Impact of shift work on irritable bowel syndrome and functional dyspepsia
A meta-analysis

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Abstract
Background: The possible association between shift work with irritable bowel syndrome (IBS) and functional dyspepsia (FD) remains controversial. The purpose of the study is to conduct a meta-analysis to explore the potential association between shift work with IBS/FD.

Methods: We searched relevant observational studies on Medline (PubMed) and Embase until June 30, 2021. Two different investigators extracted data and assessed the quality of each study independently. The meta-analysis was used to evaluate the pooled odds risk (OR) between shift work and IBS/FD.

Results: Eight studies were included ultimately. Shift workers were more likely to suffer from IBS. The OR of shift work was 1.81 (95% confidence interval 1.42; 2.32) with low heterogeneity ($P < .05, I^2 = 0\%$) for IBS. However, no evidence of the association was observed between shift work and the risk of FD. The OR of shift work was 0.87 (95% confidence interval 0.62; 1.23) ($P > .05$) for FD.

Conclusions: There was a positive association between shift work and IBS. The prevalence of IBS was 81% higher among shift workers than among non-shift workers. Shift work was probably a risk factor for IBS. The low heterogeneity supports the reliability of the results. However, there was no significant association between shift work and FD. The strength of the evidence was limited and further prospective cohort studies were needed.

Abbreviations: CI = confidence interval, FD = functional dyspepsia, FGIDs = functional gastrointestinal disorders, IBS = irritable bowel syndrome, OR = odds risk.

Keywords: functional dyspepsia, irritable bowel syndrome, meta-analysis, observational study, shift work

1. Introduction

Functional gastrointestinal disorders (FGIDs) are characterized by upper and lower symptoms with no definite organic or biochemical abnormalities. Irritable bowel syndrome (IBS) and functional dyspepsia (FD) are the most common among FGIDs and have received more attention for affecting the quality of life and social functioning. For example, IBS affects 7% to 16% of Americans[1] and the overall prevalence of dyspepsia was 21%.[2] Alteration in motility, immunity, visceral sensitivity, intestinal barrier integrity, and psychological factors have been proved vital mechanisms in IBS.[3–5] However, the correlation between lifestyle and IBS/FD remains insufficient.

In daily life, shift work is quite common. This is partly because some occupations have to keep people on the job 24 hours a day (such as medical staff), and partly because enterprises have to improve production efficiency. Rotating shift forms include morning shift/night shift/rotating shift, periodic shift, and irregular shift. Over the past few decades, increasing attention and researches have pointed to the possible negative health effects of shift work. Shift work has been proved to increase the risk of cardiovascular disease and metabolic disorders.[6,7]
Some researchers believed that medical students in the overnight call were not associated with the development of IBS.\textsuperscript{[8]} But Borko Nojkov et al confirmed that shift work contributed to the development of IBS. The association between shift work and IBS/FD is controversial. Therefore, we conducted a meta-analysis of published observational studies to review epidemiological evidence on the association between shift work and IBS/FD.

2. Materials and methods

2.1. Search strategy and selection criteria

In accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, we searched published studies through Medline (PubMed) and Embase from inception to June 30, 2021. We identified all pertinent literature that associate between shift work and FGIDs, including FD and IBS. We used (“dyspepsia” or “IBS” or “irritable bowel syndrome”) and (“shift work” or “rotating shift work” or “night shift work” or “work at night” or “irregular work schedule”) as retrieval strategy. The diagnosis of IBS/FD in all included literatures was referred to Rome II criteria and Rome III criteria.\textsuperscript{[9,10]} The cases included in the literature belong to the secondary study and no patient privacy involved, so ethical approval was waived.

Studies were identified based on predefined inclusion criteria: the study was designed as a case-control or cohort study or cross-sectional study; the exposure of interest was shift work, the outcome was morbidity IBS/FD, 95% confidence interval (CI) or sufficient information to report win odds risk (OR) or relative risk (RR) for calculation. In addition, non-human studies, clinical trials, reviews, letters, duplicate literature, and studies that examined other associations were excluded. Subsequently, 2 investigators (Nian Wang and Xinghuang Liu) independently reviewed eligible articles by titles and abstracts and then by full texts. Any discrepancy between the 2 investigators was solved by a discussion with the senior investigator (Dr Tao Bai).

2.2. Data extraction and quality assessment

We extracted the following data from each eligible article: name of the first author, publication year, country, study design, data sources, subject number, age, diagnose of IBS/FD, the definition of shift work, the proportion of females, confounder adjusted and OR/relative risk/hazard ratio (95% CI). The Agency for Healthcare Research and Quality\textsuperscript{[11]} was applied to evaluate the cross-sectional studies. The Agency for Healthcare Research and Quality has an 11-item checklist. If it was answered “YES”, the item scored “1”; “NO” or “UNCLEAR” would be scored “0”. A score of more than 7 is considered as high quality, a score of 4 to 6 as moderate-quality, while a score of less than 4 as low quality. Any disagreements were resolved by consensus.

2.3. Data synthesis and meta-analysis

In this meta-analysis, all statistical analyses were performed with R 3.6.0 (Stata Corporation, TX). The OR value and 95% CI of each study were combined to obtain the combined OR value and 95% CI. P < 0.05 was regarded as a significance level. The heterogeneity among the studies was assessed by I2 statistics. If the result of the heterogeneity test was I2 > 50%, the random-effects model was applied. Otherwise, the fixed-effects model was used. Subgroup analysis was conducted to explore the potential influence of variables on pooled effects (such as origin country). Sensitivity analysis was conducted to evaluate the potential effect of the results. All statistical methods were predetermined.

3. Results

3.1. Literature characteristic and quality evaluation

A total of 69 items were retrieved. Of these, 23 articles were excluded because they were reviews, not English, non-human studies, or duplicate literature. After evaluating the full texts of the remaining articles that may be relevant for this meta-analysis, 38 of 46 were excluded for no association or no relevant data. In total, 8 studies were included. The detailed flowchart of the selection process on eligible studies was shown in flow diagram. Table 1 summarizes the 8 pieces of literature that met the inclusion criteria. All the included literature could be attributed to cross-sectional studies. Data were obtained from single-center studies and the questionnaire was taken from medical staff. The sample size ranged from 51 to 468. Shift schedules were classified as rotating shift, day shift, and night shift. In the 8 articles included, 4 articles covered both IBS and FD. Six studies used Rome III criteria to define IBS/FD and the 2 used Rome II criteria. As for the definition of shift work, 4 studies used self-reported, 1 study used overnight call requirements, 1 study was determined by researchers, 1 study used the record, and 1 study did not mention. The proportion of females in the 2 studies was 100%. The result of the quality assessment was presented in Table 2. Among the 8 articles, 7 were of high quality, 1 was of medium quality.

3.2. Overall meta-analysis of the association between IBS and shift work

When IBS was used as an outcome, the 8 studies were analyzed to seek whether the association was positive or negative. The heterogeneity test showed that I2 = 0 and the fixed effect model was selected. The OR and 95% CI of 8 studies were quantitatively combined, and the pooled OR and 95% CI was 1.81 (1.42; 2.32) (Fig. 1). It suggested that shift workers had an 81% increase in the prevalence or incidence of IBS compared with non-shift workers. We conducted subgroup analysis to explore the sources of heterogeneity and influence by region (Europe, America, and Asia). The pooled OR were 1.76 (95% CI 1.2; 2.58) and 1.81 (95% CI 1.42; 2.32), respectively (Fig. 2). This subgroup analysis had no statistical significance for heterogeneity. Sensitivity analysis was performed to test the robustness of our study findings. The pooled OR was 1.81 (95% CI 1.42; 2.32) after excluding studies without adjusting covariates (Fig. 3). The sensitivity analysis indicated that shift work obviously increased the risk of IBS.

3.3. Overall meta-analysis of the association between FD and shift work

When FD was used as an outcome, the pooled OR was 0.87 (95% CI 0.62; 1.23) (Fig. 4). The results showed that there was no significant correlation between shift work and FD. The pooled OR was 0.87 (95% CI 0.62; 1.23) and there was no statistical significance. Due to the limited number of included literature, no publication bias test was performed.
| Study               | Rogers et al | Zhou et al | Lu et al | Wells et al | Nojkov et al | Koh et al | Kim et al | Wang       |
|--------------------|--------------|------------|----------|-------------|--------------|-----------|-----------|------------|
| **Publication year** | 2021         | 2021       | 2006     | 2012        | 2010         | 2014      | 2013      | 2008       |
| **Country**        | USA          | China      | Singapore| UK          | Korea        | Korea     | Korea     | China      |
| **Study design**   | Cross-sectional | Cross-sectional | Cross-sectional | Cross-sectional | Cross-sectional | Cross-sectional | Cross-sectional | Cross-sectional |
| **Data sources**   | Single center; questionnaire research of nurses | Single center; questionnaire research of nurses | Single center; questionnaire research of nurses | Single center; questionnaire research of medical studies | Single center; questionnaire research of nurses | Single center; questionnaire research of nurses | Single center; questionnaire research of nurses | Single center; questionnaire research of nurses |
| **Subject number** | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 | Day shift: 24; Night shift: 27 |
| **Age (yrs)**      | 21–59 years old (mean 32.9±10.0) | 22–55 years old (mean 31.4±8.4) | 20–60 years old (median: 29) | 20–36 years old (mean: 25.0±2.1) | None | None | None | Mean 30.4±7.9 years old |
| **Diagnose of IBS/FD** | Rome III criteria | Rome III criteria | Rome III criteria | Rome III criteria | Rome III criteria | Rome III criteria | Rome III criteria | Rome III criteria |
| **Definition of shift work** | Self-reported | Self-reported | Overnight call requirements | Self-reported | Rome III criteria | By the researchers | Rome III criteria | Rome III criteria |
| **Proportion of female** | 96% | 100% | 47.7% | 89.6% | None | None | None | None |
| **Confounder adjusted** | None | None | None | None | None | None | None | None |
| **OR/RR/HR (95% CI)** | OR: 1.67 [0.45, 6.41] | OR: 1.88 [1.03, 2.49]; FD: OR: 0.76 [0.42, 1.21] | OR: 1.90 [0.60, 5.21] | OR: 2.14 [1.14, 3.74]; FD: OR: 0.71 [0.29, 1.70] | OR: 1.88 [1.03, 2.49]; FD: OR: 0.76 [0.42, 1.21] | OR: 1.32 [0.47, 3.74]; FD: OR: 0.71 [0.29, 1.70] | OR: 2.36 [1.01, 5.47]; FD: OR: 0.98 [0.46, 2.09] | OR: 1.67 [0.65, 4.67]; FD: OR: 1.50 [0.72, 3.21] |

CI = confidence interval, FD = functional dyspepsia, FGIDs = functional gastrointestinal disorders, HR = hazard ratio, IBS = irritable bowel syndrome, OR = odds risk, RR = relative risk.
4. Discussion

This study systematically reviewed the existing epidemiological evidence on the association between shift work and IBS/FD. Systematic review and meta-analysis found that shift work was an independent risk factor for IBS, but not significantly associated with FD.

Gastrointestinal activity and functions are regulated by circadian rhythms 24 hours a day.\cite{12} Shift work may contribute to circadian disturbances. Circadian rhythms also remain in the gastrointestinal system, and it regulates gastrointestinal motility, secretion, immunity, and metabolism.\cite{13} It has been documented that circadian disruption probably alters the gut microbiota, leading to an inflammatory state associated with shift work.\cite{14} A study had shown that disrupted circadian rhythms in the gut are linked to gastrointestinal disorders such as constipation and IBS.\cite{8,15} Melatonin regulates gastrointestinal motility and sensation, such as improving bowel habits and alleviating abdominal pain or bloating in patients with IBS.\cite{16} Melatonin is influenced by the 24-hour light-dark cycle and is a reliable marker of the circadian rhythm system.\cite{17} Razavi et al.\cite{18} revealed that night shift workers are exposed to more light than day workers and therefore have lower levels of melatonin in their urine. Low-dose melatonin accelerated intestinal motility, while high-dose did the opposite.\cite{19,20}

Shift work was associated with an increased risk of adverse mental health outcomes in general, and depressive symptoms in particular.\cite{21} Resident physicians who were on call more than 6 times a month had significantly poorer sleep quality and higher anxiety and depression scores compared to other colleagues.\cite{22} It is well known that patients with IBS often have symptoms such as...
as anxiety and depression. This may partly explain the increased incidence of IBS associated with shift work.

This study found no association between FD and shift work. The imbalance between the core circadian physiology and the work schedule is thought to be the main cause of shift work resulting in sleepiness and sleep disruption.[23] Vege et al.[24] revealed that impaired sleep quality was not associated with FD in the general population. Matsuzaki et al.[25] reported that no independent relationship between FD and sleep disorders after adjusting for the severity of reflux and bowel symptoms. However, the study on the relationship between FD and shift work has some shortcomings. There were only 4 studies included. The subjects were from the single-center, all of which were nursing-related staff. Therefore, the results of the study need to be further confirmed.

Our study demonstrated that IBS and FD are more common among staff in shift workers than those working the day shift. Shift work is an independent factor for risk of IBS. Moreover, adjusting for the severity of reflux and bowel symptoms.

![Figure 2. Pooled fixed-effect OR and 95% CI for the association of shift work and IBS by the region. CI = confidence interval, IBS = irritable bowel syndrome, OR = odds risk.]

| Study                        | TE  | sTE  | Odds Ratio | OR   | 95%–CI Weight |
|------------------------------|-----|------|------------|------|---------------|
| **region = Europe and America** |     |      |            |      |               |
| Ann E. Rogers et al          | 0.51| 0.6776| 1.67       | [0.44; 6.30] | 3.5%          |
| Malcolm Wells et al           | 0.18| 0.3547| 1.20       | [0.60; 2.40] | 12.7%         |
| Borko Nojkow et al            | 0.76| 0.2494| 2.14       | [1.31; 3.49] | 25.6%         |
| Fixed effect model            |     |      | 1.76       | [1.20; 2.58] | 41.8%         |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.0309$, $p = 0.41$ |     |      |            |      |               |
| **region = Asia**             |     |      |            |      |               |
| Hui–Qing Zhou et al           | 0.63| 0.2252| 1.88       | [1.21; 2.92] | 31.4%         |
| Wei Zhen Lu et al             | 0.64| 0.5049| 1.90       | [0.71; 5.11] | 6.3%          |
| Seong–Joon Koh et al          | 0.28| 0.5291| 1.32       | [0.47; 3.72] | 5.7%          |
| Hye In Kim et al              | 0.86| 0.4310| 2.36       | [1.01; 5.49] | 8.6%          |
| Xue–Yan Wang                  | 0.51| 0.5030| 1.67       | [0.62; 4.48] | 6.3%          |
| Fixed effect model            |     |      | 1.86       | [1.34; 2.57] | 58.2%         |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.94$ |     |      |            |      |               |

**Figure 2.** Pooled fixed-effect OR and 95% CI for the association of shift work and IBS by the region. CI = confidence interval, IBS = irritable bowel syndrome, OR = odds risk.

| Study                        | Odds Ratio | OR   | 95%–CI     |
|------------------------------|------------|------|------------|
| Omitting Ann E. Rogers et al | 1.82       | [1.42; 2.34] |         |
| Omitting Hui–Qing Zhou et al | 1.79       | [1.32; 2.41] |         |
| Omitting Wei Zhen Lu et al   | 1.81       | [1.40; 2.34] |         |
| Omitting Malcolm Wells et al | 1.93       | [1.48; 2.51] |         |
| Omitting Borko Nojkow et al  | 1.71       | [1.29; 2.28] |         |
| Omitting Seong–Joon Koh et al| 1.85       | [1.43; 2.39] |         |
| Omitting Hye In Kim et al    | 1.77       | [1.37; 2.29] |         |
| Omitting Xue–Yan Wang        | 1.83       | [1.41; 2.36] |         |

**Fixed effect model**

1.81 [1.42; 2.32]

**Figure 3.** Sensitivity analysis for the cross-sectional studies used IBS as the exposure factor. IBS = irritable bowel syndrome.
shift work has no significant correlation with FD. There are some
limitations in this meta-analysis. Firstly, the definitions of shift
work in the included literature were inconsistent. In the included
literature, there were about day work and shift work,[26–29] night
work and shift work,[30] and regular work and shift work.[31]
Secondly, the diagnostic criteria for IBS and FD in the literature
are not completely consistent. These may lead to some deviation
from the results and conclusions. We have included the currently
available cohort studies and performed subgroup analysis. Due
to the limited number, the application of the results and
conclusions of this study should be considered in combination
with other factors.

Author contributions
Tao Bai and Zhaohong Shi were involved in conception and
generation of the study protocol and study design. Nian Wang
and Xinghuang Liu reviewed the literatures, meta-analysis,
as well as have written. Weixiang Ye verified the data. Tao Bai was
responsible for resolving disagreements in data selection,
synthesis, and assessment. Nian Wang and Xinghuang Liu
contributed equally to this study. The manuscript is approved by
all authors for publication.

Data curation: Nian Wang.
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Writing – original draft: Nian Wang.

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