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P-141. Liver Retransplantation in HIV-Infected Patients: A Multicenter and Multinational Cohort Study.

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Background: Information on liver retransplantation (reLT) in HIV-infected patients is very limited. We describe the indications, main characteristics, and outcome of reLT in HIV-infected patients included in 8 prospective national cohorts comprising HIV-infected liver recipients.

Methods: We analyzed data from 37 HIV-infected patients who underwent reLT between 1997 and 2012 in Spain (14 patients), USA (9), Italy (5), Germany (4), UK (2), Switzerland (1), Portugal (1), and Argentina (1).

Results: Median (IQR) age was 47 (42-50) years and 92% were men. HIV-1 infection was acquired by injecting drug use or sexual transmission in 19 and 12 cases, respectively. The indication of primary liver transplantation (LT) was cirrhosis by HCV, HCV and HBV, or HBV infection in 28, 4, and 5 cases, respectively. Fourteen patients (38%) had hepatocellular carcinoma. At primary LT, median (IQR) CD4 cells/mm3 was 295 (212-394) and plasma viral load was <200 copies/mL in 81% of patients while 97% of cases were on antiretroviral therapy (ART). reLT was indicated because of vascular thrombosis, primary graft nonfunction, chronic rejection, HCV recurrence, and other indications in 13, 7, 6, 7, and 4 cases, respectively. reLT was urgent (early, ≤30 days) in 19 cases (51%) and elective (late, >30 days) in 18 cases (49%). Median (IQR) MELD at reLT was 23 (21-31). All patients received a liver graft from a cadaveric donor. After a median (IQR) follow-up of 21 (2,57) months, 19 (51%) of the 37 HIV-infected patients with reLT died. Overall patient survival rate (95% confidence intervals) after reLT at 1, 3, and 5 years was 54% (36,68), 51% (34,65), and 51% (34,65), respectively. Survival rates at 1 and 3 years for HIV-infected patients who underwent early reLT (≤30 days, N=19) vs late reLT (>30 days, N=18) was 42% vs 66% and 42% vs 66%, respectively (p=0.186). Survival rates at 1 and 3 years for HIV/HCV-infected patients with a negative (N=15) vs a positive (N=22) plasma HCV RNA viral load at reLT was 80% vs 35% and 80% vs 30%, respectively (p=0.008). HCV recurrence was the main cause of death (7 cases, 37%). Two (40%) of the 5 HIV/HBV-infected reLT patients died (survival at 1,3 and 5 years was 80%). HIV infection was controlled with ART after reLT in most cases.

Conclusions: Medium-term survival after reLT was poor in HIV-infected patients. Post-reLT outcome was better among HIV/HCV-coinfected patients with undetectable plasma HCV RNA at reLT and HIV/HBV-coinfected patients.

BACKGROUND

Information on liver retransplantation (reLT) in HIV-1-infected patients is scarce.

OBJECTIVE

To describe indications, main characteristics and outcomes of reLT in recipients with HIV-1 infection included in 8 prospective national cohorts of HIV-infected liver recipients.

PATIENTS & METHODS

- Prospective multicenter cohort study of all HIV-1-infected patients who underwent reLT in Spain, USA, Italy, Germany, UK, Switzerland, Portugal and Argentina.
- The criteria for primary LT and reLT were the same as for the patients without HIV-infection.
- Study period: 1997-2012
- Variables: Sociodemographic, HIV (stage, CD4 cell count, plasma HIV-1 RNA viral load, ART), liver disease (etiology, MELD), first LT and reLT indications and characteristics at baseline and at follow-up were collected using a standardized CRF.

HIV inclusion criteria for primary LT

	Spain*	Italy	U.K.	U.S.A.
Previous C events:				
- Opportunistic infections	Some**	None in the previous year.	None after HAART-induced immunological reconstitution.	Some †
- Neoplasms	No	No		Some‡
CD4 cell count/mm3	>100§	>200 or >100 if decompensated cirrhosis	>200 or >100 if portal hypertension	>100§
Plasma HIV-1 RNA VL BDL on cART***	Yes	Yes	Yes	Yes

** Tuberculosis, *Pneumocystis jirovecii* pneumonia or esophageal candidiasis; † PML, chronic cryptosporidiosis and multidrug-resistant fungal infection are exclusion criteria; ‡ Visceral Kaposi sarcoma and NHL are exclusion criteria. §Patients with previous OIs should have >200 CD4 cells/mm3; ***If Plasma VL was detectable, post-OLT supression with HAART should be predicted in all patients.

***Drug abuse: No heroin or cocaine abuse for >2 years; No alcohol abuse for >6 months.**

STATISTICAL ANALYSIS

- Continuous variables were expressed as median and interquartile range (IQR)
- For comparisons between continuous variables, Mann-Whitney U test was employed. For categorical variables, the chi-square test or Fisher test was used.
- Survival analyses were performed with the date of reLT as the start date. Lost of follow-up and death from any cause were treated as failures. Survival time was estimated using the Kaplan–Meier product-limit method; the curves of the different groups were compared using the generalized log-rank test.
- Statistical significance was defined as a bilateral p-value <0.05.

Number of Patients with Liver Retransplantation (reLT) According to the Participant Country (1997-2012)

	Number Primary LT	Number reLT (%)
Spain	270	14 (5)
USA	125	9 (7)
Italy	118	5 (4)
Germany	30	4 (13)
UK	24	2 (8)
Argentina	10	1 (11)
Portugal	13	1 (8)
Switzerland	10	1 (10)
Total	600	37 (6)

Main characteristics of liver reLT in HIV-infected patients (1997-2012)

Age (year)*	**47 (42,50)**
Male gender	**34 (92%)**
HIV risk factor	
- Former i.v. drug use	**19 (51%)**
- Sexual	**12 (33%)**
- Other	**6 (16%)**
Calendar year	
- 1997-2001	**2 (5%)**
- 2002-2006	**9 (24%)**
- 2007-2012	**26 (70%)**

* Median (IQR)

Main characteristics before first LT

Primary LT indication	
- HCV infection	28 (76%)
- HBV infection	5 (13%)
- HCV + HBV coinfection	4 (11%)
- Hepatocellular carcinoma	14 (38%)
HCV Genotype	
- GT 1 or GT 4	24 (75%)
- GT 2 or GT 3	5 (16%)
- Other GT / Unknown	3 (9%)

Main characteristics HIV Infection

Before primary LT

- On HAART	35 (95%)
- CD4 cells/mm3*	295 (212,394)
- Plasma HIV viral load BDL	30 (81%)

Before reLT

- On HAART	34 (92%)
- CD4 cells/mm3*	246 (126,354)
- Plasma HIV viral load BDL	25 (67%)

*Median (IQR)
BDL: Below detection limit

Donor characteristics

Primary LT donor (n=17)

- Age*	55 (45,60)
- ≥ 65 years	4 (24%)
- Donor brain death by trauma	4 (24%)

reLT donor (n=31)

- Age*	48 (31,59)
- ≥ 65 years	4 (13%)
- Donor brain death by trauma	7 (19%)

*Median (IQR)
BDL: Below detection limit

Main characteristics before reLT

Indication for reLT

- Vascular complications	13 (35%)
- Primary non-function	8 (22%)
- Rejection	6 (16%)
- HCV recurrence	6 (16%)
- Other*	4 (11%)

MELD score at reLT** 23 (21,31)

*HCV recurrence plus rejection, massive liver necrosis, perfusion/toxic injury and cholangiocarcinoma in one case each.

**Median (IQR)
BDL: Below detection limit

Main characteristics before reLT

Type of reLT according to interval between primary and reLT (days)

- Early reLT (≤ 30 days)	19 (51%)
- Late reLT (>30 days)	18 (49%)

HCV ARN positive at reLT

- Positive	22 (59%)
- Negative*	15 (41%)

*Including 5 HBV/HIV coinfected patients

Outcomes after reLT

Length of follow-up (months)	**21 (2,57)***
Third LT	**2 (5%)****
	19 (51%)
Mortality	
Cause of death	
- HCV recurrence	**7 (37%)**
- Non-AIDS infections	**6 (32%)**
- Miscellaneous***	**6 (26%)**

* Median (IQR); ** Both patients died within one month from third LT

*** Stroke, 2 cases and PNF, left heart failure, rejection and massive bleeding after reLT

Univariate analysis of mortality

	Alive N=18	Dead N=19
Interval between primary and reLT		
- Early reLT (≤ 30 days)	7 (39%)	12 (63%)*
- Late reLT (>30 days)	11 (61%)	7 (37%)
HCV ARN positive at reLT		
- Positive	7 (47%)	15 (88%)**
- Negative (including HBV)	11 (53%)	4 (12%)
HBV infection	3 (60%)	2 (40%)***

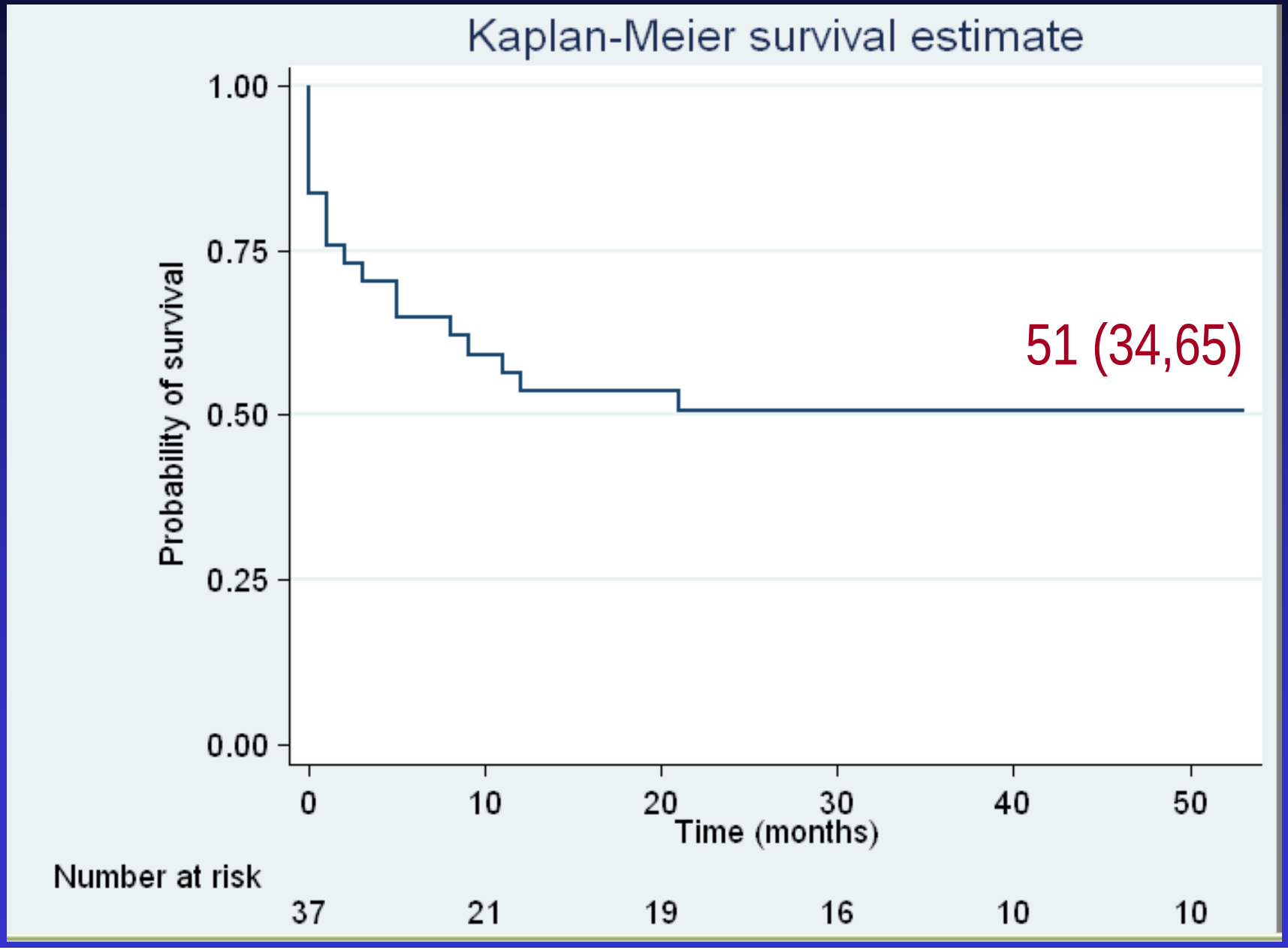
* *P*=0.25; ** *P*=0.03

*** One case died early due to surgical complications and the other case died 15 years after reLT.

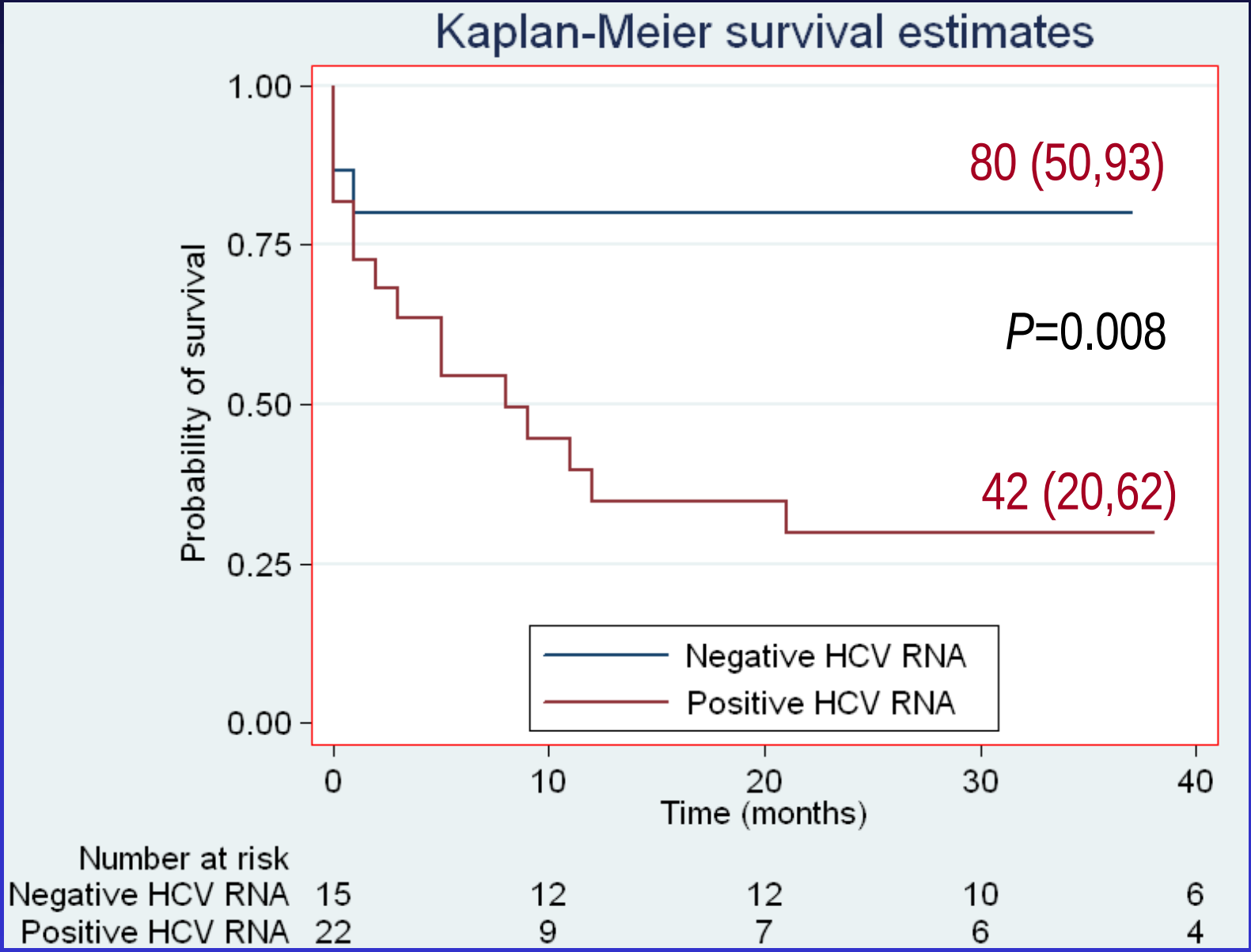
Overall patient survival rates

Characteristics	No.	1-yr	3-yr	5-yr	*P*-value
Overall patient survival	37	54%	51%	51%	
HCV RNA status at reLT					0.008
- Positive	22	35%	30%	30%	
- Negative	15	80%	80%	80%	
Interval from first LT (days)					0.180
- Early (0-30)	19	42%	42%	42%	
- Late (>30)	18	66%	60%	60%	
MELD Score at reLT					0.026
- ≤25	24	66%	62%	62%	
- >25	13	31%	31%	31%	

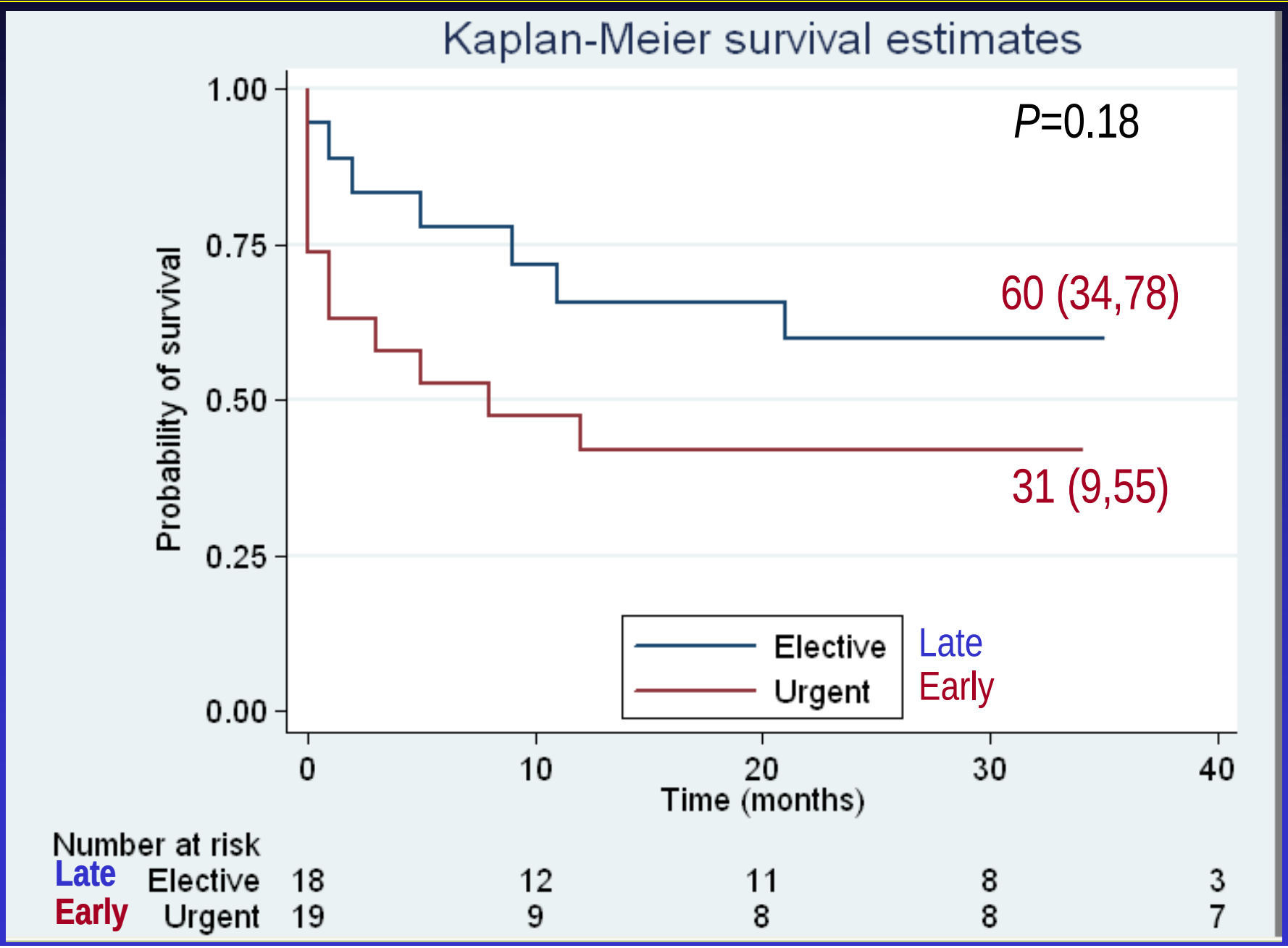
Overall patient survival rate after reLT



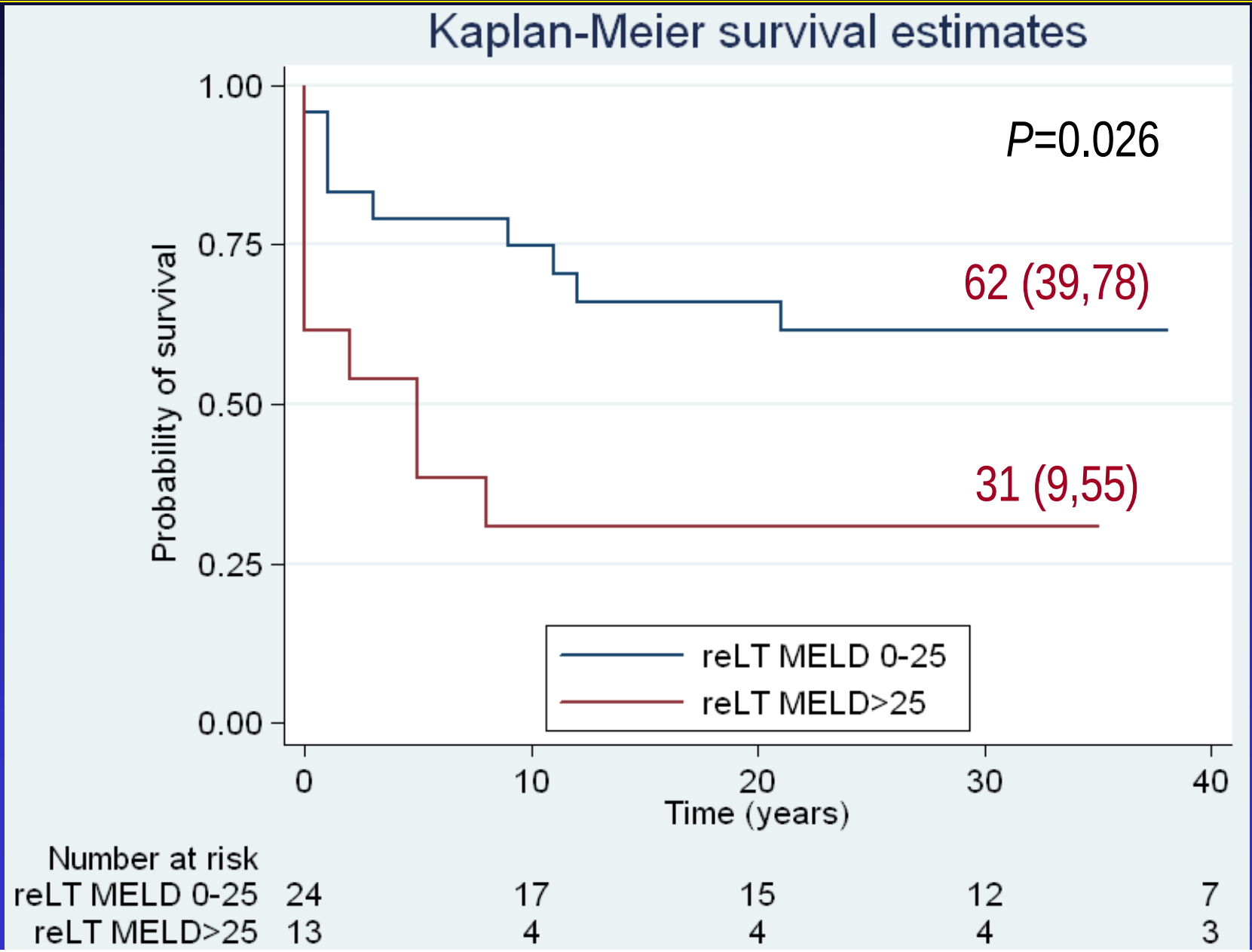
Patient survival rates at 3 years according to HCV RNA status at reLT



Patient survival rate at 3 years according type of reLT



Patient survival rate at 3 years according to pre-reLT MELD score



CONCLUSIONS

- This is the first international cohort of patients with HIV-infection who underwent liver retransplantation (reLT). Most cases of reLT were performed during the last 6 years.
- Vascular complications were the most common cause of early reLT. Only 7 patients (19%) underwent reLT due to HCV recurrence.
- Overall survival rates at 1, 3 and 5 years were 54%, 51% and 51%, respectively. Most deaths (89%) occurred within the first year of reLT.
- Survival in patients with positive plasma RNA HCV viral load and in patients with a high MELD score is poor and, therefore, the indication for re-transplantation in these two subsets of patients is questionable in the current setting of organ shortage. Conversely, patients without HCV replication had a good mid-term prognosis with survival rates at 3 years of 80%.
- Larger studies and longer follow-up are needed to confirm these results.

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