

Original article

SARS-COV-2 screening in allogeneic hematopoietic stem cell donors: Implications for the evaluation process and eligibility

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ABSTRACT

Introduction: Soon after the onset of the SARS-CoV-2 pandemic, viral screening by nasopharyngeal swab became mandatory for allogeneic hematopoietic stem cell (HSC) donor eligibility.

Methods: We described our monocenter experience with allogeneic HSC donors from February 1 to the October 31, 2020 to verify whether the introduction of SARS-CoV-2 screening altered the donor eligibility and/or entailed a prolongation of the evaluation process.

Results: A total of 21 allogeneic HSC donors were screened during the above-mentioned period upon request by the local transplant physicians or by the Italian Bone Marrow Donor Registry; among the HSC donors ($n = 17$) who completed the eligibility process and further received the nasopharyngeal swab, all but one were negative for the presence of SARS-CoV-2. The positive donor remained asymptomatic for the whole duration of the infection, which lasted six weeks. However, he was temporarily excluded from donation. The median duration of the evaluation process was not significantly different, compared to the same period of 2019 (p -value = 0.11).

Conclusion: The mandatory SARS-CoV-2 screening in allogeneic HSC donors allowed for the detection of 6% positivity in this monocenter series over a 9-month period. Despite the inconvenience of this unexpected non-eligibility, the exclusion of a SARS-CoV-2 positive donor represented an important safety measure for the donor, with respect to a new and still partially unknown virus. The screening did not alter the length of the donor evaluation and thus, did not cause a delay in the eligibility process.

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Introduction

Soon after the onset of the SARS-CoV-2 pandemic, viral screening by nasopharyngeal swab became mandatory for allogeneic hematopoietic stem cell (HSC) donor eligibility in Italy, both for related and unrelated ones¹. The measure was conceived as a precaution for the health of both HSC donor and recipient, as on one hand, the impact of the mobilization regimen or bone marrow harvest is unknown among SARS-CoV-2-positive individuals, albeit asymptomatic, and on the other hand, the transmission of SARS-CoV-2 through HSC donation cannot be formally excluded; in March 2020 the information about what soon became a deadly virus across the world was quite limited and therefore, a cautionary approach seemed the most reasonable. Later on, and so far, no evidence of viral transmission through blood donation came from the clinical experience^{2,3}; nonetheless, a SARS-CoV-2-negative screening result is still recommended for the eligibility of HSC donors⁴. To the best of our knowledge, although mobilization and donation did not seem to adversely impact the course of infection in the asymptomatic donors who have been reported so far^{5,6}, any detrimental effect of mobilization or bone marrow harvest (including general anesthesia, decrease of hemoglobin level, donation-related pain and fatigue) on the donor's health cannot be formally excluded, with respect to a still partially unknown virus. According to the indications from the Italian *Centro Nazionale Trapianti*¹ released on the March 3, 2020, a SARS-CoV-2-specific nasopharyngeal swab by the reverse transcriptase-polymerase chain reaction (RT-PCR) had to be added to the already established blood, urine and imaging exams during the work-up, but its exact timing was not defined, as long as it were performed before initiating the patient conditioning regimen, being negative for the donor eligibility. In addition, graft cryopreservation was intended to further enhance the process safety⁷.

Herein we describe our monocentric experience with allogeneic HSC donors who were evaluated for donation from the March 1 to October 31, 2020 in order to verify whether the introduction of SARS-CoV-2 screening altered the donor eligibility or entailed a prolongation of the evaluation process.

Methods

We performed the SARS-CoV-2-specific nasopharyngeal swab after having completed all the eligibility tests, i.e., one or two days before the planned initiation of mobilization by the Granulocyte Colony-Stimulating Factor, but we did not receive any request for bone marrow harvest in this period; this choice was made because an earlier SARS-CoV-2 screening would have required a second test in 5–7 days, given the incubation period and the high number of infected people in

our region in the first wave of March/April 2020. The same timing was maintained onwards and up to the time of writing. The test was performed by the RT-PCR (GeneFinder™ COVID-19 Plus RealAmp Kit, ELITech; Allplex™ 2019-nCoV Assay, Seegene) on nasopharyngeal swab samples collected by three different physicians from the Apheresis team in the cited period; results were available within the 24 h following its execution⁸. Informed consent for the HSC donation was obtained from all the donors; the study was exempt from approval by an ethics board.

Results

During the above-mentioned nine-month period, a total of 21 allogeneic HSC donors were screened at the *ASST Grande Ospedale Metropolitano Niguarda*, Milano, Italy and started the suitability and eligibility evaluation process upon request by the local transplant physicians or by the Italian Bone Marrow Donor Registry (IBR), this latter in favor of unrelated patients. There were HLA-identical siblings ($n = 7$), haploidentical related donors ($n = 12$) and unrelated ones ($n = 2$); the median age was 37 years (range: 20–64) and the male/female ratio was 13:8. Among the HSC donors ($n = 17$) who completed the eligibility process and further received the nasopharyngeal swab, all but one were negative for the presence of SARS-CoV-2 and proceeded to donation. As of March 2021, no signs or symptoms of SARS-CoV-2 infection emerged during their post-donation follow-up. **Figure 1** shows the evaluation process together with the causes of unsuitability or non-eligibility of the HSC donors. The only SARS-CoV-2 positive donor was a 20-year-old male, an unrelated donor, who thus was temporarily excluded from donation; he remained asymptomatic for the whole duration of the infection, lasting six weeks from the positive swab up to the two consecutive negative ones that proved the clearance of infection. After that time, his exclusion was confirmed due to the elapsed time to transplant for the current recipient, but he remains available for future donations on behalf of the IBMDR. The median duration of the entire evaluation process for the 16 donors was 35 days (range: 10–123) and was not significantly different, when compared to the 14 donations during the same period of 2019, for which a median of 57 days (range: 23–124) was recorded (p -value by the Mann-Whitney U test = 0.11).

Discussion

Herein we report our experience with 21 consecutive allogeneic HSC donors who underwent SARS-CoV-2 screening by nasopharyngeal swab before the eligibility to donate and found one asymptomatic SARS-CoV-2-positive donor; despite the exclusion of this donor due to the detected infection, no delay in the evaluation process for all the donors was

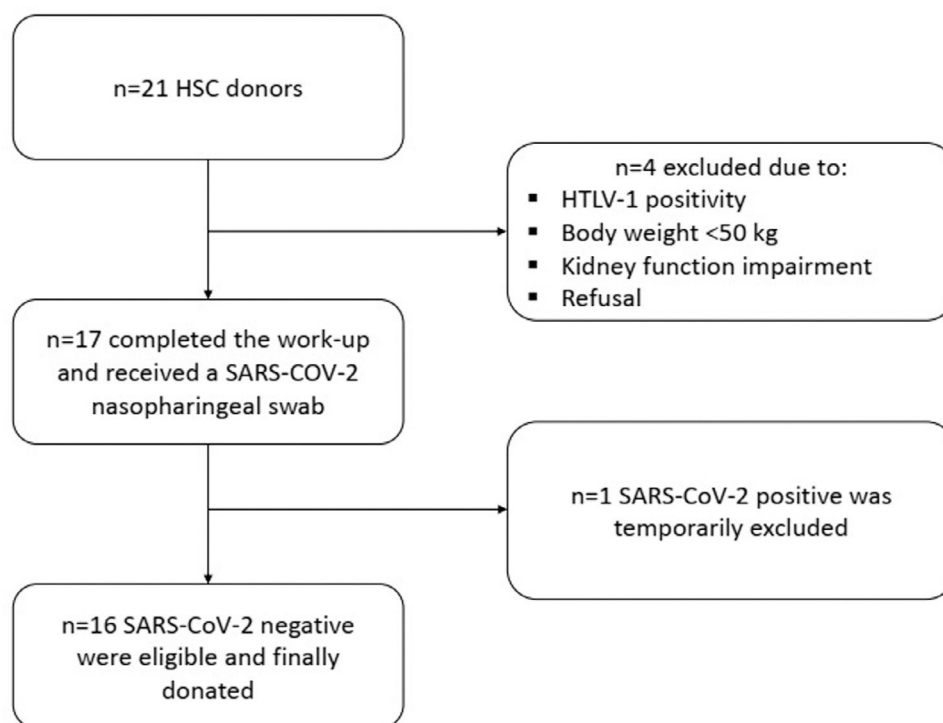


Figure 1 – Evaluation process with the causes of unsuitability or non-eligibility of the HSC donors.

observed and the duration of the entire process was not significantly different, with respect to the year before.

It is noteworthy that the presence of the SARS-CoV-2 positive test in 6% of our HSC donor series (one in the 17 donors who received the nasopharyngeal swab) is consistent with the seroprevalence of 5.2% (95% CI: 2.4 - 9.0) among the healthy blood donors in our area⁹. Although we cannot exclude false-negative findings among our 16 asymptomatic donors due to the well-known intrinsic limitations of the technical procedure¹⁰ or operator-related issues, the lack of evidence of SARS-CoV-2 infection during their follow-up, especially in the immediate post-donation period, appears to be reassuring in this sense. Furthermore, two recent reports on HSC transplantation from SARS-CoV-2-positive donors did not mention any unfavorable infection outcome among the donors, nor any viral transmission through the HSCs^{5,6}.

Conclusion

In conclusion, the mandatory SARS-CoV-2 screening in allogeneic HSC donors allowed for the detection of a 6% positivity ($n = 1$ donor) in this monocentric series over a nine-month period. Despite the inconvenience of such a non-eligibility, we believe that the exclusion of the SARS-CoV-2 positive donor represented a safety measure for the donor himself, with respect to a new and still partially unknown virus. Importantly, the SARS-CoV-2 screening did not alter the length of donor evaluation and thus did not cause a delay in the eligibility process.

Authorship contributions

R.C.: conceptualization, investigation and writing - original draft; F.A., E.V., M.P., I.C., A.M.M., L.B., N.S., S.P., L.M. and S.R.: investigation and writing - review & editing; D.F., C.V. and F.S.: resources; E.D. and G.G.: writing - review & editing.

Conflicts of interest

The authors declare no conflicts of interest.

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REFERENCES

1. Prot. 503/CNT 2020 Del 3 Marzo. Aggiornamento Delle Misure Di Prevenzione Della Trasmissione Dell'infezione Da Nuovo Coronavirus (SARS-CoV-2) in Italia attraverso Il Trapianto Di organi, Tessuti e Cellule". Available from: http://www.trapianti.salute.gov.it/imgs/C_17_cntAvvisi_231_0_file.pdf [cited 2020 March 3].
2. Cappy P, Candotti D, Sauvage V, Lucas Q, Boizeau L, Gomez J, et al. No evidence of SARS-CoV-2 transfusion transmission despite RNA detection in blood donors

- showing symptoms after donation. *Blood*. 2020;136:1888–91.
3. Gambacorti-Passerini C, Ruggeri M, Aroldi A, Piazza R, Mazzi A, De Silvestro G, et al. Transfusion of blood products derived from SARS-CoV-2+ donors to patients with hematological malignancies. *Transfus Apher Sci*. 2021;60(3):103105. <https://doi.org/10.1016/j.transci.2021.103105>.
 4. Ljungman P, Mikulska M, de la Camara R, Basak GW, Chabannon C, Corbacioglu S, et al. The challenge of COVID-19 and hematopoietic cell transplantation; EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy. *Bone Marrow Transplant*. 2020;55(11):2071–6. <https://doi.org/10.1038/s41409-020-0919-Erratum>. in: *Bone Marrow Transplant*. 2020 Jun 8.
 5. Leclerc M, Fourati S, Menouche D, Challine D, Maury S. Allogeneic haematopoietic stem cell transplantation from SARS-CoV-2 positive donors. *Lancet Haematol*. 2021;8(3):e167–e69.
 6. Anurathapan U, Apiwattanakul N, Pakakasama S, Pongphitcha P, Thitithanyanont A, Pasomsub E, et al. Hematopoietic stem cell transplantation from an infected SARS-CoV-2 donor sibling. *Bone Marrow Transplant*. 2020;55(12):2359–60.
 7. Hamadani M, Zhang MJ, Tang XY, Fei M, Brunstein C, Chhabra S, et al. Graft cryopreservation does not impact overall survival after allogeneic hematopoietic cell transplantation using post-transplantation cyclophosphamide for graft-versus-host disease prophylaxis. *Biol Blood Marrow Transplant*. 2020;26(7):1312–7.
 8. Alteri C, Cento V, Antonello M, Colagrossi L, Merli M, Ughi N, et al. Detection and quantification of SARS-CoV-2 by droplet digital PCR in real-time PCR negative nasopharyngeal swabs from suspected COVID-19 patients. *PLoS ONE*. 2020;15(9):e023631.
 9. Valenti L, Bergna A, Pelusi S, Facciotti F, Lai A, Tarkowski M, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 outbreak in Milan. *Blood Transfus*. 2021;19:181–9.
 10. Valenti L, Bergna A, Pelusi S, Facciotti F, Lai A, Tarkowski M, et al. Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19. *J Clin Microbiol*. 2020;58: e00297–20.