Relationship between the period from symptom onset to confirmation and the prevalence: results from 159 COVID-19 patients using public information through the data crawling

Myung-Bae Park, Eun Young Park 3rd, Taesic Lee, Jinhee Lee

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Abstract

Background: In general, early intervention based on early diagnosis of the disease is considered to be very important for improving the health outcome. However, there is still not enough evidence of how medical care that is based on the early diagnosis of confirmed cases can affect the COVID-19 treatment outcomes.

Objective: Accordingly, we aimed to investigate the effects of the duration from the onset of clinical symptoms to confirmation on the duration to the resolution of COVID-19 (release from quarantine).

Methods: For preliminary data collection, we performed data crawling to extract data from social networks, blogs, and official websites operated by local governments. We collected data from the 4,002 confirmed cases from 33cities reported until May 31, 2020, for whom sex and age information could be verified. Subsequently, 2,494 patients with unclear symptom onset date and 1,349 patients who had not been released or had no data about the release date were excluded. Thus, 159 patients were finally included in this study. To investigate whether rapid confirmation reduces the prevalence period, we divided the duration from symptoms to confirmation (S2C) into quartiles, 1Q, 2Q, 3Q, and 4Q, of ?1, ?3, ?6, and ?7 days. We investigated the duration from symptoms to release (S2R) and confirmation to release (C2R) according to these quartiles. Furthermore, we performed multiple regression analysis to investigate the effects of rapid confirmation after symptom onset on the treatment period, duration of prevalence, and the duration until the release from isolation.

Results: We performed multiple regression analysis to investigate the association between rapid confirmation after symptom onset and the total prevalence period (faster release from isolation). S2C showed a negative association with C2R (T-value = ?3.58; p=0.0005) and a positive association with S2R (T-value = 5.86; p<0.0001) that were statistically significant.

Conclusions: Duration from symptom onset to the confirmation date is an important variable for predicting prevalence, and these results support the hypothesis that rapid S2C could reduce S2R. Clinical Trial: N/A

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Relationship between the period from symptom onset to confirmation and the prevalence: results from 159 COVID-19 patients using public information through the data crawling

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Running Title: Early diagnosis and period prevalence of COVID-19

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Ethical approval

This study was conducted in accordance with the Declaration of Helsinki, and all of the materials used in the article were only publicly available data. Moreover, all of those data are non-identifying data, and anyone can use it.

Author Contributions

M-B Park initiated the idea and led the formal analysis. JH Lee and EU Park initiated the idea and reviewed and edited the final draft of the article. TS Lee reviewed related articles and statistical analysis. All authors reviewed and approved the final version of this article.

Conflicts of Interest

The authors declare no potential conflicts of interest.

Availability of data and materials

If you need the processed data, please contact the author to request the data.

Keywords: COVID-19, SARS-CoV-2, symptoms onset, duration of prevalence, confirmation, South Korea

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Conclusions: Duration from symptom onset to the confirmation date is an important variable for predicting prevalence, and these results support the hypothesis that rapid S2C could reduce S2R.

INTRODUCTION

The COVID-19 Outbreak

The novel coronavirus disease (COVID-19) was first reported on December 31, 2019, in cases of pneumonia with an unknown etiology in Wuhan, China [1], and subsequently spread to the neighboring countries, including South Korea and Japan [2]. On March 11, 2020, the World Health Organization (WHO) reported a total of 118,000 confirmed cases and approximately 4,000 deaths due to COVID-19 in 114 countries. On the afternoon of the same day, the WHO formally declared COVID-19 as a global pandemic [3]. The first confirmed case, a Chinese woman in her 30s, in South Korea was reported on January 20, 2020, followed by another confirmed case, a 55-year-old man who had visited Wuhan, China. Subsequently, COVID-19 appeared to be stably controlled for almost a month; however, the number of cases increased explosively after February 20, whereby South Korea became the second country after China to experience the beginning of an epidemic. Subsequently, on February 29, the number of daily incidence of confirmed cases peaked at 900 and has since been on a downward trend. As of November 30, 2020, a total of 64 million cumulative confirmed cases have been reported worldwide [4].

Treatment and management of confirmed COVID-19 cases in South Korea

The WHO defines a confirmed case of COVID-19 as a person with a laboratory-confirmed COVID-19 infection, regardless of clinical signs and symptoms [5]. The symptoms mainly include fever, cough, shortness of breath, and breathing difficulties [6], although more than 15% of cases are asymptomatic [7]. In South Korea, individuals who have entered the country or have been in close contact with a confirmed COVID-19 case must undergo a test for COVID-19. The rapid antigen test (RAT) is an efficient tool for rapid confirmation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, although it is not used as an official tool for a confirmatory diagnosis in view of the capacity of laboratories to conduct the requisite number of tests and the number of confirmed and suspected cases. In the early stages of the COVID-19 epidemic, confirmatory testing involved two stages: pan-coronavirus and base sequencing analysis. However, real-time polymerase chain reaction (RT-PCR) has been used subsequently for basic confirmation [8]. Individuals who are suspected of having COVID-19 based on the clinical presentation of symptoms or close contact with a confirmed COVID-19 patient are diagnosed based on test results from two clinical samples, one each from the upper and lower respiratory tract [8, 9]. RT-PCR requires at least 24 h for the results to become available, and everyone who is tested is quarantined until the final diagnosis is determined.

The treatment strategy for COVID-19 can generally be divided into supportive care, respiratory support, symptomatic treatment, nutritional support, and psychological intervention [10]. Moreover, antibiotics can be administered to prevent secondary infections [11]. Furthermore, remdesivir is prescribed as an antiviral treatment for SARS-CoV-2, although its effectiveness is being debated [12, 13]. South Korea classifies patients according to the disease severity, and patients with high severity are treated in hospitals dedicated to infectious diseases and at national inpatient treatment centers. Patients who are classified as having mild symptoms or those not require inpatient treatment due to improvement in clinical symptoms may be admitted to residential treatment centers. In these facilities, the medical staff monitors patients at least twice a day.

COVID-19 is highly contagious and, therefore, confirmed patients must avoid contact with other people and should immediately be placed in quarantine [14-16]. In general, early intervention based on early diagnosis of the disease is considered to be very important for improving the health outcome [17-19]. However, most of the studies on COVID-19 conducted thus far have focused on preventing the spread of the disease by quickly identifying confirmed patients and minimizing their contact with other people [15, 20]. In contrast, there is very little evidence of how medical care that is based on the early diagnosis of confirmed cases can affect the COVID-19 treatment outcomes. Accordingly, we aimed to investigate the effects of the duration from the onset of clinical symptoms to confirmation on the duration to the resolution of COVID-19 (release from quarantine).

MATERIALS AND METHODS

Data Collection

South Korea comprises 228 si (cities), gun (counties), and gu (districts), with 17 metropolitan city and province levels, including Seoul, its capital. All local governments disclose basic information online on official websites about confirmed cases. Almost all Korean local governments have made public information such as symptom date, release date, and age of the confirmed case by anonymization until the first half of 2020. We used the crawler through Python's 'selenium' module, and additionally used 'BeautifulSoup' and 'Pandas' libraries to collect data. In the early stage of the pandemic, the local government de-identified the information of the confirmed person and disclosed the movement, region, and age. At this time, many people connected to the local government's homepage to check this, and the server was overloaded. Accordingly, many local governments have provided information to their official social networks and blogs to distribute data traffic and improve access to information. Therefore, we only collected information on local government official websites, social networks, and blogs, and did not use information from other sites that are not

guaranteed to be reliable. For preliminary data collection, we performed data crawling to extract data from social networks, blogs, and official websites operated by local governments. Second, the data were manually reviewed and revised. Data completed in this manner underwent a final review and revision process that included the use of various check codes to complete the final data set. Data were extracted and made for June 1-7, 2020 (Figure 1)

Study design and participants

We collected data from the 4,002 confirmed cases from 33cities reported until May 31, 2020, for whom sex and age information could be verified. Subsequently, 2,494 patients with unclear symptom onset date and 1,349 patients who had not been released or had no data about the release date were excluded. Thus, 159 patients were finally included in this study.

A confirmed case of COVID-19 was defined based on a confirmed diagnosis from positive RT-PCR results on two or more clinical specimens, regardless of clinical signs and symptoms [21]. To be released from isolation, at least 7 days must pass from the day of confirmation; the patient must be afebrile without the administration of any antipyretic agents, and the clinical symptoms must show an improving trend. In addition, the patient must test negative on two consecutive PCR tests, each conducted at least 24 h apart [22].

Statistical Analysis

We performed descriptive analysis on the mean, minimum, and maximum values for the duration from symptoms to release (S2R), symptoms to confirmation (S2C), and confirmation to release (C2R) according to the sex and age of the patients. To investigate whether rapid confirmation reduces the prevalence period, we divided S2C into quartiles, 1Q, 2Q, 3Q, and 4Q, of ≤1, ≤3, ≤6, and ≥7 days. We investigated S2R and C2R according to these quartiles. Furthermore, we performed multiple regression analysis to investigate the effects of rapid confirmation after symptom onset on the treatment period, duration of prevalence, and the duration until the release from isolation.

To measure the predictive power of S2R, we used logistic regression (LR) after setting S2R and other variables (age, sex, and S2C) as the dependent and independent variables, respectively. We transformed the days of S2R into tertiles (T1, T2, and T3). Two scenarios were evaluated as follows: (1) the classification of early S2R after setting T1 and T2–3 as one and zero coding, respectively, and (2) the classification of late S2R after setting T3 and T1–2 as one and zero coding, respectively. We randomly divided the data into training and test sets by ratios of 70% and 30%, respectively. We determined two lists of variables with the following combinations: (1) age + sex and (2) age + sex +

S2C. We constructed an LR model using a training set to predict early or late S2R. Thereafter, we measured the predictive performance of early or late S2R in the test sets. With 100 iterations of the random division of training and test sets, we measured the average performance of the classification for early or late S2R.

RESULTS

The study population (n=159) included 67 men (42.1%) and 92 women (57.9%), whereas age groups appeared in the following order: 40–59 years (44.7%), 20–39 years (37.1%), ≥60 years (13.2%), and 0–19 years (5.0%). The mean S2C was 6.1 days and mean C2R was 25.3 days. The S2C was shorter among females (5.6 days) than among males (6.7 days), whereas the C2R was similar for males (25.4 days) and females (25.2 days). The S2R was 32.1 and 30.8 days among males and females, respectively. With regard to age, the S2C was longest in the 0–19 years group (7.9 days), followed by the 40–59 years (7.3 days), 20–39 years (5.0 days), and ≥60 years (4.3 days) groups. The C2R was longest in the ≥60 years group (27.8 days), whereas S2R was longest in the 40–59 years group (33 days; Table 1).

Both C2R and S2R were investigated by quartiles of S2C, and 4Q, 3Q, 2Q, and 1Q were ≥7, 4–6, 2–3, and 1 day(s), respectively. The S2R was shortest, at 28.5 days, when the S2C was 1Q (≤1 day), followed sequentially by 2Q, 3Q, and 4Q with 28.9, 31.6, and 36.5 days, respectively. The results indicated that the prevalence increased with an increase in S2C (Figure 2).

We performed multiple regression analysis to investigate the association between rapid confirmation after symptom onset and the total prevalence period (faster release from isolation). Sex and age did not show a significant association with C2R and S2R. However, S2C showed a negative association with C2R (T-value = −3.58; p=0.0005) and a positive association with S2R (T-value = 5.86; p<0.0001) that were statistically significant (Table 2).

We measured the informative power of the S2C to predict early or late S2R. We found that S2C proposed an improved performance for both models ($p < 0.001$, for the early S2R and the late S2R models) compared to the model that used age and sex as input features (Figure 3).

DISCUSSIONS

Rapid diagnosis of confirmed cases enables prompt infection control and environmental decontamination of patients with suspected infection and places, such as environmental decontamination of related places and the management of close contacts [9]. Most of the studies published to date have tended to approach the early detection of COVID-19 from the perspective for

the prevention of infection and its spread [23]. Reducing the time to isolation through rapid diagnosis has been proven to help prevent the spread of SARS-CoV-2 infection [15, 21, 23]. In this context, studies published to date have claimed that early detection of COVID-19 is important because it can lower the mortality rate [24, 25]. However, such a claim is an inference based on general medical knowledge about pneumonia and complications but is not rooted in actual COVID-19 data.

Through linear regression analysis, we verified that the S2C is a factor that influences S2R. In addition, we used LR to test the predictors of S2R and found that the inclusion of the S2C variable in the model significantly increased the predictive power. Therefore, S2C is an important variable for predicting prevalence, and these results support the hypothesis that rapid S2C could reduce S2R. Consequently, this study demonstrated that rapid diagnosis leads to faster release from isolation. If COVID-19 could be diagnosed early, the symptoms and progression of disease could be controlled with only simple treatment, and the reduced number of severe patients could allow the stable availability of hospital beds [20]. In the current COVID-19 pandemic, confirmed COVID-19 patients in many countries are not receiving proper treatment because of the shortage of medical resources; thus, efficient use of limited medical resources is desperately needed. Under such circumstances, treating patients and releasing them from isolation as quickly as possible is one of the most important strategies for infectious disease control. Clinically, shortening the treatment period could be one of the best methods to improve the personal safety and quality of life of patients as well as the safety of medical staff and to reduce the workload of medical staff.

Anyone with symptoms or suspected of being infected should be tested immediately, and the intervention must take place as soon as possible upon confirmation. Delays in the confirmation of COVID-19 increase the social burden of the spread of an infectious disease but also contributes to the clinical burden of an increase in the prevalence period. Results of regression analysis in this study showed that sex and age were unassociated with the prevalence and isolation periods. Such findings are not consistent with a previous study which reported that the prognosis of COVID-19 is influenced by age [10]. The earlier study focused on the qualitative aspect of health or medical condition after treatment or release from isolation [10], whereas this study investigated the prevalence period. Therefore, a direct comparison is difficult because of the differences in the level of variables. The COVID-19-related mortality rate is higher among the older population [5, 26] and, therefore, rapid diagnosis is important for the elderly. The elderly population has a high likelihood of having underlying diseases and onset of complications, whereas the risk of disease progression to severe conditions is also higher. Thus, it is inevitable that a higher mortality is to be expected and, therefore, early intervention through rapid confirmation is expected to reduce the mortality rate [27].

Consequently, considering the results from this and previous studies, rapid confirmation could shorten the prevalence period, lead to better prognosis, and reduce the mortality rate. A long with the advancement in diagnosis for COVID-19, such as nucleic acid tests, the polymerase chain reaction (PCR) method which is considered as the ‘gold standard’ for the detection of virus, the rapid confirmation is very important to not only prevent the spread of disease but also enable better patient care.

This study has some limitations. First, we could not distinguish between severely and mildly ill patients, and it is possible that the prevalence period may differ between these two groups. Second, the study only considered a quantitative variable of S2R, instead of clinical outcomes such as complications and post-treatment prognosis. Third, a sufficiently large sample size could not be obtained. Fourth, because we had used only the crawled data from on-line, other factors besides S2C that could affect S2R could effect as uncorrected bias in the results of the study. Nonetheless, this study obtained information on the confirmed diagnosis date for all patients, although many cases did not have symptom onset date. This was due to the fact that many patients could not accurately remember their symptom onset date. To overcome these, efforts to secure a record on the date of symptoms onset in the clinical field are necessary, and if the results of additional studies should be conducted considering severity and treatment.

CONCLUSION

Duration from symptom onset to the confirmation date is an important variable for predicting prevalence, and these results support the hypothesis that rapid S2C could reduce S2R. Consequently, this study demonstrated that rapid diagnosis leads to faster release from isolation.

Table 1. Characteristics of 159 confirmed COVID-19 cases and their S2C, C2R, and S2R

Subjects (%, SD)			**Dependent variables**	**Independent variables**	
			S2C (SD) Min, Max	C2R (SD) Min, Max	S2R (SD) Min, Max
(N=159)	Mean		6.1(8.9) −1, 48	25.3 (12.0) 4, 72	31.4 (12.8) 7, 73
Sex	Male	67 (42.1%)	6.7(10.4) −1, 48	25.4 (12.7) 7, 72	32.1 (13.4) 11, 73
	Female	92 (57.9%)	5.6 (7.6) 0, 47	25.2 (11.6) 4, 69	30.8 (12.4) 7, 70
Age	Mean	42.0 (14.7) 1, 81			
	0-19	8 (5.0%)	7.9 (11.0) −1, 33	22.3 (12.9) 12, 44	30.1 (15.7) 14, 54
	20-39	59 (37.1%)	5.0 (6.6) 0, 48	24.4 (12.1) 4, 69	29.4 (13.3) 7, 70
	40-59	71 (44.7%)	7.3 (11.0) 0, 47	25.7 (11.7) 7, 72	33 (11.9) 14, 73
	60-	21 (13.2%)	4.3 (3.6) 0, 12	27.8 (12.9) 6, 54	32.1 (13.6) 9, 60

S2C: Duration from symptom onset to the confirmation date

C2R: Duration from the confirmation date to release

S2R: Duration from symptom onset to release

Table 2. Association between S2C, C2R, and S2R based on the results of multiple regression analysis

Characteristics	Categories	C2R	S2R
		T (*P*)-value	T (*P*)-value
Sex	Male (Ref.) vs female	−0.55 (0.58)	−0.55 (0.58)
Age	60 over (Ref.) vs 40-59	0.30 (0.76)	0.30 (0.76)
	vs 20-39	0.83 (0.41)	0.83 (0.41)
	Vs 0-19	0.94 (0.34)	0.94 (0.34)
S2C (days)		−3.58 (<0.001)	5.86 (<0.001)
F		2.99 (0.01)	7.66 (<0.001)
R^2		0.089	0.200
Adj. R^2		0.059	0.174

S2C: Duration from symptom onset to the confirmation date

C2R: Duration from the confirmation date to release

S2R: Duration from symptom onset to release

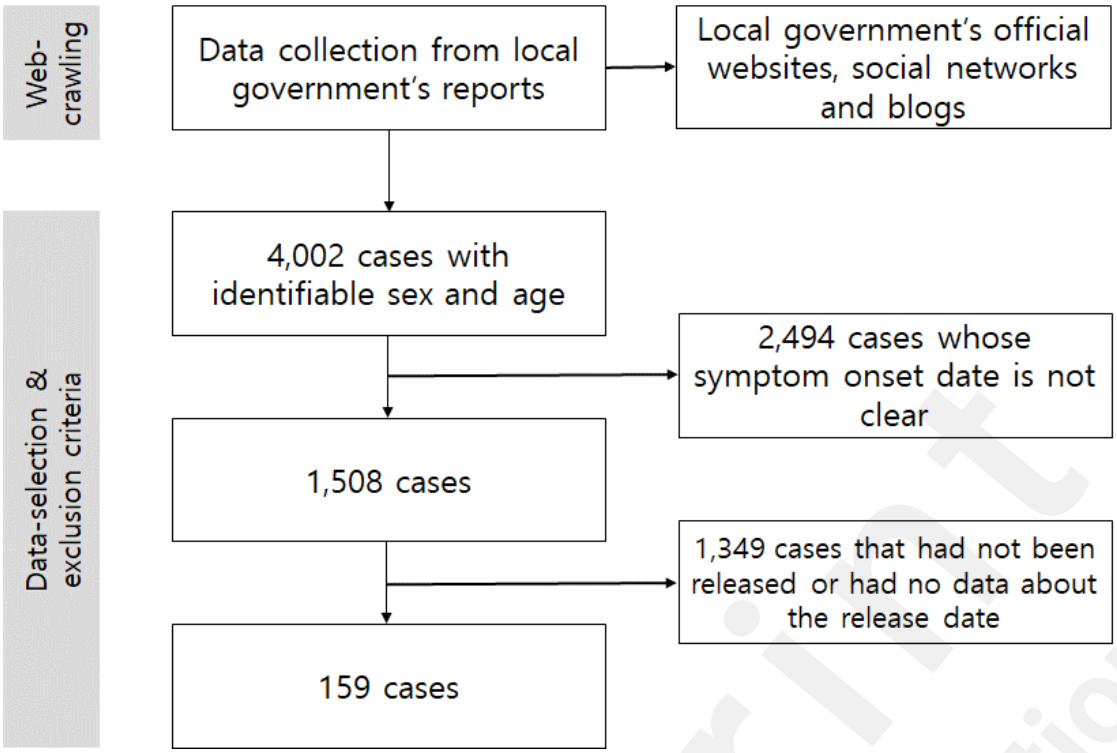

Figure 1. Flowchart for data extraction

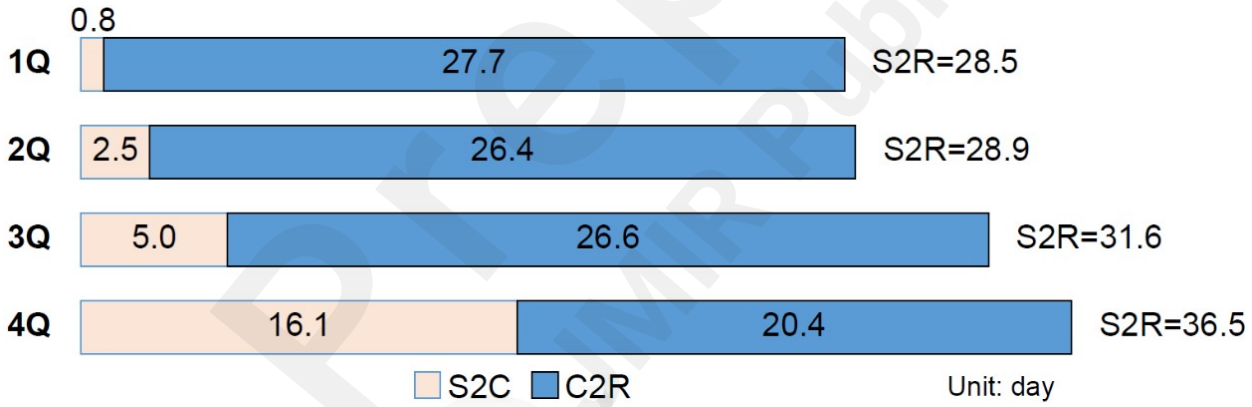

Figure 2. The duration from the confirmation date to release (C2R) and from the symptom onset to release (S2R) according to the duration from symptom onset to confirmation (S2C) quartile

The subjects were grouped into quartiles based on the duration from symptom onset to confirmation. 1Q: ~1 day (mean age: 42.5 years), 2Q: 2–3 days (mean age: 43.8 years), 3Q: 4–6 days (mean age: 39.5 years), and 4Q: ≥7 days (mean age: 42.6 years).

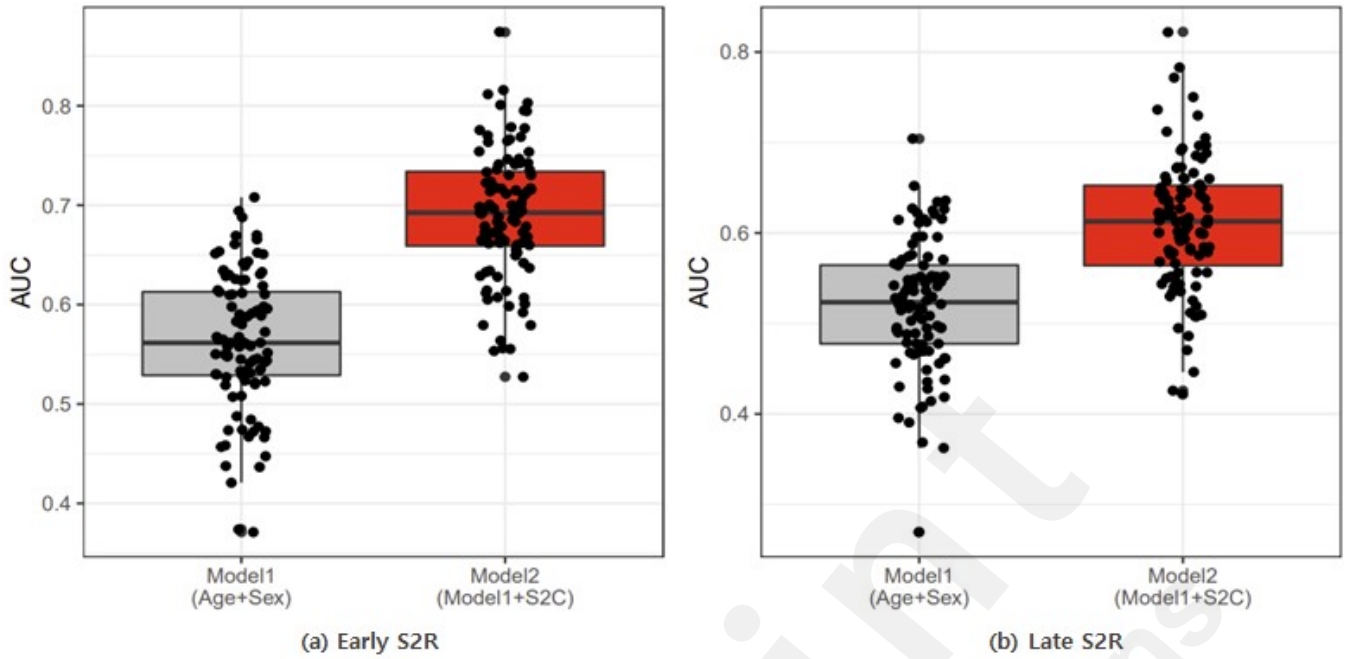

Figure 3. Predictive power determined through logistic regression (LR) after setting S2C and other variables (age, sex, and S2C).*The analysis comprises 100 iterations by the random division of training and test data sets.

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Supplementary Files

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