Trauma and COVID-19: Clinical and Paraclinical similarities between Trauma Patients with Positive and Negative PCR Tests

Golnar Sabetian¹, Hossein Abdolrahimzadeh Fard², Mina Ostovan¹*, Sina Azadikhah¹, Farid Zand³, Mansoor Masjedi⁴, Naeimehossadat Asmarian¹

¹Department of Intensive Care Medicine, Trauma Research Center, Shahid Rajaee (Emtiaz) Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
²Trauma Research Center, Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
³Department of Anesthesia and Critical Care Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
⁴Anesthesiology and Critical Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

*Corresponding author: Mina Ostovan
Address: Trauma Research Center, Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.
e-mail: Ostovanmina@gmail.com

Objectives: To compare clinical and paraclinical similarities between trauma patients with positive RT-PCR tests (PCR+ve) and the RT-PCR negative ones (PCR -ve).

Methods: This is a case-control study, where cases had a PCR+ve and controls had a negative result. Two groups were compared regarding (para) clinical values. Multivariable binary logistic regression analysis investigated the variables predicting COVID-19 and the mortality rate.

Results: Both groups were similar regarding the clinical findings and comorbidities (p>0.05). PCR+ve group had lower lymphocyte count (1.41 [1.45] vs. 1.66 [1.61], p=0.030), CPK level (411 [928.75] vs. 778 [1946.5], p=0.006) and CRP level (17 [42.5] vs. 24 [50.75], p=0.004). However, none of these findings were significant in the multivariable analysis. Finally, PCR+ve group had increased odds of death (OR=2.88; 95% CI=1.22-7.41).

Conclusion: Unlike our primary hypothesis, the study failed to mark any significant (para) clinical features guiding us to detect COVID-19 earlier in trauma patients. Moreover, the PCR+ve group is at increased mortality risk. A larger, multicentric prospective study should be designed to address this issue.

Keywords: Trauma; COVID-19; Diagnostic approach; Mortality rate.

Introduction

According to the World Health Organization (WHO), COVID-19 is responsible for more than 6 million deaths until April 16, 2020 [1]. The clinical picture varies from asymptomatic carriers to severe conditions leading to Systemic Inflammatory Response Syndrome (SIRS) and Multi-organ Dysfunction Syndrome (MODS) [2]. Therefore, detecting affected patients is not always feasible, especially in emergency conditions such as trauma [3].
Similar to COVID-19, trauma patients are at risk of developing various clinical conditions, including SIRS and MODS. These two clinical entities share several clinical and para-clinical similarities [4]. Therefore, trauma staff has faced several challenges in dealing with trauma patients during the COVID-19 pandemic. First, the clinical values are neither specific nor informative. We could not thoroughly attribute the general and respiratory symptoms such as fever, myalgia, cough, chest pain, and shortness of breath to the trauma, especially when there is a risk of concomitant COVID-19 infection [5]. Second, the para-clinical measures, such as quantitative reverse transcription-polymerase chain reaction (RT-PCR) and computed tomography (CT), lack sensitivity and specificity in the trauma setting. Moreover, our previous study has shown that chest CT images could not completely differentiate COVID-19 and trauma-related findings such as pulmonary contusions [6].

There is growing evidence of an increase report in mortality rate among COVID-19 patients compared with none COVID ones following surgeries. A multicenter retrospective study reported that the concomitant COVID-19 doubled the mortality risk in orthopedic and trauma patients [7]. Compared to the patients with negative RT-PCR tests, Thakrar et al., [8] showed a higher 30-day mortality rate in orthopedic patients with positive RT-PCR results. Other studies investigating orthopedic and trauma patients showed similar results [9, 10]. Therefore, the stakeholders suggest delaying elective or even semiurgent surgeries if the patients have a concomitant COVID-19 infection [10].

Trauma, however, is a non-deferrable condition that needs emergent, life-saving treatments. Concerning COVID-19, some issues should be addressed. First, trauma staff is at increased risk of unprotected close contact with the patients [3]. Second, they should assess the patients’ conditions to dwindle possible patient-to-staff or patients-to-patients viral transmission. Moreover, patients with a decreased level of consciousness cannot provide informative COVID-19-related history [11].

Therefore, it is essential to know how COVID-19 affects the paraclinical and clinical course of trauma patients. To the best of our knowledge, not many studies have addressed this issue. Therefore, in this case-control study, we compared the clinical and paraclinical conditions between COVID+ve and -ve trauma patients. Our primary aim was to investigate any differences between these two groups. Finally, we sought to know how such possible differences affect patients’ outcomes.

Materials and Methods

This case-control study was conducted according to the Strengthening the Report of Observational Studies in Epidemiology (STROBE) Statements [12]. All adult trauma patients admitted to Shahid Rajae Trauma Hospital from February 20, 2020, to June 21, 2021, were recruited. A pilot study conducted in our center had shown that the mortality rates (proportion of subject: q1 and q0) in the PCR+ve and PCR-ve groups are 18% and 5%, respectively. Considering the type I error (α) 5%, power 80%, and based on the formula comparing two proportions, the sample size was calculated to be 95 patients in each group. We selected patients by census sampling as cases (N=100 patients). We selected control groups by systematic random sampling (N=100 patients). Base on sorted patient list selected one patient form 46 patient randomly by chart number. There is no difference in age and gender between case and control groups (Table 1).

The RT-PCR+ve group (case) had at least one positive PCR test during hospital admission or the last two weeks prior to the admission. If the first RT-PCR test was negative (control), the second test was conducted three days later from the lower respiratory tract. The indications for RT-PCR tests were detailed in our previous study [13]. All unstable, unconscious patients or those who required live-saving interventions are assessed with the RT-PCR tests (Stage1). Stage 2 focuses on the clinical and epidemiological risk factors, including the history of acute respiratory symptoms, positive epidemiological risk factors, temperature>38°c, Respiratory rate >20/min, or O2 saturation<90%. Patients with at least two of these criteria were evaluated with RT-PCR and CT images. In the next stage (Stage 3), the presence of leukocytosis with lymphopenia and elevated ESR or CRP are the main indications for the RT-PCR test. In the last stage, if a patient does not meet any criteria mentioned above, they will be monitored considering the emerging COVID-19-related signs and symptoms [13]. The RT-PCR -ve group consisted of patients with negative PCR tests and negative COVID-19-related chest CT findings.

The inclusion criteria were (1) adult patients (age≥18 years old), (2) admitted to our hospital from February 20, 2020, to June 21, 2021, and (3) assessed with COVID-19 RT-PCR tests and chest CT images. The exclusion criteria were (1) age less than 18 years of age, (2) patients without chest CT images, (3) having incomplete medical records, and (4) died/discharged/released from the hospital less than 24 hours after hospital presentation, because such patients have incomplete records. The demographic features, laboratory and clinical data during the first 24 hours after hospital admission, mechanism of injury, and injury severity score (ISS) were collected. Any missing data were retrieved after reviewing patients’ medical records. “Other” MOI was selected if the exact MOI could not be determined. A blind board-certified radiologist reviewed the chest CT images according to the RSNA criteria provided by the Radiological Society of North America [14]. The ICU-related variables were obtained from
Iran Intensive Care Unit Registry (IICUR). IICUR was approved by the Ethics Committee of Shiraz University of Medical Sciences in 2018 (Ethic Number IR.SUMS.REC.1397.559) and recognized by the Iran Ministry of Health as the first and the only registry of adult ICU in Iran. Since then, it has been expanded to other ICUs all over the country. The primary purpose of IICUR is to provide a platform for researchers, clinicians, and administrators where they can collaborate to measure, report, benchmark, and improve ICU and hospital outcomes such as mortality and length of stay. The primary purpose of IICUR is to provide a platform for researchers, clinicians, and administrators where they can collaborate to measure, report, benchmark, and improve ICU and hospital outcomes such as mortality and length of stay. The primary purpose of IICUR is to provide a platform for researchers, clinicians, and administrators where they can collaborate to measure, report, benchmark, and improve ICU and hospital outcomes such as mortality and length of stay. The primary purpose of IICUR is to provide a platform for researchers, clinicians, and administrators where they can collaborate to measure, report, benchmark, and improve ICU and hospital outcomes such as mortality and length of stay.

The primary outcome was the in-hospital mortality rate. The secondary outcome was hospital and ICU length of stay, ventilator days, and complications such as acute renal failure, acute hepatic failure, thrombosis, and secondary bacterial infection.

Data were analyzed using SPSS software version 27 (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was used for each variable to assess normal distribution. Quantitative variables were described as mean (SD) or median with interquartile range (IQR) when appropriate, and the student sample t-test or Mann-Whitney tests were used to compare variables between the PCR+ve and -ve groups. Frequency (%) and Chi-square or Fisher exact tests were used to describe and analyze qualitative measures. Multivariable binary logistic regression analysis was done to investigate the variables predicting COVID-19 (primary analysis) and mortality rate (secondary analysis). In all comparative tests, statistical significance was set for a two-tailed p-value less than 0.05.

This study was conducted in line with the Declaration of Helsinki. The institutional review board and ethics committee of Shiraz University of Medical Sciences has approved this study with the ethics number of IR.SUMS.REC.1400.276. This study was deemed exempt from the need for consent. Results

Four thousand six hundred eighty-three patients were tested for COVID-19. Of those, 635 tests (13.5%) were positive (PCR+ve group). The mean (SD) age of all included patients was 48.11 (21.81). About three-fourths of them were men. Table 1 shows that the PCR+ve and -ve groups are similar in terms of

Table 1. Demographic features of enrolled patients by COVID-19 status (n=200).

| Demographic Characteristics | COVID-19 PCR+ test | p value |
|----------------------------|-------------------|--------|
|                            | Negative (n=100) | Positive (n=100) |
| Age, Mean (SD)             | 48.11 (21.11) | 48.10 (22.69) | 0.997 |
| Male Gender, n (%)         | 75 (75)          | 76 (76)      | 0.869 |
| ISS, Median (IQR)          | 14 (17)          | 14 (18)      | 0.507 |
| ISS, n (%)                 |                  |              |       |
| 1-8                        | 23 (23)          | 25 (25)      | 0.897 |
| 9-15                       | 29 (29)          | 26 (26)      |       |
| 16-24                      | 21 (21)          | 24 (24)      |       |
| 25-49                      | 27 (27)          | 24 (24)      |       |
| ≥ 50                       | 0                | 1 (1)        |       |
| APACHE4, Median (IQR)      | 13 (7)           | 12 (10)      | 0.374 |
| NEWS’2 score, Median (IQR) | 5 (5)            | 5 (5)        | 0.656 |
| Shock Index, Median (IQR)  | 0.68 (0.24)      | 0.69 (0.25)  | 0.732 |
| Comorbidities*, n (%)      |                  |              |       |
| Smoker                     | 11 (11)          | 3 (3)        | 0.027 |
| Opium                      | 10 (10)          | 5 (5)        | 0.179 |
| Liver Disease              | 1 (1)            | 1 (1)        | >0.999 |
| Diabetes                   | 10 (10)          | 7 (7)        | 0.447 |
| Ischemic Heart Disease     | 8 (8)            | 5 (5)        | 0.390 |
| Hypertension               | 19 (19)          | 16 (16)      | 0.577 |
| End-Stage Renal Disease    | 3 (3)            | 2 (2)        | >0.999 |
| Obstructive Lung Disease   | 6 (6)            | 3 (3)        | 0.498 |
| Restrictive Lung Disease   | 0                | 2 (2)        | 0.497 |
| Neurologic Disorders       | 3 (3)            | 3 (3)        | >0.999 |
| Cerebrovascular Accident   | 3 (3)            | 2 (2)        | >0.999 |
| Seizure                    | 1 (1)            | 3 (3)        | 0.621 |
| Rheumatoid Arthritis       | 3 (3)            | 1 (1)        | 0.621 |

*PCR: Polymerase chain Reaction; SD: Standard Deviation; ISS: Injury Severity Scale; APACHE: Acute Physiology and Chronic Health Evaluation; IQR: Interquartile range; NEWS: National Early Warning Score; Several Comorbidities were asked and only positive ones were reported.
ISS ($p=0.897$), shock index ($p=0.732$), APACHE II ($p=0.374$), and NEWS scores ($p=0.656$). The smoking frequency was significantly higher in the PCR -ve group (11% vs. 3%, $p=0.027$). Other comorbidities were reported almost uniformly.

Table 2 outlines the injury-related features and presenting vital signs. The mechanisms of injury distribution and the presenting vital signs differ between the two groups, although they were not statistically significant. The PCR -ve patients had a higher rate of chest wall trauma (47% vs. 30%, $p=0.013$).

According to the guidelines provided by RSNA criteria, the chest CT images were reviewed by a board-certified radiologist and intensivist and summarized in Table 3. Normal (42.0%), atypical (27.0), and typical (21.0%) chest CTs were the three most frequent RSNA classifications in the PCR+ve group. Moreover, the overall incidence of rib fracture was significantly higher among PCR+ve group. We categorized the rib injuries according to the number of involved ribs. Other findings were not significant. Out of twenty-two PCR -ve patients with rib fractures, nineteen cases (86.4%) had three or more rib fractures. Other radiological findings were similar.

The COVID-19-related signs and symptoms are reported in Table 4. PCR+ve patients reported more headache (6% vs 0%, $p=0.029$) and myalgia (22% vs 4%, $p<0.001$). Other clinical findings were almost similar between the groups and were insignificant.

### Table 2. Injury-related characteristics of enrolled patients by COVID-19 status (n=200).

| Variables                      | COVID-19 PCR+ test | $p$ value |
|--------------------------------|--------------------|-----------|
|                                | Negative (n=100)   | Positive (n=100) |
| Mechanism of Trauma            |                    |            |
| Falling                        | 37 (37)            | 41 (41)    | 0.102    |
| RTAb                           | 60 (60)            | 48 (48)    |          |
| Penetrating                    | 1 (1)              | 5 (52)     |          |
| Other Blunt Trauma             | 2 (2)              | 6 (6)      |          |
| Associated injuries            |                    |            |
| Head and neck                  | 38 (38)            | 50 (50)    | 0.087    |
| Spine                          | 22 (22)            | 12 (12)    | 0.060    |
| Chest                          | 47 (47)            | 30 (30)    | 0.013    |
| Abdominopelvic                 | 23 (23)            | 17 (17)    | 0.289    |
| Extremities                    | 37 (37)            | 33 (33)    | 0.553    |
| Presenting Vital Signs         |                    |            |
| GCS≤8                          | 22 (22)            | 14 (14)    | 0.141    |
| SBP≤90                         | 10 (10)            | 5 (5)      | 0.179    |
| PR*, mean (SD*)                | 88.67 (17.35)      | 91.63 (17.08) | 0.226 |
| SPO2%                          | 94 (4)             | 95 (4)     | 0.246    |
| RR*                            | 16 (4)             | 17 (2)     | 0.091    |
| T*                             | 37 (1.55)          | 37 (1.5)   | 0.176    |

*PCR: Polymerase Chain Reaction;  *RTA: Road Traffic Accident; *GCS: Glasgow Coma Scale; *SBP: Systolic Blood Pressure in mmHg; *PR: Pulse Rate (beat/min); *SD: Standard Deviation; *SPO2: Oxygen Saturation; *RR: Respiratory Rate; *T: Temperature in degree of Celsius; *were reported as Median and interquartile range. Others were described as frequency and percentage.

### Table 3. Computed tomography findings of enrolled patients by COVID-19 status (n=200).

| Chest CT b findings, n (%) | COVID-19 PCR+ test | $p$ value |
|---------------------------|--------------------|-----------|
|                            | Negative (n=100)   | Positive |
| RSNA c                     |                    |           |
| Typical                   | 0                  | 21 (21)   | <0.001   |
| Indeterminate             | 10 (10)            | 10 (10)   | >0.999   |
| Atypical                  | 51 (51)            | 27 (27)   | <0.001   |
| Normal                    | 39 (39)            | 42 (42)   | 0.666    |
| Lung involvement*         | 18.03 (12.30)      | 21.47 (15.88) | 0.189 |
| Pneumothorax              | 13 (13)            | 6 (6)     | 0.091    |
| Hydrothorax               | 18 (18)            | 18 (18)   | >0.999   |
| Rib Fracture              | 22 (22)            | 10 (10)   | 0.021    |
| ≥3                        | 19 (86.4)          | 5 (50.0)  | 0.018    |
| 2                         | 3 (13.6)           | 2 (20.0)  |          |
| 1                         | 0                  | 3 (30.0)  |          |
| Diaphragmatic Rapture     | 1 (1)              | 3 (3)     | 0.621    |
| Emphysema                 | 11 (11)            | 5 (5)     | 0.118    |

*PCR: Polymerase Chain Reaction; *CT: Computed Tomography; *RSNA= Radiological Society of North America; *patients with normal chest CT were excluded.
Table 4. Clinical signs and symptoms of enrolled patients by COVID-19 status (n=200).

| Presenting Signs and Symptoms, n (%) | COVID-19 PCR* test | p value |
|-------------------------------------|---------------------|---------|
|                                     | Negative            | Positive |         |
| Flu-like symptoms                   |                     |         |         |
| Fever                               | 37 (37)             | 27 (27)  | 0.130   |
| Cough                               | 12 (12)             | 11 (11)  | 0.825   |
| Myalgia                             | 4 (4)               | 22 (22)  | <0.001  |
| Respiratory Distress                | 31 (31)             | 23 (23)  | 0.203   |
| Chest Pain                          | 1 (1)               | 3 (3)    | 0.621   |
| Headache                            | 0                   | 6 (6)    | 0.029   |
| Neurological Symptoms               |                     |         |         |
| Anosmia                             | 0                   | 2 (2)    | 0.497   |
| Ageusia                             | 0                   | 0       | 0       |
| Decreased LOCª                      | 18 (18)             | 17 (17)  | 0.852   |
| Dizziness                           | 0                   | 2 (2)    | 0.497   |
| GI symptoms                         |                     |         |         |
| Abdominal Pain                      | 1 (1)               | 0       | >0.999  |
| Nausea                              | 0                   | 1 (1)    | >0.999  |
| Vomiting                            | 0                   | 0       | 0       |
| Diarrhea                            | 0                   | 0       | 0       |
| Anorexia                            | 5 (5)               | 0       | 0.059   |

*PCR: Polymerase Chain Reaction; LOC: Level of Consciousness

Table 5. On-hospital Arrival Laboratory findings of enrolled patients by COVID-19 status (n=200).

| Laboratory Data, Median (IQRª)      | COVID-19 PCR* test | p value |
|-------------------------------------|---------------------|---------|
|                                     | Negative            | Positive |         |
| White Blood Cells, *10^6/L          | 12.65 (7.17)        | 10.75 (7.27) | 0.024   |
| Lymphocytes count, *10^6/L          | 1.66 (1.61)         | 1.41 (1.45) | 0.030   |
| NLRc                                | 5.77 (6.26)         | 6.25 (6.7)  | 0.617   |
| Hemoglobin, gr/dL                   | 13.3 (3.05)         | 13.35 (3.73) | 0.993   |
| Platelet, *10^6/L                   | 212.5 (74.25)       | 208.5 (95)  | 0.531   |
| BUNª, mg/dL                         | 16 (6.75)           | 15 (9.82)  | 0.612   |
| Creatinine, mg/dL                   | 1.11 (0.33)         | 1.03 (0.44) | 0.032   |
| Sodium, mEq/L                       | 137 (4)             | 138 (4)    | 0.499   |
| Potassium, mEq/L                    | 4 (0.6)             | 4 (0.7)    | 0.354   |
| Calcium, mg/dL                      | 8.2 (0.90)          | 8 (0.80)   | 0.127   |
| Magnesium, mg/dL                    | 1.8 (0.3)           | 2 (0.45)   | 0.005   |
| PT, sec.                            | 12.9 (1.85)         | 12.7 (1.87)| 0.732   |
| PTT, sec.                           | 27 (4)              | 32 (9)     | <0.001  |
| INRª                                | 1.21 (0.27)         | 1.17 (0.26)| 0.720   |
| AST*, U/L                           | 49 (47)             | 34.5 (41)  | 0.027   |
| ALT*, U/L                           | 32 (42)             | 35 (36)    | 0.892   |
| ALK.P, U/L                          | 147 (84.25)         | 150 (82.75)| 0.835   |
| Direct Bilirubin, mg/dL             | 0.31 (0.2)          | 0.32 (0.25)| 0.360   |
| Total Bilirubin, mg/dL              | 0.84 (0.55)         | 0.79 (0.47)| 0.225   |
| Albumin, g/Dl                       | 3.3 (0.9)           | 3.3 (0.75) | 0.817   |
| Total Protein, g/dL                 | 5.6 (1.3)           | 5.4 (1)    | 0.287   |
| CPK*, U/L                           | 778 (1946.5)        | 411 (928.75)| 0.006   |
| LDH, U/L                            | 719.5 (649.75)      | 506 (425)  | 0.006   |
| ESR*, mm/h                          | 21.5 (47.75)        | 23 (41.5)  | 0.588   |
| CRP*, mg/L                          | 24 (50.75)          | 17 (42.5)  | 0.004   |
| Ferritin, µg/L                      | 287 (613)           | 301 (507)  | 0.597   |
| D-Dimer, ng/mL                      | 3254 (6163)         | 2542 (4911)| 0.435   |
| Fibrinogen, mg/dL                   | 269 (85.5)          | 242 (75)   | 0.105   |
| Troponin, pg/mL                     | 11.5 (50.98)        | 3.9 (24.1) | 0.019   |

*PCR: Polymerase Chain Reaction; IQR: Interquartile range; NLR: Neutrophil to Lymphocyte Ratio; BUN: Blood Urea Nitrogen; PT: Prothrombin Time; PTT: Partial Thromboplastin Time; INR: International Normalized Ratio; AST: Aspartate Aminotransferase; ALT: Alkaline Aminotransferase; ALK.P: Alkaline Phosphatase; CRP: C-reactive Peptide; ESR: Erythrocyte Sedimentation Rate; CRP: C-reactive Peptide
We run a complete laboratory profile to find any significant differences guiding us to diagnose COVID-19 among trauma patients. The results of the univariate analysis are shown in Table 5. The PCR+ve group had a significantly lower median of white blood cells (10.75 [7.27] vs. 12.65 [7.17], \( p = 0.024 \)), lymphocyte (1.41 [1.45] vs. 1.66 [1.61], \( p = 0.030 \)), creatinine (1.03 [0.44] vs. 1.11 [0.33], \( p = 0.032 \)). Interestingly, the serum level of creatinine phosphokinase, lactate dehydrogenase, and C-reactive peptides was lower in the PCR+ve group than in the negative group (Table 5). However, none of these findings were significant in the multivariate regression analysis.

Considering the outcomes, a significantly higher number of patients in the PCR+ve group were admitted to ICU wards than in the negative group (82.0% vs. 69.0%, \( p = 0.030 \)). Clinically, the PCR-ve group was intubated more frequently with more invasive ventilation supports. However, they were not statistically significant (\( p = 0.495 \) and \( p = 0.389 \), respectively). Finally, the in-hospital mortality rate (\( p = 0.160 \)) and complications, as well as the hospital and ICU length of stay (\( p = 0.631 \) and 0.608, respectively), were comparable between the two groups (Table 6).

We recruited all \( p \)-values > 0.2 in the multivariate regression analysis to find a pattern detecting COVID-19 among trauma patients. None of these findings were significant (results were not shown). Moreover, we run a second analysis to determine how these findings affect the mortality rate (Table 7). The multivariable logistic regression analysis shows that comparing the PCR -ve patients, PCR+ve ones had increased odds of death (OR=2.88; 95% CI=1.22-7.41). With each day of ICU admission, the Odds of death increase by 13% (OR=1.13; 95% CI=1.07-1.20).

**Discussion**

Trauma and COVID-19 share similar clinical and paraclinical similarities. According to the current study, univariate analysis showed that PCR+ve trauma patients had a significantly lower chest wall trauma rate, lower incidence of rib fractures, and a higher rate of ICU admission. The incidence of headaches among trauma patients who tested positive for COVID-19 was higher than in the PCR-ve groups. More patients in the PCR+ve group received steroids, and the incidence of multiple rib fractures (≥3 ribs) was lower in the PCR+ve group. However, none of these para-clinical values showed statistical significance with regard to the multivariate analysis. Trauma could easily mimic or even mask the signs and symptoms of COVID-19 diseases. Both conditions could elevate body temperature, induce hypoxia and alter the respiratory rate, heart rate, and blood pressure. On the other hand, post-traumatic hypothermia could mask COVID-19-induced fever.

Trauma and COVID-19 disease are both polyphasic inflammatory conditions. Laboratory results vary widely regarding the severity and the phases

| Outcomes                  | COVID-19 PCR test | \( p \) value |
|---------------------------|-------------------|--------------|
| Intubation                | Negative          | Positive      |
| MV Days\(^a\)             | 44 (44)           | 38 (38)      | 0.495        |
| Ventilation               | 5 (7)             | 5 (6)        | 0.402        |
| O2 supply                 | 56 (56)           | 62 (62)      | 0.389        |
| Invasive MV               | 44 (44)           | 38 (38)      |              |
| FiO2 ≥40%                 | 59 (59)           | 62 (62)      | 0.329        |
| Complications             |                   |              |              |
| Thrombosis                | 6 (6)             | 7 (7)        | 0.774        |
| Bleeding                  | 7 (7)             | 8 (8)        | 0.788        |
| Sepsis                    | 30 (30)           | 25 (25)      | 0.428        |
| Acute Liver Injury        | 4 (4)             | 1 (1)        | 0.369        |
| Acute Kidney Injury       | 5 (5)             | 10 (10)      | 0.179        |
| ICU Admission Rate        | 69 (69)           | 82 (82)      | 0.030        |
| In-hospital mortality     | 11 (11)           | 18 (18)      | 0.160        |
| Survivors HLOS\(^a\)      | 4 (4)             | 4 (4)        | 0.631        |
| Survivors ICU-LOS\(^a\)   | 4 (9)             | 4 (5)        | 0.608        |
| Steroids                  | 34 (34)           | 63 (63)      | <0.001       |
| Inotrope                  | 11 (11)           | 9 (9)        | 0.637        |

\(^a\) were reported as Median and interquartile range. Others were described as frequency and percentage

| Significant Predictors    | Mortality Odds Ratio (95% CI) | \( p \) value |
|---------------------------|-------------------------------|--------------|
| Duration of ICU Admission | 1.135 (1.073-1.200)           | <0.001       |
| Covid Positive            | 2.884 (1.122-7.414)           | 0.028        |
during which the patients present to the hospital. Inflammatory markers such as CRP, LDH, and CPK are routinely associated with more severe viral infections and worse outcomes among critically ill or septic patients [15-17]. These reports were inconsistent with our results. In our study, however, the patients were admitted to the hospital due to trauma (not COVID pneumonia). Moreover, we could not precisely track the time interval between the onset of COVID-19-related signs and symptoms and hospital admission. Therefore, these lab findings taken on hospital arrival are unreliable enough to help us predict patient outcomes.

Previous reports showed radiological similarities between COVID-19 and trauma patients sustaining chest wall trauma [6, 13, 18, 19]. These results are consistent with the previous study, which has shown that trauma patients with pulmonary contusions presented to a trauma center before the COVID-19 pandemic. They have shown that 80% of such patients had bilateral ground-glass opacity (GGO), which was a typical feature of COVID-19 (5). The CT images of 14 patients were reviewed by Akdogan et al., and 92.9 % and 85.7% had peripherally located GGO and subpleural lines, respectively [20]. Considering these similarities, CT images are not always a reliable differentiating tool. We suggest that the images should be reviewed with caution in the trauma setting when the risk of COVID-19 concurrent infection is high.

Considering the lower incidence of chest wall trauma, the overall rib fractures, and multiple (≥3) rib fractures, we primarily inferred that the volume of lung involvements should have been less in PCR+ve patients. However, the volume of lung involvement was higher in the PCR+ve group compared with that of the PCR -ve group, although it was not significant. Some researchers hypothesized that SARS-CoV-2 viruses increase lung parenchyma fragility resulting in a higher lung involvement with the same or even less severe trauma [13].

The secondary analysis showed that the PCR+ve trauma patients sustained more than 2.5-fold increased odds of death. Previously conducted studies support this finding [21-23]. An international multicenter study has shown that patients have a higher mortality rate and pulmonary complications following emergency general surgeries [24]. Several mechanisms are attributed to the increased mortality rate among trauma patients with positive PCR results in the literature. These were pulmonary and thrombotic complications [25, 26]. However, these complications were similar in our study. This discrepancy may be due to the fact that PCR-positive patients in the different studies did not have the same COVID-19 severity and disease activity [27]. During a propensity-matched study, Yeates et al., [27] failed to show any significant differences between the two trauma groups (PCR+ve and -ve groups), consistent with our results. Another contributing factor to the increased mortality rate among our trauma patients with PCR+ve results may be the higher rate of steroids used in this group. Several studies reported that over-prescribing steroids were associated with increased mortality [28-31].

There were several limitations of this study. First, although we considered several strategies to address confounders, residual ones may skew our results. Second, considering the time interval, the chance of false-negative RT-PCR results could not be ignored entirely. Although the RT-PCR test is specific, several factors affect the sensitivity, such as operators’ skills, the kits’ sensitivity, and the time interval when the test was done. Therefore, the chance of including asymptomatic, PCR-ve patients could not be ruled out. Third, it was also unclear when the patients’ symptoms started.

Last but not least, our study lacks the immunological assay investigating the serum level of inflammatory cytokines. Therefore, we do not know the exact differences in the immunological profiles between the two groups. We suggest a larger, multicentric prospective study be designed that carefully assesses the effect of different severities of COVID-19 patients on clinical and para-clinical characteristics of trauma patients. We have shown that comparing the clinical and paraclinical values is generally inconclusive. The multivariate regression analysis failed to mark any of these values guiding us to detect COVID-19 earlier in trauma patients. Moreover, trauma patients with positive PCR tests are at increased mortality risk. We suggest a larger, multicentric prospective study to be designed that carefully assesses the effect of different severities of COVID-19 patients on the clinical and paraclinical characteristics of trauma patients.

Declarations

Ethics approval and consent to participate: This study was approved by the institutional review board and the ethics committee of Shiraz University of Medical Sciences. Ethic number: IR.SUMS. REC.1400.276

Consent for publication: Not applicable

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Authors’ contributions: GS, MO, SA, and HA designed the study. MO, SA, and HA were responsible for data collection. NA conducted the analysis and interpretation of data. FZ, MM, and NA drafted the manuscript, and GS, MM, and HA revised it critically for important content. All authors...
read and approved the final manuscript.

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**References**

1. In: Organization WH. COVID-19 Dashboard 2022 [updated April 16, 2022]. Available from: https://covid19.who.int.
2. Wang T, Du Z, Zhu F, Cao Z, An Y, Gao Y, et al. Comorbidities and multi-organ injuries in the treatment of COVID-19. *Lancet*. 2020;395 (10228):e52.
3. Sawhney C, Singh Y, Jain K, Sawhney R, Trikha A. Trauma care and COVID-19 pandemic. *J Anaesthesiol Clin Pharmacol*. 2020;36 (Suppl 1):S115-S120.
4. Fouldsresht H, Ghamar Talepoor A, Eskandari N, Norouzian M, Ghezelbash B, Beyranvand MR, et al. Potential Immune Indicators for Predicting the Prognosis of COVID-19 and Trauma: Similarities and Disparities. *Front Immunol*. 2022;12:785946.
5. Abdolrahimzadeh Fard H, Mahmudi-Azer S, Abdulzahraa Yaqoob Q, Sabetian G, Ianpour P, Shayan Z, et al. Comparison of chest CT scan findings between COVID-19 and pulmonary contusion in trauma patients based on RSNA criteria: Established novel criteria for trauma victims. *Chin J Traumatol*. 2022;25 (3):170-176.
6. Abdolrahimzadeh Fard H, Mahmudi-Azer S, Sefidbakht S, Ianpour P, Bolandparvaz S, Abbasi HR, et al. Evaluation of Chest CT Scan as a Screening and Diagnostic Tool in Trauma Patients with Coronavirus Disease 2019 (COVID-19): A Cross-Sectional Study. *Emerg Med Int*. 2021;2021:4188178.
7. Clement ND, Hall AJ, Makaram NS, Robinson PG, Patton RFL, Moran M, et al. IMPACT-Restart: the influence of COVID-19 on postoperative mortality and risk factors associated with SARS-CoV-2 infection after orthopaedic and trauma surgery. *Bone Joint J*. 2020;102-B (12):1774-1781.
8. Thakrar A, Chui K, Kapoor A, Hambidge J. Thirty-Day Mortality Rate of Patients With Hip Fractures During the COVID-19 Pandemic: A Single Centre Prospective Study in the United Kingdom. *J Orthop Trauma*. 2020;34 (9):e325-e329.
9. Karayiannis PN, Roberts V, Cassidy R, Mayne AJW, McAuley D, Milligan DI, et al. 30-day mortality following trauma and orthopaedic surgery during the peak of the COVID-19 pandemic: a multicentre regional analysis of 484 patients. *Bone Jt Open*. 2020;1 (7):392-397.
10. Kaufman EJ, Ong AW, Cipolle MD, Whitehorn G, Ratnasekera A, Stawicki SP, et al. The impact of COVID-19 infection on outcomes after injury in a state trauma system. *J Trauma Acute Care Surg*. 2021;91 (3):559-565.
11. Joseph T, Civil I. Trauma care in a low-COVID pandemic environment: A new normal. *Injury*. 2020;51 (6):1245-1246.
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370 (9596):1457-7.
13. Abdolrahimzadeh Fard H, Borazjani R, Sabetian G, Shayan Z, Boland Parvaz S, Abbassi HR, et al. Establishment of a novel triage system for SARS-CoV-2 among trauma victims in trauma centers with limited facilities. *Trauma Surg Acute Care Open*. 2021;6 (1):e000726.
14. Simpson S, Kay FU, Abbarra S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Document on Reporting Chest CT Findings Related to COVID-19: Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *Radiol Cardiothorac Imaging*. 2020;2 (2):e200152.
15. Henry BM, Aggarwal G, Wong J, Benoît S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. *Am J Emerg Med*. 2020;38 (9):1722-1726.
16. Su D, Li J, Ren J, Gao Y, Li R, Jin L, et al. The relationship between serum lactate dehydrogenase level and mortality in critically ill patients. * Biomark Med*. 2021;15 (8):551-559.
17. Lu J, Wei Z, Jiang H, Cheng L, Chen Q, Chen M, et al. Lactate dehydrogenase is associated with 28-day mortality in patients with sepsis: a retrospective observational study. *J Surg Res*. 2018;228:314-321.
18. Sabetian G, Feiz F, Shakibafard A, Fard HA, Sefidbakht S, Safari SH, et al. Challenges of diagnosis of COVID-19 in trauma patients: A case series. *Trauma*. 2021;23 (3):218-29.
19. Chen LR, Chen ZX, Liu YC, Peng L, Zhang Y, Xu Q, et al. Pulmonary contusion mimicking COVID-19: A case report. *World J Clin Cases*. 2020;8 (8):1554-1560.
20. Akdogan O, Yapar D, Topcu H, Arslan S, Boyaci H, Yilmaz YA, et al. Traumatic lung pathologies confused with COVID-19. *Medicine*. 2022;11 (2):712-6.
21. Elkbali U, Sen-Crowe B, Morse JL, Wyse RJ, Berg GM, Garland JM, et al. Trauma Prevalence and Resource Utilization During 4 COVID-19 “Surges”: A National Analysis of Trauma Patients From 92 Trauma Centers. *J Surg Res*. 2022;276:208-220.
22. Sheets NW, Fawibe OS, Mahmoud A, Chawla-Kondal B, Ayutyanont N, Plurad DS. Impact of the COVID-19 Pandemic on Trauma Encounters. *Am Surg*. 2021;314821029858.
23. Balakumar B, Nandra RS, Woffenden H, Atkin B, Mahmood A, Cooper G, et al. Mortality risk of surgically managing orthopaedic trauma during the COVID-19 pandemic. *Bone Jt Open*. 2021;2 (5):330-336.
24. COVIDSurg Collaborative. Mortality and pulmonary complications in emergency general surgery patients with COVID-19: A large international multicenter study. *J Trauma Acute Care Surg*. 2022;93 (1):59-65.
25. Doglietto F, Vezzoli M, Gheza F, Lussardi GL, Domenicucci M, Vecchiarelli L, et al. Factors Associated With Surgical Mortality and Complications Among Patients With and Without Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA Surg*. 2020;155 (8):691-702.
26. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with peripoperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020;396 (10243):27-38.

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27. Yeates EO, Grigorian A, Schellenberg M, Owattanapanich N, Barmparas G, Margulies D, et al. COVID-19 in trauma: a propensity-matched analysis of COVID and non-COVID trauma patients. *Eur J Trauma Emerg Surg*. 2021;47(5):1335-1342.

28. Mishra GP, Mulani J. Corticosteroids for COVID-19: the search for an optimum duration of therapy. *Lancet Respir Med*. 2021;9(1):e8.

29. Sarkar S, Khanna P, Soni KD. Are the steroids a blanket solution for COVID-19? A systematic review and meta-analysis. *J Med Virol*. 2021;93(3):1538-1547.

30. Bahl A, Johnson S, Chen NW. Timing of corticosteroids impacts mortality in hospitalized COVID-19 patients. *Intern Emerg Med*. 2021;16(6):1593-1603.

31. Liu J, Zhang S, Dong X, Li Z, Xu Q, Feng H, et al. Corticosteroid treatment in severe COVID-19 patients with acute respiratory distress syndrome. *J Clin Invest*. 2020;130(12):6417-6428.