Several pathogens, such as Epstein–Barr, varicella-zoster, and hepatitis A viruses, can trigger AIH onset.[4] In addition, some reports described a relationship between vaccination (*i.e.*, hepatitis A and influenza virus) and the development of AIH,[5–8] suggesting a potential role of both virus and vaccine in unmasking AIH in predisposed individuals. Thus, the occurrence of acute or chronic liver disease following viral infection or vaccination should raise the suspicion of AIH in the presence of other autoimmune disorders.

Although the causal link between the SARS-CoV-2 vaccine and AIH cannot be definitively established, our case report suggests that this association could be more than coincidental. Indeed, the medical history negative for liver disease as well as the coexistence of another autoimmune disorder, the reasonable lag time between exposure to the triggering factor, the typical onset of symptoms, the laboratory/histopathological findings and finally the excellent response to therapy are all pieces of the puzzle that reinforce the hypothesis of an association between AIH and SARS-CoV-2 vaccination.

In summary, since the vaccination campaign against SARS-CoV-2 is reaching extraordinary coverage rates, healthcare providers should be aware of the potential association between the vaccine and the onset of immunomediated disorders in patients with a history of autoimmune diseases.

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Alba Rocco, Costantino Sgamato, Debora Compare declare no conflict of interest.

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Authors' contributions
Alba Rocco, Costantino Sgamato and Debora Compare: patient care, writing of the manuscript, and revision of the final version of the manuscript. Gerardo Nardone made a critical revision of the letter to the Editor.

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L-GrAFT and EASE scores in liver transplantation: Need for reciprocal external validation and comparison with other scores

To the Editor:

We read with great interest the recent article by Agopian *et al.* on the validation of the liver graft assessment following transplantation (L-GrAFT) score for prediction of early allograft failure (EAF).[1] EAF was defined as the failure of the graft (identified by retransplant or death) for any reason at 90 days after liver transplantation.[1,2] Adopting an innovative "kinetic" approach which included calculation of the AUC and slope of aspartate aminotransferase, bilirubin, platelet count, and international normalized ratio (INR), the L-GrAFT[1,2] was reported to outperform both the model for early allograft function (MEAF)[3] and early allograft dysfunction (EAD)[4] scores,

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Table 1. Comparison between EASE-score and other prognostic scores predictive of EAF.*

	C-statistic	95% CI	*p* value
EASE score[5]	0.87	0.83–0.91	
DRI[8]	0.53	0.46–0.59	<0.001
EAD[4]	0.70	0.63–0.75	<0.001
D-MELD[6]	0.60	0.54–0.67	<0.001
New ET-DRI[7]	0.55	0.49–0.62	<0.001
MEAF[3]	0.73	0.67–0.79	<0.001
L-GrAFT$_{10}$[2]	0.72	0.65–0.78	<0.001

DRI, Donor Risk Index; EAD, Early Allograft Dysfunction score; D-MELD, Donor age x MELD score; New ET-DRI, New Euro-Transplant Donor Risk Index; MEAF, Model for Early Allograft Failure score; L-GrAFT$_{10}$, Liver Graft Assessment Following Transplantation. EASE score shows the highest C-statistic at 90 days. The *p* values refer to the comparison of the indicated score against EASE-score. EASE-score has a high discrimination ability (absence of overlap of 95% CI between EASE score and other scores).
*ClinicalTrials.gov (NCT03858088).

namely the strongest validated scores available to date in this setting. The authors used a cumulative retrospective database from 4 North American (n = 3,201) and 7 European (n = 222) large volume centers.[1] The L-GrAFT has 2 calculation modalities: at 7 days (L-GrAFT$_7$) and at 10 days (L-GrAFT$_{10}$). Twenty-eight and 40 data entries are needed to calculate the scores, respectively. Both L-GrAFT scores were validated in the US cohort, while only the score at 7 days was validated in the European cohort. For the L-GrAFT$_7$, the authors report a C-statistic of 0.78 and 0.82 in the US and European cohort, respectively. Unfortunately, calculation of L-GrAFT scores is rather complex due to the significant number of requested data entries and their estimation intrinsic nature. Moreover, dedicated software is not yet available, and its logarithmic transformation does not help daily use.

On these bases, we herein provide a counterpoint to L-GrAFT offering additional evidence about early liver graft dysfunction prediction. Starting from the seminal study by Agopian *et al.*,[1] we have recently validated the L-GrAFT$_{10}$ on a population of 1,609 patients transplanted between 2016 and 2017 in 14 Italian centers and obtained a C-statistic of 0.72.[5] Using the original L-GrAFT components, we have further refined and simplified the L-GrAFT$_{10}$ formula reducing the number of data entries from 40 to 17. The beta-coefficients were re-calculated, and additional donor and recipient parameters were tested in 8 models. The final comprehensive score for EAF assessment, namely the early allograft failure simplified estimation (EASE) score, was internally validated through bootstrap and externally validated on a UK database (2 centers, 570 patients). The characteristics of both databases and the EASE-score formula are reported in Table S1 and S2, respectively. Notably, the overall prevalence of grafts from donors after cardiac death (DCD) and machine perfused (MP) grafts was 6.8% and 5.8%, respectively. Because neither of these categories were significant predictors, EASE can also be used as a precise algorithm to measure graft quality in translational studies that include high-risk DCD and MP grafts.

Unlike L-GrAFT$_{10}$, the EASE score does not include INR. Its AUC and slope are based on a lower number of evaluations (4 *vs.* 10), and no logarithmic transformation was used for bilirubin. Furthermore, the EASE score includes the following, easy-to-be-retrieved additional parameters: model for end-stage liver disease (MELD) score at transplant, number of intraoperatively transfused packed red blood cells (PRBCs), hepatic vessel thrombosis on day 10, and center volume (≥70 or between 36 and 69 cases per year).

As a result, the EASE achieved a C-statistic of 0.87 (95% CI 0.83–0.91) in the derivation set and outperformed all previously developed scores to predict EAF (Table 1).[1–4,6–8] With respect to the comparison with the L-GrAFT (C-statistic 0.72; 95% CI 0.65–0.78), the difference was significant using the DeLong test.[9] Although one could argue that a researcher-derived bias cannot be excluded, we invite the L-GrAFT developers to test the EASE score on both the North-American and COPE databases.

The EASE score also achieved an excellent C-statistic (0.93; 95% CI 0.89–0.97) for prediction of EAF at 30 days and was further validated in the UK cohort with a C-statistic of 0.78. Furthermore, it allows for stratification of liver grafts into 5 classes, with the highest one including cases to be referred for early retransplantation. The online EASE-score calculator is available at

Listing a patient for retransplant is often challenging, and surgeons and transplant hepatologists are frequently reluctant in the absence of objective signs of graft failure.[10] In our opinion, the inclusion of MELD, PRBCs, and hepatic vessel thrombosis is essential for an innovative and comprehensive definition of EAF. Notably, thrombosis of a hepatic vessel is a well-known indication for early retransplant. However, medical and endovascular treatments of thrombosis are now more efficacious than in the past, and several patients without associated liver failure recover. From this perspective, parenchymal and vascular causes of failure are linked in an innovative definition of EAF. Prediction of 90-day outcome and early identification of patients in need of retransplantation remain a priority. The choice of the best algorithm requires multiple external validation studies. A further step could be to design a prospective international validation study to enroll a larger number of cases and include series from small-volume centers.

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Conflict of interest
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Authors' contributions
AWA and QL wrote the letter, UC, RR and PDS revised and approved the final version of the letter.

Data availability statement
The data that support the findings of this study are available from the corresponding author, upon request.

Supplementary data
Supplementary data to this article can be found online at https://doi/org/10.1016/j.jhep.2020.12.009.

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An unequivocal formula to calculate L-GrAFT score is needed

To the Editor:

We read with interest the article by Agopian *et al.* entitled: "Multicenter validation of the liver graft assessment following transplantation (L-GrAFT) score for assessment of early allograft dysfunction".[1] Because early liver allograft dysfunction is difficult to assess, L-GrAFT emerges as a promising tool to detect such

Table 1. An example of the impact of rounding of coefficients on risk estimates using the unrounded (L-GrAFT$_{10}$ calculator provided in the supplement of the Agopian *et al.* study[1]) and rounded coefficients.

Predictor	Log OR	OR	Variable value	Log OR rounded
Intercept	9.77			
AUC log AST	-0.429459177	0.650861	51.73551342	-0.429
AUC log AST, squared	0.004621305	1.004632	2676.563348	0.005
Slope log AST (early)	4.607190144	100.2022	-0.205468062	4.607
Slope log AST (early), squared	4.412900349	82.50842	0.042217125	4.413
Log max INR	0.889739754	2.434496	0.405465108	0.890
AUC log TBIL	-0.04852114	0.9526372	22.36992196	-0.049
AUC log TBIL, squared	0.00362542	1.003632	500.4134084	0.004
Slope log TBIL	5.336266599	207.7357	-0.010094796	5.336
AUC log PLT	-0.046205313	0.9548459	44.91034035	-0.046
Slope log PLT	-5.248974974	0.0052529	0.171097045	-5.249
Slope log PLT squared	13.08633488	482306.4	0.029274199	13.086
	L-GrAFT$_{10}$	-2.39	With rounded factors:	-1.17
	Odds ->	0.09		0.31
	Individualized risk	8.36%		23.68%

AST, aspartate aminotransferase; AUC, area under curve calculated as 10-day mean * 10; early slope, slope of linear regression of values in first 7 days post-transplant; INR, international normalized ratio; OR, odds ratio; PLT, platelets; TBIL, total bilirubin.

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