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Chest CT scan findings in World Trade Center workers

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ABSTRACT

We examined the chest CT scans of 1,453 WTC responders using the International Classification of High-resolution CT for Occupational and Environmental Respiratory Diseases. Univariate and bivariate analyses of potential work-related pleural abnormalities were performed with pre-WTC and WTC-related occupational exposure data, spirometry, demographics and quantitative CT measurements. Logistic regression was used to evaluate occupational predictors of those abnormalities. Chest CT scans were performed first at a median of 6.8 years after 9/11/2001. Pleural abnormalities were the most frequent (21.1%) across all occupational groups In multivariable analyses, significant pre-WTC occupational asbestos exposure, and work as laborer/cleaner were predictive of pleural abnormalities, with prevalence being highest for the Polish subgroup (n = 237) of our population. Continued occupational lung disease surveillance is warranted in this cohort.

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Introduction

Over 50,000 people participated in the rescue and recovery efforts at the World Trade Center (WTC) site after the terrorist attack on September 11, 2001 (9/11). This highly diverse population consisted of first responders, construction workers, engineers, utility service workers, and volunteers.[1] WTC rescue and recovery workers were exposed to a poorly characterized mixture of toxicants, alkaline dust, gases, and fumes, including glass fibers, gypsum, concrete, paper, various building construction materials, and asbestos.[2,3] The workers were additionally exposed to other physical and psychological stressors,[2] and developed various diseases of the lower airway and other body systems.[4–6]

Chest computed tomography (CT) imaging adds objective information to the characterization of the WTC-related lower airway diseases (LAD) but, thus far, no standardized and systematic method of reporting and grading CT scan findings has been utilized. In this study, we sought to report the range of abnormalities found in the first available chest CT scan of a diverse group of WTC workers. Since pleural abnormalities, suggestive of asbestos-related disease, were the most frequent group of CT abnormalities, we also report in this study their associated occupational exposures.

Methods

Study participants and procedures

The study population consisted of workers who participated in the rescue, recovery, cleanup, and service restoration of the WTC disaster site from September 11, 2001 (9/11) to June, 2002. All subjects participated in the screening, surveillance, and clinical programs of the WTC Clinical Center of Excellence of the Selikoff Centers for Occupational Health, at Mount Sinai Medical Center, in New York City. The study was approved by the Mount Sinai Program for the Protection of Human Subjects, and restricted to subjects who provided informed consent for participation in research studies. The recruitment, screening, and surveillance protocols have been reported previously.[7] Participants included workers from virtually all occupations involved in the rescue, recovery, search, and service restoration of the WTC disaster site, except firefighters. Beginning in July 2002, program participants were offered a baseline screening examination followed by periodic surveillance and health evaluation visits at subsequent 12–18 month intervals. Examinations included reviews of symptoms, diagnoses, spirometry, laboratory tests, and chest radiography.

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Subjects for this study were part of the sub-cohort (n = 1,641) evaluated by the WTC Pulmonary Evaluation Unit (WTC PEU) from 2003 to 2012, who underwent CT imaging as part of their diagnostic evaluation. Table OS1 presents a comparison of the characteristics of this subcohort with those of the entire cohort of participants in the programs of the Mount Sinai WTC HP Clinical Center.[8] All chest CT studies were obtained at Mount Sinai Hospital in General Electric® or Siemens® multidetector row CT scanners. CT studies were performed using a protocol[9] with a radiation dose at 120 kVp, and a mean of 146 (SD 69) mAs, with subjects in the supine position, from the lung apices to the bases in a single breath hold at maximum inspiration, and with section thickness not exceeding 1.5 mm. All deidentified and coded chest CT images were stored and catalogued during the past 5 years in the WTC PEU Chest Image Archive, during which time the studies were re-evaluated by radiologists blinded to the identity and clinical information of the participants. The first CT scan available per patient was included in this study sample. The radiologists utilized the International Classification of High-resolution Computed Tomography for Occupational and Environmental Respiratory Diseases (ICOERD) to classify and grade each study. The protocol and reliability of this classification have been documented.[10,11] In brief, chest CT findings classified by this method include 8 main domains: well defined rounded opacities, irregular and/or linear opacities, ground glass opacities, honeycombing, emphysema, large opacities, inhomogeneous attenuation, and pleural abnormalities. The first 5 of those domains are semiquantitatively scored from 0 to 18 as sum grades. For descriptive purposes, we present group results for sum grades of 0, 1–2, and 3 or more.

Spirometry was performed as previously described.[8] Bronchodilator response was assessed after administering 180 mcg of albuterol by metered-dose inhaler, and repeating spirometry after 15 minutes. Predicted values for forced expiratory flows (forced vital capacity, FVC, and first-second forced expiratory volume, FEV_1) were calculated for all subjects, based on reference equations from the third National Health and Nutrition Examination Survey (NHANES III),[12] and all testing, ventilatory impairment pattern and bronchodilator response definitions, and interpretative approaches followed American Thoracic Society recommendations.[13,14]

Covariates included gender, age on 9/11/2001, body mass index (BMI) and weight status, race/ethnicity, smoking status, occupation, and pre-WTC- and WTC-related occupational exposures. BMI served to group weight status into underweight (BMI <18 kg/m^2), normal (BMI 18–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (BMI$\geq$30 kg/m^2). A subject was considered a lifetime nonsmoker if (s)he had smoked less than 20 packs of cigarettes (or 12 oz. of tobacco) in a lifetime, or less than 1 cigarette/day (or 1 cigar/week) for one year. A minimum of 12 months without tobacco use was required to deem a subject a former smoker. Race/ethnicity was categorized into the following four groups: Latino, non-Latino White, non-Latino Black, or non-Latino other race. An occupational physician (RED) recoded, grouped, and labeled pre-WTC occupations into the following 6 categories: (1) management, business, science, arts, service, sales, or office occupations ("management/services"); (2) construction trades, maintenance, and natural resources ("construction trades"); (3) construction and demolition laborers, asbestos handlers, and building cleaners ("laborers/cleaners")[15]; (4) production, transportation, and material moving ("transportation"); (5) law enforcement specific and military ("law enforcement"); and (6) unemployed, retired, or unknown ("unemployed/retired", n = 46, excluded from the study). Previous work demonstrated that most WTC workers performed duties corresponding to their pre-WTC occupation.[1] We defined significant pre-WTC occupational exposures dichotomously as self-reported exposure from "a few times per week" to "daily", in the course of usual occupation before September 11, 2001, to one or more of the following list of 11 vapors, dust, gases, and fumes: asbestos, Cadmium, diesel and non-diesel exhaust, general, mineral, and silica/sand dust, wood dust, fiberglass, industrial cleaning solutions, and welding fumes. For our analyses of pleural abnormalities, we used the same definition, but restricted it to asbestos. For descriptive purposes, WTC exposure included two dichotomous variables: arrival at the site within 48 hours of the attack,[4] and cumulative exposure duration greater than 60 days.

Statistical analyses

Univariate and bivariate analyses were performed on the study variables. Continuous variables are presented as either mean and standard deviation (SD), or median and interquartile range (IQR), as appropriate. Associations between study variables and outcomes were evaluated using chi-square (or Fisher's exact) tests, as well as Wilcoxon's rank sum test as appropriate.

Missing data in the dichotomous CT abnormality questions were imputed from the respective scored CT abnormality questions. Where an observation reported a CT abnormality sum grade, this value replaced the dichotomous response so that a score of 0 was imputed as 'no', and any score >0 was imputed as 'yes.'

Multivariate logistic regression was used to estimate the effects of our exposures of interest on pleural abnormalities. We created two models using two relevant pre-WTC occupational exposure variables as main predictors: (1) significant asbestos exposure, and (2) occupational category. We utilized a modified backward procedure to select variables for these models. Variables were eliminated from the model during the backwards procedure when the significance for the β estimate exceeded 0.2. All unselected variables were subsequently added to the resulting model one at a time, and retained if they altered the β estimate for the main predictor by greater than 10%. We considered the following covariates for these models: age on 9/11/2001, gender, BMI, race/ethnicity, smoking status, arrival at the WTC site, and duration of exposure. Multicollinearity was excluded by the variance inflation factor method.

All analyses were performed using the SAS statistical package (SAS v. 9.3; SAS Institute, Cary, NC).

Results

There are 1641 subjects in the WTC PEU Chest CT Imaging Archive. We excluded 56 subjects with missing values on 4 or more CT abnormality questions, 86 with missing data on covariates included in the multivariate models, and 46 who had either retired or had missing information on occupation on 9/11/2001. The study sample thus consisted of 1,453 subjects.

Table 1 shows the distribution of the demographic, occupational exposure and clinical characteristics, and other covariates of interest. The subjects were predominantly male, aged a median of 42 (IQR 36–48) years on 9/11/2001. Their WTC exposure duration was a median of 77 (IQR 28–139) days, and 745 (51.3%) arrived within the first 48 hours following the terrorist attack. Substantial proportions also reported daily occupational exposures to vapors, dust, gases, and/or fumes (46.2%), and to asbestos (24.4%). Spirometric studies showed normal FVC, reduced FVC, or obstructive impairment in 854 (58.8%), 418 (28.8%), and 181 (12.5%) subjects, respectively. Additionally, bronchodilator response was observed in 171 (13.5%).

Table 2 summarizes the main chest CT abnormalities, according to the ICOERD classification, in studies obtained a median of 6.8 (IQR 5.7–8.6) years after 9/11/2001. Pleural abnormalities were the most frequent type of abnormalities, found in 307 (21.1%) of the subjects, and were classified as visceral and parietal in 13.8% and 9.5% of the subjects, respectively. Well defined rounded and irregular/linear opacities were also found in more than 10% of the subjects, although with relatively low (1–2) sum grades.

Table 3 presents the bivariate analyses of the study variables and the presence of pleural abnormalities.

Table 1. Demographic, occupational, and clinical characteristics of the study population (n = 1,453).

Characteristic	N	%
Gender		
Male	1213	83.5
Female	240	16.5
Age on 9/11/2001, *median (IQR), years*	42	(36–48)
Height, *median (IQR), meters*	1.73	(1.65–1.80)
Race/ethnicity		
Non-Latino White	769	34.3
Latino	498	52.9
Non-Latino Black	135	9.3
Non-Latino other	51	3.5
Occupation		
Management/services	261	18.0
Construction trades	270	18.6
Laborers/cleaners	468	32.2
Transportation	90	6.2
Law enforcement	364	25.1
Weight status		
Normal	255	17.9
Obese	530	37.1
Overweight	638	44.7
Underweight	5	0.4
Pre-WTC occupational exposure (Significant)	671	46.2
Asbestos exposure (Significant)	355	24.4
Smoking status		
Never smoker	782	53.8
Former smoker	388	26.7
Current smoker	283	19.5
Arrival at WTC site ≤48 hours	745	51.3
WTC exposure duration ≥ 60 days	868	59.7
Spirometry pattern		
Normal	854	58.8
Low FVC	418	28.8
Obstruction	181	12.5
Bronchodilator response (Present)	171	13.5

There were significant unadjusted associations of pleural abnormalities with older age, lower BMI, non-Latino White race/ethnicity, work as a laborer/cleaner, and having reported significant pre-WTC occupational exposure to asbestos. Spirometric studies showed a very similar distribution in diagnostic patterns (normal, reduced FVC, or obstructive impairment), with a slightly lower FEV_1% predicted in subjects with pleural abnormalities. That slight difference was seen only in the subgroup of subjects with visceral pleural abnormalities (83.8%, SD 18%, vs. 80.2%, SD 19.7%, $p = 0.01$).

Table 4 presents two logistic regression models of pre-WTC occupational exposures and pleural abnormalities: model 1 had significant pre-WTC asbestos exposure as the main predictor, and model 2 had pre-WTC occupational group as the main predictor. In this analysis, occupational exposure to asbestos before 9/11/2001 was significantly associated with 1.42-fold increased odds of pleural abnormalities (Model 1). In the multivariable analysis of occupational group, work as laborer/building cleaner was significantly associated with 1.65-fold increased odds of pleural abnormalities. Table 4 also presents unadjusted odds ratios obtained by logistic regression, for comparison with the adjusted results.

Table 2. Distribution of radiological abnormalities in the study population (n = 1453). CT scan abnormalities are reported according to the ICOERD classification, on the first available chest CT scan from WTC responders and volunteers (n = 1453), and obtained a median of 6.8 years after 9/11/2001. Sum grades (which can range from 0 to 18) are reported for 5 of those domains.

Chest CT findings	N	%
Pleural abnormalities		
Any	307*	21.1
Parietal present	134	9.5
Visceral present	199	13.8
Well defined rounded opacities		
Present	145	10.0
Sum grade 1–2	104	7.2
Sum grade ≥3	41	2.8
Irregular/linear opacities		
Present	193	13.3
Sum grade 1–2	131	9.0
Sum grade ≥3	62	4.3
Ground glass opacity		
Present	114	8.0
Sum grade 1–2	71	5.0
Sum grade ≥3	43	3.0
Honeycombing		
Present	13	0.9
Sum grade 1–2	6	0.4
Sum grade ≥3	7	0.5
Emphysema		
Present	142	9.9
Sum grade 1–2	68	4.7
Sum grade ≥3	74	5.2
Large opacities		
Present	10	0.7
Inhomogeneous attenuation		
Present	188	13.0

*33 (2.3%) subjects had both parietal and visceral pleural abnormalities.

With regards to other covariates, both age on 9/11/2001 and BMI showed significant adjusted associations with the outcome in model 1, but BMI did not in model 2 (Table 4). Per every 10-year increase in age on 9/11/2001, the odds of pleural abnormalities increased in models 1 and 2 by about 18% and 16%, respectively. Per every 5 kg/m^2 increment in BMI, the odds of pleural abnormalities decreased in models 1 and 2 by 13% and 12%, respectively. We found no significant association of either WTC exposure duration or early arrival at the WTC site with pleural abnormalities, but we found that their inclusion altered the β estimate for occupation in model 2 (Table 4) by more than 10%, and both were subsequently included in that model.

After examination of model 2 (in Table 4), we conducted *post hoc* analyses for potential confounding. We focused attention on our previously described[15] sizeable subgroup of first-generation immigrant Polish laborers/asbestos handlers/building cleaners (n = 237, 16.3% of our entire study sample, and 50.6% of that occupational group). Compared to the rest of our sample, that subgroup, exclusively of non-Latino White race/ethnicity, had a significantly higher predominance of male sex (95.8% vs. 81.1%), median age (48 [IQR 42–52.5] vs. 41 [IQR 36–46] years), and status as current or former tobacco smokers (65.8% vs. 42.3%). More importantly, 70% of Polish laborers reported significant pre-WTC occupational exposure to asbestos, and accounted for almost half (166/355) of all WTC workers with such exposure. Close to a third (77/237) of the Polish laborers had pleural abnormalities, and accounted for 25.1% (77/307) of all WTC workers with such finding. In an exploratory analysis adding a race/ethnicity category of non-Latino White/Polish to both models in Table 4 left such category as the only significant predictor of pleural abnormalities (data not shown).

Discussion

To our knowledge, this is the first study that uses a standardized method for identifying and grading chest CT abnormalities in the WTC cohort, and one of the largest published to date using the ICOERD system. Using the first available chest CT study, a median of 6.8 years after the terrorist attack to the WTC, we found a non-negligible prevalence of possibly work-related imaging abnormalities. Of these, pleural abnormalities were by far the most frequent and we found them to be associated with both significant self-reported pre-WTC occupational asbestos exposure, and with work as laborer/cleaner (which also included the asbestos handlers). Older age and lower BMI were also associated with those abnormalities. Importantly, our study showed the presence of pleural abnormalities across all occupational groups and, in particular, identified the first-generation Polish immigrant laborers/asbestos handlers/building cleaners as the subgroup most likely to exhibit such abnormalities.

Chest CT imaging increases detection of occupational lung diseases, including asbestos-related diseases. The retrospective and systematic review with the ICOERD classification[10] recorded findings that were often missed or poorly quantified in routine clinical readings. Although its precise role is still under discussion, CT scanning will play a role in occupational lung disease surveillance.[16–19] In our study, an interesting finding was the predominance, among the pleural abnormalities, of those of the visceral type (including diffuse pleural thickening, pleural tags, parenchymal bands, rounded atelectasis), which tend to be associated with higher cumulative fiber dose exposures than parietal pleural abnormalities (i.e., pleural plaques).[20] No case in this series has been diagnosed with asbestosis, although cases with some of the associated findings (honeycombing, irregular/linear opacities) will have to be followed closely.

Table 3. Bivariate associations study variables for WTC responders who underwent CT evaluations with the presence and absence of pleural abnormalities recorded on the ICOERD form.

	Pleural abnormalities				
	Present	%	Absent	%	p value*
n	307	21.3	1146	78.9	—
Age *(median, IQR) years*	43 (37–50)		42 (36–48)		**0.014**
Height *(median, IQR) meters*	1.73 (1.68–1.80)		1.73 (1.65–1.80)		0.199
BMI *(median, IQR), kg/m^2*	28.1 (25.1–31.6)		28.6 (26.0–31.7)		**0.002**
Gender					
Male	259	21.4	954	78.6	0.639
Female	48	20.0	192	80.0	
Race/ethnicity					
Non-Latino White	184	23.9	585	76.1	**0.040**
Non-Latino Black	24	17.8	111	82.2	
Latino	92	18.5	406	81.5	
Non-Latino Other	7	13.7	44	86.3	
Weight status					
Underweight	0	0	5	100.0	0.067
Normal	69	27.1	186	72.9	
Overweight	130	20.4	508	79.6	
Obese	104	19.6	426	80.4	
Smoking status					
Current smoker	66	23.3	217	76.7	
Former smoker	87	22.4	301	77.6	0.153
Never smoker	154	19.7	628	80.3	
Pre-WTC occupations					
Management/services	50	19.2	211	80.8	**0.004**
Construction trades	55	20.4	215	79.6	
Laborers/cleaners	125	26.7	343	73.3	
Transportation	19	21.1	71	78.9	
Law enforcement	58	15.9	306	84.1	
Pre-WTC asbestos exposure					
Yes	95	26.8	260	73.2	**0.003**
No	212	19.3	886	80.7	
Pre-WTC occupational exposures					
Yes	150	22.4	521	77.6	0.289
No	157	20.1	625	79.9	
Arrival at WTC site					
$\leq$ 48 hours	150	20.1	595	79.9	0.341
$>$ 48 hours	157	22.2	551	77.8	
WTC exposure duration					
$>$60 days	175	20.2	693	79.8	0.271
$\leq$60 days	132	22.6	453	77.4	
Spirometry pattern					
Normal	183	21.4	671	78.6	
Low FVC	81	19.4	337	80.6	0.457
Obstruction	43	23.8	138	76.2	
Expiratory flows					
FEV_1, *%predicted (mean, SD)*	81.4 (19.2)		83.8 (18.0)		0.04
FVC, *%predicted (mean, SD)*	81.6 (17.4)		82.8 (15.6)		0.26

*p values calculated for continuous variables with the Wilcoxon's rank sum test.

Our study demonstrates the persistent risk of asbestos-related disease across the rich spectrum of occupations[1] involved in the WTC disaster site rescue, recovery, and service restoration, in relation to their pre-WTC exposures. This risk was highest for laborers/cleaners (and particularly the first-generation Polish immigrants), a category created[15] to include construction and demolition laborers, asbestos handlers, and building cleaners, because these workers often performed those functions interchangeably. These findings underscore the need for continued prevention of asbestos-related diseases and surveillance of exposed workers of all categories, while paying particular attention to those most intensely exposed.

Age on 9/11/2001 and lower BMI were also found to be predictors of pleural abnormalities, although inconsistently. Age is both an indicator of cumulative lifelong exposures, and also an expected predictor given the well-known long latency of all asbestos-related lung diseases. Lower BMI was a weak risk factor, and one possible explanation is that radiologists may be more likely to exclude pleural abnormalities in obese subjects, who often have subpleural adipose tissue accumulation.

The lack of significance of WTC exposure indicators is not surprising in an analysis of an occupational respiratory disease with very long latency. We found, however, that both WTC exposure indicators altered effect estimates for occupation in model 2. That finding in all

Table 4. Unadjusted and adjusted analyses of pleural abnormalities by history of significant occupational asbestos exposure (model 1), or pre-WTC occupational group (model 2) as main predictor.

Parameter		Unadjusted				Model 1				Model 2			
		OR	95% CI		P	OR	95% CI		P	OR	95% CI		P
Asbestos Exposure	No	reference			**0.0029**	reference			**0.0174**	n.a.			
	Yes	1.53	1.16	2.02		1.42	1.06	1.89					
Occupational Categories	Management/services	reference			**0.0044**	n.a.				reference			**0.0116**
	Construction trades	1.08	0.70	1.66						1.05	0.68	1.63	
	Laborer/ cleaners	1.54	1.06	2.23						1.61	1.10	2.39	
	Transportation	1.13	0.62	2.04						1.20	0.66	2.18	
	Law enforcement	0.80	0.53	1.21						0.81	0.52	1.25	
Age on 9/11	10-year increment	1.25	1.09	1.44	**0.0012**	1.18	1.02	1.37	**0.0246**	1.16	1.00	1.34	0.0580
WTC arrival ≤ 48 hours	No	reference			0.3410	-*				reference			0.3828#
	Yes	0.89	0.69	1.14						1.14	0.85	1.54	
BMI	5 kg/m² increment	0.89	0.78	1.01	0.0675	0.87	0.76	0.99	**0.0394**	0.88	0.79	1.01	0.0583
WTC exposure	<60 days	reference			0.2714	reference			0.1579	reference			0.0736#
	≥60 days	0.88	0.67	1.12		0.83	0.64	1.08		0.79	0.60	1.02	
Race/ethnicity	Non-Latino White	reference			**0.0416**	reference			0.1538	reference			0.1180
	Non-Latino Black	0.69	0.43	1.10		0.72	0.44	1.15		0.74	0.46	1.20	
	Latino	0.72	0.54	0.95		0.80	0.60	1.06		0.75	0.56	1.00	
	Other non-Latino	0.51	0.22	1.14		0.53	0.23	1.19		0.55	0.24	1.27	

*Eliminated from the model ($p > 0.2$).
#Included in model due to confounding or parameter alteration (>10% change in β estimate).

likelihood related to the patterns of arrival and exposure duration for laborers/cleaners, the highest risk group.[15]

The strengths of this study relate to having the largest set of chest CT images collected thus far in WTC workers, the systematic reevaluation of those studies with a standardized method to classify potentially work-related abnormalities, the range of occupations in our cohort,[1] and the amount of data on relevant risk factors. The main limitations relate to the lack of detailed ascertainment of environmental exposures to asbestos, and the relatively crude indicators of such exposure available for study. More extensive investigation of those exposures needs to be presented in order to continue the effort to control asbestos-related lung diseases. Although, compared to chest radiography, chest CT scan increases the sensitivity in the detection of pleural and pulmonary abnormalities consistent with occupational lung diseases, interreader variation is almost as common as with chest radiography,[21] and pleural abnormality findings have to be interpreted with caution, particularly in subjects with no clear exposure history,[22] or those with exclusively visceral pleural abnormalities.[23]

This study provides a baseline for needed surveillance of this cohort, with pre- and WTC-related occupational exposures. Although pleural plaques are generally considered a benign process, they are certainly a marker of pulmonary exposure, and have been recently suggested as an independent risk factor for death among exposed workers.[24] Other abnormalities that may portend more severe forms of lung disease will also require vigilance.

In summary, our study showed the prevalence of potentially work-related chest imaging abnormalities of the WTC rescue and recovery workers. Although we found subgroups and risk factors associated with potential asbestos-related pleural abnormalities, it is important to underscore the findings across all of the occupational subgroups examined. We have demonstrated the utility of chest CT for detecting, and of a standardized method for characterizing potentially work-related imaging abnormalities, and have also established a baseline for continued surveillance of this population. Future studies need examine the other frequent abnormalities observed, and their longitudinal evolution.

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Author Contributions

Study conception and design: RED; Acquisition, analysis, and interpretation of data: all authors; Critical revision for important intellectual content: All authors; Statistical analysis: JW, JTD, RED, XL, and JCC; Obtained funding: RED; Administrative, technical, or material support: RED; Study supervision: RED. All authors approved the final version of the manuscript before submission.

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