Supplement to:

Von Willebrand factor facilitates MELD-independent risk stratification on the waiting list for liver transplantation

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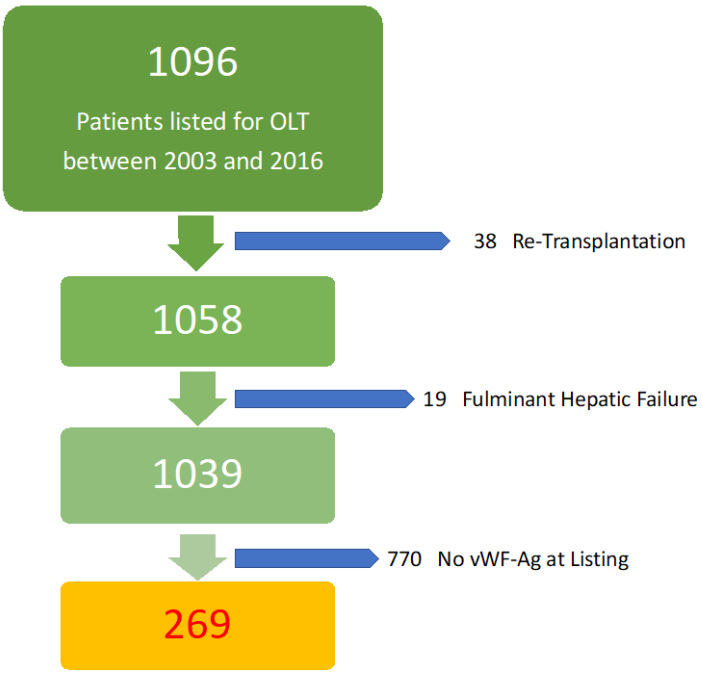
Supplemental Tables

Supplemental Table 1. Cohort Comparison

Parameter	Study Cohort (N=269) Median (range) N (%)	Patients without vWF-Ag (N=770) Median (range) N (%)	p-value
Sex			0.121
Male	203 (75.5)	543 (70.5)	
Female	66 (24.5)	227 (29.5)	
Age at listing (years)	56 (15-73)	54 (0-72)	**0.004**
Patients ≤ 15 years	1 (0.4)	25 (3.2)	**0.009**
MELD score	16 (6-40)	16 (6-40)	0.700
Indication for LTx			
Alcoholic cirrhosis	89 (33.1)	251 (32.6)	0.883
Tumor	62 (23.0)	160 (20.8)	0.434
Viral hepatitis	42 (15.6)	151 (19.6)	0.147
Biliary disorders	23 (8.6)	76 (9.9)	0.526
AI hepatitis	14 (5.2)	23 (3.0)	0.091
Cryptogenic cirrhosis	13 (4.8)	33 (4.3)	0.707
Other indications	26 (9.7)	76 (9.9)	0.923
Incidence of waiting list outcome*			0.697
Transplanted	196 (72.9)	390 (71.6)	
DoL	73 (27.1)	155 (28.4)	
Three-month mortality	31 (11.5)	94 (12.2)	0.772

vWF-Ag= von Willebrand factor antigene, MELD= model of end-stage liver disease, AI=autoimmune, DoL = death on list.
*after exclusion of de-listed patients.

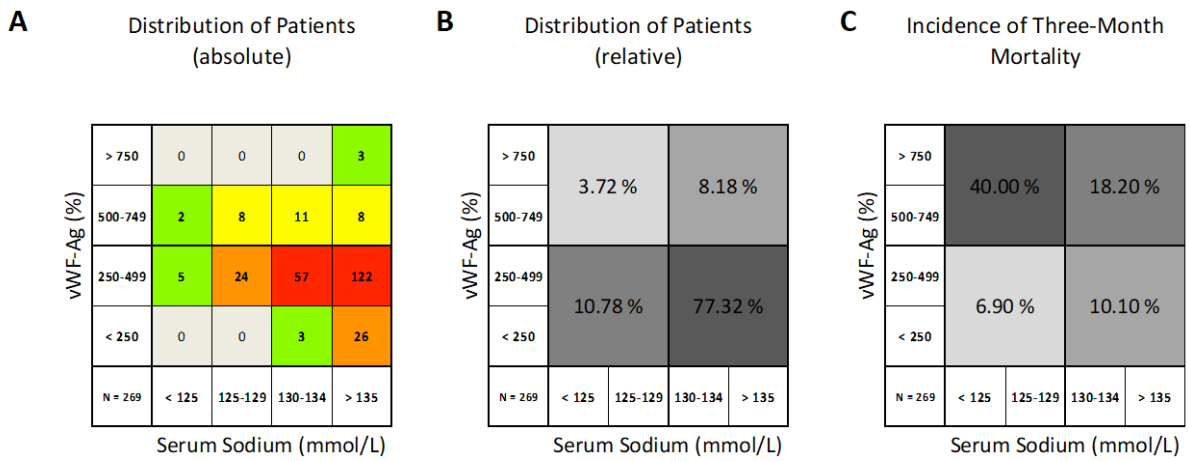
Supplemental Figures



Supplemental Fig.1 Flowchart illustrating the number and reasons for patient exclusion.

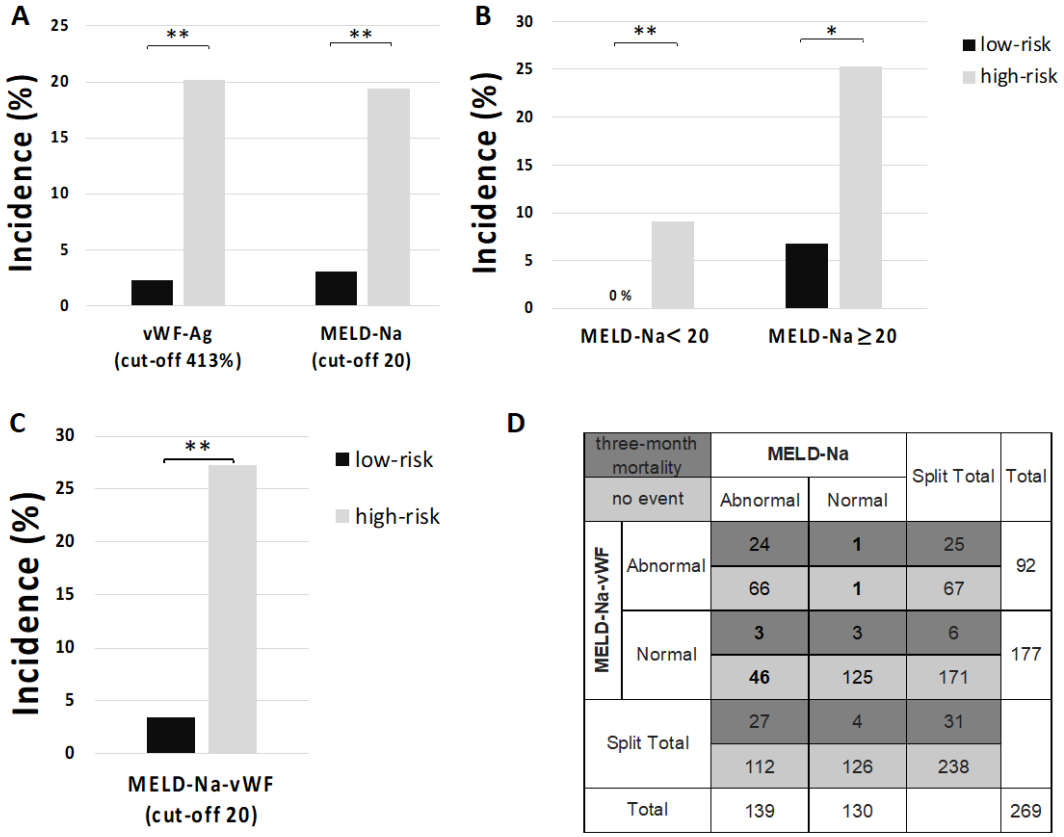
This figure illustrates the exclusion process of patients. Of note, no data for vWF-Ag was available for patients that were excluded due to clinical deterioration. Within the final cohort (N=269), 31 patients died within the first three months on the waiting list, who were compared to the remaining cohort consisting of patients who already underwent OLT at this time point and patients who survived at least three months on the waiting list.

(OLT = orthotopic liver transplantation)



Supplemental Fig.2 Association of vWF-Ag with sodium in patients awaiting OLT.

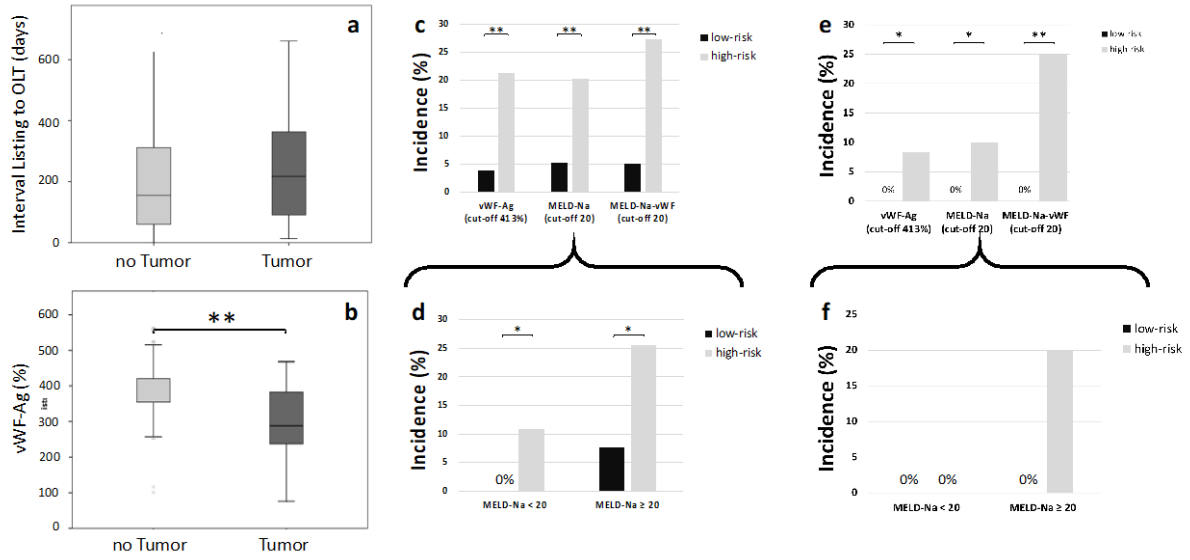
In order to evaluate a potential redundancy of vWF-Ag and serum sodium correlative analysis was performed. The distribution of patients is shown in absolute (A) as well as in relative (B) measures. Further, the incidence of three-month mortality is shown in regard to levels of vWF-Ag and serum sodium.



three-month mortality		MELD-Na		Split Total	Total
no event		Abnormal	Normal		
MELD-Na-vWF	Abnormal	24	**1**	25	92
		66	**1**	67	
	Normal	**3**	3	6	177
		46	125	171	
Split Total		27	4	31	
		112	126	238	
Total		139	130		269

Supplemental Fig.3 VWF-Ag allows risk stratification on the waiting list independent of MELD-Na and its incorporation does improve the predictive potential for three-month survival on the waiting list.

The cohort was divided according to the defined cut-off for vWF-Ag at 413%. Patients above this cut-off were found to show a significantly higher incidence for mortality within three months on the waiting list, which was comparable to a MELD-Na cut-off at 20 points (A). Interestingly, vWF-Ag was found to sub-stratify patients also in patients with low (<20) and high (≥20) MELD-Na score (B). Subsequently, the optimal cut-off for MELD-Na-vWF was identified at 20 points, which shows a good discriminatory potential for three-month survival (C). Further, net reclassification improvement (NRI) was calculated (D), which shows an improvement in the predictive potential of MELD-Na when vWF-Ag was included. (* $p<0.05$, ** $p<0.005$)



Supplemental Fig.4 Subgroup analysis.

As patients suffering from tumors were previously shown to have an advantage in terms of waiting list survival, an additional subgroup analysis was performed in this cohort (Tumor) as well as for the remaining cohort (no Tumor). Interestingly, at our institution patients with tumors show a tendency towards a longer waiting period on the list prior to OLT when compared to patients suffering from chronic liver diseases (median Interval no Tumor = 155 days, median Interval Tumor = 218 days, p=0.092; a). Further, patients with tumor showed lower levels of vWF-Ag at listing when compared to the remaining cohort (median vWF-Ag no Tumor = 420%, median vWF-Ag Tumor = 288%, p<0.001; b). Of note, the data for prediction of early waiting list mortality (i.e. < 3 months) was reproducible after exclusion of tumor patients (vWF-Ag: 3 of 80 [3.8%] in vWF-Aglow vs 27 of 127 [21.3%] in vWF-Aghigh, p<0.001; MELD-Na: 4 of 78 [5.1%] in MELD-Nalow vs 26 of 129 [20.2%] in MELD-Nahigh, p=0.003; MELD-Na-vWF: 6 of 119 [5.0%] in MELD-Na-vWFlow vs 24 of 88 [27.3%] in MELD-Na-vWFhigh, p<0.001; c). This was also the case for the prediction of early waiting list mortality according to vWF-Ag after dividing the cohort in patients with low or high MELD-Na scores (MELD-Na < 20: 0 of 41 [0.0%] in vWF-Aglow vs 4 of 37 [10.8%] in vWF-Aghigh, p=0.031; MELD-Na ≥ 20: 3 of 39 [7.7%] in vWF-Aglow vs 23 of 90 [25.6%] in vWF-Aghigh, p=0.020; d). Ultimately, the cohort of tumor patients was analyzed separately, which revealed a consistency of the data gathered in the entire cohort. Patients with tumors and dyeing within three months on the waiting list were identified by all predictive parameters assessed (vWF-Ag: 0 of 50 [0.0%] in vWF-Aglow vs 1 of 12 [8.3%] in vWF-

Aghigh, p=0.040; MELD-Na: 0 of 52 [0.0%] in MELD-Nalow vs 1 of 10 [10.0%] in MELD-Nahigh, p=0.022; MELD-Na-vWF: 0 of 58 [0.0%] in MELD-Na-vWFlow vs 1 of 4 [25.0%] in MELD-Na-vWFhigh, p<0.001; e). Again, the prediction according to vWF-Ag held through after stratification into MELD-Na low/high patients (MELD-Na < 20: 0 of 45 [0.0%] in vWF-Aglow vs 0 of 7 [0.0%] in vWF-Aghigh, p=NA; MELD-Na ≥ 20: 0 of 5 [0.0%] in vWF-Aglow vs 1 of 5 [20.0%] in vWF-Aghigh, p=0.292; f). *p<0.05, **p<0.005.