Investigating Types and Frequency of Vascular Findings in Pulmonary CT Angiography of Baker females with Pulmonary Complaints in Comparison with Chronic Obstructive Pulmonary Disease

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ABSTRACT
Still in many places all over the world including East Azerbaijan Province and particularly in rural areas, women use traditional methods such as using oven and organic fuels (wood, turd) to bake bread. It has been shown that the smoke organic fuels in places with inadequate ventilation for a long term may cause a range of problems in the respiratory system. CT angiography is a good and less invasive method in evaluating pulmonary vascular system. This study tried to compare CT angiography findings in the lungs of bread-cooking women with respiratory complaints and females with COPD and no history of bread cooking. In this case-control setting, 36 patients in the bread-cooking group (case) and 36 patients with COPD in the control group underwent lung CT angiography. Pathologic findings including dilation of the bronchial arteries, hyper vascularization of the bronchial arteries, changes in pulmonary trunk diameter, silent embolism and any other abnormal changes were documented and compared between the two groups. The mean duration of bread-cooking was 4.78±3.17 years (2-12). Abnormal vascular findings in lung CT angiographies of the bread-cooking women with respiratory complaints were dilation of the bronchial arteries (22.2%), hyper vascularization of the bronchial arteries (8.3%), silent embolism (11.1%) and parenchymal emphysematous changes (13.9%). They were documented in the COPD group in 36.1%, 27.8%, 27.8% and 3.33% of the patients, respectively. Accordingly, the frequency of hyper vascularization of the bronchial arteries and parenchymal emphysematous changes was significantly higher in the COPD group than in the bread-cooking women. In contrast, the mean diameter of the pulmonary trunk was significantly higher in the bread-cooking group (3.32 vs. 3.17 cm). Abnormal findings in lung CT angiography of bread-cooking women with respiratory symptoms are frequent and in some cases, they are different from findings in the lungs of women with COPD and no previous history of bread-cooking.

Keywords: Bread-cooking, COPD, CT Angiography
INTRODUCTION
Despite enormous progress in food production and processing industry, there are still many areas, particularly rural, in which the traditional ways of baking bread are predominantly employed. Many less developed areas in the province of East Azerbaijan, Iran, are good examples in this regard that use home hand-made furnaces fueled by organic material such as wood and turd [1].
Using such material as the fuel specially when there is not sufficient ventilation may cause various types of respiratory disease [2]. Constrictive and obstructive pulmonary diseases with or without a superimposed allergic reaction are good examples of such problems that are seen among households using organic fuels including bread-baking females. In different studies conducted all over the world, it has been shown that the prevalence of such respiratory disease is significantly higher among bread-baking women compared to their matched controls [3-5].
Development of such problems in this particular population has been attributed to the toxic components of smoke of burning organic materials inside traditional furnaces as well as flour contamination [6]. Accordingly, it is expected that the involvement of pulmonary vasculature should be more common in this group compared to normal population, which may lead to further problems in the cardiovascular system [7].
Changes in diameter of the bronchial arteries, hypervascularization, pulmonary trunk widening and abnormal changes in pulmonary tissue are among the most important findings in CT angiography of patients with COPD that are supposed to be present to some degrees in bread-cooking women [8-9].
Accordingly, despite the presence of multitude of studies reporting pulmonary problems in traditionally bread bakers and persons in close contact with flour and similar products, to the best of the authors’ knowledge there is no study about lung angiographic findings in these patients. It is not clear whether the schemes associated with restrictive and constrictive pulmonary conditions are present in patients with bread-baking history. So, this study tries to compare pulmonary vascular findings using CT angiography between patients with both pulmonary problems and bread-baking history and those with chronic obstructive pulmonary disease (COPD) with no significant history of traditional bread baking.

MATERIAL AND METHODS
In this descriptive-analytic, case-control, prospective study, pulmonary CT angiography findings in patients with bread baking history and pulmonary complaints and women with COPD and no previous traditional bread baking attending to Imam Reza Teaching Hospital between December 2016 through July 2016 were compared with each other. Written informed consents were obtained form the patients. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences.
Bread-baking women (traditionally) with respiratory complaints who were candidates of pulmonary CT angiography were considered as the case group (36 patients). Patients in this group had at least 2 years of bread-baking history and complained of respiratory symptoms. Patients with a history of smoking/shisha use, and those with known pulmonary disease and/or right cardiac problems were excluded. The control group included women with definite diagnosis of COPD without a previous history of bread baking, who were candidates of pulmonary CT angiography on the attending physician’s discretion (36 patients). The two groups were age-matched.
All patients in both groups underwent thorough physical examination, conventional spirometry (FEV1, FVC, TLC and RV measurement) and pulmonary vascular CT angiography. Presence/absence of pulmonary obstructive/restrictive condition and its severity on the basis of spirometry findings were reported in each patient by the attending pulmonary specialist. Two radiologist examined CT angiographic images independently, without knowing other patients related information. A third radiologist was arbitrated when there was a controversy. Pulmonary CT angiography findings were as follows: Increased diameter of bronchial artery (over 2 mm), presence of bronchial artery hypervascularization on the discretion of radiologist, diameter of the pulmonary trunk, presence of silent embolism, any abnormal change in the pulmonary vascular structure, and emphysematous changes in the pulmonary tissue. In the case group, presence/absence of abnormal CT angiographic findings was compared between various severities of pulmonary obstruction (according to spirometry findings).

**Statistical analysis**

Data were presented as mean±standard deviation and frequency (%). Spss software ver. 16 was used. The independent samples t-test was used for comparing quantitative data. The chi-square test or the Fisher’s exact test was used for comparing qualitative data. Correlation between quantitative variables was examined reporting the Pearson coefficient (r). A p-Value less than 0.05 was considered statistically significant.

**Results**

There were 36 patients in the bread-baking group and 36 patients in the COPD group. The two groups were comparable for the mean age (62.03±6.76 years vs. 60.00±7.94 years, p=0.25), mean height (161.72±7.47 cm vs. 161.81±7.49 cm, p=0.96) and the mean weight (66.92±13.56 kg vs. 65.64±11.40 kg, p=0.67). The mean duration of bread baking was 4.78±3.17 years (2-12). Respiratory findings in the case group were as follows: FEV1, 2.06±0.20; FVC, 3.15±0.26; FEV1/FVC, 65.50±5.50; TLC, 88.89±7.28; RV, 89.31±8.63. Signs and symptoms of the patients are summarized and compared between the two groups in Table 1. Accordingly, only pleurodynia was significantly more frequent in the case group.

| Sign/symptom | Cases (n=36) | Controls (n=36) | p-value |
|--------------|-------------|----------------|---------|
| Dyspnea      | 27 (75%)    | 30 (83.3%)     | 0.38    |
| Pleurodynia  | 27 (75%)    | 18 (50%)       | 0.03*   |
| Cough        | 33 (91.7%)  | 33 (91.7%)     | -       |
| Sputum       | 23 (63.9%)  | 24 (66.7%)     | 0.80    |

*Statistically significant

Previous disease was present in 14 patients (38.9%) in the case group and 11 patients (30.6%) in the control group (p=0.46). These diseases were hypertension in 8 cases, arthritis in 3 patients, diabetes mellitus in 2 cases and hypothyroidism in 1 patient in the case group. In the control group, there were 6 patients with hypertension, arthritis in 2 patients, diabetes mellitus in 2 cases and cataract in 1 case in the control group. The diagnosis was obstructive disease in 16 patients (44.4%), restrictive disease in 8 patients (22.2%) and a combination of both in 3 patients (8.3%) in the case group.
severity of the disease was mild in 19 patients (70.4%), moderate in 6 patients (22.2%) and severe in 2 cases (7.4%), whereas it was mild in 17 controls (47.2%), moderate in 15 controls (41.7%), and severe in 4 controls (11.1%); with no significant difference between the two groups (p=0.18). Pulmonary CT angiography findings are summarized in Table 2.

Table 2. Pulmonary CT angiography findings in bread baking and control women

| Variable                               | Cases  | Controls | p-value |
|----------------------------------------|--------|----------|---------|
| Increased diameter of bronchial artery | 8 (22.2%) | 13 (36.1%) | 0.20    |
| Pulmonary artery hypervascularization  | 3 (8.3%)  | 10 (27.8%) | 0.03*   |
| Silent embolism                        | 4 (11.1%) | 10 (27.8%) | 0.07    |
| Parenchymal emphysematous changes      | 5 (13.9%) | 12 (33.3%) | 0.05*   |
| Pulmonary trunk diameter (cm)          | 3.32±0.54 | 3.17±0.68 | 0.02*   |

*Statistically significant

Accordingly, while pulmonary hypervascularization and parenchymal emphysematous changes were significantly more frequent in controls (odds ratio, OR, 4.23, p=0.03 and OR=3.1, p=0.05, respectively); the mean diameter of the pulmonary trunk was significantly higher in the case group (p=0.02).

Pulmonary CT angiography findings in the bread-baking group are presented on the basis of the severity of pulmonary involvement in Table 3.

Table 3. Pulmonary CT angiography findings in bread-baking women according to the severity of involvement

| Variable                               | Normal (n=9) | Mild (n=19) | Intermediate/severe (n=8) | p-value |
|----------------------------------------|--------------|------------|--------------------------|---------|
| Increased diameter of bronchial artery | 0 (0)        | 0 (0)      | 8 (100)                  | <0.001* |
| Pulmonary artery hypervascularization  | 0 (0)        | 0 (0)      | 3 (37.5)                 | 0.01*   |
| Silent embolism                        | 0 (0)        | 1 (5.3)    | 3 (37.5)                 | 0.03*   |
| Parenchymal emphysematous changes      | 0 (0)        | 0 (0)      | 5 (62.5)                 | <0.001* |
| Pulmonary trunk diameter (cm)          | 3            | 3          | 4                        | <0.001* |

*Statistically significant

Accordingly, the frequency of increased diameter of the bronchial artery, pulmonary hypervascularization, silent embolism, and emphysematous parenchymal changes were significantly higher in patients with intermediate/severe disease. The mean diameter of the pulmonary trunk was also significantly higher in this group of patients (p<0.001).

There was a significant, positive correlation between the diameter of the pulmonary trunk and the duration of bread baking (r=0.64, p<0.001). In other words, with increasing time of bread baking, the diameter of the pulmonary trunk also increased (Figure 1).
DISCUSSION
In this study pulmonary system CT angiography results were compared between women complained of respiratory symptoms with traditional bread baking history and women with COPD but without such a history. The diagnosis of pulmonary disease in the bread-baking group included obstructive disease (44.4%), restrictive disease (22.2%) and obstructive-restrictive disease (83%). In 25% of patients there was no specific pulmonary disease. These results were in conformity with previous reports depicting that in patients who were exposed to long-term smoke of organic fuels could develop a wide range of pulmonary problems such as constrictive disease, interstitial lung disease, cancer, asthma and recurrent infections of the lower respiratory tract [10-14]. In a meta-analysis by Hu et al it has been also shown that long-term exposure to the smoke of organic materials may increase the risk of constrictive-obstructive disease significantly [15]. Haidarnejad and Ghaffari in a study in our center examined 42 bread-baking women with respiratory disease in spirometry, evidences of mild to severe obstructive diseases were present in 47%, mild to severe obstructive-restrictive disease 26% and mild to severe restrictive disease in 14% of patients. Only in 13% of women the spirometry results were found normal [1].
As it is clear the reported rate in the present study is very similar to that of the mentioned report. In other words, despite a 20-year difference between the time of our study and the above study, there are still pulmonary problems in bread-baking women and may cause respiratory consequences [16-20].
In a newer study in Greece, Patouchas et al 58 laborer in the section of bread production using traditional methods were examined using pulmonary functional tests and
plethysmography. Results were indicative of restrictive and constrictive diseases in the lungs in 12.6% of patients [21]. In comparison with our findings, the reported rate in above study is less than ours, possibly because of differences between the studies in terms of circumstances, time of smoke exposure and the type of fuel.

On the basis of our findings, abnormal vascular findings in CT angiography of the lungs of the studied women were the increased diameter of bronchial arteries (22.2%), hypervascularization of bronchial arteries (8.3%), silent embolism (11.1%) and emphysematous changes in the lung parenchyma (13.9%); and the mean diameter of the pulmonary trunk was 3.17 cm. In comparison, the rates of bronchial artery hypervascularization and parenchymal emphysematous changes were significantly higher in COPD group, whereas the mean diameter of the pulmonary trunk was higher in the bread-baking group.

In a study by Ozbay et al, findings of spirometry and pulmonary CT scan were examined in 30 women with COPD without previous smoking but a positive exposure to the smoke of biomaterials. According to the findings of CT scan the most frequent findings were the increased pulmonary volume, increased thickness of interlobular septum, local emphysematous regions and broncho vascular arborisation [22]. In a study by Rivera et al, pulmonary CT findings were compared between women with COPD due to biomaterial smoke and smoking. It was shown that although vascular changes were prominent in the both groups, they were more common in the former group [23].

As it is seen, in oppose to our findings the frequency of bronchial artery hypervascularization was significantly higher in the COPD group. The reason for this discrepancy could be including COPD cases resulting from both smoke and smoking in the mentioned study; whereas in our series COPD cases were just a small fraction.

For example in a study by Menchini et al it was shown that bronchial artery hypervascularization is a frequent feature in patients with COPD [8]. However, a higher frequency of emphysematous changes in COPD patients compared to bread-baking women in the present work has been previously emphasized; In a study by Kara et al CT findings high resolution CT scan findings were compared between 30 symptomatic females with a previous exposure to biomaterial smoke and 30 controls. In this study, emphysematous changes were significantly more common in the case group (63% vs. 3%) [24]. In a study by Rivera et al cadavers of 21 women with smoking-induced COPD and 27 women with biomaterial smoke-induced COPD were examined. Emphysematous changes and increased thickness of pulmonary arteries were more common in the first and the second groups, respectively [23]. In a study by González-García et al two groups of women with respiratory symptoms attributable to wood smoke (19 cases) and smoking (12 cases) were compared. In this study, emphysematous changes were seen more common in the latter group [25]. In a study by Camp et al 21 patients with COPD and no previous history of smoking but exposure to biomaterial smoke and 22 women with smoking-induced COPD were examined using CT scanning. Accordingly, in conformity with our findings emphysematous changes were significantly more common and more severe in the smokers [26].

An increased diameter of the main pulmonary artery trunk in CT is a major finding indicative of pulmonary hypertension [27-29]. Therefore, the increased diameter of pulmonary trunk in bread-baking women compared to that in COPD patients may indicate a higher frequency of pulmonary hypertension in the same group.
This surmise that a long-term exposure to biomaterial smoke may cause pulmonary hypertension is not new in the literature and has been emphasized in other studies, too [30], [30-31], [32]. In a study by Sertogullarindan et al results of CT angiography of the respiratory system were examined in patients with a previous exposure to biomaterial smoke. 104 women in the case group and 20 controls were recruited. In line with our findings, they also showed that the mean diameter of the main pulmonary artery was significantly higher in the case group (3.7 cm vs. 2.7 cm). Accordingly, the authors concluded that pulmonary hypertension was more common in the case than in the control group [33]. In a review article by Assad et al it was concluded that in COPD due to biomaterial smoke, in comparison to smoking-induced type, the bronchial involvement is more widespread, the emphysematous changes are less and the pulmonary hypertension is more severe [34]. We also reached a similar conclusion [35-36].

Another important finding in our study was a significant, direct association between abnormal findings in CT angiography with the severity of involvement determined by spirometry. In a study by Arslan et al the effect of biomaterial smoke on the respiratory system was examined in 21 female cases and controls. Restrictive-constrictive changes were more frequent in the case group. In high-resolution CT the frequency of fibrotic changes and increased thickness of peribronchoalveolar was 7 and 5 times more than that in controls, respectively. In line with our findings, a significant positive correlation was found between the severity of disease on the basis of spirometry and the extent of the mentioned changes [37]. In a study by Sertogullarindan et al it was shown that women with a positive history of exposure to biomaterial smoke a significant correlation presents between the severity of pulmonary hypertension and the severity of pulmonary disease [32].

In addition to such a finding, we also showed a significant positive correlation between the diameter of the pulmonary trunk and the duration of bread baking. Zhou et al also showed that there is a direct correlation between the extent of decreased pulmonary function and the time of exposure to biomaterial smoke. They reported this conclusion in a study on 966 patients with COPD and a positive history of exposure to biomaterial smoke [38].

Various mechanisms have been suggested to explain differences between respiratory systems in patients with previous exposure of biomaterial or cigarette smoke; although the composition of any type of smoke may be similar-or at least share common features-on the basis of the origin of biomaterial smoke, the combustive efficacy and the percentage of ambient humidity the effect on the respiratory system varies [26].

Despite this fact, some studies have suggested that this heterogeneity is due to differences in the composition of the two types of smoke, which despite similar size of the particles comparable pathophysioligic processes are present [39].

The age of first exposure is important, because it has been shown that in bread-baking women, for example, even fetus in the uterine may be affected untowardly. The fact that women and children are more exposed to the smoke of biomaterials is because of their more frequent exposure in comparison with men, which in turn, increases the culminate dose of exposure significantly. On the other hand, an exposure at younger ages leads to frequent respiratory infections that affect structures and functions of this system [39].

Inspiration of the two types of the smoke is also different. In the biomaterial group, a consistent tidal breathing pattern is present, whereas in the cigarette smoke group there is biphasic pattern: the smoke enters the mouth in the first place and then after a short time
pause and mixing with more air enters the lungs [40]. Deep inspiration of cigarette smoke causes the entrance of the smoke into deeper regions of the lung parenchyma and this may explain the emphysematous phenotype of COPD in smokers [26].

The present study is the first one in the literature that correlated CT angiography findings in the respiratory system of women with a history of bread baking and a group of controls with COPD. For more definite conclusions and defining exact mechanism of the physiopathology, however, further studies are needed.

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