plausibility, we conclude that cigarette smoking is a convincing risk factor for bladder cancer among Japanese population. However, the strength of association might be somewhat weaker than that in Europe and America.

Supplementary data

Supplementary data at http://www.jjco.oxfordjournals.org.

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Conflict of interest statement

None declared.

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Appendix 1

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