Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

implementation of the DRSS into clinical practice could contribute to informing relevant therapeutic decisions (ie, with regards to the selection of the intensity of conditioning), the decision to a specific post-transplant maintenance strategy (eg, by hypomethylating compounds),[3] the velocity of withdrawal of immunosuppressive agents, or the application of donor lymphocyte infusion. Third, the intervals of residual disease measurement by PCR techniques, next-generation-sequencing,[4] and multiparameter flow cytometry, as well as chimerism analyses, could be scheduled during the post-transplant period with the help of this new prognostic system (patients with more adverse risk profiles could be candidates for more frequent testing in the post-transplant period if therapeutic consequences are available).

Shouval and colleagues' study continues previous efforts[5] that have aimed to develop more precise risk stratification systems that can be applied to a comprehensive spectrum of haemato-oncological disorders in the allogeneic HSCT context. The cohort in their study, with more than 47000 patients, is one of the largest so far reported in the this setting. By including molecular markers for risk stratification in patients with acute myeloid leukaemia, Shouval and colleagues indicate a possible trend for further development of such risk stratification system for the future: molecular mutation profiles determined by next-generation-sequencing will exert an increasing role, probably comprising comprehensive marker panels in patients with acute myeloid leukaemia and other entities (eg, myelodysplastic syndrome or myeloproliferative neoplasm).

Beyond that, the inclusion of the pre-transplant measurable residual disease status by molecular genetics (eg, *NPM1* mutation),[6] and multiparameter flow cytometry[7] could be an interesting additional option for a more accurate assessment of the remission status within the respective risk stratification systems. Araki and colleagues showed that the outcome of patients who have acute myeloid leukaemia with measurable residual disease (MRD) and are in morphologic remission at the time of HSCT showed similarities to patients with active disease at this timepoint.[7] Transplantation study groups should investigate MRD as an additional parameter, preferably in close collaboration between both clinicians and laboratory specialists. It should be emphasised that more comprehensive molecular mutation patterns and sophisticated measurable residual disease methods could impose novel challenges for the combination of different haemato-oncological entities within one transplant risk score. Therefore, future risk classification systems for transplantation might be tending to focus on single disease entities rather than disease-spanning scores.

We declare no competing interests.

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Allogeneic haematopoietic stem cell transplantation from SARS-CoV-2 positive donors

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of COVID-19, but up to half of people infected with the virus are asymptomatic.[1] Moreover, SARS-CoV-2 RNAemia might occur in about 15% of symptomatic patients but also in a minority of those who are asymptomatic,[2] making possible—yet unconfirmed to date—the possibility of viral transmission through blood products,[3,4] in particular in the setting of allogeneic haematopoietic stem cell transplantation (HSCT).

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Here we report two cases of patients with acute myeloid leukaemia from our hospital who were transplanted in early October, 2020, with peripheral blood stem cells harvested from donors who tested positive for SARS-CoV-2 by RT-PCR on nasopharyngeal swabs at the time of cell collection.

Patient one is aged 60 years and reached first complete remission of acute myeloid leukaemia with myelodysplasia-related changes after induction chemotherapy. The patient then received consolidation with intermediate-dose cytarabine and was directed to haploidentical HSCT after reduced-intensity conditioning, using post-transplantation cyclophosphamide as prophylaxis for graft versus host disease. The donor was the patient's 22-year-old child.

Patient two is aged 64 years and reached first complete remission of a *RUNX1*-mutated acute myeloid leukaemia after induction chemotherapy. After receiving two consolidation courses with intermediate-dose cytarabine, a relapse occurred with profound pancytopenia and a marrow blast level of 13%. Meanwhile, the patient developed pulmonary invasive fungal infections and was referred for HSCT from a 50-year-old sibling donor.

For the **World Marrow Donor Association website** see https://wmda.info

In both cases, the donors tested negative for SARS-CoV-2 by RT-PCR on nasopharyngeal swabs 8 days before transplantation. However, at time of cell collection, both donors were tested again and found to be positive although still asymptomatic. Acute infection was found in the donor for patient two on the basis of seroconversion for anti-nucleoprotein and a significant increase in total anti-S1 antibodies (appendix).[5]

See **Online** for appendix

With regards to the benefit–risk balance for each recipient, recipients received their transplantations on the same day as collection, with recipients being tested twice a week for SARS-CoV-2 on nasaopharyngeal swabs and plasma. All tests remained negative over a 4-week follow-up period. Both recipients developed fever at some point after transplantation, without other symptoms suggesting COVID-19 illness.

The COVID-19 pandemic has created substantial barriers to timely donor assessment, cell collection, and graft transport. In the 14 days before donation, donors should practice good hygiene and isolate themselves as much as feasible during this period. Unnecessary travel should be avoided. Some guidelines recommend that donors should be tested for SARS-CoV-2 so that results are available before their admission for the collection procedure.[6]

Stem cell products can be frozen at the collection site or recipient-treating centre if substantial transport delays related to travel restrictions are likely. Indeed, cryopreservation of stem cell products is a secure approach in the pandemic context, preventing unexpected and undesirable events, such as transport delays or last-minute disqualification of a donor who is symptomatic and SARS-CoV-2 positive on the day of collection, that could preclude timely delivery of the graft to a patient who has already received the pre-transplantation conditioning regimen. Using this logistical organisation, cryopreserved grafts will be expected to be received at the recipient-treating centre before the start of conditioning. In parallel, cryopreservation might be used with the aim to apply a formal post-donation so-called cryo-quarantine period whereby a donation will only qualify for release if the donor tests negative or remains symptom-free at the end of the cryo-quarantine period. Although theoretically decreasing the risk of viral transmission from asymptomatic donors to recipients, systematically applying such a cryo-quarantine period remains debatable. First, as highlighted in the World Marrow Donor Association recommendations (updated as of Dec 8, 2020), failure to qualify for release can occur as a result of COVID-19 exposure that occurs after collection. Second, in the absence of symptoms, a positive nasopharyngeal swab on day 14 after collection or later is not consistent with the presence of pre-symptomatic SARS-CoV-2 infection at the time of collection. Third, cryopreservation for a minimum quarantine of 2 weeks might be directly harmful due to the urgent need for the transplantation in patients with aggressive, hard-to-control, underlying diseases such as acute leukaemia. In non-malignant diseases, such as severe aplastic anaemia, fresh cells rather than frozen cells have been found to be better for blood and marrow transplantation, in correlation with graft cell loss induced by the cryopreservation process.[7] Fourth, the two cases we reported here suggest that, despite the absence of pathogen-reduction treatment as is used for transfusion products, peripheral blood stem cells that have been harvested from donors who are SARS-CoV-2 positive might not lead to haematogenous viral transmission. Notably, this absence of transmission has been previously reported in a paediatric patient who received a bone marrow transplantation harvested from

a sibling donor who tested positive for SARS-CoV-2 by RT-PCR on nasopharyngeal swabs although they were asymptomatic.[8]

Finally, independent of risk to patient, strong ethical issues also exist regarding cryopreservation of donor stem cell products, particularly in the setting of voluntary unrelated donors. Cryopreservation results in a substantial increase of non-transfused unrelated donor stem cell products, possibly related to progression of the underlying malignancy in the recipient or acquisition of additional comorbidities during the quarantine period.[9]

Beyond the possibility of blood or HSCT transmission risk, important public health considerations and a variety of community measures around the world are having a major effect on HSCT donors and collection facilities. In this rapidly evolving pandemic, the situation in many countries is likely to change quickly in the coming months and years. The transplantation community has to remain vigilant to the evolving definition of risk-adapted procedures, taking advantage of the accumulation of knowledge in the field.

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