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Use of convalescent plasma in patients with COVID-19

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Abstract

Introducton: We wished to evaluate the clinical effectiveness of convalescent plasma (CP) in coronavirus disease 2019 (COVID-19) patients treated in hospitals in the Kuyavian-Pomeranian Voivodeship, including the impact of treatment duration and CP antibody titer on the course of hospitalization and patient survival in relation to other risk factors.

Material and methods: This was a retrospective analysis of clinical data of CP use in hospitals in the Kuyavian-Pomeranian Voivodeship.

Results: A total of 3,596 patients had available clinical data. In 59% of patients, CP was administered during the initial 24 hours of hospitalization (median: 1 day, range 1–49). In cured patients, hospital length of stay correlated with time of CP administration (p <0.001), i.e. the sooner the COVID-19 convalescent plasma (CCP) was administered, the shorter the hospitalization. Overall survival in analyzed COVID-19 patients was 78.3%, and it was better when CP was administered during the first day of hospitalization (79.9% vs. 86.8%, p = 0.057), in younger patients (91.0% vs. 76.2% for patients <50 years and older, respectively; p <0.001); in patients not requiring invasive ventilation (78.7% vs. 26.9%, p <0.001), in good performance status patients (92.5% vs. 81.0% and 68.6% in patients in moderate and poor performance status, respectively; p <0.001); and in patients without comorbidities (88.6% vs. 75.9%, p <0.001). In turn, blood group and titers of antibodies against severe acute respiratory syndrome coronavirus 2 in CP had no impact on survival. In multivariate analysis, the following factors increased the risk of death from COVID-19: general clinical status at admission (poor > moderate > good), comorbidities, mechanical ventilation required. Risk of death was decreased in younger patients (continuous variable), while administration of CP within the first day of hospitalization had borderline significance (p = 0.077). The use of CP was a safe therapeutic approach. Mild reactions were reported after just 5/9,356 (0.05%) transfusions.

Conclusions: The early administration of CP had a beneficial effect on the clinical course of treatment in COVID-19 patients.

Key words: convalescent plasma, COVID-19, SARS-CoV-2

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Introduction

Treatment with plasma collected from people with a history of viral infections is a long-established method of treating some infectious diseases, especially when neither effective therapy nor a means of preventing the spread is available. Convalescent plasma (CP) was used, for example, during the Spanish flu pandemic of 1918–1920. According to data from that time, patients with pneumonia caused by the influenza virus who received convalescent human

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blood products had a clinically significant reduction in the risk of death. In addition, CP was also used in the treatment of measles, mumps, chicken pox, as well as cytomegalovirus or parvovirus B19 infections. The World Health Organization (WHO) also recommended the use of convalescent plasma during the Ebola hemorrhagic fever (EHF) epidemic [1]. The use of CP was also investigated in the severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) outbreak in 2003, the H1N1 influenza virus pandemic in 2009–2010, and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012. Both anti-MERS and anti-SARS therapies have shown better therapeutic effects in patients receiving CP compared to the control group [2, 3]. However, the best effects were observed in 2009 during the AH1N1 flu pandemic, where the mortality rate in the group treated with convalescent plasma was significantly lower than in the control group (20.0% vs. 54.8%) [4].

In reaction to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, on 10 April, 2020, the Polish Ministry of Health, following European Commission guidelines, informed the Blood Donation Centers (RCKiK, *Regionalne Centrum Krwiodawstwa i Krwiolecznictwa*) in Poland about the possibility of launching a program of plasma collection from COVID-19 convalescents, which was immediately implemented [5, 6]. At the start of the pandemic, the use of COVID-19 convalescent plasma (CCP) was an immediately available, low-risk, experimental therapy.

On 25 April, 2020, the Agency for Health Technology Assessment and Tariffication (AOTMiT) published 'Polish diagnostic, therapeutic and organizational recommendations for the care of individuals infected with SARS-CoV-2 or exposed to a SARS-CoV-2 infection'. This document highlighted the potential therapeutic value of CCP, albeit as a method requiring further studies. In addition, the 'Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists. Annex no. 2 as of 13 October, 2020' organized and standardized the procedure of treatment with CCP use. According to the aforementioned recommendations, the administration of c. 200–400 mL of CCP should be considered in the full-blown stage of infection (viral multiplication), usually in the first week of the disease, when saturation (SpO_2) is below 95%, and the patient requires hospitalization.

The aim of this study was to analyze data on the effectiveness of the use of SARS-CoV-2/COVID-19 convalescent plasma in patients treated for COVID-19.

Material and methods

Study design

We analyzed the first year of receiving and using CCP by the RCKiK in Bydgoszcz, i.e. 1 May 2020 to 30 April 2021. The studied population included hospitalized patients in the Kuyavian-Pomeranian Voivodeship, based on data obtained from hospitals, including: the impact of treatment duration and CCP antibody titer on the course of hospitalization and patient survival in relation to other risk factors. Only patients treated with CCP were eligible.

Methods

Data on CCP use in patients treated for COVID-19 was obtained from the RCKiK in Bydgoszcz and from hospitals in the Kuyavian-Pomeranian Voivodeship where plasma from convalescents was used. The staff accepting orders for CCP recorded the routine data required for all blood components, such as the name of the hospital, the name of the ordering physician, the name and surname of the patient and his/her blood group, data regarding patient's performance status, date of admission, age, saturation, the type of oxygen therapy used, respirator use, and the presence of comorbidities [7, 8]. In addition, hospitals in the Kuyavian-Pomeranian Voivodeship were asked to provide data including: donation number, name and surname of the patient who received it, admission date, transfusion date, and discharge/death date.

Definitions

Convalescent (recoverer) — a person who has been infected with the SARS-CoV-2 virus asymptomatically or symptomatically, with varying degrees of COVID-19 symptoms intensity, which has been confirmed by the available molecular or antigen tests.

COVID-19 convalescent plasma (CCP) — plasma collected from a person who has been infected with the SARS-CoV-2 virus asymptomatically or symptomatically with varying degrees of COVID-19 symptoms intensity, which has been confirmed by the available molecular or antigen tests. This is plasma obtained from whole blood or by automated plasmapheresis. A unit of FFP typically has a volume of c. 200 mL, depending on the preparation method used.

Concomitant diseases — this denotes simultaneous presence of a chronic condition which is a risk factor in reference to COVID-19 therapy. Due to the nature of SARS-CoV-2 infection, these include physiological conditions such as pregnancy and puerperium.

Clinical course and severity of COVID-19

COVID-19 is a disease characterized by a highly variable clinical course. Since the beginning of the COVID-19 pandemic, the following disease form scale has been adopted [9]:

- asymptomatic infection: without any clinical symptoms and signs, and chest imaging results normal, whereas 2019-nCoV nucleic acid test result is positive
- mild: symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Physical examination shows congestion of pharynx and no auscultatory

abnormalities. Some cases may have no fever or have only digestive symptoms such as nausea, vomiting, abdominal pain, and diarrhea;

- moderate: with pneumonia, frequent fever, and cough (mostly dry cough, followed by productive cough); some may have wheezing, but no obvious hypoxemia such as shortness of breath, and lungs can hear sputum or dry and/or wet snoring. Some cases may have no clinical signs and symptoms, but chest computed tomography shows lung lesions, which are subclinical;
- severe: early respiratory symptoms, such as fever and cough, may be accompanied by gastrointestinal symptoms, such as diarrhea. The disease usually progresses at ~1 week, and dyspnea occurs with central cyanosis. Oxygen saturation is <92% with other hypoxia manifestations;
- critical: children can quickly progress to acute respiratory distress syndrome or respiratory failure and may also have shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury. Organ dysfunction can be life-threatening.

Statistical methods

The results were evaluated with statistical analysis. Non-categorical variables were compared using the Mann-Whitney test for two groups and the Kruskal-Wallis test for more than two groups; categorical variables were compared using the chi-square test, with simultaneous calculation of the odds ratio (OR) with a corresponding 95% confidence interval (CI). Patient survival was the primary endpoint. Correlations between two parameters were analyzed by Spaerman test, with rho coeffcient. Overall survival (OS) was time from day of admission to hospital to completion of follow-up or death. OS curves were estimated by the Kaplan-Meier method and compared with the log-rank test. Moreover, in predefined groups, a univariate Kaplan-Meier analysis of individual survival prognostic factors was performed. Additionally, a multivariate Cox analysis of survival prognostic factors was performed. Multivariate analysis included factors with p value of <0.01 in univariate analysis. The results of multivariate analysis are presented as OR with 95% CI. An OR value >1 indicates an increased risk of therapeutic failure. An OR value <1 indicates a risk reduction. P <0.05 was considered statistically significant. The analysis was performed using the statistical package SPSS 27.0 (IBM SPSS Statistics).

Results

Patient characteristics

Clinical data on the use of the preparations in the Kuyavian-Pomeranian Voivodeship were obtained for 3,596 patients from ten hospitals. In total, 5,178.6 units of CCP were transfused (not all data was complete) out of all 9,313.5 units (9,356 packs) of CCP dispensed to hospitals in this region. The characteristics of these patients are presented in Table I. The analyzed group of patients hospitalized for

Table I. Patient characteristics (n = 3,596)

Parameter	Value
Sex, n [%]:	
• female	1,455 (40.5)
• male	2,141 (59.5)
Median age (range) [years]:	68 (1.3–100)
• <18	2
• 18–65	1,481
• > 65	1,969
• missing data	147
Blood group, n [%]:	
• 0	1,077 (29.9)
• A	1,455 (40.5)
• AB	332 (9.2)
• B	732 (20.4)
General condition before plasma administration, n [%]:	
• poor	1,123 (31.2)
• moderate	2,044 (56.8)
• good	380 (10.6)
• missing data	49 (1.4)
Need for mechanical ventilation before plasma administration, n [%]:	
• yes	28 (0.8)
• no	3,515 (97.7)
• missing data	53 (1.5)
Presence of comorbidities, n [%]:	
• yes	2,818 (78.4)
• no	591 (16.4)
• missing data	187 (5.2)
Day of first dose, median (range) [days]:	1 (1–49)
• 1	2,127
• 2	701
• 3–7	649
• >7	119
Day of discharge from hospital, median (range) [days]:	12 (1–131)
• missing data	101
Fatal outcome, n [%]:	
• yes	758 (21.1)
• no	2,741 (76.2)
• missing data	97 (2.7)

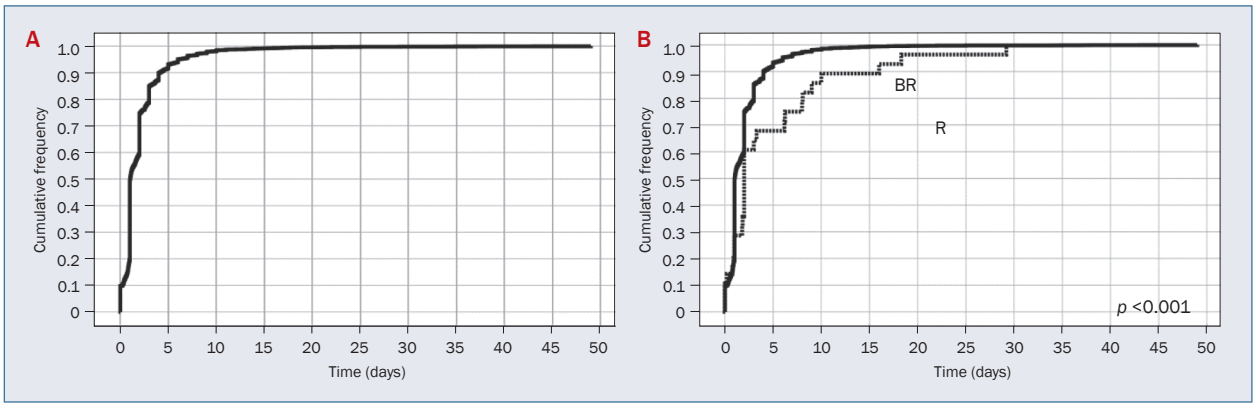

Figure 1. Cumulative frequency of first plasma dose administration by time from hospitalization: **A.** Overall for all analyzed patients; **B.** For patients undergoing mechanical ventilation (R), and non-mechanically ventilated (BR)

COVID-19 and treated with CCPs predominantly included men (59.5%), median age 68 years (range 1.3–100). Comorbidities were diagnosed in 78.4% of patients. In the majority of patients, the general condition assessed by the attending physician was moderate (56.8%); however, 31.2% of patients were in a poor general state. Some patients (n = = 28, 0.8%) already required the use of mechanical ventilation. The majority of patients (n = 2,127; 59.1%) received CCP on the first day of hospitalization. Length of hospital stay was 1–131 days (median 12).

Time of first CCP administration

The median time from hospital admission to ordering and administration of convalescent plasma was 1 day (range: 1–49) with 92% of patients receiving plasma before the fifth day of hospitalization (Figure 1A). Comorbidities did not affect earlier plasma administration. There were no differences in terms of the time of plasma administration depending on the patient's age, regardless of adopted value. A similar time-dependence was observed for each age group, regardless of the cut-off point. However, the plasma preparation was earlier administered to patients not requiring mechanical ventilation (Figure 1B; p <0.001). The median number of convalescent plasma transfusions in COVID-19 patients was 1, range 1–4. Single plasma administration was given to 3,240 patients (90.15%), with two, three and four administrations in 334 (9.30%), 17 (0.47%) and three (0.08 %) patients, respectively. The time from hospital admission to plasma administration did not impact survival, and the distribution of plasma first dose administration was identical in patients who survived and who died.

Duration of hospitalization depending on CCP administration time

A correlation was found between the time from hospital admission to administration of the first plasma dose and

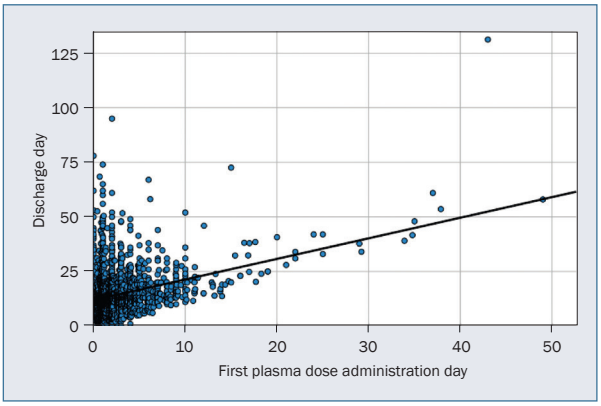

Figure 2. Correlation between time from hospital admission to first plasma dose administration and discharge day, rho = 0.16; p <0.001. Scatter plot of observed actual data with estimate of linear dependence equation for day of first plasma dose administration and discharge day: y = 0.9x + 11.9

discharge day, rho = 0.16; p <0.001 (Figure 2). The relationship was proportional in all analyzed patients, as well as in patients who died.

Administration of CCP on the first day after hospital admission resulted in a statistically significant reduction of length of stay (LoS) in survivors, in patients in good or moderate general condition, in patients with or without comorbidities, and in patients not requiring mechanical ventilation (Table II). There was no evidence of a relation between anti-SARS-CoV-2 antibody titers and LoS.

Effect of CCP on treatment outcomes

The overall survival rate of all plasma-treated COVID-19 patients included in the analysis with available clinical data was 78.3% (Figure 3A). A plateau was reached by day 30, and there were no COVID-19-related deaths after day 50.

Table II. Effect of COVID-19 convalescent plasma (CCP) administration on first day of hospitalization on length of stay

Patient groups	CCP administration on first day of hospitalization, median (range) [days]	CCP administration after first day of hospitalization, median (range) [days]	*p*
Total	12 (1–78)	13 (1–131)	<0.001
Survivors	12 (1–78)	13 (1–131)	<0.001
Patients who died	7 (1–68)	10 (1–51)	<0.001
General condition:			
• good	11 (1–46)	13 (1–131)	<0.001
• moderate	12 (1–74)	13 (1–95)	<0.001
• poor	12 (1–78)	13 (1–67)	0.055
Comorbidities:			
• yes	12 (1–78)	13 (1–131)	<0.001
• no	10 (1–32)	12 (2–44)	<0.001
Mechanical ventilation needed:			
• yes	13 (1–23)	13 (3–58)	0.401
• no	12 (1–78)	13 (1–131)	<0.001

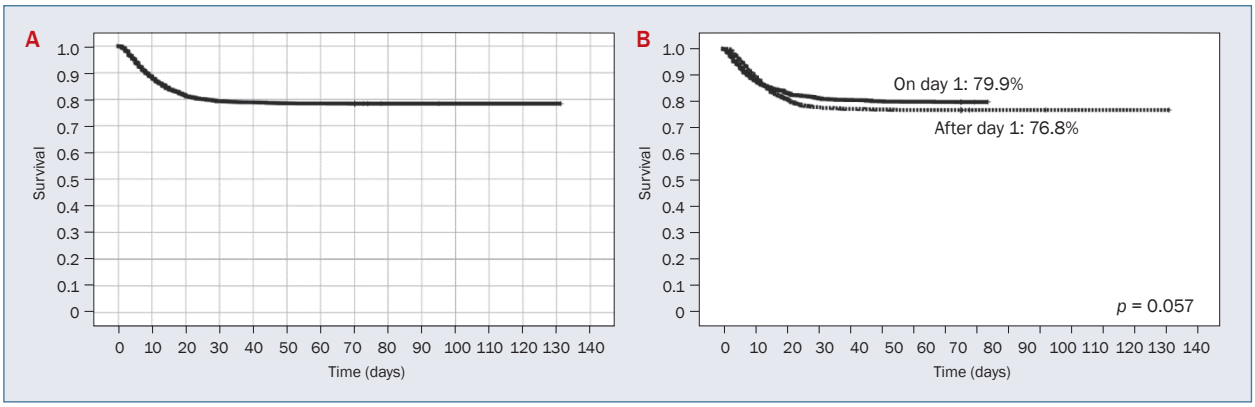

Figure 3. Overall survival: (**A**) coronavirus disease 2019 (COVID-19) patients who received COVID-19 convalescent plasma (78.3%) (**B**) depending on first plasma dose administration time (day 1 vs. day >1, $p = 0.057$)

Importance of CCP use in treatment of COVID-19 patients

Patient survival was improved when plasma was administered within the first day of hospitalization (79.9% vs. 76.8%, $p = 0.057$) (Figure 3B). However, the following factors showed no effect on survival: number of plasma doses administered, blood group, titers of anti-SARS-CoV-2 antibodies in the plasma preparation, and the total number of units of anti-SARS-CoV-2 antibodies transfused in the plasma to the patient.

Analysis of remaining risk factors associated with death

Regardless of the adopted age range, cure rates were better in younger patients. The survival of patients <50 years and >50 years was 91.0% and 76.2%, respectively (p <0.001) (Figure 4A). The general condition of the patients at the time of plasma ordering was of significant importance for survival. Survival rates in patients in good, moderate and poor general condition were 92.5%, 81.0%, and 68.6%, respectively (p <0.001) (Figure 4B). In patients without comorbidities, survival rate was 88.6%, while the presence of comorbidities reduced survival in COVID-19 patients to 75.9% (p <0.001) (Figure. 4C), including atrial fibrillation (n = 79) (Figure 4D) or previously diagnosed thrombosis or embolic events (n = 12) (Figure 4E). Survival rate in patients non-mechanically ventilated at the time of plasma administration was 78.7%, while in patients with mechanical ventilation it was 26.9% (p <0.001) (Figure 4F).

Multivariate analysis of risk factors associated with death

The multivariate analysis included all factors with p value of <0.1 in the Kaplan-Meier analysis, i.e. age (<50 years vs. >50 years), comorbidities (presence or absence),

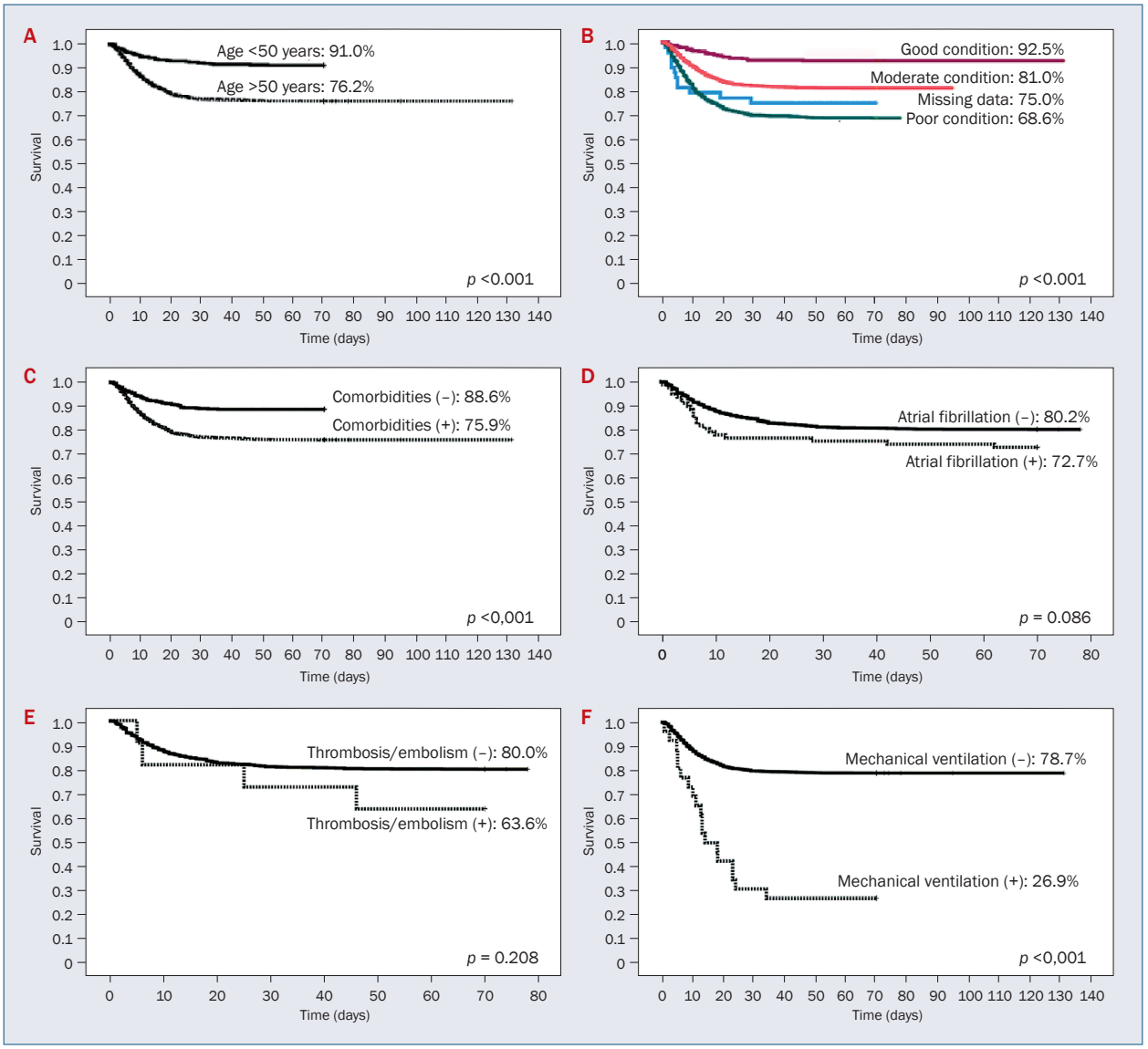

Figure 4. Overall survival in COVID-19 patients, depending on: (**A**) age; (**B**) general condition at time of plasma ordering; (**C**) presence of comorbidities; (**D**) known atrial fibrillation; (**E**) previous thrombosis or embolic events; (**F**) need for mechanical ventilation

mechanical ventilation (yes vs. no), general condition (moderate vs. good and poor vs. good) and the time of plasma administration (on day 1 vs. after day 1). It was shown that four factors influenced survival: age <50 was a favorable prognosis factor, while the unfavorable prognosis factors included presence of comorbidities, severe or moderate general condition, and the need for mechnical venstilation. Plasma administration on the first day of hospitalization had a borderline effect on OS improvement (Table III).

Analysis of post-transfusion adverse reactions

Between 1 May 2020 and 30 April 2021, a total of 9,356 packages of convalescent plasma were transfused to

Table III. Multivariate analysis of death risk factors

Parameter	OR	95% CI	*p*
Age <50 years	0.5	0.4–0.7	<0.001
Comorbidities	1.6	1.2–2.0	<0.001
Mechanical ventilation	3.1	1.8–5.1	<0.001
General condition:			<0.001
• moderate *vs.* good	1.7	1.4–2.0	
• poor *vs.* good	5.5	1.8–17	
Plasma administration on day 1	0.9	0.8–1.1	0.077

OR — odds ratio; CI — confidence interval

COVID-19 patients in the Kuyavian-Pomeranian Voivodeship. There was no serious post-transfusion reaction at this time. Five mild post-transfusion reactions were reported, accounting for 0.05% of all transfusions. These occurred in five different patients: two women and three men aged 28–73 (median 40). In four cases, these were typical mild allergic reactions. In the fifth case, the clinical symptoms included hypotension, anxiety, vomiting, and tachycardia.

Discussion

This paper presents data on the effectiveness of convalescent plasma in COVID-19 patients treated in hospitals in the Kuyavian-Pomeranian Voivodeship, based on information obtained from these hospitals.

The most important results show that the use of convalescent plasma as close to symptom onset as possible had a beneficial effect on the COVID-19 clinical course, including a reduction of hospitalization LoS in survivors and a tendency to improve survival rate in patients receiving CCP within the first day of hospitalization. The study showed that the early use of plasma had a beneficial effect on patients' clinical condition. The time of plasma administration correlated with the reduction of hospitalization LoS. The use of CCP on the first day increased survival rate, although this correlation was only on the borderline of statistical significance. These results were confirmed by numerous clinical observations of doctors from hospitals in the Kuyavian-Pomeranian region, emphasizing the improvement of the general condition in patients receiving CCP.

Analyzing the influence of CCP on treatment outcomes, a correlation was shown between the time from hospital admission to first plasma dose administration and the discharge day: faster first dose plasma administration correlated with shorter LoS, except for patients requiring mechanical ventilation and in poor general condition, where the result was on the borderline of statistical significance. Survival rate was also better when plasma was administered within the first day of hospitalization (79.9% vs.76.8%, $p = 0.057$). Statistical significance was not achieved in that case, however, the results were on the borderline of statistical significance, indicating a marked trend toward improvement. Practically this means that in the group of 2,127 patients receiving CCP on the first day, a difference of 3.1% in these results could transfer into saving 66 lives. In this light, we must underscore that we analyzed the clinical data from only 3,596 patients out of 7,182 who received CCPs, which constituted 50.1%. The actual number of survivors thanks to CCP use could probably be twice as large.

The analysis of risk factors associated with death due to COVID-19 showed a borderline positive role of the early administration of CCPs. Only patients who received CCPs were analyzed in this study. The multivariate analysis showed that four factors had an adverse effect on survival: older age of patient, presence of comorbidities, severe or moderate general condition, and the need to use mechanical ventilation.

Patients' general condition at the time of plasma ordering was important for survival. Survival rates in patients in good, moderate and poor general condition were 92.5%, 81.0%, and 68.6%, respectively ($p < 0.001$). In patients non-mechanicallly ventilated at the time of plasma administration, the survival rate was 78.7%, while in patients on a mechanical ventilator it was 26.9% ($p < 0.001$). In severely ill patients with the need to use mechanical ventilation, there was no evidence of a relation between early plasma administration and hospital LoS, which is consistent with the REMAP-CAP study results, in which critically ill patients (n = 2,011, of whom 1,084 received CCPs) were given plasma upon Intensive Care Unit (ICU) admission within 48 hours of randomization. There was no evidence of benefit from the use of convalescent plasma together with standard care compared to standard care alone in terms of mortality and other analyzed endpoints, including the primary endpoint i.e. days with not receiving organ support in ICU.

Evaluation of the effectiveness of CCPs in COVID-19 therapy must be carried out in the context of the development of therapeutic methods for this disease and the collection of scientific evidence. CCP was introduced at a time when the first evidence of chloroquine and hydroxychloroquine ineffectiveness had appeared, there were no antiviral drugs effective against the SARS-CoV-2 virus, no scientific evidence of the value of steroids and cytokine inhibitors, and when there were no specific monoclonal antibodies at all, and no information on a possible vaccine against SARS-CoV-2. Since the advent of COVID-19, research has been ongoing around the world to explore different treatment options for this disease (Figure 5). Antiviral, anti-inflammatory, anti-clotting, and antibiotics have been used in the treatment of COVID-19, but in most cases, the effectiveness of these methods has not been confirmed in large, randomized controlled trials.

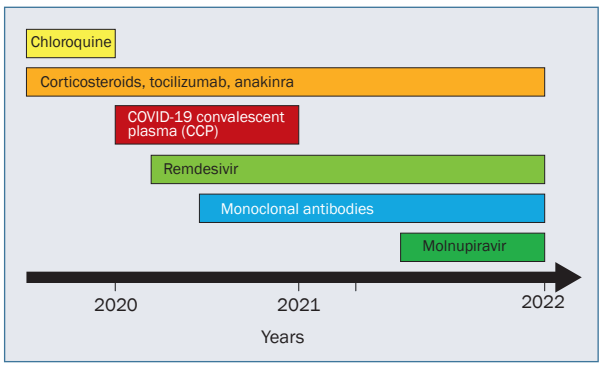

Figure 5. Main therapeutic methods in coronavirus disease 2019

Table IV. American Association of Blood Banks (AABB) recommendations on coronavirus disease 2019 convalescent plasma (CCP) use

1.	When making risk benefit decisions, one should consider the risk of CCP as comparable to standard (SARS-CoV-2 non-immune) plasma
2.	CCP is optimally effective when transfused as close to symptom onset as possible. CCP is unlikely to provide benefit for patients with late-stage disease or on mechanical ventilation
3.	The effectiveness of CCP is related to the antibody quantity within a unit; high-titer CCP is superior to low-titer CCP. A single high-titer unit should be sufficient for most patients
4.	In the absence of group B or group AB CCP, the transfusion of group A or group O CCP with low anti-A/B titer may be acceptable for group B and group AB patients
5.	Additional randomized, controlled clinical trial data is needed to fully assess CCP efficacy and to identify which specific patient populations would benefit most

SARS-CoV-2 — severe acute respiratory syndrome coronavirus 2

At the end of 2020, CCP had become one of the main treatment options for patients with symptomatic COVID-19, when the first reports of the effectiveness of this method began to appear. 2021 brought a significant number of reports on this subject, and most of them showed either little or no effectiveness of this method. However, it should be emphasized that, except for the RECOVERY study, most of the analyses included relatively small numbers of patients, so we must be cautious before making conclusions about a lack of efficacy. In addition, the RECOVERY study did not resolve many issues, including the effectiveness of very early or early administration of CCPs.

Summarizing the results of the most important studies published in 2021 on the use of CCPs in the treatment of COVID-19 patients, isome points stand out clearly: the lack of CCP effectiveness in hospitalized COVID-19 patients, and no effect of high-titer CCPs on the improvement of survival, the length of hospitalization, disease progression or the use of mechanical ventilation (RECOVERY trial) [10]. In a systematic review and meta-analysis by Janiaud et al. [11], no analyses were performed regarding antibody titers (high vs. low), early (<72 h) vs. late CCP use, or effects in patients not undergoing mechanical ventilation. However, CCP appears to be effective when properly administered taking into account the titer, timing of administration, and the patient's clinical condition. CCP use is effective if high-titer CCP is administered early, i.e. <72 hours from symptom onset, or in patients with mild COVID (i.e. <30 breaths per min; saturation >93%) [12–14]. Randomized controlled trials have shown that CCP is a safe therapy, similarly to saline infusion [14–16]. CCP can play an important therapeutic role if used before natural antibodies response [17], although in transplant recipients as well as oncology and hematology patients it can be used even in the later stages of disease (>72 h from symptoms onset) [18, 19]. In the study by Thompson et al. [20], CCP use resulted in a higher survival rate (deaths in 143 CCP vs. 823 patients in control group) (HR = 0.60, 95% CI = 0.37–0.97) [20]. A total of 238 oncohaematological patients have reported benefits from the administration of CCPs [21].

On 1 June, 2021, the AOTMiT updated its recommendations, whereby, due to the failure to confirm the effectiveness of the intervention in most randomized trials and their meta-analyses, the routine use of convalescent plasma in hospitalized COVID-19 patients was not recommended. This recommendation was based on an analysis of available scientific publications as part of a review of scientific reports regarding the use of convalescent plasma in the treatment of COVID19.

The current American Association of Blood Banks (AABB) recommendations regarding CCP use are set out in Table IV [22]. These show that immunosuppressed patients can benefit most from the use of CCPs. Nevertheless, due to the development of technology for monoclonal antibodies production, including casirivimab/imdevimab, interest in the use of CCPs gradually decreased in the second half of 2021. On 29 December, 2021, the RCKiK in Bydgoszcz for the last time dispensed CCP for therapeutic use.

Therapy with convalescent plasma is effective and well tolerated in most cases. Serious adverse reactions are rarely reported. Especially when convalescent plasma is used in the treatment of various viral infections, it can be stated that such a procedure reduces mortality, decreases viral load, and consequently shortens the hospitalization time and accelerates the convalescence process. Convalescent plasma was an immediately available and low-risk experimental therapy.

Conclusions

The early use of convalescent plasma had a beneficial effect on the treatment of COVID-19 patients. The time of plasma administration correlated with the reduction of length of hospital stay in survivors. Survival rate was better when plasma was administered within the first day of hospitalization (79.9% vs. 76.8%, $p = 0.057$). The titer of protective antibodies in the plasma preparation has not been shown

to be of importance for the length of hospitalization or patient survival. The risk factors for COVID-19 therapy failure included: older age (as a continuous variable), presence of comorbidities, poor or moderate general condition, and the need for mechanical ventilation. Plasma administration on the first day of hospitalization showed a borderline effect on survival rate improvement ($p = 0.077$).

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Authors' contributions

KG — data collection, data analysis, writing manuscript. JS — study design, data collection, data analysis, supervision.

Conflict of interest

None.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; uniform requirements for manuscripts submitted to biomedical journals.

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