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Bladder Cancer in South Korea: Analysis of Trends and Risk Factors of Bladder Cancer in South Korea Using a Nationwide Database

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Purpose: The purpose of this study was to evaluate the incidence rate and trend of bladder cancer in South Korea using a nationwide database. In addition, we aimed to determine the risk factors and their influence on the incidence of bladder cancer.

Materials and Methods: We extracted data from the health insurance database and estimated the incidence rate of newly developed bladder cancer from 2007 to 2019. In addition, we conducted further analysis of 10,210,654 individuals who underwent general health check-ups in 2009 to investigate the risk factors for bladder cancer. Variables associated with bladder cancer were evaluated using Cox regression analysis.

Results: Bladder cancer significantly increased especially in the last 10 years. In 2019, 21.07 people per 100,000 were diagnosed with bladder cancer, whereas 13.62 people per 100,000 were diagnosed with bladder cancer in 2007. The compound annual increase rate from 2007 to 2019 was 3.7%. Among 10,210,654 individuals who had general health check-ups in 2009, bladder cancer was diagnosed in 83 people per 100,000 population in the 10-year follow-up. After adjusting for other variables, smoking-related variables were most significantly associated with bladder cancer incidence, followed by metabolic syndrome and its related variables. In the further analysis of the effect of smoking on bladder cancer according to sex, the smoking amount was more significantly associated with bladder cancer incidence in women compared to that in men.

Conclusions: The crude incidence of bladder cancer continuously increased in South Korea during the last 10 years. Smoking, in addition to sex, age, and metabolic syndrome-related variables, was significantly associated with bladder cancer, especially in women.

Key Words: Incidence, Smoking, Urinary bladder neoplasms

INTRODUCTION

Bladder cancer was ranked as the 10th most common cancer and the 6th most common male cancer worldwide in 2020 [1]. Although the incidence of bladder cancer is higher in men than in women without regional differences [2], it is significantly affected by region: bladder cancer incidence is significantly lower in Asian countries than in Western

countries [1, 3]. In addition, trends in bladder cancer incidence also vary by region [4]. These findings are thought to be affected by several factors associated with bladder cancer, including smoking behaviors and environmental factors [5, 6].

Not only well-known risk factors, such as smoking, but also ethnicity could influence the incidence and oncological outcomes of bladder cancer [6, 7]. In addition, the policies and awareness about smoking, which also influence secondhand smoking [8], and smoking types, such as nonfilter cigarettes, could vary from country to country. Some studies reported that the relative risk of bladder cancer among the Asian population was lower than that in other populations [9, 10]. In other words, a country-based national analysis of the incidence, incidence trend, and risk factors for bladder cancer is needed to accurately determine the country-specific incidence trend and risk factors for bladder cancer.

In 2019, bladder cancer was the 12th most common cancer and 4,895 patients were newly diagnosed with bladder cancer in South Korea [11]. Bladder cancer severely impairs the quality of life [12]. Moreover, due to the frequent intravesical recurrence after transurethral resection of bladder tumors and intensive follow-up strategies, medical expenses for bladder cancer cannot be ignored [13]. Therefore, it is essential to check the current status of the incidence rate, incidence trend, and risk factors for bladder cancer using a nationwide database in South Korea, which will serve as a basis for future medical policy decisions. To demonstrate the current status of bladder cancer in South Korea, the Korean Urological Oncology Society launched the bladder cancer fact sheet project in 2022. In this study, we aimed to identify the current status of bladder cancer in South Korea and estimate the incidence rate and trend of bladder cancer using a nationwide database. In addition, we sought to determine the risk factors and their influence on the incidence of bladder cancer in a nationwide general health check-up cohort.

MATERIALS AND METHODS

1. Incidence and Trend of Bladder Cancer

In South Korea, medical expenses in approximately 98% of the population were covered by the National Health Insurance Service [14] and the data were collected by the National Health Insurance Sharing Service (NHISS). We extracted 2005–2019 data from the NHISS. Among these, we excluded the patients who visited medical facilities with bladder cancer between 2005 and 2006 to calculate the patients with newly diagnosed bladder cancer after January 2007. Bladder cancer was defined using the Korean Standard Classification of Diseases (KCD) version 6, based on the International Classification of Diseases 10th revision, as code C67 and V193, cancer-specific insurance codes in Korea. Those with ages <20 years were also excluded from the analysis. Using these data, the incidence rate and incidence trend of newly developed bladder cancer per 100,000 population were estimated from 2007 to 2019 after subdividing the population according to sex and age. The compound annual increase rate for newly diagnosed bladder cancer was also calculated.

2. Variables Associated With Newly Diagnosed Bladder Cancer

Among approximately 38 million people, 10.5 million people who underwent general health check-ups in 2009 were initially selected for further analysis. After excluding patients who were diagnosed with bladder cancer from 2005 to 2008 and those without required data, 10,210,654 people were finally included in the further analysis. Baseline characteristics were analyzed using the 2009 health check-up data. Continuous variables were assessed using means±standard deviations and categorical variables were assessed using numbers with percentages.

The presence of hypertension, diabetes, dyslipidemia, abdominal obesity, and metabolic syndrome was determined using the KCD code, medication data, and general health check-up data (Supplementary Table 1). Smoking status, smoking amount, and drinking amount were assessed using the questionnaires included in the general health check-up. Drinking status was categorized as follows: nondrinker; 0 g/day; mild drinker, >0 and <30 g/day; and heavy drinker, ≥30 g/day. The residential areas were classified into 2 groups: urban versus rural. Metropolitan cities were defined as urban areas and the others as rural areas.

The incidence of bladder cancer according to sex and age

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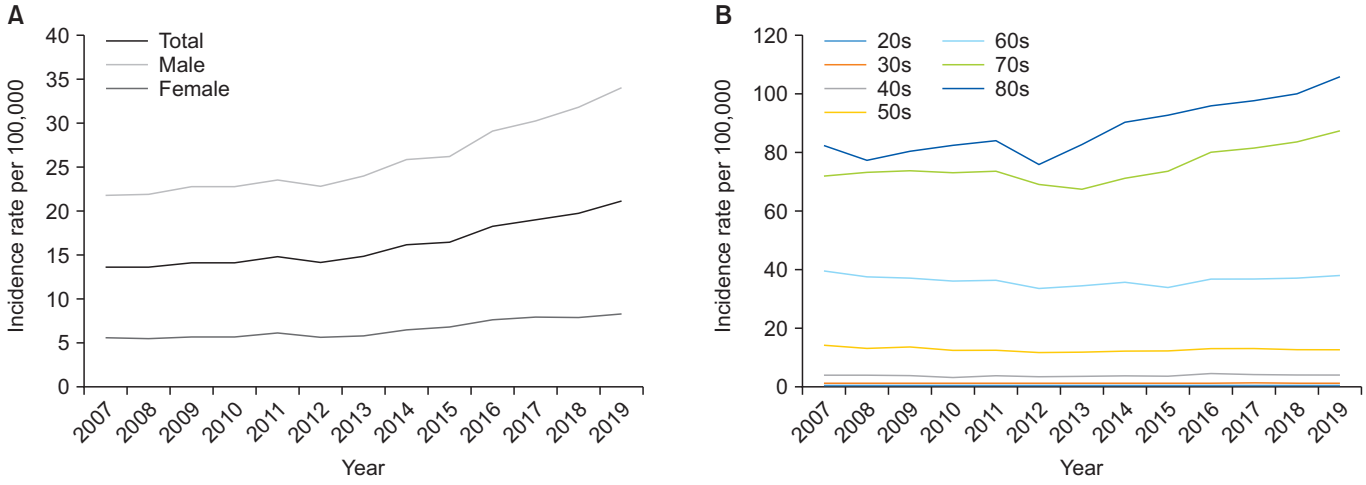

Fig. 1. Trends in bladder cancer incidence. (A) Trends in bladder cancer incidence according to sex. (B) Trends in bladder cancer incidence according to age.

group (≥20 and <40 years, ≥40 and <65 years, and ≥65 years) was determined using Kaplan-Meier analysis and compared using a log-rank test. Using univariate and multivariable Cox regression analysis, we developed 3 models for assessing the effects of variables on the incidence of newly diagnosed bladder cancer: model 1 was unadjusted; model 2 was only adjusted for age and sex; and model 3 was adjusted for all other variables.

As smoking, in addition to sex and age, was determined as the most powerful variable associated with bladder cancer, we further analyzed the interactions between smoking, age, and sex. P-values for interactions in each model were calculated and compared. A p-value of <0.05 was considered statistically significant.

3. Research Ethics

This study was performed according to the Helsinki Declaration (http://www.wma.net/en/30publications/10policies/b3/) and approved the Institutional Review Board (IRB) of Seoul Metropolitan Government - Seoul National University Boramae Medical Center (IRB No. 07-2021-25). A written informed consent is waived by IRB.

RESULTS

The incidence rate of bladder cancer per 100,000 population significantly increased especially during the last 10 years (Fig. 1). In 2019, 21.07 people per 100,000 were diagnosed with bladder cancer, whereas 13.62 per 100,000 persons were diagnosed with bladder cancer in 2007. The compound annual increase rate from 2007 to 2019 was 3.7%. Newly diagnosed bladder cancer significantly increased in both male and female populations. When age stratification was performed, the increment in the incidence of bladder cancer was significant in those older than 70 years, although there were no significant increments in those under 70 years (Supplementary Table 2).

Individuals who underwent health check-ups in 2009 were included in the further analysis. The mean age of this population was 47.1 years and the mean body mass

Table 1. Patients' baseline characteristics (n=10,210,654)

Characteristic	Value
Age (yr)	47.1±14.1
Body mass index (kg/m^2)	23.7±3.2
Hypertension	2,725,576 (26.69)
Diabetes	881,632 (8.63)
Dyslipidemia	1,769,656 (17.33)
Abdominal obesity	2,001,110 (19.6)
Smoking status	
None smoker	6,126,317 (60.0)
Ex-smoker	1,425,970 (14.0)
Current smoker	2,658,367 (36.0)
Smoking amount (pack-year)	6.2±11.6
Drinking status	
None drinker	5,296,037 (51.9)
Mild drinker	4,110,114 (40.3)
Heavy drinker	804,503 (7.9)
Residence	
Urban	4,606,962 (45.1)
Rural	5,603,692 (54.9)

Values are presented as mean±standard deviation or number (%).

index was 23.7 kg/m^2 (Table 1). The percentage of each metabolic component in this population was as follows: hypertension, 26.7%; diabetes mellitus, 8.6%; dyslipidemia, 17.3%; abdominal obesity, 19.6%; and metabolic syndrome, 24.9%. Smoking status was as follows: nonsmoker, 60.0%; ex-smoker, 14.0%; and current smoker, 26.0%. The mean smoking amount was 6.2 pack-years, the mean duration of smoking was 7.2 years, and the mean daily amount of smoking was 0.3 pack.

Bladder cancer was diagnosed in 83 people per 100,000 population in the 10-year follow-up (Fig. 2). The bladder cancer incidence rate was significantly higher in men than women (315 vs. 79 individuals per 100,000 population, p<0.001). In addition, the bladder cancer incidence rate was significantly associated with old age (≥20 and <40 years vs. ≥40 and <65 years vs. ≥65 years: 20 vs. 180 vs. 845 individuals per 100,000 population, p<0.001).

In univariate analysis, all metabolic syndrome-related variables, smoking-related variables, and residential areas were significantly associated with newly diagnosed bladder cancer (Table 2). After age and sex adjustment, smoking-related variables, including smoking status and smoking amount, were the most powerful risk factors for newly diagnosed bladder cancer, followed by metabolic syndrome and metabolic syndrome-related variables. Drinking amount and residential area were also related to newly diagnosed bladder cancer. After adjusting for all variables, smoking-related variables remained the most powerful variables associated with newly diagnosed bladder cancer. Metabolic syndrome-related variables, drinking amount, and residential area were also associated with newly diagnosed bladder cancer.

In the further analysis of the effects of smoking on bladder cancer, the effects of smoking amount on newly diagnosed bladder cancer were more powerful in women than men, not only in the unadjusted model but also in the adjusted model, including models 2 and 3 (Table 3). In addition, the effects of smoking on newly diagnosed bladder cancer were more prominent in older people after adjusting for all variables.

DISCUSSION

The incidence of bladder cancer varies significantly by geographic region and might be affected by several factors including exposure to smoking, occupational factors [15], arsenic in drinks [16], or availability and accessibility to cystoscopy or imaging studies [17]. In addition, these variables are influenced by socioeconomic status, regional characteristics, or sociopolitical situation. In other words, although risk factors for bladder cancer would be similar worldwide, the incidence rate and trend of bladder cancer and the magnitude of the effect of each risk factor on bladder cancer incidence could vary from country to country. In the current study, we identified the current status of bladder cancer in South Korea, including the incidence rate and trend of bladder cancer. In addition, we evaluated the actual magnitude of each risk factor for bladder cancer in Koreans using a nationwide database.

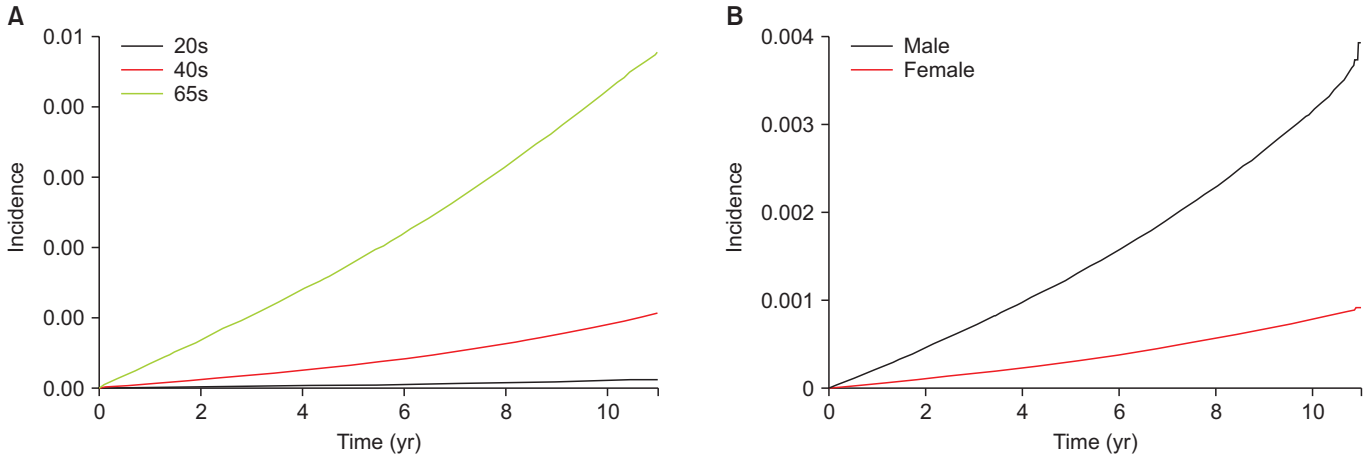

Fig. 2. Incidence of bladder cancer according to age and sex. (A) Age group. (B) Sex.

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Table 2. Variables associated with bladder cancer incidence

Variable	Total (n)	Bladder cancer (n)	Model 1		Model 2		Model 3	
			HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Diabetes				<0.001		<0.001		<0.001
No	9,329,022	17,836	Reference		Reference		Reference	
Yes	881,632	4,165	2.60 (2.51–2.69)		1.22 (1.18–1.27)		1.13 (1.09–1.18)	
Hypertension				<0.001		<0.001		<0.001
No	7,485,078	10,632	Reference		Reference		Reference	
Yes	2,725,576	11,369	3.04 (2.96–3.12)		1.16 (1.13–1.19)		1.10 (1.07–1.13)	
Dyslipidemia				<0.001		<0.001		<0.001
No	8,440,998	16,532	Reference		Reference		Reference	
Yes	1,769,656	5,469	1.59 (1.54–1.64)		1.17 (1.13–1.20)		1.08 (1.05–1.12)	
BMI (kg/m^2)				<0.001		<0.001		<0.001
<25	6,878,893	13,985	Reference		Reference		Reference	
≥25	3,331,761	8,016	1.18 (1.15–1.21)		1.10 (1.0–1.13)		1.01 (0.97–1.04)	
Abdominal obesity				<0.001		<0.001		<0.001
No	8,209,544	15,495	Reference		Reference		Reference	
Yes	2,001,110	6,506	1.74 (1.69–1.79)		1.17 (1.14–1.21)		1.10 (1.06–1.14)	
Smoking status				<0.001		<0.001		<0.001
None	6,126,317	9,250	Reference		Reference		Reference	
Ex	1,425,970	5,615	2.64 (2.55–2.73)		1.31 (1.26–1.36)		1.30 (1.25–1.35)	
Current	2,658,367	7,136	1.80 (1.74–1.85)		1.61 (1.55–1.66)		1.64 (1.58–1.70)	
Smoking amount (pack-year)				<0.001		<0.001		<0.001
0	6,126,317	9,250	Reference		Reference		Reference	
<10	1,577,998	1,989	0.83 (0.79–0.87)		1.07 (1.02–1.13)		1.08 (1.03–1.14)	
<20	1,181,476	2,834	1.60 (1.53–1.67)		1.31 (1.25–1.37)		1.32 (1.26–1.38)	
≥20	1,324,863	7,928	4.10 (3.98–4.22)		1.66 (1.61–1.72)		1.66 (1.61–1.72)	
Drink status				<0.001		<0.001		<0.001
None	5,296,037	11,423	Reference		Reference		Reference	
Mild	4,110,114	8,274	0.93 (0.90–0.95)		1.00 (0.97–1.03)		0.89 (0.87–0.92)	
Heavy	804,503	2,304	1.33 (1.28–1.39)		1.10 (1.05–1.15)		0.97 (0.93–1.02)	
Residence				0.673		<0.001		<0.001
Urban	4,606,962	9,975	Reference		Reference		Reference	
Rural	5,603,692	12,026	0.99 (0.97–1.02)		0.89 (0.86–0.91)		0.89 (0.87–0.92)	

Model 1, unadjusted; model 2, only adjusted for age and sex; model 3, adjusted for all other variables; HR, hazard ratio; CI, confidence interval; BMI, body mass index.

In the last decade, the crude incidence rate of bladder cancer significantly increased in South Korea, especially in those aged 70 years or older. These findings are thought to be associated with the rapid aging of the Korean population, in addition to increased health check-ups in older people. In 2000, South Korea became an aging society, with over 7% of its population 65 years or older, and in 2017, South Korea became an aged society, with over 14% of its population aged 65 years or older [18]. Based on the cancer statistics in Korea, the compound annual growth rate of bladder cancer incidence from 2008 to 2017 was 3.0%, which is similar to 3.7% in the current study [19, 20]. However, the age-standardized incidence was consistent between 2008 and 2017, which supports our hypothesis. Although the age-standardized incidence of bladder cancer did not change, the increment in the crude incidence of bladder cancer in Korea should not be overlooked because the treatment for bladder cancer in elderly patients is challenging due to the risk of decreasing quality of life without prolonging survival [21, 22]. In addition, considering that the life expectancy in Koreans continues to increase rapidly [23], political support for elderly patients with bladder cancer is urgently needed.

As shown in previous studies, smoking amount and smoking status were the most powerful risk factors for bladder cancer in the current study. However, interestingly, the magnitude of the effects of smoking on bladder cancer was smaller in the current study than that reported in other studies: 1.64-fold vs 2-4-fold for current smokers [24]. A previous Japanese study reported similar results, which the authors attributed to filtered cigarettes [9]. Similar findings, smaller effect sizes of smoking on lung cancer, were also observed in lung cancer research. Although these findings

Table 3. Effects of smoking amount (pack-year) on bladder cancer incidence by sex and age

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value†	HR (95% CI)	p-value†	HR (95% CI)	p-value†
Sex						
Male		<0.001		<0.001		<0.001
0	Reference		Reference		Reference	
<10	0.41 (0.38–0.43)		1.04 (1.00–1.10)		1.05 (1.00–1.11)	
<20	0.74 (0.70–0.77)		1.29 (1.23–1.35)		1.30 (1.24–1.36)	
≥20	1.89 (1.82–1.95)		1.64 (1.59–1.70)		1.64 (1.59–1.70)	
Female						
0	Reference		Reference		Reference	
<10	0.75 (0.61–0.90)		1.49 (1.23–1.81)		1.52 (1.26–1.85)	
<20	2.12 (1.61–2.79)		1.60 (1.22–2.10)		1.61 (1.23–2.12)	
≥20	4.30 (3.34–5.54)		2.15 (1.67–2.77)		2.15 (1.67–2.77)	
Age						
20–39 Years		<0.001		0.003		0.002
0	Reference		Reference		Reference	
<10	1.75 (1.45–2.10)		0.98 (0.81–1.18)		0.98 (0.82–1.18)	
<20	2.62 (2.14–3.21)		1.10 (0.90–1.35)		1.09 (0.89–1.34)	
≥20	4.43 (3.32–5.91)		1.47 (1.10–1.97)		1.45 (1.09–1.93)	
40–64 Years						
0	Reference		Reference		Reference	
<10	1.75 (1.63–1.88)		1.01 (0.94–1.08)		1.02 (0.95–1.09)	
<20	2.44 (2.30–2.58)		1.27 (1.20–1.35)		1.28 (1.21–1.36)	
≥20	3.85 (3.68–4.02)		1.59 (1.51–1.66)		1.58 (1.50–1.65)	
≥65 Years						
0	Reference		Reference		Reference	
<10	2.36 (2.18–2.54)		1.25 (1.15–1.35)		1.26 (1.16–1.36)	
<20	2.74 (2.57–2.93)		1.36 (1.27–1.46)		1.38 (1.29–1.47)	
≥20	3.44 (3.29–3.58)		1.66 (1.59–1.74)		1.68 (1.61–1.76)	

Model 1, unadjusted; model 2, only adjusted for age and sex; model 3, adjusted for all other variables; HR, hazard ratio; CI, confidence interval.
†p-values for interactions in each model.

need to be validated, smoking patterns, smoking amount, and use of filtered cigarettes could be the reasons for this phenomenon named "smoker's paradox" [25]. As not only the smoking status but also the smoking amount in the current study had smaller effects than those reported in previous Western research [26], we conjecture that the "smoker's paradox" is also present in bladder cancer although more research is warranted.

Interestingly, the magnitude of the effects of smoking on bladder cancer incidence was higher in women as reported in previous studies [26, 27]. Considering the smoking behavioral differences between men and women, such as the number of puffs per cigarette and the size of the remaining cigarette butt after smoking, this finding is quite convincing because women are thought to intake less carcinogen during smoking when compared to men with the same amount of smoking [28]. Considering that the smoking rate did not decrease in Korean women unlike in men [29], it is thought that there is a need to implement active smoking cessation education, especially for female smokers. Although the reason for this finding needs to be elucidated, it is possible to make these data available to the general public to promote their awareness and understanding so as to induce smoking cessation and, hopefully, lower the future risk of bladder cancer, especially in women.

In this study, all metabolic syndrome-related variables were also associated with newly diagnosed bladder cancer although the magnitude of their effects was modest, which is consistent with previous studies [30]. However, due to the complexity of the determination of the association between bladder cancer incidence and metabolic syndrome, it is difficult to conclude the actual influence of metabolic syndrome on bladder cancer. However, it would be important for clinicians to recognize this fact and suspect bladder cancer in patients with hematuria accompanied by metabolic syndrome and carefully examine these patients.

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This study was limited by its retrospective design and operational definition. In addition, the lack of occupational and dietary data is another limitation of the current study. However, considering that this is a nationwide study with a large study population and a long duration of follow-up, it would be useful not only for establishing medical policies in Korea and raising public awareness but also for improving the understanding of clinicians on the current status of bladder cancer in Korea.

CONCLUSIONS

In South Korea, the crude incidence of bladder cancer significantly increased during the last decade, especially in those 70 years or older. The most significant risk factors for newly diagnosed bladder cancer were smoking status and amount, followed by metabolic syndrome-related variables. Considering the magnitude of the effect of smoking on newly diagnosed bladder cancer, especially in women and older people, more active smoking cessation education for these populations is needed.

NOTES

- Supplementary Materials: Supplementary Tables 1 and 2 can be found via https://doi.org/10.22465/juo.2346000400002.
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