ORIGINAL ARTICLE

Comparison of donor scores in bilateral lung transplantation—A large single-center analysis

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Objectifying donor lung quality is difficult and currently there is no consensus. Several donor scoring systems have been proposed in recent years. They all lack large-scale external validation and widespread acceptance. A retrospective evaluation of 2201 donor lungs offered to the lung transplant program at the Medical University of Vienna between January 2010 and June 2018 was performed. Five different lung donor scores were calculated for each offer (Oto, ET, MALT, UMN-DLQI, and ODSS). Prediction of organ utilization, 1-year graft survival, and long-term outcome were analyzed for each score. 1049 organs were rejected at the initial offer (group I), 209 lungs declined after procurement (group II), and 841 lungs accepted and transplanted (group III). The Oto score was superior in predicting acceptance of the initial offer (AUC: 0.795; CI: 0.776–0.815) and actual donor utilization (AUC: 0.660; CI: 0.618–0.701). Prediction of 1-year graft survival was best using the MALT score, Oto score, and UMN-DLQI. Stratification of early outcome by MALT was significant for length of mechanical ventilation (LMV), PGD3 rates, ICU stay and hospital stay, and in-hospital-mortality, respectively. To the best of our knowledge, this study is the largest validation analysis comparing currently available donor scores. The Oto score was superior in predicting organ utilization, and MALT score and UMN-DLQI for predicting outcome after lung transplantation.

KEYWORDS
clinical research / practice, donors and donation, donors and donation: donor evaluation, lung transplantation / pulmonology, organ procurement and allocation, organ transplantation in general

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1 | BACKGROUND

Scarcity of donor organs continues to be an unsolved problem in lung transplantation (LTx) and insufficient utilization of donor lungs is a major contributor. Currently, lungs are used in only around 20%–30% of multi-organ donors.[1,2] The lack of a consensus on how to adequately assess donor lung quality plays an important role for this issue. Routinely reported quality criteria for donor lungs include donor age, smoking status, oxygenation capacity, bronchoscopy and radiological findings, sputum gram stain, inflammatory parameters, history of intravenous drug abuse, length of intubation, and evidence of chest trauma. Nowadays there is sufficient evidence that donor lungs outside of the classical quality criteria have comparable short- and long-term outcomes.[3-6] Consequently, several research groups have published scores to stratify the risk of using extended criteria donor lungs. Currently, there are five scoring systems claiming to predict organ utilization and/ or posttransplant outcome based on variables available at the time of offer (Table 1). The Oto score was published in 2007 by the Melbourne group[7] and consists of five parameters largely corresponding to traditional standard donor criteria. Notably, paO2/FiO2 (arterial partial pressure of oxygen/fraction of inspired oxygen) ratio is perceived most important and the variable is given double weight. An adaptation of the Oto score was presented by Smits et al. based on multicenter data from Eurotransplant (ET).[8] This ET score added a donor history variable, introduced separate classes for missing values, and removed the double weight on the paO2/FiO2 ratio. Grimm et al. were the first to propose a scoring system based on both donor and recipient factors (MALT score). Derived from the United Network of Organ Sharing (UNOS) data, it aimed to predict 1-year mortality after lung transplantation.[9] The group at the University of Minnesota in Minneapolis developed a Donor Lung Quality Index (UMN-DLQI) based on a survey including 11 international transplant centers.[10] This resulted in the most complex of the scores including 16 factors, and it aimed to distinguish between more and less favorable offers. The most recent and rather basic score was published by Whited et al. from the group at Louisville, Kentucky in 2019. The Objective Donor Scoring System (ODSS) is based on UNOS data and only incorporates donor age, smoking history, diabetes mellitus diagnosis, and donor African-American race.[11]

To date, none of these scoring systems have gained widespread use in clinical lung transplantation or scientific reporting. Therefore, we aimed to evaluate the likelihood to accept a lung offer as well as organ utilization for all of the above described scores. In addition, we analyzed to what extent the five scores could predict perioperative outcomes and graft survival.

2 | PATIENTS AND METHODS

2.1 | Study cohort

Ethics approval was granted by the institutional review board of the Medical University of Vienna (EK-Nr 2063/2018). A total of 2201 lung donor offers to the Vienna Lung Transplant Program between January 2010 and June 2018 were analyzed. 1049 of those offers were immediately declined for organ quality (group I). Other reasons for refusal such as inadequate size-matching, lack of a suitable recipient, center capacity or logistics were excluded. Of the 1152 initially accepted organs, procurement surgeons rejected 190 lungs due to unacceptable organ quality at the time of procurement. Nineteen lungs were procured and subjected to ex vivo lung perfusion (EVLP), but ultimately declined for poor organ quality. These 209 organs were included in group II. Seven donation after circulatory death (DCD) donors did not progress to circulatory death after switch-off and were excluded from the analysis. A total of 936 lung donors were successfully utilized for lung transplantation. Twenty-one single-lung transplantations, 10 combined organ transplantations, and 61 re-transplantations were excluded in order to obtain a more homogenous group for outcome analysis. In three cases, donor information could not be retrieved, resulting in 841 patients assigned to group III (Figure 1).

2.2 | Donor and recipient data

A list of all lung donors offered to the lung transplant program at the Medical University of Vienna was provided by the ET organization. Detailed data for all organ offers were retrieved from the official ET donor registry. Perioperative as well as postoperative follow-up data for transplanted recipients (group III) were obtained from our institutional databases. Primary graft dysfunction (PGD) at different time points was assessed according to 2016 ISHLT guidelines.[12] Radiological assessment for grading PGD was provided by trained chest radiologists of the Department of Biomedical Imaging and Image-guided Therapy of the Medical University of Vienna.

2.3 | Calculation of donor scores

An overview of the five different donor scores, their factors, and weighing of the components is presented in Table 1. For all scores with a chest x-ray variable, computed tomography (CT) reports were also taken into consideration. In case of a discrepancy between the two, the more recent result was used. For scores not specifically addressing missing values, unremarkable findings were assumed in case of missing x-ray and CT. The MALT score and the UMN-DLQI were only calculated for successfully transplanted donors (group III), since they include recipient-bound variables and no recipient was specified for rejected donors. The lung allocation score (LAS) factor of the UMN-DLQI was calculated using the waiting list urgency status (high-urgent: 2 points; non-urgent: 0 points) for all patients transplanted before December 2011 (the time when the LAS system was implemented by ET).

2.4 | Probability of utilization

For Oto score, ET score, and ODSS, the probability to accept an initial donor offer and send an explant team was calculated.

TABLE 1 Overview of donor score features

Scoring systems overview	Oto score	ET score	ODSS	MALT score	UMN-DLQI
Alternative name	—	Lung donor score	Objective Donor Scoring System	Mortality after LTx	Donor Lung Quality Index
Published	2007, Melbourne group	2010, Eurotransplant group	2019, Louisville, KY group	2015, Johns Hopkins group	2016, Minneapolis, MN group
Region	Australia	Europe (ET region)	North America	North America	North America
Design	Single center	Registry/Multi center	UNOS Registry	UNOS Registry	Multi center/Single center
Derivation cohort	87	6080	9408	7336	56
Validation cohort	138	751	9408	1849	967
Main prediction objective	Offer acceptance and utilization	Offer acceptance and utilization	Overall graft survival	1-year mortality	Offer acceptance and utilization
Secondary outcomes [not significant]	P/F ratio at 12 h, LMV, PGD at 72 h, 30-day mortality, 1-year survival, [ICU stay]	1-year survival	[Freedom from BOS]	Overall survival	[30-day and 1-year survival, PGD 1–3 within 72 h]
Quality categories					
- Best	- Low Oto score (≤7)	- Class 1 (≤6)	- Low risk (0)	- Low risk (0–11)	- High UMN-DLQI (≥40)
- Intermediate	-	- Class 2 (7–8)	- Intermediate risk (1)	- Intermediate risk (12–21)	-
- Lowest	- High Oto score (>7)	- Class 3 (≥9)	- High risk (>1)	- High risk (≥22)	- Low UMN-DLQI (<40)
Parameters (points)	5, Donor only	6, Donor only	4, Donor only	9, Donor and Recipient	16, Donor and Recipient
	Maximum points: 18	Maximum points: 19	Maximum points: 5	Maximum points: 51	Maximum points: 50
	- Donor age (0–3)	- Donor age (1–3)	- Donor age (0–2)	- Donor age (0–5)	- Donor age (0–2)
	- Smoking history (0–3)	- Smoking history (1–2)	- Smoking history (0–1)	- Recipient age (0–7)	- Smoking history (0–2)
	- Chest X-ray (0–3)	- Chest X-ray (1–2)	- Diabetes mellitus (0–1)	- Previous thoracic Tx (0–5)	- Recipient LAS (0–2)
	- Secretions (0–3)	- Secretions (1–5)	- African-American (0–1)	- Preoperative KPS score (5–7)	- Ischemic time (0–1)
	- P/F ratio (0–6)	- P/F ratio (1–3)		- Preoperative GFR (4–6)	- P/F ratio (0–3)
		- Donor history (1–4)		- Preoperative Albumin (0–4)	- Procurement complexity (0–2)
				- ICU pre-transplant (0–6)	- Active pneumonia (0–4)
				- ECMO pre-transplant (0–7)	- Aspiration injury (0–3)
				- CMV risk status (0–4)	- Pre-existing lung disease (0–4)
					- Pulmonary edema (0–3)
					- Contusions (0–2)

(Continues)

Table 1 (Continued)

Scoring systems overview	Oto score	ET score	ODSS	MALT score	UMN-DLQI
					- Pulmonary malignancy (0–5)
					- Donor transmitted disease (0–4)
					- Extrapulmonary malignancy (0–5)
					- Size Mismatch (0–3)
					- Pos. retrospective xmatch (0–5)

Abbreviations: BOS, bronchiolitis obliterans syndrome; CMV, cytomegalovirus; ECMO, extracorporeal membrane oxygenation; ET, Eurotransplant; ICU, intensive care unit; KY, Kentucky; LAS, lung allocation score; LMV, length of mechanical ventilation; LTx, lung transplantation; MN, Minnesota; P/F ratio, ratio of arterial partial pressure of oxygen/fraction of inspired oxygen; PGD, primary graft dysfunction; pos, positive; UNOS, United Network for Organ Sharing; xmatch, crossmatch.

Furthermore, the predictive value of these scores for implantation of a procured lung (transplanted vs. canceled at procurement or after EVLP) was evaluated. These analyses were not performed for MALT score and UMN-DLQI, since no recipient was specified for rejected lungs.

2.5 | Recipient outcome

For all 841 transplanted donor lungs, stratification of recipient outcome was analyzed for the categories of each individual score. The following parameters were evaluated: incidence of PGD grade 3 at t72 hours, total length of mechanical ventilation (LMV), length of intensive care unit (ICU) stay and length of total hospital stay, in-hospital mortality, 1-year graft survival, and overall graft survival. Median posttransplant follow-up was calculated using the reverse Kaplan-Meier method.

2.6 | Statistical analysis

Statistical analysis was performed in IBM SPSS 24 (IBM Analytics, Armonk, NY) and R version 3.5.1.[13] For descriptive statistical analysis, categorical variables were compared with the Chi-squared test or Fisher's exact test as applicable. Continuous variables were compared using the Kruskal-Wallis test with Dunn-Bonferroni correction, and T-test or ANOVA with Tukey's test, respectively.

Stratification of recipient outcomes by each score was analyzed by Chi-squared test with post hoc Bonferroni-Holm correction for categorical outcome variables (PGD 3 at t72 hours, in-hospital mortality) and Kruskal-Wallis test with post hoc Dunn-Bonferroni correction was used for continuous outcome variables (LMV, length of ICU stay, and length of hospital stay) after testing for normality using Shapiro-Wilk test and histograms.

Prediction of initial acceptance, utilization after procurement, and 1-year graft survival by different scores were compared by receiver operating characteristic (ROC) analysis using the pROC R package.[14] Pairwise comparisons between the area under the receiver operating characteristic curve (ROC-AUC) values obtained for different scores were performed using the roc.test function with default parameters. Only donors where all three or five respective donor scores could be calculated were included in these analyses.

Long-term graft survival was analyzed by Kaplan-Meier curves and log-rank tests. In case of significant results in multiple group comparisons, pairwise log-rank tests with Bonferroni-Holm-corrected p-values were added. Figures were created using R or GraphPad Prism 8 (GraphPad Software, La Jolla, CA).

3 | RESULTS

3.1 | Donor demographics

Detailed donor demographics are presented in Table 2. Donors rejected at the time of offer (group I) were significantly older than donors rejected at procurement (group II) and donors used for transplantation (52 ± 17 years vs. 45.6 ± 15 vs. 40.8 ± 15 years; $p < .001$). Causes of death differed significantly between the groups ($p < .001$). There was a higher rate of head trauma (11.1% vs. 19.2% vs. 10.4%) in group II compared to groups I and III. Last available arterial partial pressure of oxygen (paO2) at 100% fraction of inspired oxygen (FiO2) at the time of offer was lowest in donors rejected at offer (358 ± 110 mm Hg) compared to those rejected at procurement (400 ± 112 mm Hg) and transplanted donors (444 ± 100 mm Hg; $p < .001$). Reasons for rejection at procurement are detailed in Table S1.

The 1049 lungs initially rejected by our center (group I) were subsequently offered to other transplant centers by ET. The majority of these donors (632; 60.2%) ultimately failed to be allocated.
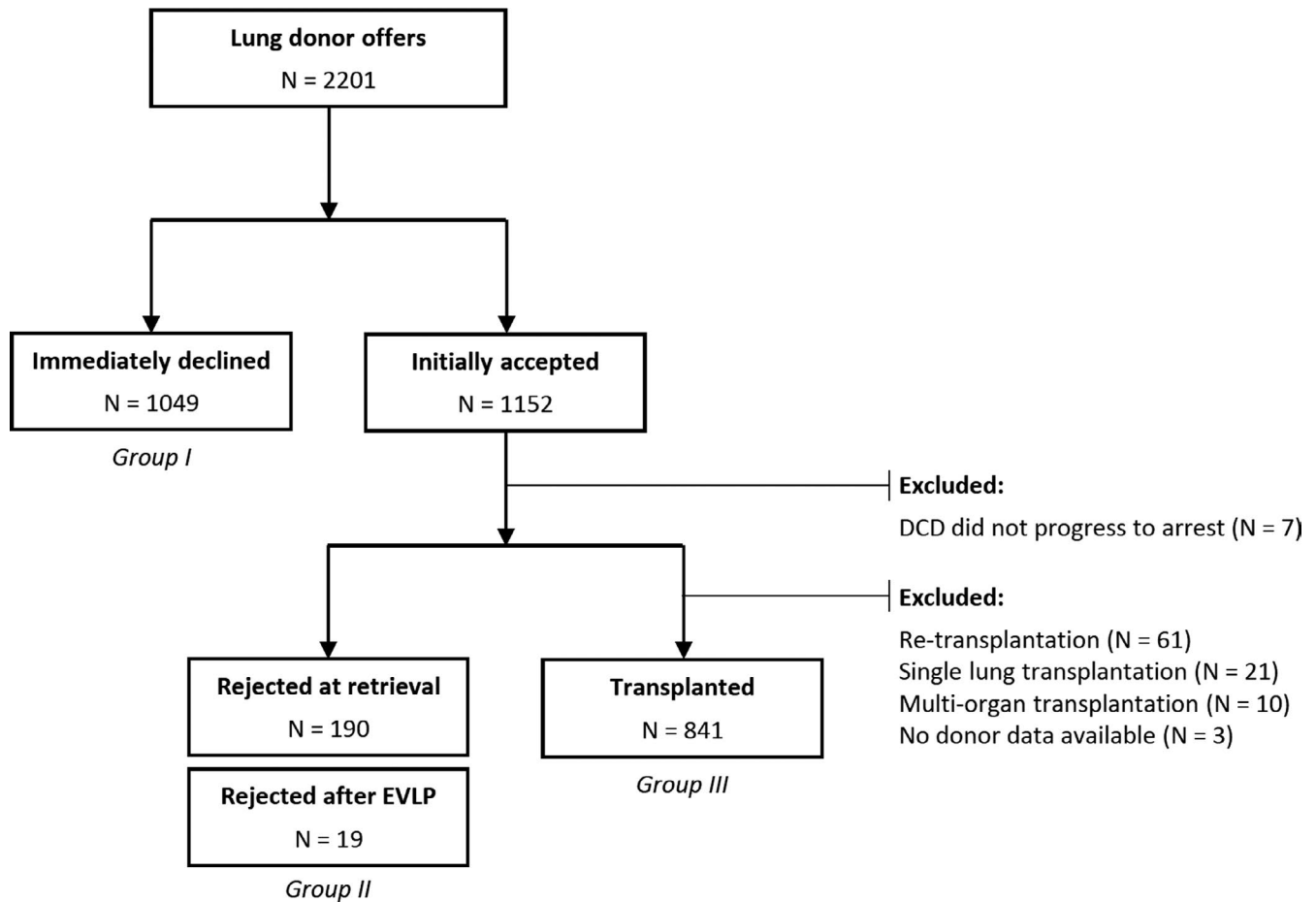
FIGURE 1 Donors were assigned to three groups: declined at offer (group I), rejected after procurement (group II), and transplanted (group III). A total of 102 donors were excluded from the analysis. EVLP, ex vivo lung perfusion; DCD, donation after cardiac death

Forty-four (4.2%) were procured but rejected after procurement. In 341 cases (32.5%), both lungs were transplanted by other centers, while in seven (0.7%) double lung offers, only one side was used. In 25 cases (2.4%), the further fate of the donor lung could not be determined. Detailed donor score distributions for subgroups of group I are depicted in Figure S1.

3.2 | Recipient demographics

A total of 841 double lung transplant recipients were included in the analysis. Chronic obstructive pulmonary disease (COPD) was the underlying diagnosis in 264 patients (31.4%), followed by pulmonary fibrosis in 217 (25.8%), cystic fibrosis in 183 (21.8%), and primary pulmonary hypertension in 76 (8.0%). Median age was 51 (interquartile range [IQR] 34–59). Preoperatively, 72 patients (8.6%) required extracorporeal life support (ECLS) bridging to transplantation. Most recipients (n = 739; 87.9%) were transplanted with intraoperative extracorporeal membrane oxygenation (ECMO) support. In 184 patients (21.8%), ECMO support was prolonged into the postoperative period according to our institutional policy.[15,16] Recipient demographics are shown in Table 3. A comparison of different recipient parameters between the categories of each

score is shown in Table S2. Median posttransplant follow-up was 66.5 months.

3.3 | Distribution of donor scores

The Oto score could be calculated for 2013 cases. Group I had the highest rate of donors (39.1%) with Oto score >7 (high-risk donors) compared to 12.9% in group II and 5.6% in group III (p < .001). A similar observation was made for the ET score. Donors rejected at the time of offer were in class 3 (high-risk) more frequently (81.9% vs. 69.2% vs. 66.3%; p < .001). The ODSS could be calculated for 2093 cases. In group I, 316 donors (30.3%) fell into the low-risk category compared to 97 (46.6%) in group II and 505 (60.0%) in group III. While percentages for intermediate risk were comparable (40.7% vs. 34.1% vs. 31.7%), group I had the highest number of high-risk donors with 303 (29.0%) versus 40 (19.3%) in group II and 69 (8.3%) in group III. All these differences were significant (p < .001). Since no recipient was specified for rejected lungs, the MALT score and UMN-DLQI could only be calculated for group III donors. Figure 2 depicts the distribution of score categories across the study groups. Figure S2 shows a comparison of distributions for Oto, ET, and ODSS

scores between DCD and DBD donors, as well as accepted and rejected EVLP lungs.

3.4 | Predicting initial acceptance of an offer for lung procurement

The predictive value for the initial decision to send out a lung procurement team was analyzed next. The Oto score showed the best prediction (ROC-AUC: 0.795; 95% CI: 0.776–0.815) compared to the ET score (ROC-AUC: 0.706; 95% CI: 0.684–0.728) ($p < .001$) and the ODSS score (ROC-AUC: 0.659; 95% CI: 0.637–0.681) ($p < .001$) (Figure 3A).

3.5 | Predicting acceptance of procured lungs for transplantation

Next, we analyzed procured donors, including 805 grafts ultimately transplanted and 201 rejected after procurement. Again, the Oto score achieved the highest ROC-AUC, indicating the highest predictive value for accepting lungs for transplantation after organ procurement (ROC-AUC: 0.660; 95% CI: 0.618–0.701), compared to the ODSS (ROC-AUC: 0.588; 95% CI: 0.546–0.629) ($p = .003$) and the ET score (ROC-AUC: 0.577; 95% CI: 0.533–0.621) ($p = .007$) (Figure 3B).

TABLE 2 Donor demographics

Donor demographics	Offer rejected (I) n = 1049	Rejected at procurement (II) n = 209	Transplanted (III) n = 841	p-value	Significant pairwise p-value
Age (mean ± SD)	52.0 ± 17	45.6 ± 15	40.8 ± 15	<.001	[#].001, [†].001, [‡].001
Gender (m%/f%)	55.3%/44.7%	58.7%/41.3%	48.2%/51.8%	.002	[†].006, [‡].014
Height (cm) (median; IQR)	170 (165–180)	170 (165–177)	170 (165–180)	.003	[†].020
Weight (kg) (median; IQR)	78.0 ± 17	74.8 ± 16	72.4 ± 16	<.001	[#]<.001, [†].012
BMI (median; IQR)	26.3 ± 4	25.5 ± 4	24.9 ± 4	<.001	[#].031, [†]<.001
Blood group (n; %)					-
A	466 (44.6%)	89 (43.0%)	352 (41.9%)	.136	
B	145 (13.9%)	30 (14.5%)	108 (12.8%)		
0	357 (34.2%)	73 (35.3%)	338 (40.2%)		
AB	76 (7.3%)	15 (7.2%)	43 (5.1%)		
Donation type (n; %)					
DBD	940 (90.1%)	205 (98.6%)	820 (97.5%)	<.001	[#].001, [†].001
DCD	103 (9.9%)	3 (1.4%)	21 (2.5%)		
Cause of death (n; %)					
Cardiac incident	38 (3.6%)	3 (1.4%)	18 (2.1%)	<.001	[#].002, [†].001, [‡].010
Cerebrovascular incident	747 (71.5%)	132 (63.5%)	572 (68.1%)		
Isolated head trauma	116 (11.1%)	40 (19.2%)	87 (10.4%)		
Malignancy	20 (1.9%)	0 (0.0%)	8 (1.0%)		
Polytrauma	64 (6.1%)	21 (10.1%)	77 (9.2%)		
Other	60 (5.8%)	12 (5.8%)	78 (9.2%)		
CPR (n; %)	241 (31.9%)	47 (22.8%)	161 (19.5%)	<.001	[#].024, [†].001
Smoking (n; %)					
Yes	476 (47.8%)	78 (37.7%)	202 (30.2%)	<.001	[#].001, [†].001, [‡].001
No	444 (44.5%)	94 (45.4%)	447 (66.7%)		
Unknown	77 (7.7%)	35 (16.9%)	21 (3.1%)		
Intubation days (median; IQR)	3 (2–6)	3 (1–6)	3 (1–5)	.001	[†]<.001
Last paO2 (mean ± SD)	358 ± 110	400 ± 112	444 ± 100	<.001	[#].001, [†].001, [‡].001
Last paCO2 (mean ± SD)	41 ± 9	40 ± 6	39 ± 6	.001	[†].001

Abbreviations: BMI, body mass Index; cm, centimeters; CPR, cardiopulmonary resuscitation; DBD, donation after brain death; DCD, donation after cardiac death; f, female; IQR, interquartile range; kg, kilograms; m, male; paCO2, arterial partial pressure of carbon dioxide; paO2, arterial partial pressure of oxygen; SD, standard deviation.

[#] 1 vs. 2; [†] 1 vs. 3; [‡] 2 vs. 3.

3.6 | Short-term outcome

Short-term results are detailed in Table 4. The Oto score correlated significantly with median hospital stay (p = .042); however, there was no statistical difference in short-term outcomes between the three risk categories of the ET score. The MALT score showed a highly significant difference in LMV (p < .001), PGD 3 rates at 72 hours (p < .001), length of ICU stay (p < .001), hospitalization (p < .001), and in-hospital mortality (p < .001). The

TABLE 3 Recipient demographics

Recipient demographics	Recipients (Group III)
	n = 841
Age (median; IQR)	51 (34–59)
Gender (m%/f%)	50.8%/49.2%
Diagnosis (n; %)	
COPD	264 (31.4%)
Fibrosis	217 (25.8%)
Cystic fibrosis	183 (21.8%)
Primary pulmonary hypertension	67 (8.0%)
A1AD	36 (4.3%)
Bronchiectasis	13 (1.4%)
LAM	9 (1.1%)
Sarcoidosis	10 (1.2%)
Other	42 (5.0%)
EVLP (n; %)	63 (7.5%)
Transplant type (n, %)	
full	390 (46.4%)
size reduced	331 (39.4%)
lobar	120 (14.2%)
Ischemic time (min) (mean ± SD)	357 ± 76
ECLS Bridging	72 (8.5%)
Type of intraoperative support (n; %)	
no support	92 (10.9%)
intraOP ECMO	739 (87.8%)
CPB	9 (1.3%)
Prolonged postOP VA ECMO	188 (22.3%)
Length of MV (h) (median; IQR)	43 (22–96)
PGD 3 at 72 hours (n; %)	28 (3.4%)
ICU stay (d) (median; IQR)	7 (5–17)
In-hospital death (n; %)	64 (7.6%)
Hospitalization (d) (median; IQR)	24 (18–37)

Abbreviations: A1AD, alpha-1-antitrypsin deficiency; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; d, days; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; f, female; h, hours; ICU, intensive care unit; intraOP, intraoperative; IQR, interquartile range; LAM, lymphangioleiomyomatosis; m, male; MV, mechanical ventilation; PGD, primary graft dysfunction; postOP, postoperative; SD, standard deviation; VA, venoarterial.

UMN-DLQI could not predict in-hospital mortality but correlated with LMV (p = .042), rates of PGD 3 (p = .009), length of ICU (p = .016), and length of hospital stay (p < .001). The risk groups of the ODSS showed differences in ICU stay (p = .016), hospitalization (p = .001), and in-hospital mortality (p = .043). Short-term outcomes for the subgroup of DCD donors (Table S3A,B) and EVLP lungs (Table S4A,B) are shown separately.

Next, we assessed the predictive accuracy of the five scores for 1-year graft survival rates. In a total of 758 donor-recipient pairs, a full set of all variables necessary for the calculation of each of the five scores was available. In the first year, 113 of these patients died while six had to be re-transplanted due to early graft failure, leading to a graft survival rate of 84.3%. The Oto score (ROC-AUC: 0.609; 95% CI: 0.556–0.662) showed the highest ROC-AUC of the three scores using only donor factors and was significantly better than the ET score, which displayed the lowest predictive capability for 1-year graft survival with a ROC-AUC of only 0.481 (95% CI: 0.425–0.536) (p = .005). The ODSS (ROC-AUC: 0.567; 95% CI: 0.517–0.617) also showed a better prediction accuracy than the ET score (p = .048) (Figure 3C). The MALT score (ROC-AUC: 0.649; 95% CI: 0.596–0.703) and the UMN-DLQI (ROC-AUC: 0.582; 95% CI: 0.528–0.637) both predicted 1-year graft survival equally well (Figure 3D).

3.7 | Long-term outcome

All scores except the ET score correlated with Kaplan-Meier graft survival. At 5 years after transplantation, graft survival in patients with low Oto score donor lungs was 73.8% compared to only 55% in those with a high score (p = .001). Recipients of low-risk donors according to the ODSS were still alive in 77.1% after 5 years, intermediate risk donors in 65.6%, and high-risk donors in 62.5% (p = .001). The MALT score mainly showed a benefit for the low-risk group (76.2%) while no difference was seen between the intermediate (65.3%) and high-risk groups (64.8%). For the UMN-DLQI categories, a superior graft survival in the low-risk category was most notable at 3 years (79.6% vs. 69.2%) and still significant at 5 years (74.4% vs. 67.7%) (p = .013). In contrast, 5-year graft survival rates of the three classes of the ET score were 74.4% vs. 70.7% vs. 72.4% (p = .766). Kaplan-Meier survival curves according to all five scores are depicted in Figure 4.

4 | DISCUSSION

To the best of our knowledge, this study represents the first direct comparison between different donor scores in a contemporary cohort of lung transplant recipients. It is also the first large external validation study for the ET, ODSS, UMN-DLQI, and MALT lung donor scores and the largest external validation study of the Oto score, which has only been previously tested in 210 potential donors in Northern Italy.[17] We found excellent prediction for the acceptance of donor offers and
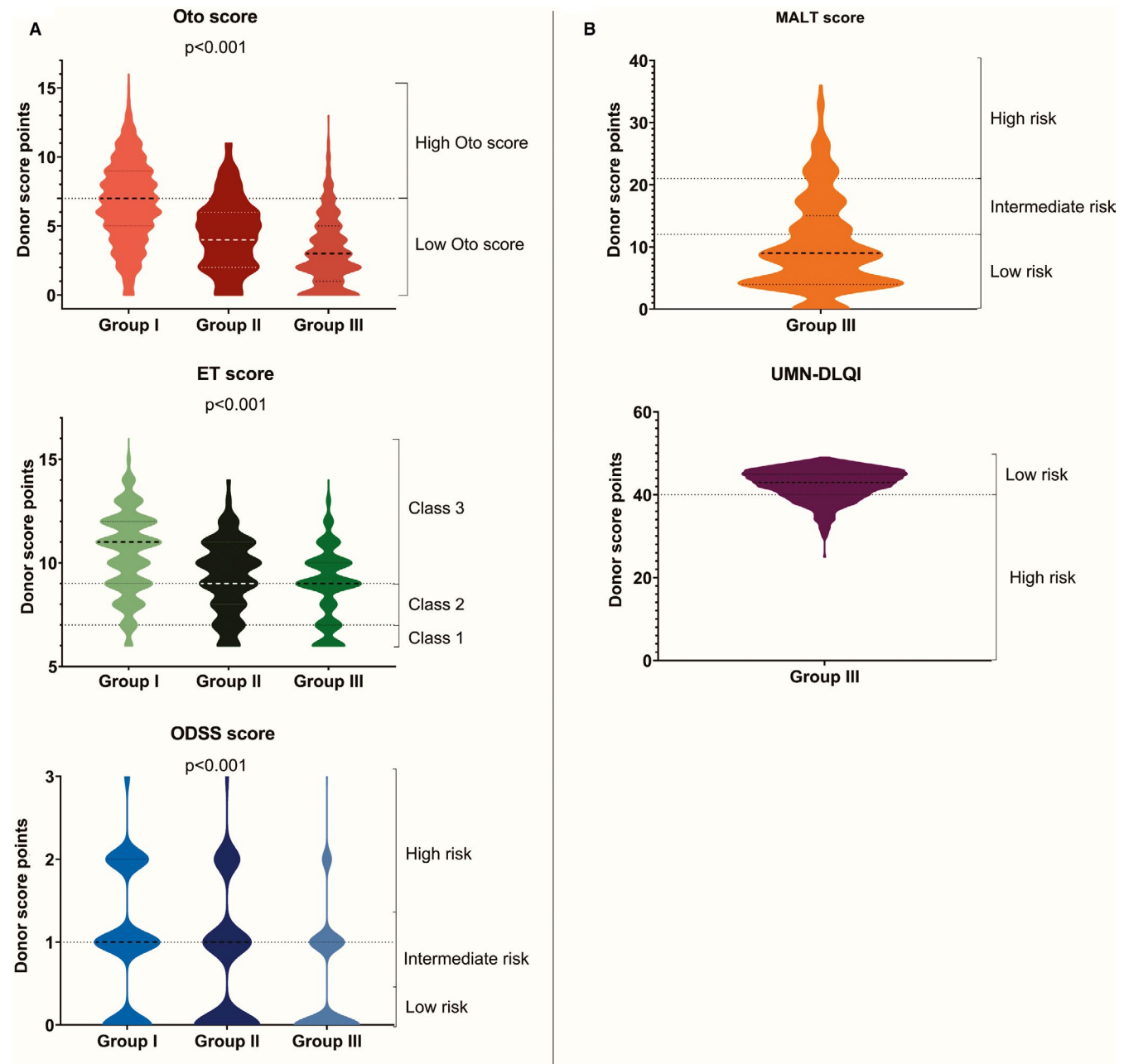
FIGURE 2 Distribution of scores in group I (organs rejected at offer), group II (organs rejected after procurement), and group III (transplanted organs). Scores using only donor factors are depicted in panel (A), and scores combining donor and recipient factors are shown in panel (B). Dotted lines signify 25%, 50% (median), and 75% quartiles [Color figure can be viewed at wileyonlinelibrary.com]

1-year graft survival for the Oto score, while it was not useful in stratifying early outcome after lung transplantation. One possible reason for this discrepancy could be that it was the oldest score analyzed in our study (published in 2007). Continuous refinements in surgical technique and posttransplant ICU care have led to markedly improved short-term results especially in the last decade. This may have reduced the power of this score to predict short-term outcome in our cohort of contemporary LTx compared to its own original cohort transplanted between 2002 and 2005. The MALT score on the other hand was excellent in predicting 1-year graft survival and in stratifying early postoperative results. The UMN-DLQI also predicted 1-year results

well and had value in stratifying most short- and long-term outcomes, along with the ODSS.

Donor pools as well as considerations on organ quality may vary geographically. All the different scores were only derived from regional cohorts. This could have an impact on the applicability of a score in different parts of the world. The ET authors sought to remedy this with their own edition of the Australian Oto score. The ODSS included African-American background as a variable rather specific to the North American region. Of note, none of our donors had African-American background. Despite this, the score correlated well with most analyzed outcomes.
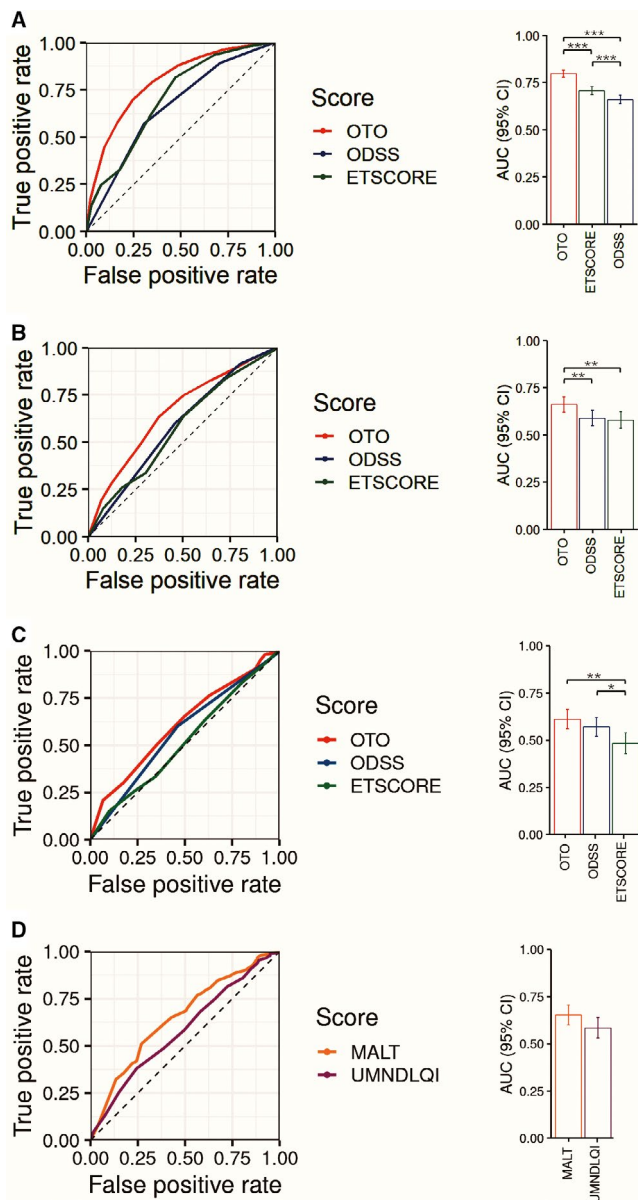
FIGURE 3 (A) The predictive value of accepting an organ offer was best for the Oto score, followed by the ET and the ODSS score. (B) The Oto score also predicted if the procured lung was ultimately transplanted most accurately, followed by the ODSS and the ET score. (C) For all successfully transplanted patients, the MALT, Oto, and ODSS scores were superior in predicting 1-year graft survival among the scores using only donor factors. (D) Both scores based on a combination of donor and recipient factors (MALT and UMN-DLQI) predicted 1-year graft survival well. Level of statistical significance is indicated as follows: *$p \leq .05$; **$p \leq .01$; ***$p \leq .001$ [Color figure can be viewed at wileyonlinelibrary.com]

Overall, the Oto score appeared to depict our current practices of organ quality assessment most accurately. We could confirm the previously published 7 points as a good cut-off for accepting an organ offer. In our cohort, only 5.6% of transplanted donors were high-risk with an Oto score >7. These patients had an impaired 1-year survival of only 70.7% compared to 85.4% of Oto score <7 donor lungs. Meanwhile, a recent publication by the Melbourne group reported

46 successfully transplanted organs with a Oto score >7 and good long-term outcome.[18] This suggests that a more liberal approach could be feasible. Using scores to predict donor acceptance is limited by the fact that they merely reflect common selection practices and do not allow deductions about the true organ quality. Nevertheless, donor scores can still play an important role by providing standardized criteria to compare donor pools and acceptance policies of different centers.

The five scores compared in this study featured a heterogeneous set of designs and parameters. They were also conceived in different eras, as the earliest started to include cases in 2001 and the most recent one ended recruitment in 2015. On the other hand, primary and secondary objectives of the individual scores were similar and they all aimed to predict 1- year or overall survival of the transplant recipient. The variables included in the early scores, such as Oto and ET score, still largely correspond to the traditional marginal donor classification.[19] The ET score added donor history to the variables, such as a known malignancy, sepsis, drug abuse, meningitis, or a positive virology including anti-CMV. In our cohort, as many as 62.1% of donors were positive for anti-CMV antibodies, resulting in 3 points being added to the score for this reason alone. This might partly explain the inferior performance of the ET score, especially since CMV status is not considered when matching a donor to a recipient at our center. The MALT score and the UMN-DLQI are the only scores to include recipient-based factors. The UMN-DLQI takes recipient LAS, size-matching, and the crossmatch into account. The MALT score even exceeds this and includes a comprehensive list of recipient parameters. It thereby integrates recent findings that preoperative performance status,[20] pretransplant kidney function[21] as well as posttransplant renal insufficiency[22] impact postoperative outcome. The excellent prediction of outcomes with these scores is in line with evidence showing that transplant outcome is more dependent on the condition of the recipient rather than the quality of the donor.[23]

Donor age was the only factor represented in all scores. However, the threshold at which donor age was considered a risk factor differed between ≥60 for the Oto score, >60 in the ET score, >64 for the MALT score, >65 for the UMN-DLQI, and >60 for the ODSS. The age limit for donor lung acceptability has been controversially discussed in the literature. Some authors have found impaired results with old-age donors,[24,25] while others reported no impact of donors aged 70 years and above on outcomes.[26,27] The paO2 at 100% FiO2 is one of the most important traditional lung quality criteria. Interestingly, it was not included in the MALT score and the ODSS, two of the more recent systems. The Oto score on the other hand places great emphasis on the paO2/FiO2 ratio by giving it double weight. The impact of donor lung oxygenation capacity on transplant outcomes has been challenged repeatedly.[28-30] Our center usually considers lungs with paO2/FiO2 ratios above 250 mm Hg acceptable, provided macroscopic organ quality is good. Smoking in multi-organ donors is a common finding. However, many lungs from moderately smoking donors can have excellent long-term function, if generalized substantial emphysema is ruled out.[31,32] Additionally, a clear survival benefit

TABLE 4 Early outcome of transplanted patients

Outcome parameters	Oto score n = 805		ET score n = 841		ODSS n = 841		
Length of mechanical ventilation (h) median (IQR)	Low: 43 (22 – 92) — High: 59 (29.5 – 119)	p = .096	Class 1: 37 (22 – 61) Class 2: 42 (22 – 114) Class 3: 45 (23 – 99)	p = .069	Low risk: 42 (22 – 88) Int. risk: 44 (22 – 99) High risk: 54 (22 – 159)	p = .150	—
PGD 3 at 72 hours n (%)	Low: 25 (3.3%) — High: 1 (2.4%)	p > .999	Class 1: 9 (3.0%) Class 2: 12 (3.0%) Class 3: 7 (5.3%)	p = .412	Low risk: 14 (2.9%) Int. risk: 8 (3.7%) High risk: 6 (4.6%)	p = .461	—
ICU stay (d) median (IQR)	Low: 7 (5 – 17) — High: 8 (5 – 21.75)	p = .350	Class 1: 6 (4 – 14) Class 2: 7 (5 – 16) Class 3: 8 (5 – 17)	p = .075	Low risk: 7 (4 – 15) Int. risk: 8 (5 – 17) High risk: 10 (5 – 30)	p = .016	†p = .015
Hospitalization (d) median (IQR)	Low: 24 (18 – 37) — High: 27.5 (21 – 47)	p = .042	Class 1: 22 (18 – 31) Class 2: 23 (19 – 39) Class 3: 25 (18 – 39)	p = .206	Low risk: 23 (18 – 36) Int. risk: 24 (18 – 36) High risk: 34 (22 – 53)	p = .001	†p = .001 ‡p = .007
In-hospital death n (%)	Low: 51 (6.7%) — High: **5 (11.1%)**	p = .232	Class 1: 7 (5.8%) Class 2: 18 (11.1%) Class 3: 39 (7.0%)	p = .157	Low risk: 29 (5.7%) Int. risk: 28 (10.5%) High risk: 7 (10.1%)	p = .043	#p = .048

Outcome parameters	MALT score n = 841		UMN-DLQI n = 780	
Length of mechanical ventilation (h) median (IQR)	Low risk: 34 (19 – 67) Int. risk: 63 (31 – 126) High Risk: 177.5 (63 – 478)	p < .001 #p < .001 †p < .001 ‡p < .001	High: 40 (22 – 89) — Low: 48 (24 – 138)	p = .042

(Continues)

Table 4 (Continued)

Outcome parameters	MALT score n = 841			UMN-DLQI n = 780		
PGD 3 at 72 hours n (%)	Low risk: 8 (1.5%)	p < .001	#p = .006	High: 14 (2.5%)	p = .009	#p = .006
	Int. risk: 11 (5.7%)		†p = .001	—		†p = .001
	High risk: 9 (9.7%)			Low: 13 (6.4%)		
ICU stay (d) median (IQR)	Low risk: 6 (4 – 10)	p < .001	#p < .001	High: 7 (4.5 – 15)	p = .016	#p < .001
	Int. risk: 12 (5 – 25)		†p < .001	—		†p < .001
	High risk: 27 (14 – 45)		‡p < .001	Low: 8 (5 – 23)		‡p < .001
Hospitalization (d) median (IQR)	Low risk: 22 (17 – 31)	p < .001	#p < .001	High: 23 (18 – 34)	p < .001	#p < .001
	Int. risk: 28 (20 – 47)		†p < .001	—		†p < .001
	High risk: 45 (31 – 64)		‡p < .001	Low: 28 (20 – 50)		‡p < .001
In-hospital death n (%)	Low risk: 24 (4.3%)	p < .001	#p = .001	High: 42 (7.3%)	p = .815	#p = .001
	Int. risk: 24 (12.2%)		†p = .001	—		†p = .001
	High risk: 16 (17.2%)			Low: 16 (7.8%)		

Abbreviations: d, days; h, hours; ICU, intensive care unit; Int., intermediate; IQR, interquartile range; PGD 3, primary graft dysfunction grade 3.

1 vs. 2; † 1 vs. 3; ‡ 2 vs. 3.

has been shown for the individual patient receiving lungs from a smoker, especially when the risk associated with reduced donor organ quality is weighed against prolonged waiting periods.[33] In summary, the value of several individual quality factors has been questioned by published evidence in recent years. This underlines the major advantage of donor scores: in contrast to traditional marginal criteria, they calculate the combination of several detrimental factors that ultimately make a lung unacceptable.

Our study has several limitations. We focused on the prediction at the time of offer and did not include scores, which combine donor parameters with early posttransplant measurements. Therefore, the Munich LTx score by Huppmann et al.[34] and the Risk Quantification for Lung Transplantation score by the Toronto group[35] were not included in our analysis. Another limitation of our study is its retrospective nature, with the possibility of miscoded or missing data. As clinical decision-making is difficult to assess retrospectively, it cannot be ruled out that borderline organs may have been accepted more liberally for high-urgent patients. While this could have a certain impact on our results, it would affect all scores in an equal way. Further prospective studies are required to clarify the value of the MALT score and UMN-DLQI to predict the likelihood of acceptance of lung offers. Although the scores have not been specifically validated for EVLP, and only the UMN-DLQI addresses DCD donors, we chose to include these cases, nonetheless, as equal outcomes have been demonstrated in the literature. Our single-center design naturally limited the number of patients that could be included. On the other hand, it provided a level of data granularity a multicenter or registry analysis could not have provided. The acceptance practices of our lung transplant program might be different to practices of other centers. However, due to data privacy restrictions, it was not possible to perform a full-scale analysis and evaluate outcomes of lungs rejected by our center but transplanted elsewhere.

In conclusion, this study offers a large external validation of currently available lung donor scores. We were able to provide the first direct comparison of these different scoring systems. Based on our analysis, the Oto score and the MALT score could be generally recommended for scientific reporting of donor data and comparing organ utilization. Moreover, these scores could be useful in adding objective parameters to aid difficult decisions whether lung offers should be declined or accepted.

DISCLOSURE

AUTHOR CONTRIBUTIONS

SS and KH conceived and designed the study; NR, DK, MM, and SS collected donor data; AB, NR, GM, MAH BM, JRM, GL, ST, and PJ collected recipient data; MW, SS, and NR performed the statistical analysis and interpreted the data; SS and KH wrote the manuscript draft; SK and WK contributed important conceptual content; all authors revised the manuscript with significant intellectual contributions.
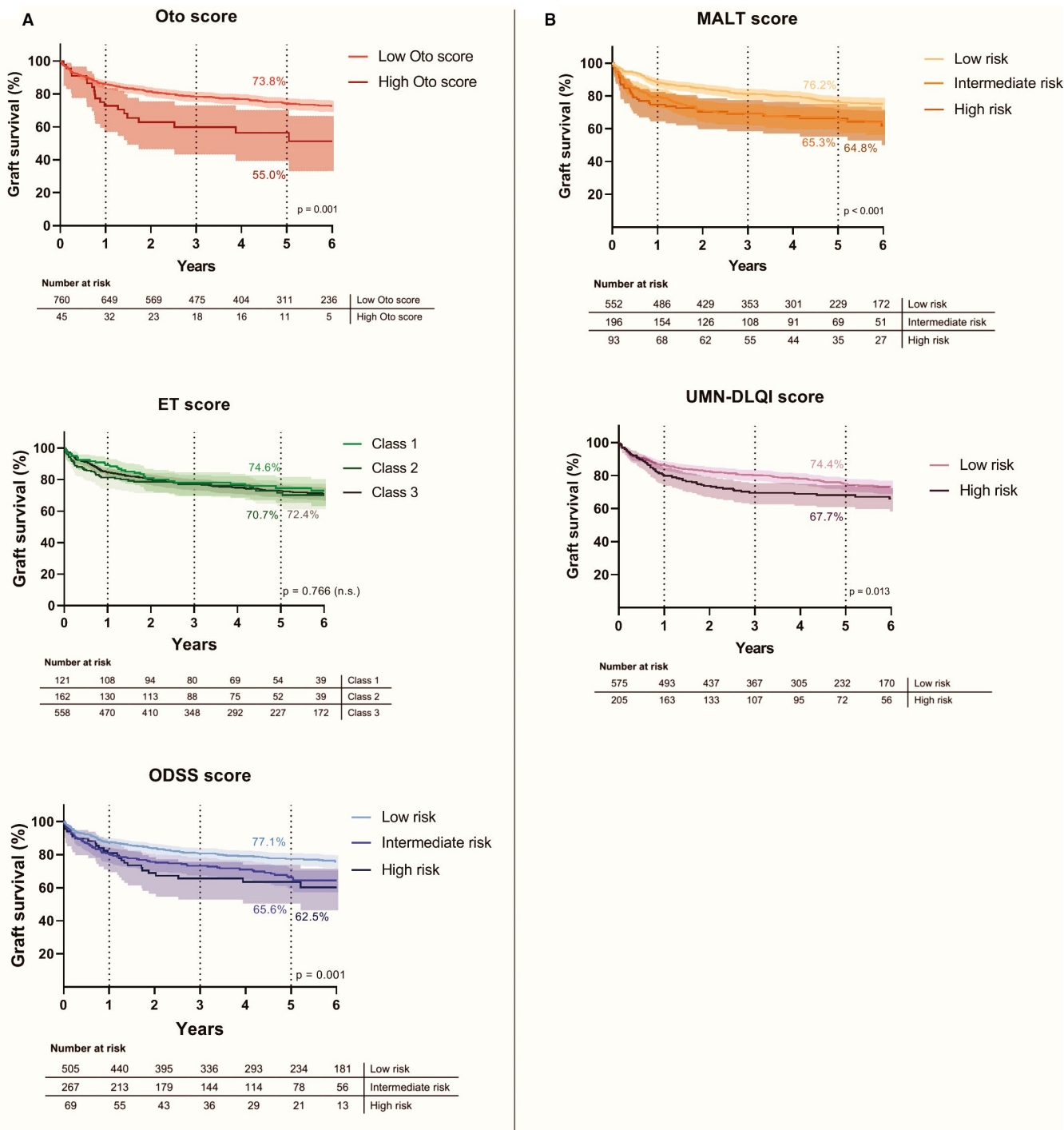
FIGURE 4 Kaplan-Meier curves of graft survival were produced for scores using only donor parameters (A) and scores combining donor and recipient parameters (B) and their respective donor organ quality categories [Color figure can be viewed at wileyonlinelibrary.com]

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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