

LETTER TO THE EDITORS

Toward a novel evidence-based definition of early allograft failure in the perspective of liver retransplant

Alfonso W Avolio^{1,2}, Andrea Contegiacomo³, Gabriele Spoletini¹, Giovanni Moschetta¹, Giuseppe Bianco¹, Salvatore Agnes^{1,2}, Marc L Melcher⁴ & Patrizia Burra⁵

1 Divisione di Chirurgia Generale e del Trapianto di Fegato, Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome, Italy

2 Dipartimento di Medicina e Chirurgia Translazionale, Università Cattolica del Sacro Cuore, Rome, Italy

3 Dipartimento di Diagnostica per Immagini, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome, Italy

4 Department of Surgery, Stanford University, Stanford, CA, USA

5 Dipartimento di Scienze Chirurgiche e Gastroenterologiche, Azienda ospedaliera universitaria, Padua, Italy

E-mail: alfonso.avolio@unicatt.it

Dear Editors,

We read with interest the study of Van den Eynde *et al.* on the effect of perfusion solutions on liver transplant outcome [1]. Graft dysfunction was analysed applying two indicators: Early Allograft Dysfunction (EAD, a dichotomous system based on transaminase, bilirubin and coagulation cut-off values) [2] and Model of Early Allograft Function (MEAF, a continuous score based on the same variables as EAD) [3]. The results showed the increased vulnerability of Histidine-Tryptophan-Ketoglutarate (HTK) preserved grafts compared to University of Wisconsin (UW) and Institute George Lopez-1 (IGL-1) ones, through the higher incidence of EAD and poorer MEAF values on the unweighted analysis (HTK > UW and IGL-1).

The debate around the definition of graft dysfunction is ongoing [4–8]. New scores emerged, fine-tuning the ability to predict organ failure when recipients' condition still allows successful retransplant [3,9]. The most utilized definition of graft dysfunction remains EAD [2], although this often encompasses conditions of reversible dysfunction.

Recently, a more accurate clinical entity, namely Early Allograft Failure (EAF), allowed a precise quantification of the overall risk of failure at 90 days, thus prompting retransplant for recipients with an unsustainable risk [9].

We developed a score named Early Allograft Failure Simplified Estimation (EASE) to predict EAF and validated it in a large external cohort [10]. Our objectives were (i) to include donor and recipient factors potentially associated with the outcome, (ii) to obtain the highest C-statistic at 30 and 90 days and (iii) to be easy to use.


The components of the EASE score are MELD, number of blood transfusions, presence of postoperative thrombosis of some hepatic vessel, trends of AST, bilirubin, platelet count and centre volume (Table S1). The stratification of grafts into five classes allows characterization of the EAF-risk (which partially overlaps with the EAD-risk), achieving a C-statistic of 0.93 (95% CI 0.89–0.97) and 0.87 (95% CI = 0.83–0.91) at 30 and 90 days, respectively. The EASE score presents several pros concerning the MEAF score used by the Authors [1]. Firstly, the inclusion of kinetics of platelets captures the capability to recover from the endothelial damage due to the ischaemia/reperfusion. Secondly, the inclusion of MELD and blood transfusions reflects the severity of the disease and the recipient's surgical complexity. Furthermore, the addition of postoperative thrombosis includes a major cause of graft failure [11]. Finally, the adjustment for centre volume improves the discrimination ability. The limitation is its complexity.

Differently from what has been done with previous complex models [3,9] to compute our score, we have now developed a web-based calculator and a smartphone APP (Fig. 1).

Results of the EASE score study allowed a comprehensive definition of EAF based on those components linked to microvascular (ischaemia-reperfusion) and macrovascular (thrombosis) injury. Donor factors, recipient conditions and technical complications [11] play a role in how the recipient can sustain graft injury, and they all share the same treatment (retransplant).

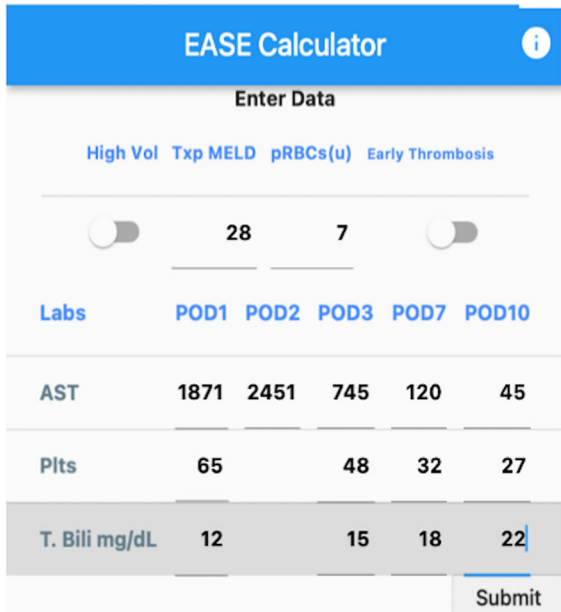
The EASE score allows the prediction and mitigation of the overall postoperative risk. It could be tested in

(a)



<https://transplanttools.com/ease-calculator/>

Transplant Tools
Mobile Apps for Organ Transplant



EASE Calculator

Enter Data

High Vol Txp MELD pRBCs(u) Early Thrombosis

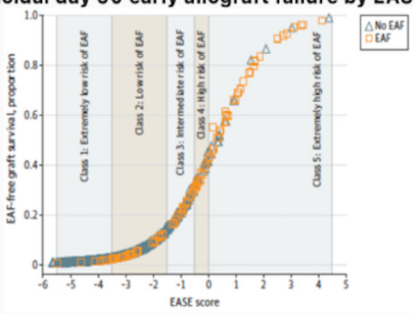
28 7

Labs POD1 POD2 POD3 POD7 POD10


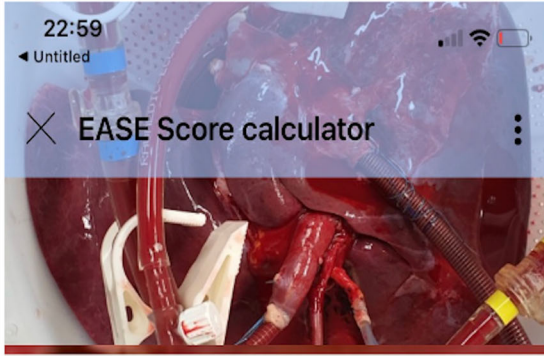
AST	1871	2451	745	120	45
Plts	65		48	32	27
T. Bili mg/dL	12		15	18	22

Submit

EASE
Unsustainable 1.
Early Allograft Failure
72.
Sigmoidal day 90 early allograft failure by EASE



(b)

EASE Score calculator

EASE score =
 + 0.044 x (MELD at transplant) +
 + 0.065 x (number of PACKED RED BLOOD CELL transfused units during surgery) +
 + 2.567 (if arterial or portal thrombosis during days 1-10) +
 + 0.000534 x (AUC*2 calculated from log_e of AST in 1, 2, 3, 7, 10 POD) +
 - 0.093 x (AUC calculated from log_e of platelet count in 1, 3, 7, 10 POD) +
 - 7.766 x (slope calculated from log_e of platelet count in 1, 3, 7, 10 POD) +
 + 0.795 x (slope calculated from bilirubin level in 1, 3, 7, 10 POD) +
 - 0.402 (if center volume ≥ 70 cases x year) +
 - 0.602

Abbreviations: MELD, model for end-stage liver disease; AUC, area under the curve; POD, post-operative day.
 Notes: Severity data entries are necessary to calculate the EASE score.
 The -0.602 constant of the EASE score results from the algebraic sum of the constant obtained by the logistic regression (-0.958) and the constant added to calibrate the unsustainable risk cutoff at the 0 threshold (+ 0.356).
 To convert bilirubin to μmol/L, multiply by 17.104. AST to μkat/L, by 0.0167.

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Contacts
 alfonso.avolio@policlinicogemelli.it
 andrea.contegiacomo@policlinicogemelli.it

Table 3. Representative cases with relative EASE scores and allograft outcomes

	Pt #520	Pt #1721	Pt #598	Pt #877	Pt #1735
MELD (+0.044)	20	14	40	19	30
PRBC (+0.065)	5	4	23	12	4
Thrombosis (+2.567)				no	no
AST day 1	253	613	11139	583	954
AST day 2	199	740	3438	517	751
AST day 3	130	125	1189	396	674
AST day 7	34	212	90	50	89
AST day 10	14	40	79	74	56
PLT day 1	32	29	20	60	
PLT day 3	41	63	67	47	
PLT day 7	54	63	33	49	12
PLT day 10	136	103	01	02	3

Home Case data **References**

Figure 1 Tools to easily calculate the EASE score. (a) QR code and a screenshot of the EASE score calculator available online ([www.transplanttools.com](https://transplanttools.com)) and also working on smartphones. (b) QR code and screenshot of the EASE score APP installable on smartphones.

the Authors' cohort [1] and in future research as an outcome measure of different perfusion solutions in the perspective of retransplant.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. EASE score formula.

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